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REVIEW ARTICLE

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An ANMS-NASPGHAN consensus document on anorectal and colonic manometry in children

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Abstract

Background: Over the last few years, the study of the colon and anorectal function has experienced great technical advances that have facilitated the performance of the tests and have allowed a more detailed characterization of reflexes and motor patterns. As a result, we have achieved a much better understanding of the pathophysiology of children with defecation problems. Anorectal and colonic manometry are now commonly used in all major pediatric referral centers as diagnostic tools and to guide the management of children with intractable constipation and fecal incontinence, particularly when a surgical intervention is being considered.

Purpose: This review highlights some of the recent advances in pediatric colon and anorectal motility testing including indications and preparation for the studies, and how to perform and interpret the tests. This update has been endorsed by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN).

KEYWORDS

anorectal manometry, children, colonic manometry, constipation, diagnosis

1 | INTRODUCTION

Over the last few years, the study of the colorectal and anorectal function has experienced great technical advances. More advanced and miniaturized probes and novel pressure recording systems have been developed. High-resolution manometry has become widely accepted and is now routinely used at all major motility centers. With the greater utilization of this technique, there has been a more detailed characterization of colonic motor patterns and anorectal function. Several research studies have enhanced our understanding of the pathophysiology of functional and organic constipation and the effects of surgery and sedation on motility testing. This review highlights some of the recent advances of pediatric colorectal and anorectal motility.

2 | BACKGROUND

Anorectal manometry (ARM) (Current Procedural Terminology- CPT 91122) is the most commonly performed motility test in children. The ARM allows assessment of anal sphincter length, tone, and function, anorectal sensory responses, rectoanal reflexes, and ability to squeeze and simulate the process of defecation. In normal individuals, the recto-anal inhibitory reflex (RAIR) is present, there is normal threshold for sensation and the urge to defecate and there are effective defecation dynamics. Colonic manometry (CM) has become an extremely valuable test in the diagnostic work-up of children with severe defecation disorders. Colonic manometry is now widely used in all major pediatric referral centers in North America and in recognition of its clinical utility, it was recently granted a CPT code (91117) in the United States. Interestingly, CM may represent the only manometry test more commonly used in children than in adults.[1] Colonic manometry evaluates intraluminal colonic pressures and their coordination. Besides its unquestionable value as a diagnostic test, CM has also been instrumental in helping understand colon physiology in children of different ages.

3 | HOW TO PERFORM THE TEST?

3.1 | Preparation for anorectal and colonic motility testing

Little preparation is needed to conduct an ARM in children. There is no need to stop medications before performing an ARM. Some

centers recommend administering an enema or a glycerin or a bisacodyl suppository on the morning of the study to assure emptying of the rectum. The preparation for CM requires detailed instructions and planning. All medications that affect colon motility should be stopped 48–72 hours prior to a CM and all patients should undergo a colonic clean out prior to the placement of the catheter.

3.2 | Equipment

The ARM probes have advanced from the standard water perfused catheters to high-resolution catheters that provide either two-dimensional intra-anal pressure measurements or more sophisticated tridimensional (3D) techniques that result in topographical representations of the entire length and circumference of the anal canal during defecation maneuvers and squeeze.[2] Newly developed 3D high-definition ARM catheters that now include up to 256 circumferentially distributed pressure sensors are increasingly used to study patients with fecal incontinence and constipation and allow identification of sphincters radial asymmetry and the contribution of the different muscles to the intra-anal pressure.[2] There are differences in the way the pressures are calculated using conventional water perfused or 3D high-definition ARM probes. While water-perfused catheter probes measure the pressure in the radial axis of the anal canal which may be radially asymmetric, the 3D high-definition ARM probe averages the high pressure of all the sensors located on the same circumference. Studies in adults have shown that the RAIR determination[3,4] and pressure readings obtained with high-resolution and conventional water-perfused ARM correlate but mean resting pressure and mean squeeze pressure are higher using 3D high-resolution manometry compared to water-perfused manometry.[4] One of the possible reasons for the higher values obtained using high-resolution probes may be that this technique only considers the highest pressure values measured in the entire anal canal.[4] Although it can be hypothesized that 3D high-resolution manometry provides a more physiological representation of the anal canal than conventional water perfused,[4] the understanding of the value of each of these novel techniques to enhance our knowledge of the pathophysiological mechanisms of the different defecation disorders in children is still evolving.

