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Three-dimensional high-resolution anorectal manometry can predict response to biofeedback therapy in defecation disorders

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Abstract

Purpose Biofeedback therapy (BT) is a simple and effective technique for managing outlet constipation and fecal incontinence. Several clinical factors are known to predict BT response, but a 50% failure rate persists. Better selection of BT responsive patients is required. We aimed to determine whether the defecation disorder type per high-resolution manometry (HRM) was predictive of BT response.

Methods We analyzed clinical, manometric, and ultrasound endoscopic data from patients who underwent BT in our department between January 2015 and January 2016. Patients were classified into four groups per the following defecation disorder classification criteria: rectal pressure > 40 mmHg and anal paradoxical contraction (type I); rectal pressure < 40 mmHg and anal paradoxical contraction (type II); rectal pressure > 40 mmHg and incomplete anal relaxation (type III); and rectal pressure < 40 mmHg and incomplete anal relaxation (type IV). An experienced single operator conducted ten weekly 20-min sessions. Efficacy was evaluated with the visual analog scale.

Results Of 92 patients, 47 (50.5%) responded to BT. Type IV and type II defecation disorders were predictive of success ($p = 0.03$) (OR = 5.03 [1.02; 24.92]) and failure ($p = 0.05$) (OR = 0.41 [0.17; 0.99]), respectively. The KESS score severity before BT ($p = 0.03$) (OR = 0.9 [0.81; 0.99]) was also predictive of failure.

Conclusion The manometry types identified according to the defecation disorder classification criteria were predictive of BT response. Our data confirm the role of three-dimensional HRM in the therapeutic management of anorectal functional disorders.

Keywords Anorectal manometry · Biofeedback therapy · Outlet constipation · Anal incontinence

Introduction

Anorectal disorders comprise two main conditions: outlet constipation (OC) and fecal incontinence (FI). Their respective prevalences are 7% and 7–15% in the general population.

Due to the high prevalence and impact of these conditions on quality of life, anorectal disorders are major public health issues [1, 2].

Anorectal manometry is currently the "gold standard" for the investigation of anorectal functional disorders. Anorectal high-resolution manometry (HRM) and three-dimensional high-definition anorectal manometry (3D-HDM) have recently been developed [3]. Due to numerous sensors and the use of a rigid probe, 3D-HDM allows a topographic analysis of pressure. Moreover, this technique has recently demonstrated that it enables the detection of pelvic floor dysfunction, such as perineal descent and internal rectal prolapse, and of sphincter defects [4–6]. In addition, HRM may improve the description of the mechanisms of defecation disorders. Indeed, although the four-type classification of defecation disorders has been first described by Rao et al with conventional manometry, its application to HRM appears to be more applicable in practice [7, 8]. The main goal of this classification scheme is to improve therapeutic management. Indeed, biofeedback therapy

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(BT) is a backbone therapy for the treatment of OC and FI and its long-term success rate of BT is approximately 50% for both indications [9]. In OC, several predictive factors of success have been described and include hard stool consistency, patient motivation, prolonged balloon expulsion time, high rectal pressure during strain, pelvic floor dysfunction, over five sessions of BT, older age, presence of dyssynergia plus absence of abdominal pain, and a low defecation index during strain [10–14]. In FI, predictive factors of BT response include being over 55 years of age, the absence of digital maneuvers, severe anal incontinence, and more than six sessions of BT [15, 16]. Conversely, prolonged use of laxatives and an increased anorectal angle are predictors of failure in patients with constipation, whereas no history of constipation, moderate incontinence, and the male sex are negative predictors in patients with incontinence [14, 16]. However, the lack of rehabilitative efficacy remains unexplained. An accurate HRM-based identification of distinct patient subgroups with anorectal functional disorders would optimize the use of BT.

The main objective of our study was to determine whether the type of defecation disorder per HRM was predictive of the response to BT.

