



High-Resolution Anorectal Manometry and 3D High-Definition Anorectal Manometry in Pediatric Settings

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8.1 Anorectal Physiology

Fecal continence and defecation are highly regulated processes ensured by the synergic and coordinated function of the rectum, pelvic floor muscles, and anal canal. The rectum functions as a reservoir for fecal material and its stretch-sensitive fibers, activated by the intraluminal distension, are essential in signaling the awareness of defecation to the central nervous system and activating spinal reflexes. The anal canal consists of the internal (IAS) and external (EAS) anal sphincters. The former, which is composed of smooth muscle cells, is innervated by the enteric nervous system and therefore not under voluntary control. It is primarily responsible for anal continence as it generates approximately 70–85% of the anal canal pressure. Conversely, the EAS, composed by skeletal muscle cells, is under the voluntary control of the sacral nerves. The two sphincters are closely adjoined and, in young children, a clear physical separation between is difficult to detect [1, 2].

The anal sphincters, the pelvic floor muscles, and the levator ani complex, which includes the puborectalis muscle, are responsible for ensuring the fecal continence at rest. Synergistically, through tonic contractions, the aforementioned structures maintain the anorectum angulated between 85° and 105° [3] and generate a pressure at the level of anal canal that exceeds the rectal pressure, hence preventing the involuntary loss of fecal material [3, 4].

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The evacuatory process is a highly regulated and voluntary function. The distension of the rectal wall above an appropriate sensory threshold provokes a temporary reflex relaxation of the IAS, named recto-anal inhibitory reflex (RAIR), which enables the luminal contents to enter the anal canal. The expulsive step, under voluntary control, is characterized by the coordinated relaxation of the EAS and pelvic floor muscles alongside with the abdominal wall contraction, which ultimately enables the passage of the stools through the anal canal [4]. If the subject is not in a socially appropriate setting to defecate, the voluntary contraction of the EAS and the puborectalis muscle prevent the defecation and the stools are returned to the colon by reverse peristalsis.

8.2 Equipment

ARM is by nature a highly technical evaluation and when knowledgeably used, provides an accurate description of anorectal neuromuscular function. However, the manometric data are reliable only if the methodology used to acquire them is accurate.

A manometric apparatus setup consists of a pressure sensor/transducer combination, which detects the pressures in the anal canal and rectum and transduces them into an electrical signal, and a recording device, which amplifies, records, and stores that electrical signal. The pressure sensor/transducer components of the manometric assembly function as a matched pair and are available in two general designs: either water-perfused catheters, connected to a pneumohydraulic perfusion pump and to volume displacement transducers, or strain gauge transducers with solid state circuitry [5].

In the last decade considerable advancements in ARM technology have been witnessed and conventional low-resolution systems have gradually been replaced by high-resolution (HRARM) and 3D high-definition manometry (HDARM). This has been achieved by a combination of new manometric assemblies allowing intraluminal pressure to be recorded from up to 256 pressure sensors spaced <0.3 mm. At the same time, advances in computer processing allow pressure data to be presented in real-time as a compact, either as two-dimensional visually intuitive “spatiotemporal plot” or more sophisticated 3D. In adults, by correlating with anatomic structures defined by MRI or 3D ultrasound, HDARM measurements allow a better definition of the contribution of different components of the anal canal and a better description of the anal canal radial asymmetry [6]. However, the role of our enhanced knowledge of the pathophysiological mechanisms of the different defecation disorders in children is still unclear.

Currently, the catheter used for 3DHRAM has an outer diameter of almost 11 mm [7]. Although the test could in theory be performed at any age, in infants the anal resting pressure could be overestimated and anal canal dynamics upon balloon distension could be misinterpreted [8]. To date, 3DHRAM has been used in children aged above 2 years.

8.3 Methodological Aspects

8.3.1 Preparation of Pediatric Patients and Caregivers

In preparation for the procedure, in children above the age of 1 year, an enema is recommended on the day or the evening prior to the day of tests. Alternatively, in those with significant fecal loading a degree of bowel preparation could be required prior to the procedure. In infants, no bowel preparation is required as they generally have soft stools [9]. Medications that can interfere with the anorectal function should be stopped before the procedure.

