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Three-dimensional high-resolution anorectal manometry: cut-off values for diagnosis of dyssynergic defecation in children

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Abstract. – OBJECTIVE: Dyssynergic defecation (DD) may be one of the most important causes of constipation, but its diagnostic criteria have not been formally validated in children. This study aims to evaluate constipated children with 3DHRAM (three-dimensional high-resolution anorectal manometry) and determine a new pediatric cut-off for DD variables.

PATIENTS AND METHODS: 205 patients diagnosed with functional constipation (FC) based on Rome III criteria were prospectively enrolled. Data were compared to a historical control group (C). Initially, the diagnosis of DD was based on adult criteria and divided into 4 types. A new cut-off value for percent anal relaxation was determined based on ROC curve analysis.

RESULTS: The FC group presented significantly lower values of percent anal relaxation during straining compared to the C group (9.5% *vs.* 20%, respectively, *p*=0.03). Based on adult criteria, DD was found in 53% of the FC group and 46% of the C group (*p*=0.3), with type II occurring most frequently (35.8%). New cut-off value of 31% for percent anal relaxation in children was derived based on the ROC curve analysis. Based on this new cut-off value, DD was diagnosed in 69.3% of constipated children, with type IV occurring most frequently (28.9%). The analysis of segmental pressure showed significant influence of segments at the locations of the puborectalis muscle and external anal sphincter.

CONCLUSIONS: We found that during bear down maneuver the percent anal relaxation variable significantly differed between patients and controls. The higher cut-off value should be used when 3DHRAM and the standard four-type classification are used to diagnose DD in children.

Key Words:
Constipation, Functional anorectal disorders, Anorectal manometry, Anorectal function testing, Children.

Introduction

Functional constipation (FC) is a common pediatric problem with a reported prevalence of up to 32.2%[1] that may be the reason for 25% of visits to pediatric gastroenterologists[2]. One of the most important causes of FC is abnormal defecation dynamics, also called dyssynergic defecation (DD). DD may contribute to the failure of conservative treatment[3]; however, implementing additional therapeutic approaches, such as pelvic floor therapy may improve outcomes[4].

Anorectal manometry is the test most commonly used to assess anorectal function in children. The procedure allows for an objective assessment of anal sphincter length, tone, thresholds of sensation (first, urge and discomfort), rectoanal reflexes, such as rectoanal inhibitory reflex (RAIR), and ability to squeeze and simulate the process of defecation (bear-down maneuver). The main indications for the test are as follows: (a) to evaluate patients with intractable constipation; (b) to evaluate patients with persistent symptoms after surgery for Hirschsprung's disease, anal sphincter achalasia, or imperforate anus repair; (c) to evaluate defecation dynamics in patients with chronic constipation; and (d) to assess rectal sensation and sphincter tone in patients with fecal incontinence[5].

In adults, the most widely used definition of DD (formerly described by the term 'anismus') is based on the presence of incomplete anal sphincter relaxation (or paradoxical anal contraction) and/or inadequate propulsive force recorded by anorectal manometry[6]. This technique can simultaneously record intrarectal pressure (a proxy for propulsive force) and intra-anal pressure during straining.

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The current diagnostic criteria for DD are based on studies in adults and have not been formally validated in children thus far. Therefore, it is difficult to implement these criteria reliably in a pediatric setting. Moreover, cut-off values were derived using conventional water-perfused manometry, and interpretation of results obtained with other technologies is uncertain[7]. The advent of three-dimensional high-resolution anorectal manometry (3DHRAM) has facilitated the determination of the contributions of different components of the anal canal in generating pressure during simulated defecation in great detail[8].

Therefore, we aimed to evaluate constipated children with 3DHRAM and determine new pediatric cut-offs for DD variables.

Patients and Methods

Study Patients

Children aged 5-18 diagnosed with FC based on the Rome III criteria[9] were prospectively enrolled in the study and underwent manometric evaluation at the Departments of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Poland. In the presence of alarm signs, additional tests were performed to exclude organic causes of constipation, including barium enema, colonic transit time study, full-thickness biopsy, and endoscopy. Patients with organic etiology of constipation were excluded from analysis.