Methods

Study population

In this monocentric retrospective study, all patients with OC or FI who had 3D-HDM and BT in our center were eligible. All examinations were performed at the Physiological Unit of the Gastroenterological Department, North Hospital, Assistance Publique-Hôpitaux de Marseille (AP-HM), France.

Inclusion criteria were as follows: age > 18 years, presence of OC and/or FI, completion of 3D-HDM prior to BT, and assessments of symptom severity with the KESS (severity scoring system for constipation) score for OC, and the Jorge and Wexner score for FI [17, 18].

Exclusion criteria were as follows: age < 18 years, unavailable severity scores, a history of proctological surgery, and failure to carry out the ten sessions. The collected clinical parameters included age, sex, height, weight, body mass index (BMI), investigation indications, medical history, surgical history, obstetrical history, proctological history, and symptom duration.

Biofeedback therapy

An experienced operator performed all BT sessions on a weekly basis. The average duration of a session was 20 min. In accordance with the recommendations and practices of our center, which is a tertiary center for the management of functional disorders, the patients underwent ten sessions.

In patients with OC, the therapeutic objectives were as follows:

– Learning abdominoperineal coordination with the correction of voluntary external anal sphincter (EAS) control, where the patient had to be able to contract the EAS independently of the abdominal muscles;
– Improving rectal sensitivity by gradually learning how to recognize decreasing volumes of rectal distension; and
– Improving the effectiveness of strain.

In patients with FI, the therapeutic objectives were to improve the following:

– Squeezing of the EAS,
– Sensory perception, and
– Coordination between rectal squeezing and EAS squeezing [19].

The symptomatic efficacy of BT was self-assessed using a visual analog scale (VAS). The VAS ranged from 0 ("no efficacy") to 5 ("symptom disappearance"). The VAS data were collected within 1 month after the last of the ten BT sessions. Patients were defined as "responders" if the VAS was greater than 3 and as "non-responders" if the VAS was less than or equal to 3 [12, 20].

Three-dimensional high-resolution anorectal manometry

The same experienced operator performed all examinations. Patients were positioned in a left lateral supine position. The 3D-HDM probe (Mano-Scan 3D; Sierra Scientific Instruments, Los Angeles, CA, USA) comprised a rigid probe with a diameter of 10 mm, with 16×16 pressure sensors distributed over a height of 64 mm and spaced 2 mm apart in the axial plane and on the circumference, which allowed simultaneous pressure recordings over the entire anal canal. For each examination, the probe was covered with a disposable sheath containing an expandable balloon. The probe was calibrated between 0 and 300 mmHg and inserted into the anal canal and rectum. No rectal preparation was performed. After pressure stabilization for 3 min, the pressure of the anal canal was recorded. The patient was asked to perform three voluntary contractions. The maximum squeezing pressure corresponded to the highest-pressure value in the anal canal, and the amplitude of the squeeze corresponded to the maximum pressure of the squeeze from which the resting pressure was subtracted. Then, the patient was asked to make three bear-down attempts to simulate defecation. The straining rectal pressure and residual anal canal pressure were measured. The relaxation percentage was calculated according to the anal canal residual pressure. The recto-anal inhibitory reflex was also assessed

by insufflation of air into the balloon in 10-mL increments, and the distension threshold that caused a drop in the anal canal pressure was measured. The balloon was deflated between each bearing [19].

Dyssynergia was defined in 3D-HDM by the absence of pressure reduction or an increase in the anal canal residual pressure during straining. Patients were classified according to the classification of defecation disorders [8]: rectal pressure > 40 mmHg and paradoxical anal contraction (type I), rectal pressure < 40 mmHg and paradoxical anal contraction (type II), rectal pressure > 40 mmHg and incomplete anal relaxation (type III), and rectal pressure < 40 mmHg and incomplete anal relaxation (type IV) (Fig. 1).