Older children are instructed to defecate if required before the test. The child should be placed in the lateral decubitus position, with knees drawn up to the chest, maintaining the hips and knees flexed at 90°. Before the probe insertion, the perianal area should be inspected and a digital rectal examination should be carried out, in order to evaluate the general anatomy, the perianal sensation, skin excoriation, and the presence of rectal impaction. Then, the lubricated manometry probe can be gently inserted into the rectum. Before starting the recording, the operator should wait for few minutes in order to allow the acclimation of anorectal area.

Pediatric gastroenterologists have often to face non-cooperative children and, especially in children under the age of 5, a study under anesthesia may be required. When that happens, only the analysis of anal sphincter resting pressures and RAIR can be performed. Moreover, the results need to be carefully evaluated as different anesthetic agents may interfere with the physiological outcomes [10–13].

Nevertheless, in some circumstances and indications undoubtedly requiring patients' cooperation a proper psychological preparation for both children and parents is certainly required. Anorectal manometry has been shown to induce significant preprocedural distress in children and adequate psychological preparation intervention has been shown to reduce anticipatory distress, to improve measurements reliability, and ultimately to better pave future treatments based on the manometric patterns [12, 14–17].

8.3.2 Study Protocol, Analysis, and Interpretation

Ideally, the full manometric protocol should aim at assessing sphincter pressures at rest and during voluntary contractions, bear-down maneuvers, rectal sensation, and reflexes. Nonetheless, the test should be tailored and the relevant parameters to assess should depend on the clinical indication.

The common parameters assessed during the ARM study are the following:

- *Resting pressure:*

The resting pressure should be recorded only after the child is relaxed and comfortable. The basal resting sphincter pressure measurement with new technology of HRAM is simply obtained by inserting the catheter and evaluating in real-time the high-pressure zone over a period of 30 s [10]. Conversely, resting

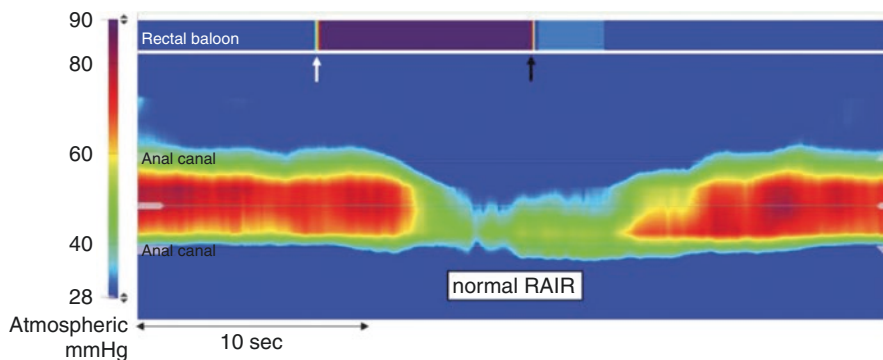


Fig. 8.1 Normal RAIR. White and black arrows point rectal balloon insufflation and deflation, respectively. The balloon inflation induces an increase in the rectal pressure, shown in the figure as purple bar. Normal RAIR is seen as a drop in anal canal pressure upon rectal balloon insufflation

pressure evaluation with low-resolution probes is usually performed through either stationary pull-through or continuous withdrawal [18]. The identification of high-pressure zone allows also the measurement of the anal canal length.

- *RAIR (recto-anal inhibitory reflex)* (Fig. 8.1):

The RAIR consists in the relaxation of IAS upon a rectal distention. In pediatrics, there are no universally agreed criteria for its definition. It is currently defined as either a dropping in pressure by >5 mmHg or $>15\%$ of the resting pressure [18]. The drop in anal pressure may be difficult to be detected especially in uncooperative children and in patients with baseline low resting pressures (e.g., under anesthesia). The RAIR has a volume-dependent response: the larger the balloon volume, the greater the degree and duration of the relaxation. Its measurement is performed by rapidly inflating the rectal balloon with incremental volumes of 5 mL in infants and newborns (up to 20 mL) and increments of 10 mL in older children [10]. If complete relaxation is not obtained, volumes up to 250–300 mL can be reached in older children to elicit the RAIR. The absence of RAIR is suggestive of colonic aganglionosis or Hirschsprung disease (Fig. 8.2). The most common reason for a false-positive RAIR is represented by the migration of the probe during the procedure, which can be prevented by securing the catheter to the anal verge. Conversely, the most frequent cause for a false-negative RAIR test is rectal dilatation (i.e., megarectum), which does not allow the balloon to stretch the rectal walls (and therefore to generate the trigger pressure for the RAIR) because of the enlarged rectal volume [18].

