



Three-dimensional High-resolution Anorectal Manometry in Children With Non-retentive Fecal Incontinence

Marcin Banasiuk,* Marcin Dziekiewicz, Magdalena Dobrowolska, Barbara Skowrońska, Łukasz Dembiński, and Aleksandra Banaszekiewicz

Department of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Poland

Background/Aims

Three-dimensional high-resolution anorectal manometry (3D-HRAM) is a precise tool to assess the function of the anorectum. Our aim is to evaluate children diagnosed with non-retentive fecal incontinence (NRFI) using 3D-HRAM.

Methods

In all children diagnosed with NRFI, manometric parameters and 3-dimensional reconstructions of the anal canal subdivided into 8 segments were recorded. All data were compared to raw data that were obtained from asymptomatic children, collected in our laboratory and published previously (C group).

Results

Forty children (31 male; median age, 8 years; range, 5-17) were prospectively included in the study. Comparison of the NRFI group and C group revealed lower values of mean resting pressure (74.4 mmHg vs 89.2 mmHg, $P < 0.001$) and maximum squeeze pressure (182 mmHg vs 208.5 mmHg, $P = 0.018$) in the NRFI group. In the NRFI group, the thresholds of sensation, urge and discomfort (40 cm³, 70 cm³, and 140 cm³, respectively) were significantly higher than those in the C group (20 cm³, 30 cm³, and 85 cm³, respectively; $P < 0.001$). In the NRFI group, 62.5% presented a mean resting pressure above the fifth percentile, and 82.5% of patients presented a maximum squeeze pressure above the fifth percentile. The comparisons between segments obtained from these patients and those obtained from the C group revealed several segments with significantly decreased pressure values in the NRFI group.

Conclusions

Our study demonstrated lower pressure parameters in children with NRFI. In patients with normal resting pressures, 3D-HRAM may reveal segments with decreased pressures, which may play a potential role in the pathomechanism of incontinence.

(*J Neurogastroenterol Motil* 2022;28:303-311)

Key Words

Child; Fecal incontinence; High-resolution manometry

Received: September 22, 2020 Revised: April 14, 2021 Accepted: May 7, 2021

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Correspondence: Marcin Banasiuk, MD, PhD

Department of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Zwirki i Wigury 63A, 02-091 Warsaw, Poland

Tel: +48-22-3179463-310, Fax: +48-22-3179463-310, E-mail: marcin.banasiuk@wum.edu.pl

Introduction

Fecal incontinence (FI) is one of the most distressing conditions in children. It is defined as the involuntary loss of feces through the anus in places inappropriate to the social context in children above the age of 4 years.¹ It may significantly decrease quality of life and lead to abnormal social functioning.^{2,3} The vast majority of patients with FI suffer from constipation, and the symptoms are due to an overflow mechanism.^{4,5} Patients with no signs of fecal retention are classified as non-retentive fecal incontinence (NRFI). Except for functional etiology, FI may be of organic origin. Among them, the most common are congenital or acquired abnormalities such as anorectal malformations, anorectal trauma or disturbances in the nervous system.⁶

To some extent, the actual mechanism of NRFI may not be recognized due to the lack of proper diagnostic methods. Three-dimensional high-resolution anorectal manometry (3D-HRAM) is a new modality for the diagnosis of anorectal function. It can be used for more scrupulous investigation of the anorectum as a result of greater resolution of the probe and its potential ability to record the pressure contribution of the different components of the anal canal.^{7,8} Moreover, it may play a role in detecting pressure defects,^{9,10} which may have an impact on continence function in patients with FI and normal mean pressure of the anal canal.

To date, only studies with conventional manometry in children with NRFI have been performed.¹¹ No studies using 3D-HRAM have been carried out, and the aim of our study is to verify whether this new manometric technique would allow for identification of mechanisms responsible for incontinence in these children that were not found in conventional manometry.

Materials and Methods

Study Subjects

Children diagnosed with NRFI (NRFI group) based on the Rome III criteria¹ were prospectively enrolled and underwent manometric evaluation. All patients underwent a thorough clinical evaluation, including physical and radiological testing, to exclude fecal retention.

The exclusion criteria were as follows: presence of rectal retention, history of surgery on the lower gastrointestinal tract prior to the study, functional constipation, and anorectal trauma.

All data were compared to raw manometric data that were

obtained from the lower gastrointestinal tract of children without symptoms and collected in our laboratory and published previously (control, C group).¹²

The study was approved by the Ethics Committee, Poland (KB7/2013). The procedures used in this study adhere to the tenets of the Declaration of Helsinki. All persons (or legal representative of children) gave their informed consent prior to their inclusion in the study.