Colonic manometry is currently performed using either water perfused or solid-state catheters with 6–36 recording ports spaced 1–15 cm apart according to the size of the patient. The use of solid state catheters that can produce tracings displayed as pressure topography plots has been found not only to be easier and safer to perform (alleviating the concerns of water overload associated with water perfused systems) but also more sensitive in recording and identifying high amplitude propagated contractions (HAPCs) compared to water perfused catheters[5] or compared to conventional tracings.[6]

Recently, a new tool has been developed for the evaluation of colon motility: fiberoptic manometry. This technique allows measurement of peristalsis with a higher fidelity by allowing a higher number of sensors than conventional solid state catheters[7] and has the ability to evaluate the distal propelling of ferrous beads through the catheter eliminating the need of fluoroscopy or other form of evaluation of colonic transit.[8, 9] This technology is yet to be evaluated in children.

Key Points

- Anorectal manometry is the most commonly performed motility test in children.
- The most accepted indication for anorectal manometry in children is the evaluation of the internal anal sphincter relaxation in response to rectal balloon distension to exclude Hirschsprung's disease.
- Colonic manometry is an extremely valuable test in the diagnostic work-up of children with severe defecation disorders.

3.3 | Catheter placement and sedation

When patients are not cooperative, sedation is required to perform the ARM. When that happens, only the resting anal pressures and the presence of the RAIR can be measured as other portions of the study cannot be performed or are not reliably reproduced under sedation. There should be careful consideration of the type of anesthetic used and the depth of sedation as some anesthetic agents even if they do not interfere with the RAIR can decrease the anal resting pressure resulting in a more difficult assessment of the RAIR. The use of preoperative midazolam or atropine does not affect the RAIR but the anticholinergic glycopyrrolate may interfere with the evaluation of the RAIR, thus resulting in falsely positive absence of RAIR.[10] Ketamine does not affect the resting anal pressure or the RAIR[10–12] but can result in self-limited "new onset" nightmares in a small proportion of patients.[13] Sevoflurane and chloral hydrate and propofol do not affect the RAIR.[10] However, propofol decreases anal resting pressure and can confound pressure measurements.[14] Neuromuscular-blocking agents should not affect the RAIR.[10]

The CM catheter is usually placed under general anesthesia during colonoscopy[15–19] but can be placed with fluoroscopy alone[20] (Fig. 1). Clipping the catheter to the colonic mucosa minimizes the risk of becoming dislodged and migrating distally throughout the study.[21] As colonoscopy in children is usually performed under general anesthesia, the potential effect of anesthesia on colon motility becomes significant. It has been suggested that the study can be performed as early as 4 hours after recovering from anesthesia[22] but others have recently reported an important effect of anesthesia on colon motility and study interpretation when the study is performed on the same day of anesthesia.[23] The study lasts a minimum of 6 hours in children, although there have been reports highlighting the utility of studying the colon over 24 hours.[24,25]

3.4 | Study procedure

Anorectal manometry - *Resting anal pressure* is recorded by averaging the values of the pressure sensors in the anal canal over a minimum of 30 seconds after a variable period of adaptation (usually 1–5 minutes).