The study exclusion criteria comprised history of surgery on the lower gastrointestinal tract, congenital anorectal malformation, anorectal trauma, and inflammatory bowel disease.

All data were compared to raw manometric data obtained from children without symptoms, which were collected in our laboratory and published previously[10].

The study was approved by the Ethics Committee of the Medical University of Warsaw, Poland (KB7/2013).

Equipment

Manometry was performed using a rigid probe to reconstruct a three-dimensional spatiotemporal plot of anal canal pressure (3DHRAM; ManoScan 360/3D; Medtronic, Dublin, Ireland) as described previously[10]. The anal canal pressure map was displayed in live mode on a monitor using specialized software (ManoScan AR 2.1, Covidien/Medtronic, Dublin, Ireland), allowing for discrimination between different pressure components.

Procedure

Patients were investigated in a supine position. Before each examination, the probe was calibrated according to the manual, lubricated, and inserted into the rectum. After an accommodation period of at least 3 minutes, conventional manometric parameters were recorded, including mean resting pressure, maximum squeeze pressure (two attempts), bear-down maneuver (performed three times), presence of RAIR, and thresholds of sensation.

Data Analysis

All conventional parameters were evaluated with dedicated software (ManoView AR v2.1; Covidien/Medtronic, Dublin, Ireland) after each procedure. Raw data from 256 sensors were used to analyze spatiotemporal plots of the anal canal. The plots were subdivided into segments as previously described[10]. Briefly, the anal canal was divided into proximal and distal high-pressure zones, which were further subdivided into anterior, posterior, left and right quadrants. Thus, pressure data from eight segments of the anal canal could be evaluated. The pressure of the puborectalis muscle (PRM) was obtained from the left, posterior and right proximal segments, and that of the external anal sphincter (EAS) from the left and right distal segments, covering their anatomical localization[8,10].

DD was initially diagnosed based on adult criteria and divided into four types as follows: adequate intrarectal pressure (> 40 mmHg) and paradoxical anal contraction (type I); inadequate intrarectal pressure (< 40 mmHg) and paradoxical anal contraction (type II); adequate intrarectal pressure (> 40 mmHg) with incomplete or absent relaxation (< 20%) of the resting anal sphincter (type III); and inadequate intrarectal pressure (< 40 mmHg) with incomplete or absent relaxation (< 20%) of the resting anal sphincter (type IV). Inadequate relaxation of the anal canal as measured by percentage of anal relaxation was a necessary criterion for DD diagnosis. To better specify the role of PRM and EAS in DD, pressures generated by these muscles were compared between patients with type I-II and type III-IV presentations.

Table I. Clinical characteristics of subjects.

Variable/Group	FC (n = 205)	C (n = 61)	*p*-value
Age (months; median (IQR)	101 (70,137)	112 (73,155)	0.3
Weight (kg; median (IQR)	27.9 (20,41)	30.6 (20,47.2)	0.2
Height (cm; median (IQR)	132 (116.2,147)	134 (120,159)	0.2
Gender (male, %)	120 (58.5%)	34 (55.7%)	0.7

IQR – interquartile range; FC – functional constipation; C – historical control group.

Statistical Analysis

The Shapiro-Wilk test of normality was used for the distribution of quantitative variables. The Mann-Whitney U test was used to test differences between groups. The χ^2 test was used to compare proportions, with Yates' correction where appropriate. Receiver operator characteristic (ROC) curve analysis was used to derive new cut-off values to discriminate between constipated and healthy individuals. Statistical significance was defined as a *p*-value of <0.05. Statistica 13 (Statsoft, OK, USA) software was used for all analyses.

Results

205 children (120 males; median age, 8 years; age range, 5-17 years) were included in the study. The clinical characteristics of the patients (FC group) in relation to the historical control group (C group) are summarized in Table I.

Compared to the C group, the FC group presented significantly lower values of mean resting pressure (89.2 mmHg *vs*. 75 mmHg, *p*=0.000), maximum squeeze pressure (211.7 mmHg *vs*. 181 mmHg, *p*=0.002) and duration of sustained squeeze (15.4 s *vs*. 11.2 s, *p*=0.005). Anal canal length was significantly higher (2.9 cm *vs*. 2.6 cm, *p*=0.04) and maximum rectal compliance was greater (1 *vs*. 0.6, *p*=0.000) in the FC group than in controls.