Equipment

Manometry was performed by using 3D-HRAM (ManoScan 360/3D; Medtronic, Dublin, Ireland). The equipment consists of a probe connected to an amplifier and recorder system, which is further connected to a computer, and all recorded data are displayed on a computer monitor. The probe is a solid-state, rigid catheter 64 mm in length and 10.75 mm in diameter. On the surface, 256 microtransducers are arranged in 16 rows along the catheter, each consisting of 16 sensors. In this way, the 16 × 16 grid of sensors is displayed on the monitor, allowing evaluation of the anal pressure as a spatiotemporal plot. Each sensor is 4 mm long and 2 mm wide, and the software interpolates the pressure between them with 1 mm intervals. The frequency of the scan is 10 Hz, and the output resolution is 0.1 mmHg.

Inside the probe, there is a lumen that connects a balloon at one end of the probe with a 60-mL syringe attached by an elastic tube at the other. This allows for air administration decimal and measurement of the thresholds of sensation and recto-anal inhibitory reflex (RAIR). The balloon is 3.3 cm long and is composed of a non-latex thermoplastic elastomer.

The topography of the anal canal pressure is displayed on the computer using specialized software (ManoScan AR version 2.1, Covidien/Medtronic) in live mode, allowing proper positioning of the probe throughout the procedure.

There is a need for calibration before each procedure in the calibration chamber. In vivo calibration in water once a week was performed to cover the pressure deviations in reaction to body temperature.

Procedure

Before the procedure the doctor and nurse met the patients and parents outside the motility lab and explained the whole test. The tests were not arranged at fixed time-slot allowing for additional support if necessary. No routine bowel preparation was used unless the presence of stool in the rectum during digital rectal investigation was found. If this was the case, a 100-mL saline enema was ad-

ministered. Patients were investigated in a supine position allowing visual contact and better interaction. Before each examination, the probe was calibrated over a range of 0-300 mmHg, lubricated with Vaseline and inserted into the rectum. The probe was held by the investigator throughout the procedure so that the proximal and distal margins of the anal canal were maintained in the proper position. After the accommodation period of at least 2 minutes, conventional manometric parameters were recorded. These parameters were recorded with a 20-second pause between each, preferably following a routine order: resting pressure, squeeze pressure (performed twice), presence of an RAIR, and thresholds of sensation. The RAIR was evaluated by rapid inflation and deflation of the balloon with incremental volumes ranging from 10-60 mL. A RAIR was defined by a 25% decrease in the mean resting pressure. Thresholds of sensation were obtained by continuous administration of air into the balloon (performed twice).

Data Analysis

All recorded data were evaluated with dedicated software (ManoView AR version 2.1; Covidien/Medtronic) after each

procedure. The software allows for the analysis of conventional manometric parameters. Data from 256 sensors were used to analyze spatiotemporal plots of the anal canal. The proximal and distal margins of the high-pressure zone (HPZ) were identified using an algorithm implemented in the original software. This establishment was performed separately for resting and squeeze states. After that, the HPZ was divided into proximal and distal parts and then into anterior, posterior, and left and right segments, as described previously.¹² This allowed for comparisons between patients of different ages and with respect to anal canal length.

Statistical Methods

The distribution of quantitative variables was tested by the Shapiro-Wilk test of normality. Based on the results of the latter test, Mann-Whitney *U* statistics were used to test differences between 2 groups. The χ^2 test was used to compare proportions. Statistical significance was defined as a *P*-value of < 0.05. Statistica 13 (Statsoft, Oklahoma, USA) was used for all analyses.

Results

Forty children (31 male; median age, 8 years; range, 5-17) were included in the study. The clinical characteristics of the subjects are summarized in Table 1.

The analysis of conventional manometric parameters revealed that children suffering from NRFI presented lower values of mean resting pressure and maximum squeeze pressure than children from the control (C) group. There were no differences between the NRFI group and the C group with regard to anal canal length, duration of sustained squeeze, minimal rectal compliance, and

Table 1. Clinical Characteristics of the Subjects

| Variable | Group | | <i>P</i> -value |
|-------------|---------------------|---------------------|-----------------|
| | NRFI (n = 40) | Control (n = 61) | |
| Age (mo) | 102.5 (86.5-145.5) | 112.0 (73.0-155.0) | 0.893 |
| Weight (kg) | 29.5 (22.9-50.0) | 30.6 (22.0-47.2) | 0.706 |
| Height (cm) | 134.0 (124.3-157.5) | 134.5 (120.0-159.0) | 0.926 |
| Sex (male) | 31 (77.5) | 34 (55.7) | 0.026 |

NRFI, non-retentive fecal incontinence.

Data are presented as median (interquartile range) or n (%).