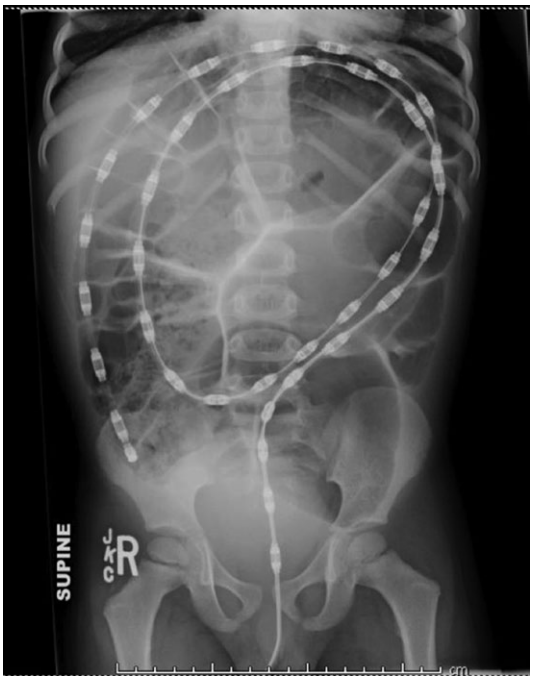

FIGURE 1 Colon motility catheter (solid state) placement with the most proximal sensor at the level of the cecum and most distal in the anal canal. Note the redundant sigmoid colon and the dilated caliber of the colon

Measuring the length of the anal canal is done by performing several pull-through maneuvers of the catheter through the sphincter complex when using a water perfused system or by using a high-resolution catheter with multiple, closely spaced recording sites. The *RAIR*- the relaxation of the internal anal sphincter in response to rectal distension - is evaluated by rapidly inflating the rectal balloon with 5 mL increments in infants and newborns up to 20 mL and by 10 mL increments in older children. The volume required to elicit the RAIR varies according to the size of the rectum and most centers recommend continuing to increase the volume to higher volumes (250–300 mL) in older children if complete relaxation is not obtained. *Squeeze effort* is usually measured as an absolute value over a maximum of 20 seconds but it can also be calculated as the squeeze increment by subtracting the resting pressure. *Rectal sensation* is tested through the insufflation of the balloon with progressively larger volumes either by the intermittent rectal distension method or through ramp inflation. The intermittent rectal distension method mimics the arrival of gas or stool in the rectum. This method consists in the inflation and total deflation of the balloon with intermittent resting periods. In the ramp inflation method, the rectum is distended progressively with larger volumes without deflation intervals. *Transient rectal sensation* is defined as the smallest volume of balloon distension that the patient perceives. The minimum volume that produces a lasting urge to defecate is defined as the *critical volume* (this can be difficult to determine in children younger than 7 years of age or in those with developmental disabilities). During *bear down effort*, the rectal pressure increases and the anal canal pressure decreases with relaxation of the external anal sphincter and pelvic floor muscles. The *balloon expulsion* test that is extensively used in adult patients with suspected pelvic outlet obstruction is not commonly utilized in children. A small pediatric study has shown that this test can help guide therapy in children with chronic constipation and outlet obstruction.[14]

The standard CM study recording consists of three phases: fasting, meal challenge and bisacodyl or other drug challenge (when needed). The study starts with a recording of fasting motility for 1–2 hours followed by the ingestion of a combined liquid and solid meal (at least 20 kcal/kg).[26] There are no specific recommendations for patients who are unable to eat by mouth or are dependent on enteral nutrition. The authors give the usual formula the patients are receiving at home (15–20 kcal/kg) as a bolus if tolerated or continuous feeds over approximately 30 minutes if not tolerated faster. If no HAPCs are seen in the fasting or postprandial state, bisacodyl 0.1–0.2 mg/kg is given through the colonic motility catheter into the lumen of the proximal colon to induce HAPCs of similar amplitude, duration, propagation velocity and migration of those occurring spontaneously.[27] Rectal bisacodyl has a similar effect but delayed by 10–15 minutes.[27] Colonic intraluminal distention also elicits HAPCs but not as consistently as intraluminal bisacodyl.[28] The study has good day-to-day reproducibility when performed 2 weeks apart in adults,[29] but such data are not available in children.

It is important to acknowledge that the protocol to perform and interpret these procedures is not standardized and may vary institutionally.