Although the median RAIR threshold value was the same in the FC and C groups (10 cm^3), constipated children often presented RAIR after the balloon was inflated to higher volumes (interquartile range [IQR]=10-30 cm^3 *vs*. 10-15 cm^3 in the FC and C groups, respectively; *p*=0.001).

The thresholds of first sensation, urge and discomfort in the FC group (50 cm^3, 80 cm^3 and 110 cm^3, respectively) were significantly higher than in the C group (20 cm^3, 30 cm^3 and 85 cm^3, respectively; *p*=0.000 for all comparisons).

The analysis of manometric variables obtained during the bear-down maneuver revealed decreased values in the FC group compared to the C group; however, the only significant parameter was the percentage of anal relaxation. The recto-anal pressure differential was negative in both groups. All results are summarized in Table II.

Based on adult criteria, 53% of constipated children presented with DD. The distribution of patients with different types of DD was 30.3% type I, 35.8% type II, 11.9% type III and 22% type IV. DD was also observed in 46% of children in the C group based on adult criteria. Thus, there was no statistically significant difference in the frequency of DD between the FC and C groups (*p*=0.3).

The ROC cut-off value for percentage of anal relaxation to discriminate between healthy controls and constipated patients was found to be 31% (Figure 1). Based on this new cut-off value,

Table II. Bear down manoeuver variables.

	FC		C		
Variable/Group	N	Median (IQR)	N	Median (IQR)	*p*-value
Residual anal pressure	182	79 (57, 106.5)	56	81.8 (53.4, 105)	0.8
Percent of anal relaxation	182	9.5 (-25.0, 30)	56	20 (-9, 46)	0.03
Intrarectal pressure	182	34.4 (23.2, 52.5)	56	42.3 (27.3, 55.5)	0.2
Rectoanal pressure differential	182	-37 (-70.1, -17.8)	56	-37.2 (-77, -15.9)	0.7

IQR – interquartile range; FC – functional constipation; C – historical control group.

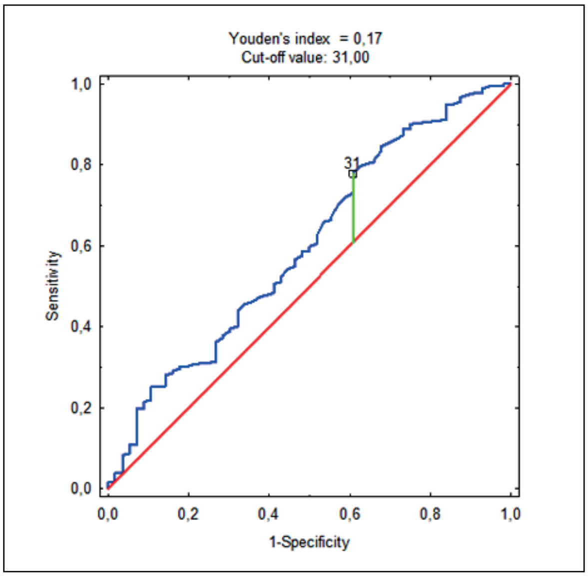

Figure 1. The ROC curve analysis with a new cut-off value for percentage of anal relaxation discriminating between healthy controls and constipated patients.

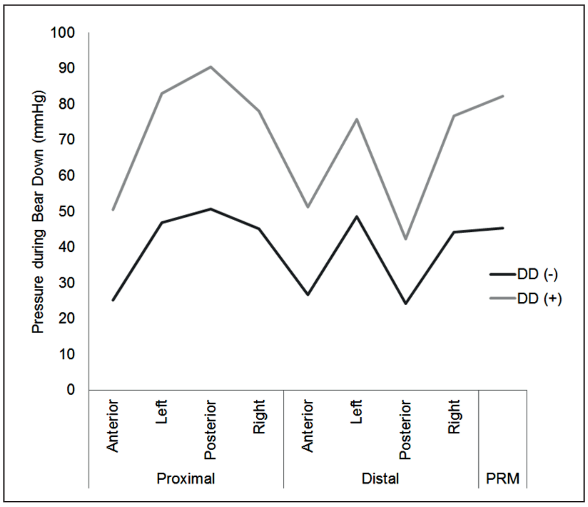

Figure 2. Segmental pressures obtained from the FC group according to DD diagnosis based on the 20% criterion for anal relaxation.

the frequency of DD in both groups was recalculated (Table III). The new distribution of different types of DD in the FC group was 23.2% type I, 27.5% type II, 20.4% type III and 28.9% type IV.