Table 2. Conventional Manometric Parameters

| Parameter | Group | | <i>P</i> -value |
|---|-------------------|---------------------|-----------------|
| | NRFI | Control | |
| Mean resting pressure (mmHg) | 74.4 (56.5-90.7) | 89.2 (81.1-103.7) | < 0.001 |
| Maximum squeeze pressure (mmHg) | 182 (145.3-218.3) | 208.5 (169.4-249.8) | 0.018 |
| Duration of sustained squeeze (sec) | 11.5 (6.6-19.9) | 15.4 (15.4-9-20.0) | 0.189 |
| Anal canal length (cm) | 2.8 (2.4-3.2) | 2.6 (2.1-3.1) | 0.451 |
| Minimal rectal compliance (cm ³ /mmHg) | 0.2 (0.1-0.2) | 0.2 (0.1-0.2) | 0.559 |
| Maximal rectal compliance (cm ³ /mmHg) | 0.8 (0.5-1.1) | 0.6 (0.5-0.9) | 0.362 |
| RAIR threshold (cm ³) | 10 (10-20) | 10 (10-15) | 0.733 |
| First sensation (cm ³) | 40 (20-120) | 20 (10-20) | < 0.001 |
| Urge (cm ³) | 70 (40-130) | 30 (20-55) | < 0.001 |
| Discomfort (cm ³) | 140 (110-170) | 85 (45-130) | < 0.001 |

NRFI, non-retentive fecal incontinence; RAIR, recto-anal inhibitory reflex.

Data are presented as median (interquartile range).

maximum rectal compliance. In both groups, the threshold of the RAIR was equal. In the NRFI group, the thresholds of first sensation, urge and discomfort were significantly higher than those in the C group. All results are summarized in Table 2.

Comparison of segmental pressures between the groups revealed significant differences. In the NRFI group, the resting pressures of all segments were significantly decreased. Lower values of maximum pressures for all segments were observed except for the proximal right, distal right and distal posterior segments (Fig. 1).

Twenty-five out of 40 (62.5%) incontinent patients presented normal mean resting pressure values (above the fifth percentile),

and 33 out of 38 (82.5%) patients presented maximum squeeze pressures within the normal range. The comparisons of the segmental pressures of these patients with those of the C group revealed several segments with significantly decreased values (Fig. 2).

All patients with normal mean resting pressure presented decreased pressures of at least 1 segment (below the fifth percentile). Majority of patients with normal maximum squeeze pressure presented normal values for segmental pressures. Only 27.2% of patients presented decreased value for at least 1 segment. All results are summarized in Table 3.

Twenty percent of patients with normal mean resting pressure

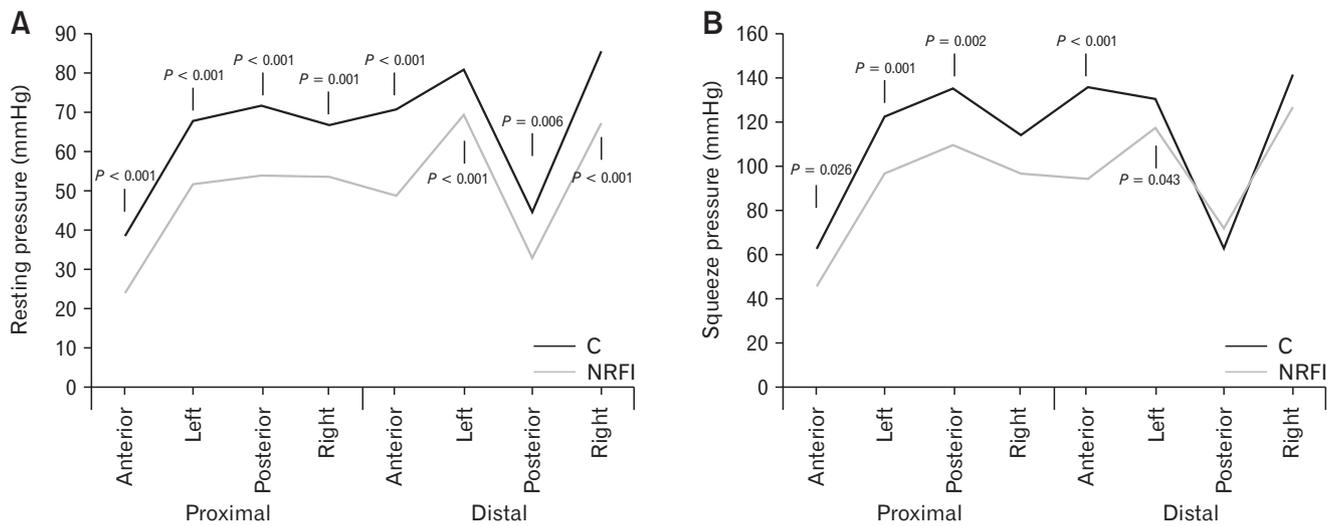


Figure 1. Comparison of segmental pressures between the non-retentive fecal incontinence (NRFI) and control (C) groups.