4 | INTERPRETATION

The effect of rectal distension on anal relaxation and rectal sensitivity is affected by the size and the type of the balloon and the location of the balloon and normal values vary from laboratory to laboratory. Normative data has been recently published for the 3D probe, demonstrating a resting pressure of 83 ± 23 mm Hg, with a mean volume to elicit the RAIR of 15.7 ± 10.9 mL.[30] The interpretation of the ARM is done mostly by evaluating the basal anal resting pressure and the normal presence of the RAIR (Fig. 2). There is usually an incremental degree of anal sphincter relaxation with increasing rectal balloon

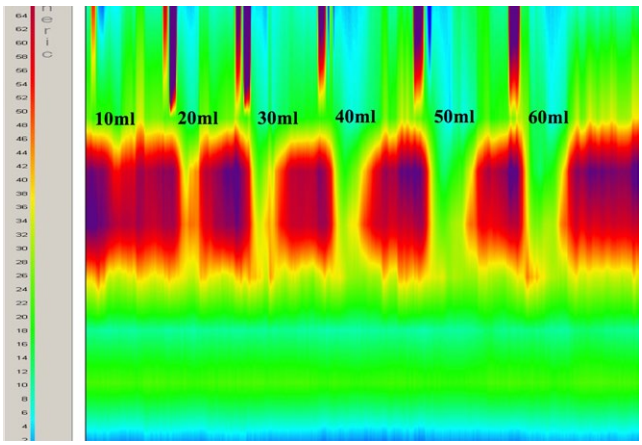

FIGURE 2 HRARM demonstrating a normal dose–response for RAIR. Note the increase in both the percentage and duration of relaxation with increasing volume for rectal distention

volume (dose–response). The RAIR is considered to be present if the balloon inflation elicits a decrease in at least 5 mm Hg[31] in the internal anal sphincter pressure. Such a small drop in anal pressure can sometimes be difficult to differentiate from movement artifact especially in an awake, uncooperative child. When the patient cooperates, one can also evaluate sensation, the presence of a normal squeeze and bear down efforts. Paradoxical contraction of the external anal sphincter and pelvic floor muscles can cause increase in anal pressure during attempted defecation and this response is classified as dyssynergia or anismus. Children with truncal hypotonia or abdominal muscle weakness can have difficulty bearing down and augment the rectal pressure during attempted defecation without necessarily increasing the anal sphincter pressure.

The interpretation of the CM is done mostly by visual inspection of the recording. Although, for obvious ethical reasons, CM has never been performed in healthy children, patterns of normal colon motility have now been established, based on observations from children with expected normal colonic physiology.[17] The colon does not have an easily recognizable fasting motility cycle like it is found in the upper gastrointestinal tract. During fasting, the colon demonstrates low-amplitude, mostly non-propulsive, segmental contractions with rare peristaltic movements.[32] Feeding stimulates more frequent and higher amplitude segmental contractions and increases the colonic tone. There is an inverse relationship between age of the child and the number of propagated contractions triggered by the ingestion of a meal.[17, 26] The presence of a gastrocolonic response to a meal is usually determined visually (Fig. 3), but a *motility index* can also be calculated by the software when the change in motor activity is not obvious. Colonic propagated contractions are classified based on their amplitude as HAPCs with pressures of at least 60 mm Hg, lasting 10 seconds and propagating for at least 30 cm and low amplitude propagating contractions with pressures less than 40 mm Hg.[32] Spontaneous HAPCs occur mostly postprandially or upon awakening, at times in clusters with one HAPC followed by others few minutes later.[13, 16, 17, 26] The onset of HAPCs in response to bisacodyl administration represents the most recognizable motility pattern in the study and the most clinically significant part of the test (Fig. 4). The identification of the HAPCs has a higher inter-observer agreement when compared to the gastrocolonic response to a meal and some have suggested the study could be abbreviated to include only the bisacodyl challenge.[33] There is consensus that the study can be considered normal when there is an increase in motility after a meal and the occurrence of spontaneous, meal-induced or bisacodyl-induced HAPC propagating to the recto-sigmoid junction.[15] Abnormal propagation of colonic contractions may indicate a segmental and milder colon motility disorder while absent HAPCs may indicate a more extensive and severe colonic dysfunction