- *Squeeze pressure* (Fig. 8.3):

It is elicited by asking the child to voluntarily contract the anal canal and it is calculated as the greatest pressure increase referred to the baseline resting pressure. In some centers, the average of three measurements is calculated [10, 18]. An increased or decreased value may be due to myogenic or neurogenic causes.

- *Endurance squeeze* (Fig. 8.4):

The child is asked to contract the anal canal as strongly as possible for at least 15- to 20-s period.

- *Rectal sensation*:

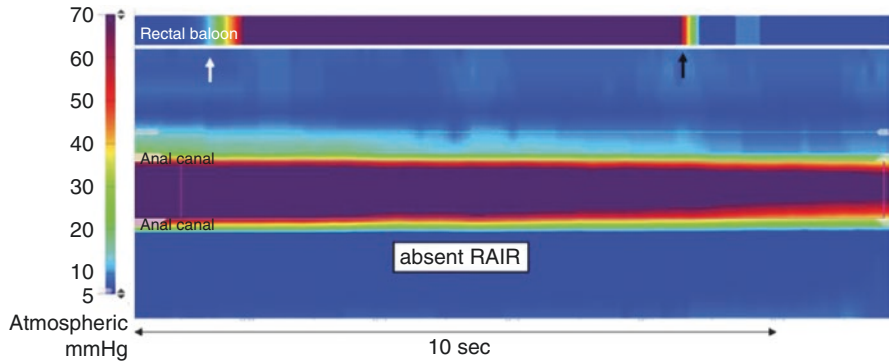


Fig. 8.2 Absent RAIR. White and black arrows point rectal balloon insufflation and deflation, respectively. The balloon inflation induces an increase in the rectal pressure, shown in the figure as purple bar. The anal sphincter pressure does not decrease upon rectal balloon insufflation. RAIR is absent in several conditions including colonic aganglionosis or Hirschsprung disease

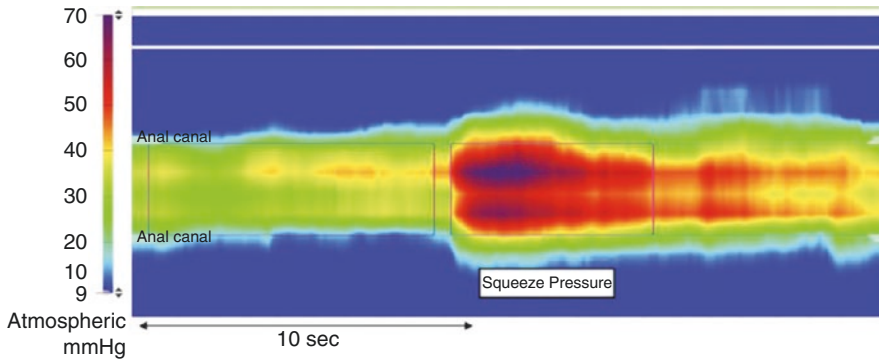


Fig. 8.3 Squeeze pressure. It is elicited by asking the child to voluntarily contract the anal sphincter. It is calculated as the greatest pressure increase referred to the baseline resting pressure

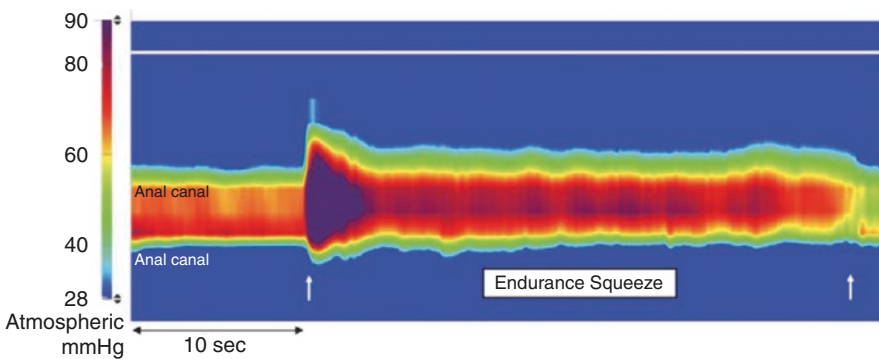


Fig. 8.4 Endurance squeeze. It is the length of time the child is able to maintain the anal canal pressure during a voluntary contraction. It is elicited by asking the child to voluntarily contract the anal sphincter as strongly as possible for a period of at least 15–20 s. The white arrows point the start and the end of the squeeze