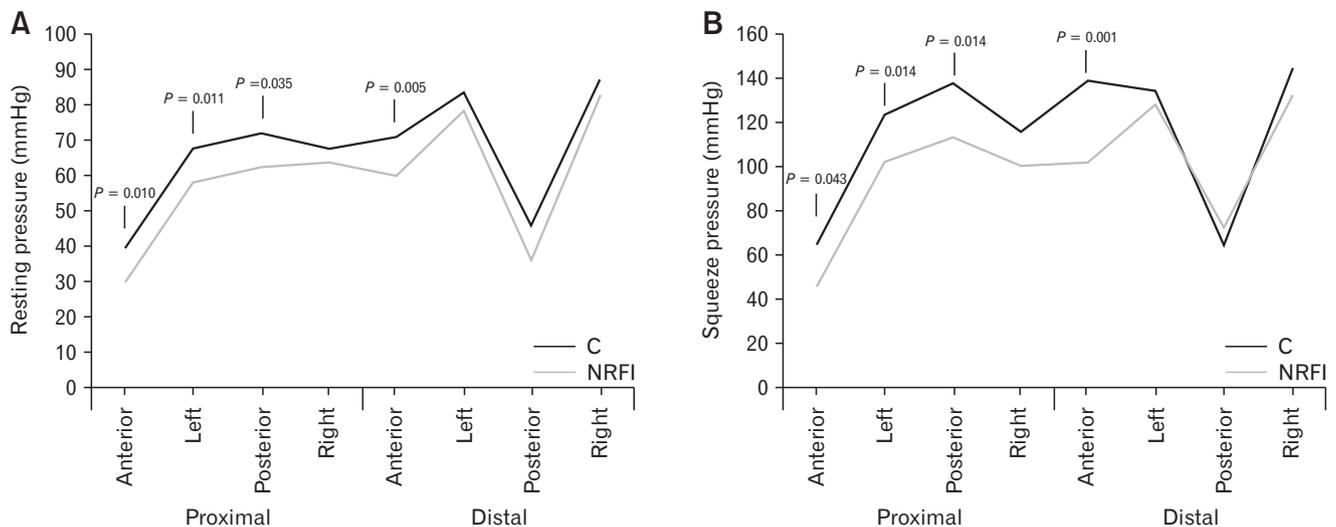


Figure 2. Comparisons of the segmental pressures of patients with resting pressures above the fifth percentile (non-retentive fecal incontinence [NRFI]) and those of the control (C) group.

Table 3. Number of Segments With Pressures Below Fifth Percentile in Patients With Normal Resting Pressure or Normal Maximum Squeeze Pressure

| Number of segments with decreased pressure | Patients with pressure value within the normal range | |
|--|--|--------------------------|
| | Mean resting pressure | Maximum squeeze pressure |
| 0 | 0 (0.0) | 24 (72.7) |
| 1 | 15 (60.0) | 7 (21.2) |
| 2 | 6 (24.0) | 1 (3.0) |
| 3 | 2 (8.0) | 0 (0.0) |
| 4 | 1 (4.0) | 0 (0.0) |
| 5 | 0 (0.0) | 0 (0.0) |
| 6 | 1 (4.0) | 1 (3.0) |

Data are presented as n (%).

presented decreased pressures of proximal posterior or distal anterior segments. Patients with normal maximum squeeze pressure also presented decreased squeeze pressures of these segments (Table 4).

Discussion

In summary, we found that in patients with NRFI, the mean resting and maximum squeeze pressures of the anal canal were significantly decreased. Moreover, all thresholds of sensation (first, urge, and discomfort) were elevated. We found that in incontinent patients presenting with a mean resting pressure within the normal range, several segments of the anal canal generated lower values of pressure. This may serve as a potential mechanism of incontinence not revealed by conventional manometry.

In the literature, no studies have utilized 3D-HRAM. Using conventional manometry, a few studies evaluated children with FI. Most of them investigated patients who suffered from overflow (retentive) incontinence, as it reflects the most frequent etiology of this disorder, making direct comparisons with our results very difficult.

In most studies in children with incontinence, the mean resting pressures of the anal canal were comparable to those obtained from healthy controls. In the largest series, 210 by Benninga,⁵ the maximum anal resting tone was found to be significantly higher in the incontinent group than in the controls and constipated children, which is a rather unexpected finding, as loss of feces should be more likely to be observed when decreased pressure of the anal canal is present.⁵ These observations were confirmed by several smaller studies.¹¹ This phenomenon may be partly explained by anxiety regarding the potential loss of feces and may lead to outlet obstruction

Table 4. Number of Patients With Mean Resting or Maximum Squeeze Pressures Within the Normal Range and Decreased Pressure of Segment of the Anal Canal

| Segment with decreased pressure | Number of patients (%) |
|---------------------------------|------------------------|
| Resting | |
| Proximal half of the anal canal | |
| Anterior | 0 (0.0) |
| Left | 2 (8.0) |
| Posterior | 5 (20.0) |
| Right | 3 (12.0) |
| Distal half of the anal canal | |
| Anterior | 5 (20.0) |
| Left | 2 (8.0) |
| Posterior | 0 (0.0) |
| Right | 1 (4.0) |
| Squeeze | |
| Proximal half of the anal canal | |
| Anterior | 1 (3.0) |
| Left | 1 (3.0) |
| Posterior | 4 (12.1) |
| Right | 0 (0.0) |
| Distal half of the anal canal | |
| Anterior | 5 (15.2) |
| Left | 1 (3.0) |
| Posterior | 2 (6.1) |
| Right | 1 (3.0) |

and overflow soiling, as this mechanism was suggested by Arhan et al.¹³ In one small study, a subgroup of non-retentive incontinent children presented decreased resting and squeeze pressures, but the differences did not reach statistical significance.¹⁴

In our group, we found resting pressures to be decreased, which is in contrast to most of the pediatric series mentioned above but in line with adult studies. In most of them, decreased pressure parameters were found,¹⁵⁻⁴³ irrespective of the etiology of symptoms.