Additionally, the manometric patterns obtained with 3D-HDM enable the identification of muscles that prevent the pressure drop in the anal canal. Indeed, the absence of pressure reduction can be caused by EAS contraction and/or puborectalis muscle contraction. Raja et al. have shown that the three-dimensional manometric image of the puborectalis muscle is easily identifiable [20]. Thus, during straining, an area of posterior superior high pressure is linked to a contraction of the puborectalis muscle, and an anterior and inferior high pressure is linked to a contraction of the EAS. Considering this additional criterion, three muscle subtypes were defined: patients with only puborectalis muscle contraction ("PB"), patients with only EAS contraction ("EAS"), and patients with both muscle contractions ("PBS") (Fig. 2). Pelvic floor disorders that can be visualized with this technique (internal rectal prolapse and perineal descent) were also systematically investigated. Internal rectal prolapse was defined in 3D-HDM as the appearance of an anterior high-pressure zone during straining combined with excessive perineal descent [5]. After straining was stopped, a return to baseline eliminated an artifact associated with probe movement [4].

Finally, the presence of a sphincter defect was also systematically investigated. In accordance with current data from the literature, a sphincter defect was described in 3D-HDM as a continuous circumferential area over which the pressure was below 10 mmHg during the resting pressure (internal anal sphincter (IAS) defect) and voluntary contraction (EAS defect) [5].

Endoanal ultrasound

Two experienced operators performed the endoanal ultrasound (EUS) scans. Patients ware positioned in a left lateral supine position. A rigid two-plane probe (linear and hemicircumferential) with a frequency of 7 MHz was used (EUP-U533; Hitachi, Japan). The probe was covered with a sheath and a water-filled balloon to maintain acoustic contact. A slow 360° rotation of the probe allowed for the analysis of the different structures of the anal canal and of the adjacent

organs. A rupture of the IAS was defined as an interruption in the hypoechogenic area and a rupture of the EAS was defined as a stop in the hyperechogenic area. The measurements of these defects were made in both linear and hemi-circumferential planes.

Regulatory aspects

As a retrospective study and in accordance with French clinical trial legislation, consent was not required. Data were anonymized and collected from the AP-HM computerized file, which was declared to the "Commission Nationale Informatique et Liberté".

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics software version 20.0 (IBM SPSS Inc., Chicago, IL, USA). Quantitative variables are presented as the mean ± standard deviation, and qualitative variables are presented as the number and percentage. The relationship between two qualitative variables (percentage comparison) was evaluated using Pearson's chi-square test or, if the theoretical headcount was less than five, with Fisher's exact test. The relationship between a quantitative variable and a qualitative variable with two modes (comparison of means) was evaluated using Student's independent sample t test or the Mann–Whitney U test if the distribution of the quantitative variable was not normal. Odds ratios are presented with their 95% confidence intervals. All tests were applied bilaterally and the results were considered as significant when $p < 0.05$.

Results

Demographic characteristics

Ninety-two patients, 78 women (85%) and 14 men (15%) with a mean age of 50.6 ± 16 years were included between January 2015 and January 2016. Forty-five (49%) patients had OC, and 47 (51%) had FI. The demographic characteristics of the population are described in Table 1.

Forty-seven (51%) patients were considered to be responders to BT and 45 (49%) were considered to be non-responders. In the OC subgroup, 23 (51%) patients were responders to BT, and 22 (49%) were non-responders. In the FI subgroup, 24 (51%) patients were responders to BT and 23 (49%) were non-responders. The flowchart is presented in (Fig. 3).