The rectal sensation can be assessed in a cooperative child (usually aged 4–5 years and over) by steadily increasing the balloon size through the inflation of progressively greater volumes of water or air. It can be performed with or without deflation intervals in between the subsequent incremental volumes (intermittent rectal distension method or through ramp inflation method, respectively) [10]. It provides further information on the child's stool perception, which can be indicative of either anorectal dysfunction or dilated rectum. Three different sensation volumes are usually recorded: (i) *the first sensation*, which represents the lowest balloon volume at which the patient feels the balloon; (ii) *the urge sensation*, defined as the lowest volume required to elicit the defecation urge; (iii) *the maximum tolerable sensation*, reached when severe urgency and pain is experienced. This may be hard to be evaluated in children younger than 7 years of age and children with developmental impairment. Sensations are usually decreased in children with dilated rectum, often due to long-lasting outlet-obstruction constipation.

- *The bear-down maneuver or push (simulated defecation)* (Fig. 8.5):

It is carried out to evaluate anorectal and pelvic floor pressure changes during a simulated defecation. Usually, this provocative test is possible to perform in children above 5–6 years of age and it requires significant cooperation. Normally, the defecation attempt should induce a simultaneous and coordinate increase in the rectal pressure and relaxation of anal sphincters. This maneuver allows clinicians to diagnose dyssynergic defecation, which is a common cause of fecal outlet obstruction.

- *Balloon expulsion test:*

It is carried out asking the child to sit on a commode or in lateral position and expel the intrarectal inflated balloon, trying to guarantee as much privacy as possible. The test is defined normal if the balloon is expelled. In pediatrics, there is

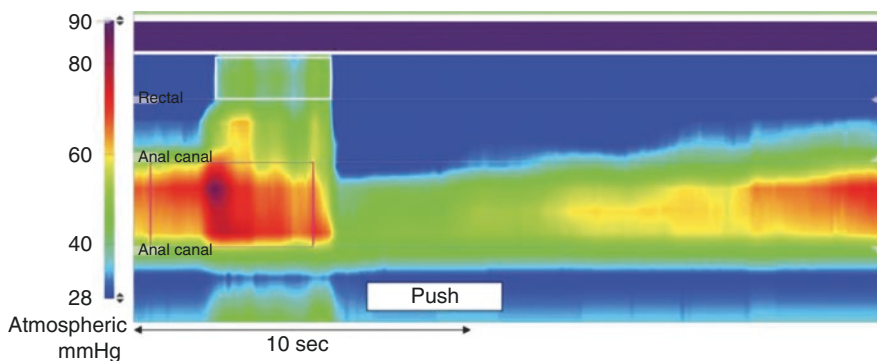


Fig. 8.5 Bear-down maneuver or push in dyssynergic defecation. It is carried out to evaluate anorectal and pelvic floor pressure changes during a simulated defecation. Normal defecation attempt induces a simultaneous and coordinate increase in the rectal pressure and relaxation of anal sphincters. In the figure, there is an increase in rectal pressure (*white square*) but paradoxical increase in anal pressure, consistent with the diagnose dyssynergic defecation, which is a common cause of fecal outlet obstruction in children

no a consensus on the time cut-off needed to expel the balloon and the ideal balloon volume. Studies have demonstrated that adult normal values can be used. Patients with dyssynergia usually fail to expel the balloon [19]. It has been demonstrated that this test in pediatric patients with outlet-obstruction type of constipation may help in tailoring therapeutic management [19].

8.3.3 Reference Values

In pediatric age, there is a lack of uniformity in terms of protocols and equipment, and hence lack of normal reference values. Moreover, normal HRAM and 3D HRAM values have been published only for adult populations [20–23], while only few studies have been performed in children with similar methodologies. Hence, the interpretation still relies on expertise of the pediatric gastroenterologists in the field. Moreover, conventional water-perfused ARM measures are routinely used in manometry reporting despite in adult literature has shown that the values with high-resolution manometry are higher than those with water perfusion [24]. Moreover, significant variability in values might depend on gender, BMI, age, use of different protocols, and the interaction between the patient and the clinician [21, 22, 25, 26].

