Values From Three-dimensional High-resolution Anorectal Manometry Analysis of Children Without Lower Gastrointestinal Symptoms

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BACKGROUND & AIMS: Three-dimensional high-resolution anorectal manometry (3DHRAM) provides a topographic image of pressure along the anal canal. We aimed to determine normal 3DHRAM values in children.

METHODS: We performed a prospective study of 61 children (34 male; mean age, 8.28 years) without any symptoms arising from the lower gastrointestinal tract who were evaluated at the Department of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Poland. Manometry procedures were performed by using a rigid probe without medication. Pressure within the anal canal and 3D images of sphincters were measured. If possible, squeeze pressure and thresholds of sensation were evaluated. The population was divided into age groups of <5 years, 5–8 years, 9–12 years, and older than 12 years.

RESULTS: The mean resting and squeeze sphincter pressures were 83 ± 23 mm Hg and 191 ± 64 mm Hg, respectively. The mean length of the anal canal was 2.62 ± 0.68 cm and correlated with age ($r = 0.49$, $P < .0001$). The mean rectal balloon volume to elicit rectoanal inhibitory reflex was 15.7 ± 10.9 cm^3. The first sensation, urge, and discomfort were observed at balloon volumes of 24.4 ± 23.98 cm^3, 45.9 ± 34.55 cm^3, and 91.6 ± 50.17 cm^3, respectively. The mean resting pressure of the puborectalis muscle was 69 ± 14 mm Hg, whereas the mean squeeze pressure was 124 ± 33 mm Hg. There was no statistically significant difference in pressure parameters between age groups. We observed a positive correlation between age and balloon volume needed to elicit discomfort ($r = 0.49$, $P < .001$).

CONCLUSIONS: In a prospective study, we determined normal values from 3DHRAM analysis of children without symptoms arising from the lower gastrointestinal tract. There were no significant differences in pressure results between children of different sexes or ages. ClinicalTrials.gov number: NCT02236507.

Keywords: Anal Sphincter Function; Reference; Standard; Diagnostic; Functional Disorder.

Anorectal manometry measures pressures of the distal part of the gastrointestinal tract. This method is noninvasive and can be used as a diagnostic tool for many functional diseases of the anorectal area (ie, constipation, fecal incontinence) and after surgery (ie, for Hirschsprung disease, anorectal malformations).[1] The most widely used method is the conventional water-perfused system that uses a 4-channel catheter.[2] A new high-resolution anorectal manometry (HRAM) system that uses circumferential sensing solid-state transducers allows for the evaluation of the anal sphincteric complex in a more detailed manner.[3] The catheter consists of at least 12 sensors located longitudinally and circumferentially and records average pressures every 7–10 mm. Three-dimensional high-resolution anorectal manometry (3DHRAM) is an advanced version of the HRAM system and has been recently introduced into clinical practice. Currently, 3DHRAM is the most precise method for assessing the anal sphincter function and may be crucial for planning and controlling surgical procedures of the anorectal area.[4,5] Although 3DHRAM use in children is increasing,

Abbreviations used in this paper: EAS, external anal sphincter; HPZ, high pressure zone; HRAM, high-resolution anorectal manometry; PRM, puborectalis muscle; RAIR, rectoanal inhibitory reflex; SD, standard deviation; 3DHRAM, three-dimensional high-resolution anorectal manometry.

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there are no normal values available for this age group. Therefore, the aim of the study was to establish normal ranges of 3DHRAM for the pediatric population.

Materials and Methods

Study Subjects

Children without symptoms arising from the lower gastrointestinal tract underwent manometric evaluation at the Department of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Poland. Exclusion criteria were as follows: age younger than 1 year and older than 18 years, history of surgery for anorectal malformations, diagnosis of constipation or fecal soiling established by Rome III criteria, diagnosis of inflammatory bowel diseases or any other type of large bowel inflammation, presence of anal fissure, anal varices, inflammation of the anorectal area, or any other disease that may interfere with the function of the anorectum. All parents and children $\geq$16 years old signed the informed consent before participation in the study. The population was divided into age groups of <5 years, 5–8 years, 9–12 years, and older than 12 years.