We found higher thresholds of sensation in our sample than other studies. In the literature, the results from sensory tests are inconsistent. Some authors reported higher (decreased sensitivity)¹¹ while others reported lower (increased sensitivity)^{5,44} thresholds of sensation. This discrepancy may be the result of different subtypes of incontinence. A proportion of patients suffer from urge incontinence as a result of increased sensitivity of the anorectum.⁴⁵ Others may present symptoms due to passive leakage of feces and higher thresholds of sensation observed during tests of sensitivity.⁴⁶ Another possible cause of this discrepancy in the literature may also be the result of differences in the physical properties of manometric balloons. The materials of most of them are compliant with the environment, and thus, the results may not be reliable.⁴⁷

In our sample, we found lower resting pressures and higher thresholds of sensation, which supports the hypothesis of interaction between these 2 variables. It was suggested that in patients with lower resting pressures, increased sensitivity may be the natural adaptive mechanism preventing fecal leakage and improving symptoms. This may explain the lower thresholds of sensation in some patients. In other patients, this mechanism may be damaged, and higher thresholds may coexist with low anal pressure, aggravating symptoms, as found in our sample.⁴⁸

The phenomenon described above may serve as another explanation of the decreased mean pressures found in our sample. Our group of patients was evaluated by a tertiary referral center after not responding to standard first-line therapy, which may reflect more severe cases of incontinence with potentially broken adaptive mechanisms.

A possible mechanism of incontinence without retention is that the higher threshold of sensation may exceed the threshold of the RAIR. Consequently, involuntary loss of feces may occur.^{49,50} In our NRFI group, the threshold of first sensation was 4-fold higher than the RAIR threshold.

The length of the anal canal is suggested to be one of the possible co-factors determining continence. We found no difference in the length of the HPZ of patients and asymptomatic children, in contrast to some authors who suggested that a longer anal canal may increase mechanical resistance to feces, resulting in good continence.⁵¹ In contrast, others hypothesized that a long HPZ may lead to the entrapment of a small amount of feces, resulting in involuntary soiling.³¹

It has been suggested that disruption of the sphincters or disturbed pressure distribution in the anal canal may compromise continence. This may be observed more often after surgery for anorectal disorders than under other circumstances.⁵²⁻⁵⁸ Three-dimensional HRAM is expected to have the ability to detect pressure defects of the anal canal pressure profile in a more detailed manner than conventional manometry.⁵⁹ It may have a potential role in detecting small but symptomatic sphincter defects that do not influence the pressure of the whole anal canal. Studies in adults comparing this technique to endoultrasonography, which is believed to be the gold standard in this field, revealed only moderate concordance.^{9,60,61} Notably, these results may be due to an unvalidated definition of the pressure defects obtained by manometry. On the other hand, not all scars observed in endoultrasonography may contribute to producing symptoms, reflecting only anatomical but not functional defects of the anal canal.

There is no consensus on how to describe the three-dimensional

(3D) spatiotemporal plot of the anal canal. The simple visual analysis proposed by Xu et al⁶² may reveal possible disturbances in pressure distribution and confirm the diagnosis of sphincteric defects, but this may be biased by subjective analysis and technical errors (eg, pressure drift of sensors according to temperature, duration of the study, and proper holding of the catheter throughout the whole study). In contrast, Zifan et al⁶³ proposed a rather complicated predictive model for evaluating 3D data obtained from incontinent patients, but the complexity limits its usefulness in routine clinical practice. To simplify the analysis of anal canal pressures, we utilized the protocol previously described.¹² We aggregate the pressures from sensors covering the HPZ and possible localization of particular muscles.

We found that in incontinent patients, all segments in the resting state and almost all segments during the squeeze maneuver were significantly decreased. This reflects the lower mean resting and maximum squeeze pressures of the anal canal in the whole incontinent group. Interestingly, in the proportion of patients with resting pressures within the normal range, several segments were still significantly decreased. Two of these segments (the proximal left and proximal posterior) reflect the part of the anal canal where the puborectal muscle operates, suggesting its role in continence mechanisms. The same observations were found in patients with normal squeeze pressures. All these findings may suggest a possible mechanism of incontinence not revealed by standard manometric variables and identify patients in whom tests of anal structure are indicated (ultrasonography) or who may potentially benefit from biofeedback therapy despite normal results from conventional manometry.