Segmental pressure in patients from the FC group who met the adult criteria for DD was significantly higher than the corresponding value in patients without dyssynergic patterns (Figure 2). The difference in pressure between patients with and without DD according to adult criteria was greater for segments covering the locations of the PRM (proximal left, posterior and right) and EAS (distal left and distal right). The difference was even greater when the definition of DD was based on 31% anal relaxation (Figure 3).

Significant differences between patients with type I-II and type III-IV presentations were found with regard to PRM and EAS pressures. Data are summarized in Table IV.

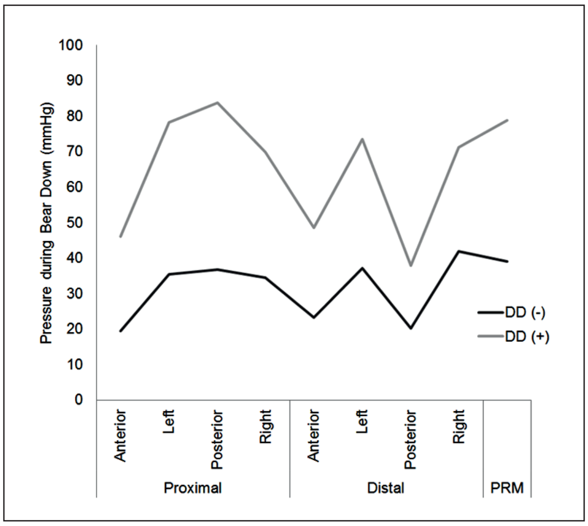

Figure 3. Segmental pressures obtained from the FC group according to DD diagnosis based on the 31% criterion for anal relaxation.

Table III. Percent of patients and controls with dyssynergic defecation (DD) pattern according to different criteria based on cut-off values for the percent of anal relaxation.

Group Cut-off value for percent of anal relaxation	FC n (%)	C n (%)	*p*-value
20%	109/205 (53.2)	34/61 (55.7)	0.3
31%	142/205 (69.3)	28/61 (45.9)	0.049

FC – functional constipation; C – historical control group.

Table IV. Bear down manoeuver variables.

Type of DD Muscles	Type I-II		Type III-IV		
	N	Median (IQR)	N	Median (IQR)	*p*-value
Diagnosis of DD based on 20% cut-off value for percentage of anal relaxation					
EAS	72	84.4 (57.7, 117)	37	67 (59.3, 80.8)	0.006
PRM	72	98 (76.9, 121.1)	37	69.9 (60.2, 80.5)	< 0.001
Diagnosis of DD based on 31% cut-off value for percentage of anal relaxation					
EAS	72	84.4 (57.7, 116.8)	70	64.2 (48.3, 78.9)	< 0.001
PRM	72	98 (76.9, 121.1)	70	67.9 (55.6, 80.2)	< 0.001

DD – dyssynergic defecation; PRM – puborectalis muscle; EAS – external anal sphincter; IQR – interquartile range.

Discussion

The present study was performed to determine the role of high-definition manometry in the diagnostic work-up of children suffering from FC, with special emphasis on evacuatory disorders. Our data revealed lower values of conventional pressure parameters (both resting and squeeze), higher values of rectal compliance and higher thresholds of sensation in patients as compared to control subjects. Based on adult criteria, DD was present in more than half of all patients and was more frequent among constipated children than in controls; however, this difference was not statistically significant. The only parameter out of the manometric bear-down variables showing a significant difference between the two groups was the percentage of anal relaxation. Given that using adult criteria might produce a bias, we performed ROC curve analysis and calculated a new cut-off value of 31% anal relaxation to better differentiate constipated patients from controls. In three-dimensional reconstructions, the important role of the PRM and EAS in DD was highlighted by the action of segments covering their anatomical locations during bear-down. The differences in pressures between patients and controls were greater in these segments than in others.