The study was approved by the Ethics Committee of the Medical University of Warsaw, Poland (KB/8/2013) and was registered at ClinicalTrials.gov (NCT02236507).

Equipment

Manometry was performed by using 3DHRAM (ManoScan 360/3D; Covidien/Medtronic, Dublin, Ireland). The manometric system is composed of a catheter attached to an amplifier and recorder system, which is then connected to the computer. The catheter measures 64 mm in length and has an outer diameter of 10.75 mm. It consists of 256 solid-state pressure sensors that are divided between 16 rows. Each row is composed of 16 circumferentially oriented sensors. The pressure is measured every 4 mm longitudinally and 2.1 mm circumferentially. Attached at the end of the probe is a non-latex balloon. A 60-mL syringe is connected to the balloon via an air channel inside the catheter. This allows for the administration of increasing air boluses into the balloon to measure the rectoanal inhibitory reflex (RAIR) and sensation thresholds. The catheter is marked to identify the posterior axis.

The software interpolates pressures between the sensors. The real-time spatiotemporal plots of the anorectum are recorded and presented in two-dimensional and 3D display on the computer monitor by using dedicated software.

Procedure

All patients were studied according to the methods described previously.[1,4,5] No routine bowel preparation or anesthesia was used. A digital rectal examination was performed before the manometric procedure. A saline enema was administered if stool was present. Patients were examined in supine position, which allowed for better cooperation with the child and was determined to be more comfortable for children watching color contour plots during the procedure.

Before each examination, a dedicated disposable sheath with a balloon was placed on the catheter, and a calibration was performed. The catheter was lubricated and gently inserted into the anorectum. An investigator held the catheter during the whole procedure with regard to the posterior mark on the probe. The depth of the probe was established so that the proximal and distal margins of the high pressure zone (HPZ) were clearly identified. After the accommodation period of 2 minutes, conventional manometric measurements were collected as follows: (1) 20 seconds of resting pressure recorded and 20 seconds of squeeze pressure recorded measured twice with 30-second break, (2) ano-anal reflex, (3) cough reflex, and (4) RAIR. The RAIR threshold was evaluated by rapid inflation and deflation of the balloon with incremental volumes ranging from 10 to 60 mL. The reflex was considered present when decrease in resting pressure reached 25%. At the end of the procedure the thresholds of sensation, urge, and discomfort were identified by continuous administration of air into the balloon (performed twice).

Data Analysis

After the examination dedicated software was used to analyze the recorded data (ManoView AR v2.1; Covidien/Medtronic). Conventional parameters were calculated by the software. Three-dimensional parameters were derived from the raw data collected by 256 sensors. The proximal and distal ends of the HPZ were established with the aid of the implemented software algorithm. Moreover, the 3D maps of the HPZ were radially divided into quadrants as previously described,[6] so that the anterior, posterior, left, and right quadrants were easily recognizable. The 4 quadrants were further divided along the length of the anal canal to the proximal and distal halves. The pressures of the puborectalis muscle (PRM) were approximated by using the anatomy of the anal canal[7–10] and the resulting mean pressures of the left, posterior, and right proximal quadrants. All authors had access to the study data and had reviewed and approved the final manuscript.

Statistical Analysis

Data analysis was conducted by using SAS (SAS Inc, Cary, NC) software. Sensor measurements were aggregated with respect to 8 quadrants. Descriptive statistics such as the mean and standard deviation (SD) were computed to summarize pressure values within each quadrant. Student *t* test was used to compare differences in selected variables between male and female subjects. Correlation was evaluated by Pearson or Spearman coefficient, depending on data distribution. Linear regression models were then used to predict the relationship between age and selected variables.