The major advantage of our study is that we investigated children with NRFI using precise technology that revealed pressure defects in the anal canal that were not observed using standard high-resolution manometry. This has the potential role of facilitating adequate individualized diagnosis (tests of anal structure) and treatment.

Our study has several limitations. The study sample was relatively small, which may bias some of the manometric parameter results. Despite this, we were able to find differences in both conventional and 3D (segmental) parameters, suggesting possible functional disturbances in anal canal architecture, and evolving symptoms. Another limitation is that we did not perform other diagnostic modalities, such as colonic manometry, that at least in part may have explained other possible mechanisms of FI. The thresholds of sensation established with manometric balloons should be validated with a barostat, which is believed to be the gold standard.

The last limitation is the size and properties of the probe. A greater diameter catheter in relation to a smaller size anal canal may produce false positive pressure readings in younger patients (obscuring some smaller pressure defects).

In conclusion, our study demonstrated lower pressure parameters and higher thresholds of sensation in children suffering from NRFI. We proved that 3D-HRAM may be a useful tool for assessing the function of the anorectum in these children, revealing more discrete mechanisms compromising the anal canal.

Financial support: Covidien/Medtronic (Ireland) provided manometric equipment (catheter and disposable sheaths).

Conflicts of interest: Marcin Banasiuk: equipment support for study; Aleksandra Banaszkiwicz, Marcin Dziekiewicz, Łukasz Dembiński, Magdalena Dobrowolska, and Barbara Skowrońska: nothing to disclose.

Author contributions: Marcin Banasiuk: study concept and design, acquisition of data, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, statistical analysis, obtained equipment support, and drafting of the manuscript; and Aleksandra Banaszkiwicz, Marcin Dziekiewicz, Łukasz Dembiński, Magdalena Dobrowolska, and Barbara Skowrońska: study concept and design, acquisition of data, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content.

References

- Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology* 2006;130:1527-1537.
- Bongers ME, Benninga MA, Maurice-Stam H, Grootenhuis MA. Health-related quality of life in young adults with symptoms of constipation continuing from childhood into adulthood. *Health Qual Life Outcomes* 2009;7:20.
- Von Gontard A, Baeyens D, Van Hoecke E, Warzak WJ, Bachmann C. Psychological and psychiatric issues in urinary and fecal incontinence. *J Urol* 2011;185:1432-1436.
- Rajindrajith S, Devanarayana NM, Benninga MA. Review article: faecal incontinence in children: epidemiology, pathophysiology, clinical evaluation and management. *Aliment Pharmacol Ther* 2013;37:37-48.
- Benninga MA, Büller HA, Heymans HS, Tytgat GN, Taminiu JA. Is encopresis always the result of constipation? *Arch Dis Child* 1994;71:186-193.
- Ambartsumyan L, Nurko S. Review of organic causes of fecal incontinence in children: evaluation and treatment. *Expert Rev Gastroenterol Hepatol* 2013;7:657-667.
- Bharucha AE, Rao SS. An update on anorectal disorders for gastroenterologists. *Gastroenterology* 2014;146:37-45, e2.
- Raizada V, Bhargava V, Karsten A, Mittal RK. Functional morphology of anal sphincter complex unveiled by high definition anal manometry and three dimensional ultrasound imaging. *Neurogastroenterol Motil* 2011;23:1013-1019, e460.
- Vitton V, Ben Hadj Amor W, Baumstarck K, Behr M, Bouvier M, Grimaud JC. Comparison of three-dimensional high-resolution manometry and endoanal ultrasound in the diagnosis of anal sphincter defects. *Colorectal Dis* 2013;15:e607-e611.
- Lee TH, Bharucha AE. How to perform and interpret a high-resolution anorectal manometry test. *J Neurogastroenterol Motil* 2016;22:46-59.
- Molnar D, Taitz LS, Urwin OM, Wales JK. Anorectal manometry results in defecation disorders. *Arch Dis Child* 1983;58:257-261.
- Banasiuk M, Banaszkiwicz A, Dziekiewicz M, Załęski A, Albrecht P. Values from three-dimensional high-resolution anorectal manometry analysis of children without lower gastrointestinal symptoms. *Clin Gastroenterol Hepatol* 2016;14:993-1000, e3.
- Arhan P, Devroede G, Jehannin B, et al. Idiopathic disorders of fecal continence in children. *Pediatrics* 1983;71:774-779.
- Benninga MA, Büller HA, Taminiu JA. Biofeedback training in chronic constipation. *Arch Dis Child* 1993;68:126-129.
- Felt-Bersma RJ, Klinkenberg-Knol EC, Meuwissen SG. Anorectal function investigations in incontinent and continent patients. Differences and discriminatory value. *Dis Colon Rectum* 1990;33:479-485; discussion 485-486.
- Thekkinkattil DK, Lim M, Stojkovic SG, Finan PJ, Sagar PM, Burke D. A classification system for faecal incontinence based on anorectal investigations. *Br J Surg* 2008;95:222-228.
- Allen ML, Orr WC, Robinson MG. Anorectal functioning in fecal incontinence. *Dig Dis Sci* 1988;33:36-40.
- Bielfeldt K, Enck P, Erckenbrecht JF. Sensory and motor function in the maintenance of anal continence. *Dis Colon Rectum* 1990;33:674-678.
- Caruana BJ, Wald A, Hinds JP, Eidelman BH. Anorectal sensory and motor function in neurogenic fecal incontinence. *Gastroenterology* 1991;100:465-470.
- Ferguson GH, Redford J, Barrett JA, Kiff ES. The appreciation of rectal distention in fecal incontinence. *Dis Colon Rectum* 1989;32:964-967.
- Fernández-Fraga X, Azpiroz F, Malagelada JR. Significance of pelvic floor muscles in anal incontinence. *Gastroenterology* 2002;123:1441-1450.
- Freys SM, Fuchs KH, Bussen D, Thiede A. [Anorectal pull-through and vector volume manometry.] *Zentralbl Chir* 1996;121:652-658. [German]
- Hallan RI, Marzouk DE, Waldron DJ, Womack NR, Williams NS. Comparison of digital and manometric assessment of anal sphincter function. *Br J Surg* 1989;76:973-975.
- Hiltunen K. Anal manometric findings in patients with anal incontinence. *Dis Colon Rectum* 1985;28:925-928.
- Hoffmann BA, Timmcke AE, Gathright JB, Hicks TC, Opelka FG, Beck DE. Fecal seepage and soiling: a problem of rectal sensation. *Dis*