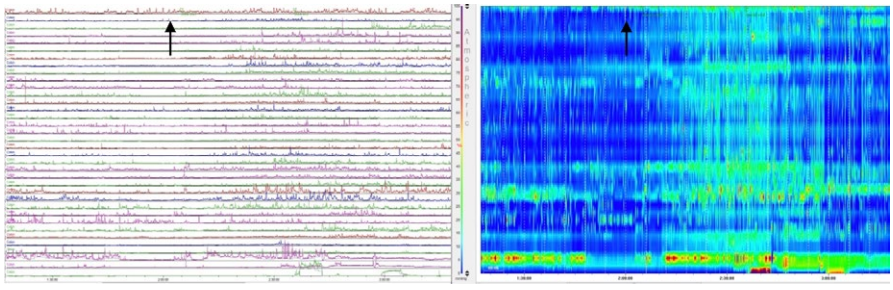

FIGURE 3 Normal gastrocolonic response to a meal. Note the increase in colon motor activity after ingestion of the meal (arrow) started

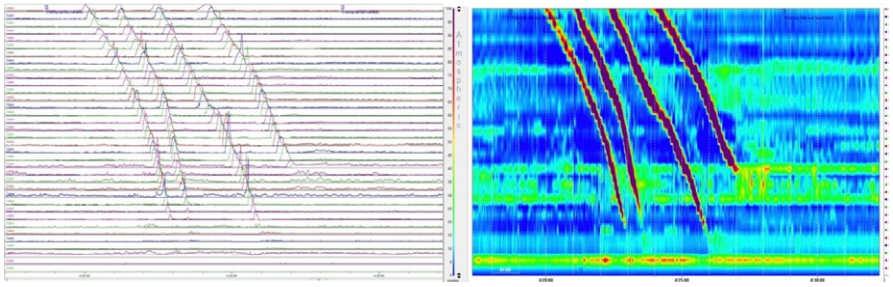

FIGURE 4 Normal HAPCs. Note that the amplitude is >60 mm Hg and the contractions are propagating to the recto-sigmoid junction

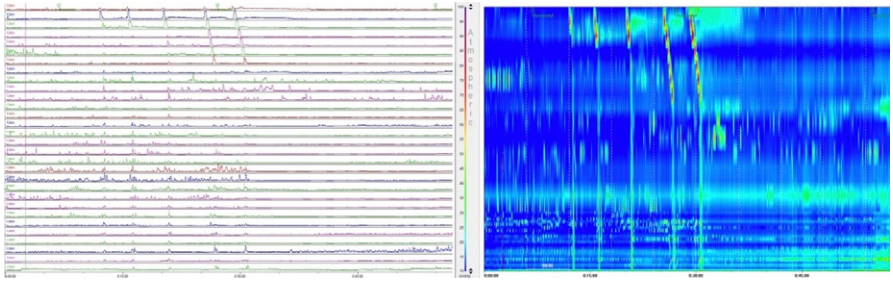

FIGURE 5 Abnormal HAPCs. Note that the contractions do not propagate beyond the transverse colon

(Fig. 5). Both the postprandial response to a meal and the presence of HAPCs have been associated with preservation of the enteric nervous system and correlate with colonic fecal movement by cine-MRI.[34] A recent report highlighted the association between bisacodyl-induced HAPC and anal canal relaxation (a "colo-anal reflex"), with most contractions resulting in anal canal relaxation as HAPC reach the splenic flexure.[35] After any type of colonic transection, CM has demonstrated that there is an increase in the number of HAPCs, probably due to the loss of a negative recto-colonic feedback, with a higher frequency of propagated contractions occurring in those patients operated for Hirschsprung's disease compared to those undergoing surgery for other indications.[36]