Results

Between December 2013 and September 2014, 61 children (mean age, 8.28 years; range, 2–17 years; 34 boys) were included in the study. There were no differences in age, weight, height, and the number of bowel movements per day between girls and boys (Table 1). The mean time of procedure was 10 minutes 9 seconds. There was no difference in manometric measurements on the basis of sex and pressure parameters between age groups (Table 2). RAIR was present in all children. In the youngest group, 7 children were able to squeeze and 5 children were able to report sensation thresholds. All of them were older than 4 years of age. Data distribution of mean resting pressure is shown in Figure 1.

In older children, an elongated HPZ (Figure 2) and higher threshold of discomfort were observed. Correlation coefficients between age and parameters are summarized in Table 3.

The mean resting pressure of the PRM was 69 mm Hg (standard deviation [SD], ±14), whereas the mean squeeze pressure was 124 mm Hg (SD, ±33).

At rest, the mean pressures of the anterior, posterior, left, and right quadrants were 112 mm Hg (SD, ±29), 115 mm Hg (SD, ±31), 153 mm Hg (SD, ±28), and 152 mm Hg (SD, ±28), respectively. The mean pressures during squeeze were 191 mm Hg (SD, ±78), 199 mm Hg (SD, ±78), 245 mm Hg (SD, ±84), and 241 mm Hg (SD, ±81), respectively. There were significant differences in the mean pressures between the sagittal and coronal quadrants. The mean pressures of all quadrants with respect to the proximal and distal halves of the anal canal are summarized in Table 4. There were statistically significant differences in the mean pressures between halves within the same quadrants ($P < .0001$), with relatively higher pressures measured in the posterior

Table 1. Clinical Characteristics of Subjects

Variable (n)	Total (61) Mean (±SD)	Male (34) Mean (±SD)	Female (27) Mean (±SD)	P value
Age (*mo*)	104.6 (55.25)	114.1 (51.1)	116 (51.27)	.88
Weight (*kg*)	32.5 (17.5)	34.59 (17.1)	36.07 (17.2)	.74
Height (*cm*)	137.75 (24.78)	137.7 (26.3)	137.6 (23.3)	.98
Bowel movements (*stools per day*)	1.18 (0.51)	1.15 (0.45)	1.22 (0.59)	.58

Table 2. Conventional Manometry Parameters Based on Sex and Subdivided Into Age Groups

Group variable	Total		Male		Female			<5 y		5–8 y		9–12 y		>12 y		
	N	Mean (±SD)	n	Mean (±SD)	n	Mean (±SD)	*P* value	n	Mean (±SD)	n	Mean (±SD)	n	Mean (±SD)	n	Mean (±SD)	*P* value
Maximum resting pressure (*mm Hg*)	61	100 (27)	34	1110 (23)	27	110 (18)	.95	9	115 (28)	19	104 (20)	19	112 (17)	14	110 (22)	.49
Mean resting pressure (*mm Hg*)	61	83 (23)	34	92 (19)	27	92 (16)	.86	9	94 (24)	19	86 (15)	19	94 (15)	14	96 (19)	.29
Maximum squeeze pressure (*mm Hg*)	58	191 (64)	33	216 (65)	25	204 (38)	.38	7	201 (60)	18	206 (40)	19	206 (59)	14	229 (65)	.58
Length of HPZ (*cm*)	61	2.6 (0.68)	34	2.8 (0.64)	27	2.6 (0.67)	.15	9	2.2 (0.5)	19	2.4 (0.4)	19	2.9 (0.6)	14	3.1 (0.7)	.00
Mechanical resistance (*cm × mm Hg*)	61	219.4 (87.14)	34	256.2 (79.32)	27	238.1 (87.69)	.4	9	195.8 (49.0)	19	208.6 (53.4)	19	270.5 (69.7)	14	305.3 (105.6)	.00
Minimum rectal compliance (*cm³/mm Hg*)	60	−0.38 (5.52)	33	0.16 (0.08)	26	0.17 (0.07)	.75	7	0.14 (0.0)	19	0.18 (0.1)	19	0.16 (0.04)	14	0.17 (0.08)	.6
Maximum rectal compliance (*cm³/mm Hg*)	60	−0.9 (0.81)	33	0.64 (0.39)	26	0.76 (0.35)	.23	7	0.53 (0.4)	19	0.75 (0.4)	19	0.68 (0.2)	14	0.7 (0.4)	.6
RAIR (*cm³*)	61	15.7 (10.9)	34	12.8 (5.67)	27	15.4 (11.68)	.29	9	13.3 (7.5)	19	11.1 (3.2)	19	13.7 (5.9)	14	18.6 (15.1)	.11
First sensation (*cm³*)	56	24.4 (23.98)	32	20.6 (14.13)	24	22.9 (29.56)	.72	5	34 (28.8)	18	25 (32.9)	19	14.7 (6.9)	14	22.1 (11.9)	.28
Urge (*cm³*)	56	45.9 (34.55)	32	39.7 (28.11)	24	43.3 (37.03)	.67	5	36 (27.0)	18	37.2 (35.9)	19	36.3 (19.8)	14	55 (39.9)	.33
Discomfort (*cm³*)	56	91.6 (50.17)	32	81.6 (46.9)	24	102 (54.59)	.19	5	48 (22.8)	18	75.8 (45.3)	19	88.2 (45.0)	14	127.1 (53.7)	.00