- Colon Rectum 1995;38:746-748.
26. Holmberg A, Graf W, Osterberg A, Pählman L. Anorectal manometry in the diagnosis of fecal incontinence. *Dis Colon Rectum* 1995;38:502-508.
 27. Kafka NJ, Coller JA, Barrett RC, et al. Pudendal neuropathy is the only parameter differentiating leakage from solid stool incontinence. *Dis Colon Rectum* 1997;40:1220-1227.
 28. Kuijpers HC, Scheuer M. Disorders of impaired fecal control. A clinical and manometric study. *Dis Colon Rectum* 1990;33:207-211.
 29. Lewicky-Gaupp C, Hamilton Q, Ashton-Miller J, Huebner M, DeLancey JO, Fenner DE. Anal sphincter structure and function relationships in aging and fecal incontinence. *Am J Obstet Gynecol* 2009;5:559, e1-e5.
 30. Monk DN, Mills P, Jeacock J, Deakin M, Cowie A, Kiff ES. Combining the strength-durations curve of the external anal sphincter with manometry for the assessment of faecal incontinence. *Br J Surg* 1998;85:1389-1393.
 31. Osterberg A, Graf W, Pählman L. The longitudinal high-pressure zone profile in patients with fecal incontinence. *Am J Gastroenterol* 1999;94:2966-2971.
 32. Parellada CM, Miller AS, Williamson ME, Johnston D. Paradoxical high anal resting pressures in men with idiopathic fecal seepage. *Dis Colon Rectum* 1998;41:593-597.
 33. Penninckx F, Lestär B, Kereemans R. Manometric evaluation of incontinent patients. *Acta Gastroenterol Belg* 1995;58:51-59.
 34. Rao SS, Ozturk R, Stessman M. Investigation of the pathophysiology of fecal seepage. *Am J Gastroenterol* 2004;99:2204-2209.
 35. Rasmussen O, Christensen B, Sørensen M, Tetzschner T, Christiansen J. Rectal compliance in the assessment of patients with fecal incontinence. *Dis Colon Rectum* 1990;33:650-653.
 36. Rasmussen OO, Sørensen M, Tetzschner T, Christiansen J. Anorectal pressure gradient in patients with anal incontinence. *Dis Colon Rectum* 1992;35:8-11.
 37. Rasmussen OO, Sørensen M, Tetzschner T, Christiansen J. Dynamic anal manometry: physiological variations and pathophysiological findings in fecal incontinence. *Gastroenterology* 1992;103:103-113.
 38. Rasmussen OO, Rønholt C, Alstrup N, Christiansen J. Anorectal pressure gradient and rectal compliance in fecal incontinence. *Int J Colorectal Dis* 1998;13:157-159.
 39. Raza N, Bielfeldt K. Discriminative value of anorectal manometry in clinical practice. *Dig Dis Sci* 2009;11:2503-2511.
 40. Read NW, Harford WV, Schmulen AC, Read MG, Santa Ana C, Fordtran JS. A clinical study of patients with fecal incontinence and diarrhea. *Gastroenterology* 1979;76:747-756.
 41. Sentovich SM, Rivela LJ, Blatchford GJ, Christensen MA, Thorson AG. Patterns of male fecal incontinence. *Dis Colon Rectum* 1995;38:281-285.
 42. Siproudhis L, Bellissant E, Juguet F, Allain H, Bretagne JF, Gosselin M. Perception of and adaptation to rectal isobaric distension in patients with faecal incontinence. *Gut* 1999;44:687-692.
 43. Stojkovic SG, Balfour L, Burke D, Finan PJ, Sagar PM. Role of resting pressure gradient in the investigation of idiopathic fecal incontinence. *Dis Colon Rectum* 2002;45:668-673.
 44. Mion F, Garros A, Brochard C, et al. 3D high-definition anorectal manometry: values obtained in asymptomatic volunteers, fecal incontinence and chronic constipation. Results of a prospective multicenter study (NOMAD). *Neurogastroenterol Motil* 2017;29:e13049.
 45. Bharucha AE, Fletcher JG, Harper CM, et al. Relationship between symptoms and disordered continence mechanisms in women with idiopathic faecal incontinence. *Gut* 2005;54:546-555.