There are no published studies using high definition manometric equipment on constipated children that compare conventional parameters to normal values. As different types of catheters may substantially influence recorded pressures[11], direct comparisons with the results of our study are not possible. Contrary to our findings, a majority of previous studies[12-15] reported resting and squeeze pressure values that were lower, but not significantly different, in constipated patients compared to controls. Our results are similar to those of studies reporting lower pressures in subgroups of patients with fecal impaction, especially when impaction resulted in megarectum[16,17]. This suggests that a higher number of cases of severe constipation was evaluated in our tertiary center.

We found higher thresholds of sensation in the FC group, which is in line with the results of most studies utilizing manometric equipment[13,14]. However, the volumetric method is biased by the properties of elastic balloons and reflects dilatation of the rectum[7,18] rather than true hyposensitivity[19]. It is worth noting that the balloons used in our study were made of non-latex, thermoplastic elastomer, which is less elastic than the latex used by others. Our results may therefore represent a more reliable recording method, although further studies are necessary to support this hypothesis. Additionally, we found that constipated children presented higher values of rectal compliance than controls. This phenomenon is an important factor predisposing to more severe symptoms[20], further supporting the increased presence of more severe cases in our tertiary center.

Defecation dynamics may play an important role in the etiology of FC. In our study, we found that DD was responsible for constipation in more than 60% of patients. Frequencies reported by others vary substantially, from 29% to as high as 90.5%[21,22]. This wide range reflects the enormous diversity in definitions and methodologies used in previous studies, with a variety of both tests and parameters[14,23,24]. Notably, all early reports were focused only on the presence of paradoxical contraction of the anal sphincter, excluding those with no increase in rectal pressure during straining[24]. Moreover, some authors allowed for movement of the catheter during bear-down (a necessary condition for the evaluation of straining)[25], which might lead to either "pseudorelaxation" of the anal canal or contraction as a result of the ano-anal reflex.

In our study, we used the definition proposed by Rao et al[26], based not only on pressure changes in the anal canal (paradoxical contraction or inadequate percentage of anal canal relaxation) but also on manometrically-registered intrarectal pressure as an equivalent of propulsive force. However, it is important to remember that the initially proposed cut-off values for relaxation and propulsive force were established arbitrarily based on pattern recognition performed by experts on highly selected samples of participants, all of whom had symptoms suggestive of DD[27]. This raises the important question of whether the proposed criteria have any discriminatory power between constipated and healthy individuals. Indeed, we found comparable proportions of patients and controls with DD, which is in line with the results of a study by Grossi et al[28] utilizing high resolution manometry in adults. Although new manometric equipment based on high-resolution catheters has facilitated the easier evaluation of different types of dyssynergia in adults[29], important concerns about the validity of this type of manometry in diagnosing DD remain. High-resolution anorectal manometry performed during straining showed high prevalence of a negative rectoanal pressure differential as a result of inadequate relaxation and/or inadequate intrarectal pressure, not only in patients with defecatory disorders but also in healthy controls[28,30,31]. A possible explanation for false positive results is that old variables have been used with new technologies. Cut-off pressure values derived from conventional manometry may not be appropriate for application to high-resolution solid-state sensor results. To address this problem, some authors proposed new parameters, such as integrated relaxation pressure[32]; however, this new variable failed to improve diagnosis of DD in a study of healthy and constipated adults when 3DHRAM was used[33]. Others proposed a new classification of DD based on principal component analysis and consolidation of dyssynergic subtypes[34]. However, this system has also failed to perform better so far, either because of difficulties with implementation in clinical practice or because there is no change in frequency of abnormal defecation compared to the old system[7].