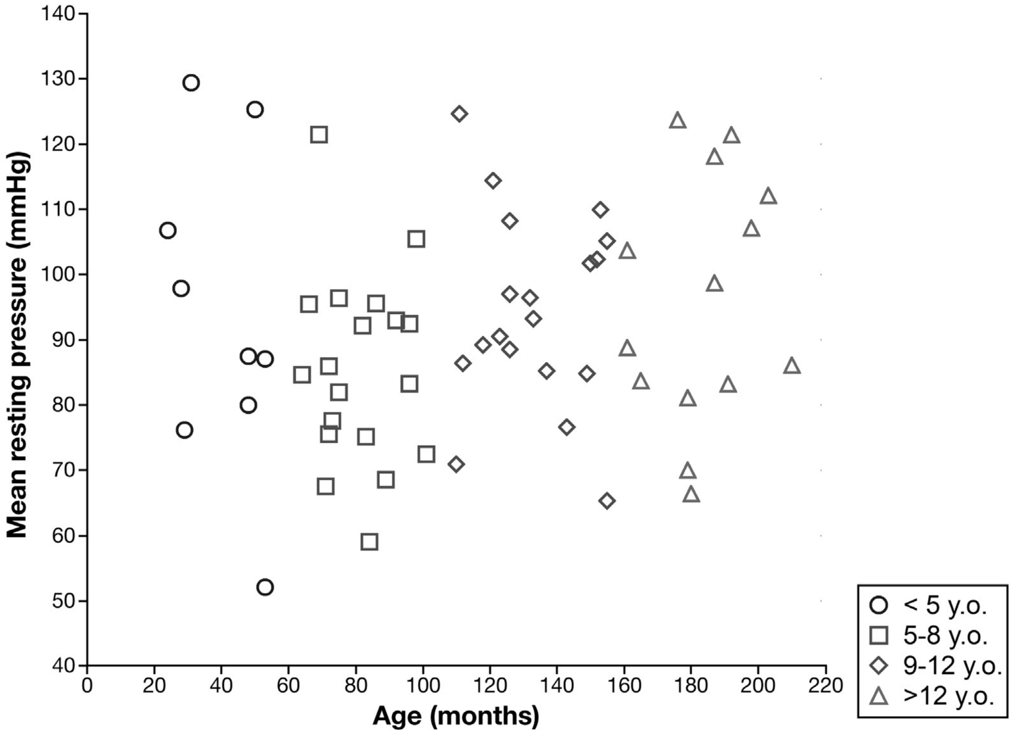

Figure 1. Data distribution of mean resting pressure in different age groups.

proximal and distal lateral quadrants during both rest and squeeze.