Fig. 1 Five patterns of three-dimensional high-definition anorectal manometry during strain. A/Normal pattern. B1–B4/ Four types of abnormal patterns. Defecation disorder classification
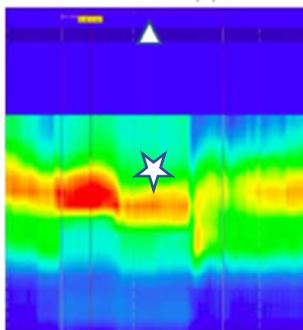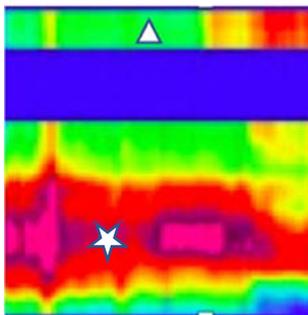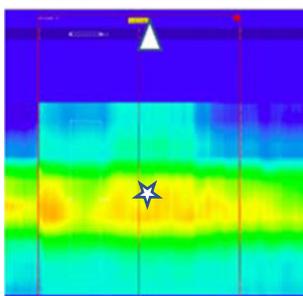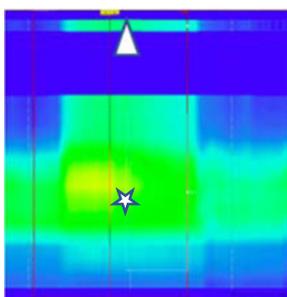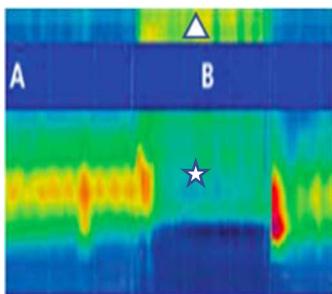
Normal:

△ Rectal Pressure > 40 mmHg

☆ Anal relaxation > 20%

Type I:

△ Rectal Pressure > 40 mmHg

☆ Paradoxical anal contraction

Type II:

△ Rectal Pressure < 40 mmHg

☆ Paradoxical anal contraction

Type III:

△ Rectal Pressure > 40 mmHg

☆ Incomplete anal relaxation

Type IV:

△ Rectal Pressure < 40 mmHg

☆ Incomplete anal relaxation

Subtype (PB)
Paradoxical anal contraction in posterior and superior area during straining

Subtype (EAS)
Paradoxical anal contraction in anterior and inferior area during straining