For all the aforementioned reasons, we decided to use the classic four types proposed by Rao et al[26], but redefined cut-offs for recorded variables. We performed ROC analysis for percentage of anal relaxation (as a necessary condition to diagnose DD) to derive a new cut-off allowing for better discrimination between patients and controls. The higher-than-previously-reported cut-off value found in our analysis is intriguing (31% *vs.* 20%) but may reflect the need to achieve greater relaxation to compensate for overall low intrarectal pressure observed in our sample.

When adult criteria were used, the most frequent type of DD in our sample was type II, i.e., most children presented inadequate propulsive force combined with paradoxical increase of pressure in the anal canal. This contrasts with adult results, where type I was the most frequently reported[26,33,35]. Notably, we did not find a significant difference in intrarectal pressure values between patients and controls. A possible explanation is that a proportion of children may not be able to generate intrarectal pressures as high as those found in adults. This is supported by the fact that in our sample, the 25th percentile for intrarectal pressure did not reach the adult cut-off (40 mmHg). Lower intrarectal pressure may also reflect the lying position in which the maneuver is performed during manometry. The push maneuver in this position is not aided by gravity as it would be in the sitting position. Moreover, straining in the lying – and thus unfamiliar – position may be a confounding factor. Finally, another explanation may be that 3D catheters do not record intrarectal pressure *in situ*. The recording is made indirectly by an external sensor, and pressure imposed on the balloon is further transduced to the external sensor. This may potentially decrease the recorded value. After redefinition of the cut-off value, the most frequent type of DD was found to be type IV, reflecting both an inadequate propulsive force and relaxation.

Even though the initial difference in frequency of DD in both groups was insignificant, the usage of high-definition manometry was able to confirm the key role of striated muscles, i.e., the EAS and PRM, in generating paradoxical contraction. Greater differences in pressure in segments covering the anatomical locations of the EAS and PRM were observed between constipated patients and control subjects. The differences were even more discernible when the new cut-off value for percentage of anal relaxation was used to recalculate segmental pressure.

The main advantage of our study is that we used the most advanced technology to report the frequency of DD in children, allowing for confirmation of the role of striated muscles in the etiology of abnormal defecation patterns. We proved that using adult criteria may not reliably diagnose abnormal defecation dynamics in children and derived new pediatric criteria. However, there are several limitations to this study. First, we did not perform additional tests, such as balloon expulsion testing (BET) or defecography to confirm evacuatory disorders. As these additional tests have not been formally validated in children, we assumed that their results may be biased and could introduce confounding results in our sample. There is substantial diversity in the types of catheters, protocols, and cut-off values for positive BET in children. Additionally, there is no published consensus on the optimal catheter type, volume of balloon distension and whether it should be filled with air or water, or the impact of additional variables, such as age and sex on the results and protocol of BET in children. Due to the striking discrepancies between the results of different tests of evacuatory function in adults, further studies validating all modalities, particularly in children, are strongly indicated. Other limitations include catheter thickness and rigidity, as well as the location of the sensor recording intrarectal pressure, all of which may influence results. Moreover, the anxiety of the child may be another limitation that may lead to a proportion of healthy controls being adjudged as fulfilling the manometric criteria for DD. The study was performed in a tertiary center and may represent a selected group of patients. Finally, formal sample size calculation was not possible due to the lack of similar studies in children, and we decided to perform a large cohort study based on feasibility, which may also produce bias.

Conclusions

Constipated patients present lower resting and squeeze pressures, higher thresholds of sensation and greater rectal compliance as compared to healthy controls evaluated by 3D manometric probe. As constipated patients and control subjects presented with similar proportions of DD based on adult criteria, a new cut-off value for percentage of anal relaxation was established. Notably, the ROC curve is almost parallel to a straight line, indicating poor discriminatory power, which is similar to the results of anorectal manometry in adults suffering from constipation. This may be due to the various causes of constipation, as well as the limitations of the manometry itself. The poor discriminatory power of manometry resulted in recommendations to use BET as a first screening test of evacuatory dysfunction in adults. The results of our study also suggest the need for additional testing. Further studies are recommended to validate other modalities such as BET or defecography to verify the incorrect defecation model in children. In the absence of access to additional diagnostic tests, when 3D manometry and the standard four-type classification are used to diagnose DD, we suggest using the higher cut-off value for percentage of anal relaxation with caution.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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