Discussion

This study provides a full data set of normal values of 3DHRAM for the pediatric population. Moreover, this is an assessment of 3DHRAM normal values that is essential for the correct interpretation of a procedure's results and for clinical decision-making.

HRAM represents a new dimension for the evaluation of anal sphincter function and pressure profile. Its ability to record pressures along the anal canal by using closely spaced sensors simplified both the procedure and the interpretation.[11] The advent of a more advanced version

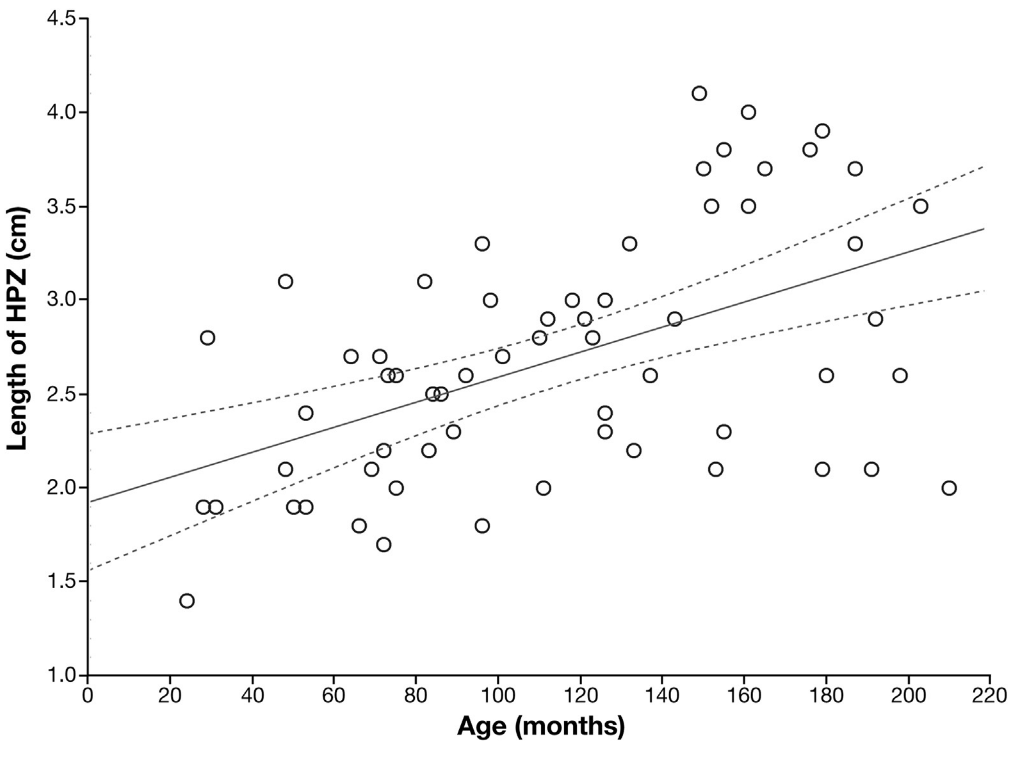

Figure 2. Correlation between age and length of HPZ (in linear regression model).

Table 3. Correlation Coefficients Between Age and Parameters

Variable	Correlation coefficient	*P* value
Maximum resting pressure	0.07	.62
Mean resting pressure	0.21	.11
Maximum squeeze pressure	0.13	.32
Length of HPZ	0.47	.00
Mechanical resistance	0.46	.00
Minimum rectal compliance	0.2	.13
Maximum rectal compliance	0.15	.27
RAIR	0.24	.07
First sensation	−0.01	.93
Urge	0.25	.06
Discomfort	0.50	.00

of HRAM, the 3DHRAM catheter, allowed for the visualization of pressures with even more detail, producing a map of pressures recorded longitudinally and circumferentially. This detailed map might be crucial for the localization of potential pressure gaps and for discriminating which part of the anal canal may be responsible for continence.[12–16] To our best knowledge, although the catheter used in our study is rigid and of greater diameter than flexible ones, it depicts pressure area with the highest resolution. This may have impact on surgical procedures, especially in children with congenital anorectal malformations. The pressure asymmetry of the anal canal observed in children after surgery for Hirschsprung disease may help in controlling and improving surgical techniques.[17] Moreover, 3DHRAM may confirm the role of PRM in continence function and tailor adequate treatment.[6]