Subtype (PBS)
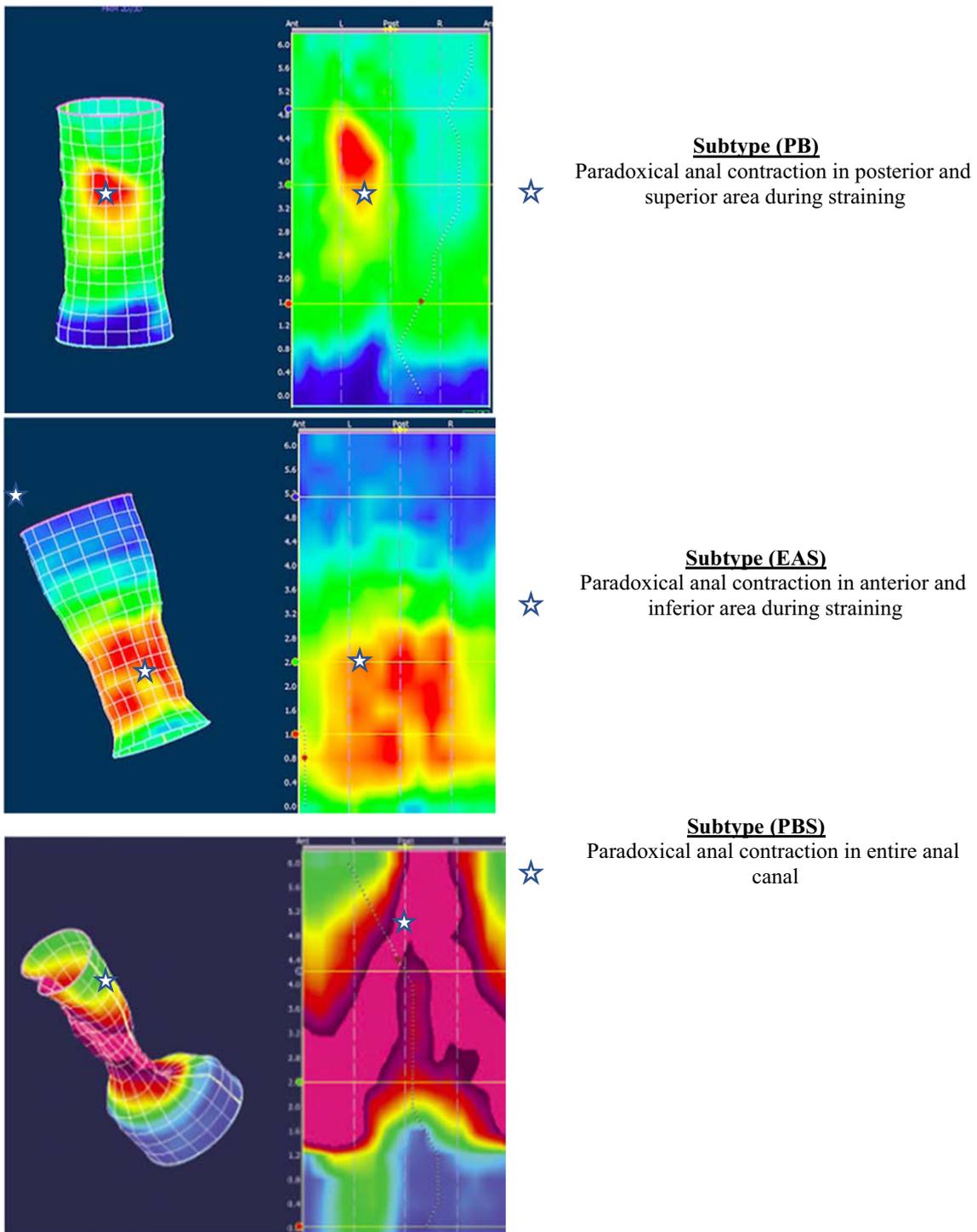Paradoxical anal contraction in entire anal canal

Fig. 2 Muscular subtypes during straining. An anal canal 3D reconstruction is shown on the left and an anal canal 2D reconstruction is shown on the right

Manometric data

Eighty-three (89%) patients were identified as having a defecation disorder with 3D-HDM. The remaining nine (11%) patients had no abnormalities during the defecation phase on the manometric line. The manometric characteristics of the population are shown in Table 2.

The distribution of these patients according to the defecation disorder classification type and muscular subtype is described in Table 3. The presence of other anomalies, which are

Table 1 Demographic characteristics

Parameters	All patients $N = 92$	Responders $N = 47$	Non-responders $N = 45$	p
Constipation n (%)	45 (49%)	23 (51.1%)	22 (48.9%)	1
Anal incontinence n (%)	47 (51%)	24 (51.1%)	23 (48.9%)	1
Male n (%)	14 (15%)	9 (64.3%)	5 (35.7%)	0.39
Female n (%)	78 (85%)	38 (48.7%)	40 (51.3%)	
Mean age (years)	50.6 ± 16.1	49.8 ± 16.7	51.4 ± 15.6	0.63
Mean VAS	3.2 ± 1.6	4.5 ± 0.5	1.8 ± 1.2	
Basal Wexner score (mean)	8.1 ± 5.5	7.42 ± 5.9	8.7 ± 5.3	0.45
Basal KESS score (mean)	19 ± 6.8	17.1 ± 6.9	21.5 ± 5.9	*0.03*
Symptom duration (days) (mean)	121 ± 166	104 ± 137	138 ± 193	0.42
Urinary incontinence n (%)	45 (48.3%)	20 (44%)	25 (56%)	0.3
Dyspareunia n (%)	8 (8.6%)	2 (25%)	6 (75%)	0.15
Vaginal delivery n (%)	55 (69%)	27 (49%)	28 (51%)	0.77
Cesarean delivery n (%)	5 (6%)	2 (40%)	3 (60%)	0.58
Instrumental maneuvers n (%)	12 (18%)	6 (50%)	6 (50%)	0.77
Episiotomy n (%)	29 (44%)	13 (38.5%)	16 (61.5%)	0.93
Perineal tear n (%)	26 (39%)	11 (32.3%)	15 (57.7%)	0.8
Height (cm) (mean)	163 ± 7.1	163 ± 6	163 ± 8	1
Weight (kg) (mean)	61 ± 10.3	64 ± 11	58 ± 10	0.08
BMI (kg/m^2) (mean)	20.4 ± 8.8	22.1 ± 8.8	19.3 ± 8.8	0.32