To date only two studies in pediatric age have been performed using HARM and 3DHARM in order to establish normative values. One study using HARM reported normal values of anorectal sphincter metrics (including resting pressure, anal canal length, and RAIR) in 180 healthy and asymptomatic newborns based on age, and segregated by preterm vs term [27]. Recently, Banasiuk et al. have published a study aimed at evaluating normal 3DHRAM values in 61 children without symptoms from the lower gastrointestinal tract [8]. Normal values in pediatric age using either low- or high-resolution manometry are summarized in Tables 8.1 and 8.2.

Further studies are needed in pediatric populations in order to reach universally agreed normal values.

8.4 Indications

The indications of ARM are the following:

- *To rule out Hirschsprung disease (HD)*

HD is characterized by the absence of ganglion cells in the myenteric and submucosal nerve plexuses in the colon and rectum secondary to an aberrant ontogenetic development of the gastrointestinal tract. Hence, due to the lack of innervation in the rectum, ARM shows a typical absence of IAS relaxation upon rectal distention. The absence of RAIR on ARM should prompt rectal suction biopsy (RSB), which is the gold standard for the diagnosis of HD. The absence of RAIR and the presence of ganglion cells at rectal suction biopsies define the condition named anal achalasia, which responds well to the treatment with botulin toxin [18].

Table 8.1 Normal manometric values in term and preterm neonates found in pediatric studies published using either low- or high-resolution anorectal manometry (Zar-Kessler et al. [18], modified)

	Equipment (technique)	Healthy patients (n)	Ages	Anal resting pressure (mmHg)	Anal canal length (cm)	RAIR threshold volume (mL)	Patients with normal RAIR (%)	Rectal pressure (mmHg)
Kumar et al. [2]	Water-perfused LR	30	3–28 D	31.07 ± 10.9	1.67 ± 0.34	9.67 ± 3.7		
			34–39 weeks of GA					
Benninga et al. [28]	Water-perfused LR	22	30–33 weeks PMA	32 ± 4		1.6 ± 0.3 ^a	92% ^a	9 ± 2
			33–38 weeks PMA	51 ± 4		1.9 ± 0.2	100%	11 ± 3
de Lorijn et al. [29]	Water-perfused LR	16	3–23 D	24.5 ± 11.4		3.4 ± 1.6 ^a	81% ^a	6.5 ± 4.8
			27–30 weeks PMA					
Tang et al. [27]	Water-perfused HRARM	85	0.5–85 D	23.1 (19.9–26.2)	1.8 (1.7–2.0)	1.6 (1.4–1.9)		
			Preterm neonates	27.7 (24.8–30.6)	1.9 (1.7–2.0)	2.2 (1.7–2.7)		
			≥31 D ^b	32.9 (29.6–36.2)	2.0 (1.7–2.3)	3.7 (2.8–4.7)		
			28–36 weeks of GA					
95	1–67 D	28.9 (25.8–32.0)	1.9 (1.7–2.1)	2.8 (2.3–3.3)				
	Term neonates	31.6 (28.9–34.3)	2.0 (1.9–2.1)	3.5 (2.9–4.0)				
	37–42 weeks of GA	39.9 (35.6–44.1)	2.3 (2.1–2.4)	4.5 (3.9–5.0)				

D days of life, LR low resolution, GA gestational age, PMA postmenstrual age

^aAir insufflation: 1–5 mL of air was directly insufflated into the rectum to elicit the RAIR, instead of inflated balloon

^bIn this group healthy patients older than 1 month of life (infants) were included

Table 8.2 Normal manometric values for infants and children found in pediatric studies published using either low- or high-resolution anorectal manometry (Zar-Kessler et al. [18], modified)