In the literature, a few studies have reported normal values for anorectal manometry in the pediatric population. There were differences in the type of equipment and methodology used. Most of the studies used conventional water-perfused equipment.[18–27] Other investigators used manometry with microtransducers[28–31] or 3 balloon systems,[32,33] or the equipment was not specified.[34–37] Moreover, the results of these studies were derived from small sample sizes subdivided into age groups, and the protocols differed among authors. There was only 1 study reporting normal values by using a high-resolution water-perfused catheter on a large cohort of 180 asymptomatic newborns.[38] The absolute values of the pressures are known to be catheter-dependent, and the parameters determined by solid-state sensors are relatively higher than those of water-perfused manometry.[39,40] There is also evidence that the results may differ on the basis of the protocol[41] and the interaction between the patient and the investigator.[42] For this reason, normative data should be collected separately for each specific catheter, and the procedure needs to be standardized with the evolution of equipment and our understanding of anorectal physiology.[43] In the adult population, normal values of HRAM[41,44] and 3DHRAM[45,46] have already been established. This is a report of normative data for 3DHRAM in a pediatric cohort.

Table 4. Pressures of All Segments Along the Anal Canal With Respect to Proximal and Distal Halves

Quadrant	Distal half Mean (±SD)	Proximal half Mean (±SD)	Total Mean (±SD)
Rest (n = 61)			
Anterior	72 (17)	41 (17)	112 (29)
Posterior	44 (20)	71 (16)	115 (31)
Left	84 (17)	69 (17)	153 (28)
Right	86 (18)	67 (16)	152 (28)
Squeeze (n = 58)			
Anterior	134 (49)	67 (33)	191 (78)
Posterior	72 (36)	138 (40)	199 (78)
Left	135 (39)	123 (37)	245 (84)
Right	141 (41)	112 (34)	241 (81)

NOTE. Pressures are expressed in mm Hg.

Intra-anal pressure is generated by 3 muscles, the internal anal sphincter, the external anal sphincter (EAS), and the PRM. During rest, approximately 50%–85% of pressure is of internal anal sphincter origin,[47,48] whereas squeeze pressures are the effect of EAS and PRM contraction. According to its specific anatomy, the anal canal is considered to be asymmetrical. In our study we observed asymmetry in children with regions that have relatively higher mean pressures in the proximal posterior and distal lateral segments of the HPZ. We analyzed 3D maps of pressure separately by using raw data from 256 sensors. The 16 × 16 grid of sensors was rearranged to simplify analysis, which allowed for a more comprehensive view of potential asymmetry. A similar observation of asymmetrical anal canals was reported by Ambartsumyan et al,[6] who reported on the asymmetry in children with constipation. In our study, the mean pressures recorded in the 4 quadrants were higher, which may be a result of different methods used to derive parameters and different types of samples (healthy vs constipated children). Although different absolute values of pressures were observed in each quadrant, the different quadrants displayed similar asymmetry.