It is obvious that interpretation of colon manometry studies requires experience and sub-specialty training. In the Guidelines for Training in Pediatric Gastroenterology by NASPGHAN published in 2013 it is stated that pediatric GI fellows should be exposed to this procedure but the numbers of studies required for the training were not specified.[37] The recommendations also state that for the practice of subspecialties like Neurogastroenterology and Motility advanced training "could be obtained in 1 of 3 ways: within the context of a standard 3-year fellowship, assuming all of the basic requirements for clinical training and scholarship are met; during an additional, dedicated fourth year of fellowship training; or postfellowship in the course of mentored, specialized practice." There are no specified metrics to assess such training, because those only exist currently for transplant hepatology.

5 | INDICATIONS

The indications of the ARM include:

1. The most common and accepted indication for ARM in children is the evaluation of the internal anal sphincter relaxation in response to rectal balloon distension to help exclude Hirschsprung's disease. Evaluation of RAIR can also be useful in children with suspected anal achalasia. The RAIR is classically absent in patients with Hirschsprung's disease, anal sphincter achalasia and after circular rectal myomectomy or complex imperforate anus repair.
2. To evaluate patients with anorectal malformations with persistent defecation problems after surgical repair.
3. To assess persistent defecation problems after surgery for Hirschsprung's disease.[38, 39] Because the anal sphincter is dysfunctional in all children with Hirschsprung's disease and the RAIR remains absent after surgery, patients can experience difficult stool expulsion and chronic constipation. In patients with Hirschsprung's disease with fecal incontinence following surgical repair the measurement of the length of the anal canal may be of relevance.
4. Select patients with hypertonic sphincter or anal achalasia that may benefit form botulinum toxin injection and evaluate the effect of botulinum toxin injection into the anal sphincter.[40–42]
5. To evaluate defecation dynamics in patients with chronic constipation. When a child attempts to defecate, rectal pressure rises and anal sphincter pressure decreases. Children with dyssynergia fail to coordinate this response. Testing for this maneuver may be falsely positive in children due to the lateral position adopted during the motility testing or the anxiety related to trying to defecate in the presence of the personnel performing the test.
6. The assessment of rectal sensation and sphincter tone are an important part of the evaluation of patients with fecal incontinence associated with neurogenic problems. The RAIR is present in patients with spinal cord lesions. Sacral agenesis is associated with lower external anal squeeze pressure and blunted sensation upon rectal distension secondary to abnormal parasympathetic innervation.[43] It has been described that children with spinal lesions have a greater likelihood of anal spasm and achieve maximum relaxation of the sphincter with smaller balloon inflation volumes.[44]

The main indications for CM include:

1. Differentiation between functional constipation and intrinsic colonic dysmotility. Colon manometry is deemed useful to differentiate children with functional constipation from those with a colonic motor disorder, such as colonic inertia. In pediatrics, functional constipation is due to a behavioral disorder, namely the child's attempt to resist and delay defecation for fear of a painful bowel movement. Thus, in these children, the colon has normal motility with an intact gastrocolonic response to a meal.[26] Some have reported the utility of CM to differentiate between colonic myopathy and neuropathy,[16] but a recent study failed to show a correlation between manometric and histologic findings.[45] Thus, the test should be reported according to the physiologic findings observed: the presence and quality of the gastrocolonic response and the HAPCs, rather than as changes consistent with neuropathy or myopathy. In patients with chronic intestinal pseudo-obstruction, the colonic motility is abnormal in the majority of cases with absence of both gastrocolonic response and HAPCs[16] however, no data is available of the clinical utility of the test in chronic intestinal pseudo-obstruction.
2. Help planning surgical interventions in selected patients with constipation refractory to medical therapy. Colon manometry can help guiding surgical interventions such as placement of an appendicostomy or a cecostomy for the administration of antegrade colonic enemas (ACE) or creation of a diverting ileostomy. Colonic manometry has been reported to be useful in predicting successful outcomes to ACE.[46, 47] The value of CM in guiding partial colonic resections is debated. Some have suggested CM may help to detect abnormal colonic segments that may benefit from surgical resection[48, 49] while others have reported that partial colonic resections do not lead to symptom improvement in the majority of patients.[50] A recent study indicated that partial resections after a failed ACE may lead to symptomatic improvement.[51]
3. Determine if a diverted colon may be re-anastomosed.[48] Clinical progress in combination with repeated CM testing are taken in consideration at the time of deciding which patients will benefit from reanastomosis or will require a resection.