VAS, visual analog scale; *BMI*, body mass index

represented by pelvic floor disorders and sphincter defects defined by 3D-HDM is described in Table 4.

Subgroup analyses

The results from the "OC" and "FI" subgroup analyses are presented in Tables 2 and 3. The type II defecation disorder ($p = 0.03$) was significantly associated with the response to BT in the OC group, and the type IV defecation disorder ($p = 0.04$) was significantly associated with the response to BT in the FI group.

EUS characteristics

Twenty-one patients (54%) had a defect in one or both anal sphincters at the time of the EUS. Seven patients (33%) (two
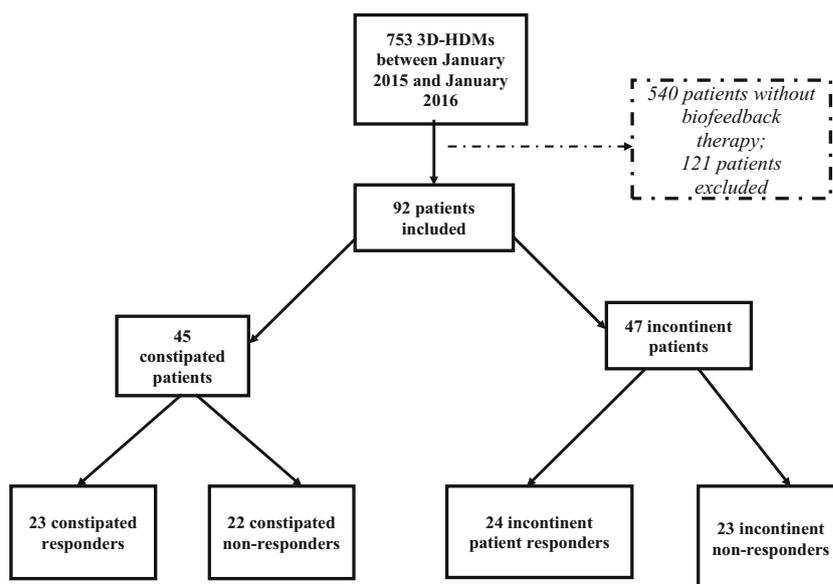
Fig. 3 Patients flowchart