	Equipment	Healthy patients (n)	Ages	Anal resting pressure (mmHg)	Anal canal length (cm)	Maximal squeeze pressure (mmHg)	RAR threshold volume (mL)	First sensation volume (mL)	Critical volume (mL)	Rectal pressure (mmHg)
Benninga et al. [3]	Water-perfused LR	13	8–16 Y	55 ± 16		182 ± 61	18 ± 10	19 ± 12	131 ± 13	
	Water-perfused LR	30	35 D–16 M	42.43 ± 8.9	1.86 ± 0.6		14.0 ± 9.5			
Li et al. [30]	Not mentioned	30	18 M–12.3 Y	43.43 ± 8.79	3.03 ± 0.52		25.0 ± 11.6			
	Water-perfused LR	10	7–14 Y		4.0 ± 0.9			28.0 ± 11.4	117.0 ± 46.2	
Surphen et al. [31]	Water-perfused LR	27	6.5–12 Y ^a	80.9 ± 24.3		141.7 ± 47.2		30.4 ± 11.9	95.6 ± 38.1	13.0 ± 13.0 (resting) 60.5 ± 22.0 (defecation)
	Solid state 3DARM	9	2–5 Y	94 (24)	2.2 (0.5)	201 (60) ^b	13.3 (7.5)	34 (28.8) ^c	36 (27) ^c	
Banasiuk et al. [8]	Solid state 3DARM	19	5–8 Y	86 (15)	2.4 (0.4)	206 (40) ^d	11.1 (3.2)	25 (32.9) ^d	37.2 (35.9) ^d	
		19	9–12 Y	94 (15)	2.9 (0.6)	206 (59)	13.7 (5.9)	14.7 (6.9)	36.3 (19.8)	
		14	12–17 Y	96 (19)	3.1 (0.7)	229 (65)	18.6 (15.1)	22 (11.9)	55 (39.9)	

M months of age, Y years of age, LR low resolution

^aApproximately^bEvaluated on seven patients^cEvaluated on five patients^dEvaluated on 18 patients

Recently, a new measure, the anal sphincter relaxation integral (ASRI), has been developed to objectively quantify the RAIR and discriminate patients with and without HD [32]. However, its role in the clinical management of patients with HD is still to be elucidated.

- *To evaluate the anorectal functions of HD children after surgical repair*

ARM plays an essential role in the post-surgical evaluation of these patients. For instance, it has been shown that the measurement of the length of the anal canal in HD children with fecal incontinence after surgical repair enables to pave further effective therapeutic management [33].

- *To evaluate the sphincter function in children with organic causes of constipation (e.g., anorectal malformation, spinal cord lesions)*

Children with anorectal malformations need an accurate functional evaluation after anorectal surgery in order to evaluate the residual anorectal function. Additionally, in the pre-surgery workup before reverting colostomy or ileostomy, ARM may be indicated in order to exclude the presence of outlet-obstruction defecation.

Spinal cord abnormalities may increase the tone of the anal sphincters as a consequence of the damage of upper motoneurons and an exaggerated contraction and anal spasms upon balloon dilation or sphincter relaxation with smaller balloon inflating volumes [34]. Conversely, in some neurological conditions the anal tone may be decreased due to abnormalities involving the lower motoneuron [35].

- *To evaluate persisting symptoms of constipation with or without fecal incontinence unresponsive to standard medical therapy*
- *To evaluate the anorectal function before and after therapeutic interventions such as botulinum toxin injection and biofeedback*
- *To assess the defecation dynamics*

The incoordination between the relaxation of the anal sphincters and pelvic floor muscles during defecation, called dyssynergic defecation, may be an underlying cause of constipation. This can be evaluated in real-time with ARM during the bear-down maneuver and, in adult population, ARM allows clinicians to differentiate dyssynergic defecation into different phenotypes according to the presence of adequate/inadequate increase in rectal pressure and failed reduction/paradoxical increase in anal pressure (type 1–4) [36]. Regardless of the type of ARM phenotype, dyssynergic defecation leads to outlet-obstruction constipation. This diagnosis can be confirmed by the inability of expelling the balloon. In children, both the bear-down maneuver and the balloon expulsion test may be falsely labelled as negative, because of the lateral position adopted during the test and the anxiety due to defecate in the presence of the clinicians [19].

8.5 Future Perspectives and Conclusions

Over the last decade, remarkable technical advances, in terms of probe miniaturization and pressure recording systems, have led to a more detailed understanding of the anorectal function. High-resolution (HRAM) and 3D high-definition

(3DHDAM) systems will gradually replace conventional low-resolution anorectal manometry. However, in children, although HRAM provides a greater characterization of defecatory disorders phenotypes, fecal incontinence, and anorectal dysmotility in adult population as well as in pediatric patients, it is still limited by the lack of standardization, interpretation, and normal data. The increasing application of new system in clinical will certainly lead to a substantial improvement of appropriate management driven by specific manometric patterns and underlying pathophysiological abnormalities.

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