4. To assess the improvement of colonic dysmotility after long-term use of ACE.[46, 52] Patients with poor response to ACE and abnormal colonic motility are likely to require a colonic resection. However, this is an important decision that is made on a case-by-case basis and involves consideration of other comorbidities, psychological and social issues that are beyond the scope of this review.
5. To evaluate persistent symptoms following surgery, specifically for Hirschsprung's disease and anorectal malformations. Colonic manometry in combination with ARM has emerged as an important tool in understanding the pathophysiology and guiding the management of persistent postoperative symptoms of patients with Hirschsprung's disease and anorectal malformations, such as imperforate anus. Treatment guided by the CM (laxatives when HAPCs were weak or absent and medications to increase stool consistency in the presence of HAPCs migrating to rectum with normal or low tone anal sphincter) resulted in a significant improvement in quality of life and frequency and consistency of bowel movements.[53,54] It has been reported that 80% of patients with imperforate anus and fecal incontinence have HAPCs propagating into the neorectum and 60% have low internal anal sphincter resting pressure. Treatment based on those findings resulted on improvement of fecal incontinence in 45% of patients.[55] In patients with imperforate anus with constipation and incontinence CM may be useful in defining the etiology by demonstrating left or total colon dysfunction and treat accordingly.

In a large retrospective study of children with defecation disorders, which included 150 CM studies, the most common indications for the procedure were lower GI symptoms (68%), persistent symptoms after corrective surgery in Hirschsprung's disease (14%), evaluation of CIPO (11%), and evaluation before considering closure of a diverting ostomy (7%). Normal colonic motility was found in 38% of children, left colon dysmotility in 17%, and total colonic dysmotility in the rest. Based on the results of the study, treatment changes were recommended in 93% of patients, resulting in symptom improvement in 78% and worsening in 4% and parental satisfaction with the interventions was 88%.[56] Up to now, no controlled, prospective studies have evaluated the utility of the test to guide therapy or predict outcome.

6 | CONCLUSION

In summary, ARM is the most performed and widely available motility study in pediatrics. Colonic manometry is now considered a "routine" diagnostic test in children and its indications and interpretation have been standardized. Improvements in technology are now making ARM and CM easier to perform and more informative. Controlled, prospective studies evaluating the impact of ARM and CM testing on medical and surgical treatment and long-term outcome are still lacking.

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DISCLOSURE

No competing interests were declared for this study. Leonel Rodriguez- Nothing to disclose. Carlo Di Lorenzo: Scientific consultant QOL Medical, IMHealth Science, Merck. Manu Sood: Scientific consultant QOL scientific. Dr. Sood's spouse is employed by AbbVie. Dr. Sood and his spouse own Abbott and AbbVie stock. Miguel Saps: Scientific consultant Forest, Quintiles, Ardelyx, QOL Medical, IMHealth Science, Nutricia. Leonel Rodriguez, Manu Sood, and Miguel Saps are members of the Pediatric Committee of ANMS. Miguel Saps is councilor of ANMS. Carlo Di Lorenzo is President of NASPGHAN.

AUTHOR CONTRIBUTION

All authors contributed to the analysis of the published data, wrote and critically reviewed the manuscript.

ABBREVIATIONS

3D, tridimensional; ACE, antegrade colonic enemas; ARM, Anorectal manometry; CM, Colonic manometry; HAPC, high amplitude propagated contraction; RAIR, recto-anal inhibitory reflex.

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