Cross-sectional studies[7] and radiologic investigations of the anal canal that were based on magnetic resonance imaging[10] and ultrasonography[49,50] in adults demonstrated the contribution of EAS in the distal half and PRM in the proximal half of the anal canal. Similar results were reported in children.[51,52] The PRM is considered to play a crucial role in the continence mechanism.[53,54] To characterize the contribution of the PRM we decided to divide the anal canal into proximal and distal parts. This allowed for the comparison of quadrants at the same level and enabled the estimation of possible contributions from the PRM and EAS separately.[10]

We determined the mean threshold volume of air to elicit RAIR to be 15.7 cm^3. Our results are consistent with previous reports that showed the mean threshold volume ranging from 11 to 50 cm^3.[18–25,27–33]

The mean length of the HPZ in children of the same median age varies from 3.0 to 3.3 cm.[22,35] Our measurements revealed a shorter span of the pressure profile compared with previous non-3DHRAM studies. The longer HPZ may be a result of the historically used pull-through technique, which elicits an ano-anal reflex and pressure increase.

The length of the HPZ in our sample was correlated with age, which is consistent with previous studies.[22,37] In our study, there were no other age-dependent parameters except for the threshold of discomfort, but the clinical significance of this observation needs to be established.

We measured a mean resting pressure higher than previously reported (83 mm Hg versus 25–67 mm Hg, respectively).[18–37] Interestingly, the mean and maximum resting pressures in our samples were even higher than those pressures reported in adults by Li et al[45] and Coss-Adame et al[46] (60.8 mm Hg and 83 mm Hg, respectively). Similarly, we observed higher maximum squeeze pressures compared with other pediatric normative values. A possible explanation of these findings is that the 3DHRAM catheter has a larger diameter than other manometric catheters and is being used in the anal canal of children, which is relatively smaller in diameter, generating higher pressures. This explanation would confirm previous observations in studies in adults by using the solid-state 3DHRAM catheter[40] and relatively high mean pressure in the youngest subgroup. In our group, voluntary squeeze pressures were higher than previously reported (90–190 mm Hg versus 190–215 mm Hg in our sample).[28,33] This discrepancy may be explained by the specific physiology of EAS. Studies in adults revealed that EAS operates at a short sarcomere length, which means that the stretch of sphincter generates a relatively higher force of contraction.[55]

In this study we observed higher thresholds determined at higher volumes of air inside the balloon than those thresholds reported by studies that used latex balloons. There is evidence that different types of balloons are vulnerable to physical conditions, ie, temperature and pressure.[56] The balloon used in our study is made of non-latex, thermoplastic elastomer, which is less elastic than latex and may produce different pressure characteristics.

The major advantage of our study is that we established 3DHRAM normal values in children. Our study also has a few limitations. The sample size is relatively small, making it impossible to determine differences according to age, but large enough to perform appropriate statistical analysis. Higher pressures recorded in the youngest group compared with other age groups may reflect the influence of the size of the catheter in relation to relatively smaller diameter of the anal canal. For that reason, the normal values may have limited application in this age group. The selection of PRM segments in the 3D pressure map was based on magnetic resonance images and ultrasonography studies in adults. We did not correlate 3D images of pressure with endoanal ultrasonography that was performed simultaneously. Therefore, our puborectalis segments might be selected with some degree of error.

Conclusions

We report normative data for 3DHRAM in children. We also present asymmetry of the anal canal in a healthy pediatric population.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at http://dx.doi.org/10.1016/j.cgh.2016.01.008.

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Conflicts of interest
The authors disclose no conflicts.

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Supplementary Materials

Measurements and Data Analysis

Anal Sphincter Pressures

Data were obtained by thick and rigid catheter with 256 sensors, with dedicated sheath and balloon (Supplementary Figure 1).

Before data evaluation all samples were corrected by using thermal compensation function. The catheters were calibrated before each procedure. Moreover, in vivo calibration procedure was performed once a week.