 46. Muñoz-Yáguie T, Solís-Muñoz P, Ciriza de los Ríos C, Muñoz-Garrido F, Vara J, Solís-Herruzo JA. Fecal incontinence in men: causes and clinical and manometric features. *World J Gastroenterol* 2014;20:7933-7940.
 47. Sauter M, Heinrich H, Fox M, et al. Toward more accurate measurements of anorectal motor and sensory function in routine clinical practice: validation of high-resolution anorectal manometry and rapid barostat bag measurements of rectal function. *Neurogastroenterol Motil* 2014;26:685-695.
 48. Frühauf H, Fox MR. Anal manometry in the investigation of fecal incontinence: totum pro parte, not pars pro toto. *Digestion* 2012;86:75-77.
 49. Hoffmann BA, Timmcke AE, Gathright JB Jr, Hicks TC, Opelka FG, Beck DE. Fecal seepage and soiling: a problem of rectal sensation. *Dis Colon Rectum* 1995;38:746-748.
 50. Lubowski DZ, Nicholls RJ. Faecal incontinence associated with reduced pelvic sensation. *Br J Surg* 1988;75:1086-1088.
 51. Martins EC, Peterlini FL, Fagundes DJ, Martins JL. Clinical, manometric and profilometric evaluation after surgery for Hirschsprung's disease: comparison between the modified Duhamel and the transanal rectosigmoidectomy techniques. *Acta Cir Bras* 2009;24:416-422.
 52. Emblem R, Diseth T, Mørkrid L, Stien R, Bjordal R. Anal endosonography and physiology in adolescents with corrected low anorectal anomalies. *J Pediatr Surg* 1994;29:447-451.
 53. Emblem R, Diseth T, Mørkrid L. Anorectal anomalies: anorectal manometric function and anal endosonography in relation to functional outcome. *Pediatr Surg Int* 1997;12:516-519.
 54. Fukata R, Iwai N, Yanagihara J, Iwata G, Kubota Y. A comparison of anal endosonography with electromyography and manometry in high and intermediate anorectal anomalies. *J Pediatr Surg* 1997;32:839-842.
 55. Fukuya T, Honda H, Kubota M, et al. Postoperative MRI evaluation of anorectal malformations with clinical correlation. *Pediatr Radiol* 1993;23:583-586.
 56. Yuan Z, Bai Y, Zhang Z, Ji S, Li Z, Wang W. Neural electrophysiological studies on the external anal sphincter in children with anorectal malformation. *J Pediatr Surg* 2000;35:1052-1057.
 57. Hedlund H, Peña A, Rodriguez G, Maza J. Long-term anorectal function in imperforate anus treated by a posterior sagittal anorectoplasty: manometric investigation. *J Pediatr Surg* 1992;27:906909.
 58. Caldaro T, Romeo E, De Angelis P, et al. Three-dimensional endoanal ultrasound and anorectal manometry in children with anorectal malformations: new discoveries. *J Pediatr Surg* 2012;47:956-963.
 59. Ambartsumyan L, Rodriguez L, Morera C, Nurko S. Longitudinal and radial characteristics of intra-anal pressures in children using 3D high-definition anorectal manometry: new observations. *Am J Gastroenterol* 2013;108:1918-1928.

60. Rezaie A, Iriana S, Pimentel M, Murell Z, Fleshner P, Zagherian K. Can three-dimensional high-resolution anorectal manometry detect anal sphincter defects in patients with faecal incontinence? *Colorectal Dis* 2017;19:468-475.
61. Wickramasinghe DP, Perera CS, Senanayake H, Samarasekera DN. Correlation of three dimensional anorectal manometry and three dimensional endoanal ultrasound findings in primi gravida: a cross sectional study. *BMC Res Notes* 2015;8:387.
62. Xu C, Zhao R, Conklin JL, et al. Three-dimensional high-resolution anorectal manometry in the diagnosis of paradoxical puborectalis syndrome compared with healthy adults: a retrospective study in 79 cases. *Eur J Gastroenterol Hepatol* 2014;26:621-629.
63. Zifan A, Ledgerwood-Lee M, Mittal RK. A predictive model to identify patients with fecal incontinence based on high-definition anorectal manometry. *Clin Gastroenterol Hepatol* 2016;14:1788-1796, e2.