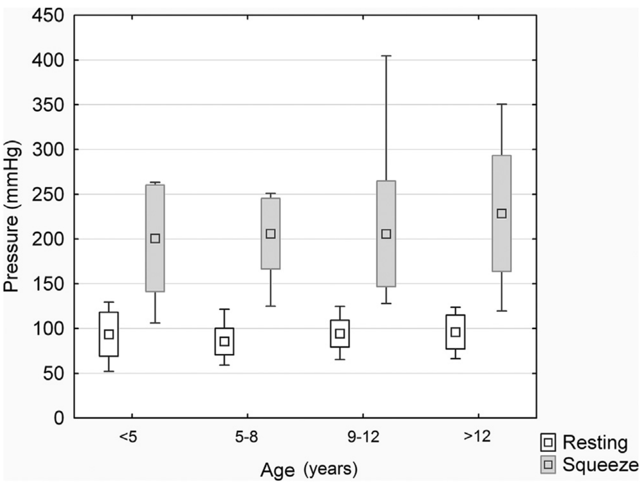
Conventional manometric parameters such as the length of HPZ were evaluated by using dedicated software (Manoview; Covidien/Medtronic). Electronic sleeve was routinely used for pressure measurements, with the lollipops manually adjusted to appropriate measurement area. Each pressure measurement was evaluated in separate time frame. All pressure parameters were referenced to atmospheric pressure. Maximum squeeze pressure was defined as the maximum average anal sphincter pressure over duration set to 1 second. The length of HPZ was defined as the length of average spatial distribution of pressure that is more than 25% of peak HPZ pressure above the intrarectal pressure. Mean and maximum values of conventional pressure parameters are shown in Supplementary Figure 2.

Raw data from 256 sensors were used to analyze 3D picture of HPZ. Proximal and distal margins (proximal and distal levels of sensors) of anal canal were established by using the same algorithm as the length of HPZ. Electronic platforms were used to subdivide sphincteric area into 8 segments and to obtain mean pressure from each segment.

Statistical Analysis

To clarify data presentation, results are expressed as mean (±SD). Before between-group comparison, mean test assumption assessment was conducted. Kolmogorov-Smirnov normality test showed significant discrepancies between empirical and normal distribution in case of several variables. No heterogenous variances were found between boys and girls and between age groups. The *t* test was chosen as the method for mean comparisons. Although normality distribution is not requisite condition for *t* test usage, *t*-test result may be affected by distribution shape. To ensure that there was no effect of distribution shape on mean comparison effect, Wilcoxon rank test was performed. Z statistic was calculated only for those variables whose distribution was not normal in at least 1 subgroup. Results based on sex are summarized in Supplementary Table 1.

Supplementary Figure 1. Catheter with dedicated sheath and balloon.



Supplementary Figure 2. Mean resting pressures (*white boxes*) and maximum squeeze pressures (*gray boxes*) of different age groups.

Supplementary Table 1. Statistical Analysis Based on Sex

Test variable	Equality of variances test		Normality assessment: Kolmogorov-Smirnov normality test (*P* value)		*t* test	Wilcoxon rank test	
	F	Pr. > |F|	Male	Female	*P* value	Z	Pr. > |Z|
Maximum resting pressure (*mm Hg*)	1.69	0.1735	>.150	>.150	.95	—	—
Mean resting pressure (*mm Hg*)	1.35	0.4367	>.150	>.150	.86	—	—
Maximum squeeze pressure (*mm Hg*)	2.90	0.0088	>.150	>.150	.38	—	—
Length of HPZ (*cm*)	1.08	0.8222	>.150	>.150	.15	—	—
Mechanical resistance (*cm* × *mm Hg*)	1.22	0.5803	<.010	>.150	.4	−1.0672	0.2859
Minimum rectal compliance (cm^3/*mm Hg*)	1.09	0.8148	.023	.023	.75	−1.3991	0.1618
Maximum rectal compliance (cm^3/*mm Hg*)	1.25	0.5695	>.150	<.010	.23	1.7943	0.0728
RAIR (cm^3)	4.25	0.0001	<.010	<.010	.29	0.4240	0.6715
First sensation (cm^3)	4.38	0.0002	<.010	<.010	.72	−0.9447	0.3448
Urge (cm^3)	1.73	0.1521	<.010	<.010	.67	0.1353	0.8923
Discomfort (cm^3)	1.35	0.4307	.076	.012	.19	1.3032	0.1925