Table 2 Manometric data

Parameters	Global population				Constipation subgroup				Anal incontinence subgroup			
	All patients	Responders	Non-responders	p	All patients	Responders	Non-responders	p	All patients	Responders	Non-responders	p
N (%)	92	47 (51%)	45 (49%)		45	23 (51%)	22 (49%)		47	24 (51%)	23 (49%)	
Mean resting pressure (mmHg)	77.5±27.3	73.9±27	81.1±27	0.21	86±27	82±24	89±31	0.44	69±25	61±28	72±18	0.23
Maximal squeezing pressure (mmHg)	189±76.4	196±76	175±69	0.19	209±68	215±73	208±62	0.76	167±72	156±57	149±67	0.12
Anal canal length (cm)	4.2±7.1	3.5±0.5	4.9±10	0.33	3.5±0.8	3.5±0.4	3.5±1	0.76	4.9±10	3.4±0.6	3.3±0.6	0.34
Anal canal residual pressure during straining (mmHg)	99±39	97±38	100±41	0.7	111±39	111±40	113±39	0.77	87±37	82±34	84±31	0.65
Anal relaxation during straining (%)	−39±70	−41±55	−37±84	0.77	−43±84	−39±46	−51±112	0.58	−34±55	−47±67%	−21±42	0.19
Mean rectal pressure during straining (mmHg)	33±20	34±21	32±19	0.67	33±20	36±22	32±19	0.60	33±20	34±22	29±17	0.91
Recto-anal inhibitor reflex (RAIR) (%)	92 (100%)	47 (100%)	45 (100%)	1	45 (100%)	23 (100%)	22 (100%)	1	47 (100%)	24 (100%)	23 (100%)	1
Mean threshold RAIR (mL)	13.3±7.4	13.9±9	12.7±5.8	0.5	13±8	14±10	12±6	0.47	14±7	15±8	14±6	0.86

Table 3 Dyssynergic patients

Parameters	Global population				"Constipation" subgroup				"Anal incontinence" subgroup			
	All patients	Responders	Non-responders	p	All patients	Responders	Non-responders	p	All patients	Responders	Non-responders	p
N (%)	82 (89%)	42 (51%)	40 (49%)	0.52	40	20 (50%)	20 (50%)	0.66	42	22 (52%)	20 (48%)	1
Type of defecation disorder												
I	22 (27%)	12 (54%)	10 (46%)	0.76	9 (23%)	6 (67%)	3 (33%)	0.24	14 (33%)	6 (43%)	8 (57%)	0.51
II	49 (59%)	21 (43%)	28 (57%)	0.05	26 (65%)	11 (42%)	15 (58%)	0.04	21 (50%)	9 (43%)	12 (57%)	0.36
III	1 (1%)	1 (100%)	0 (0%)	0.33	1 (1%)	1 (100%)	0 (0%)	1	0 (0%)	0	0	N/A
IV	10 (13%)	8 (80%)	2 (20%)	0.03	4 (11%)	2 (50%)	2 (50%)	0.36	7 (17%)	7 (100%)	0 (0%)	0.07
Muscular subtype												
(PBS)	62 (78%)	32 (52%)	30 (48%)	0.52	26 (65%)	14 (54%)	12 (46%)	0.96	36 (90%)	18 (50%)	18 (50%)	0.41
(PB)	20 (22%)	10 (50%)	10 (50%)	0.52	14 (35%)	6 (43%)	8 (57%)	0.96	6 (10%)	4 (67%)	2 (33%)	0.41
(EAS)	0	0	0	N/A	0	0	0	N/A	0	0	0	N/A

EAS, external anal sphincter

Table 4 Pelvic floor disorders and anal sphincter defects (manometric defects)

Parameters	Values	Responders	Non-responders	p
Perineal descent n (%)	33 (36%)	15 (46%)	18 (54%)	0.52
Mean length of perineal descent (mm)	1.7 ± 6.1	13.3 ± 3	15.3 ± 8	0.36
Internal rectal prolapse n (%)	20 (22%)	9 (45%)	11 (55%)	0.58
Defect of internal anal sphincter (IAS) n (%)	12 (13%)	7 (58%)	5 (42%)	0.76
Degree of IAS defect	57.3 ± 69.4	24 ± 41	115 ± 76	*0.03*
Defect of external anal sphincter (EAS) n (%)	1 (1%)	1 (100%)	0 (0%)	1
Degree of EAS defect	20	20	0	1

[29%] with outlet constipation and five [71%] with anal incontinence) had isolated defects of the IAS with a mean size of 94° ± 40°. One patient (1%) (incontinent) had an isolated defect of the EAS with a mean size of 90°. Thirteen patients (62%) (five [38%] with outlet constipation and eight [62%] with anal incontinence) had defects of the EAS and defects of the IAS with mean sizes of 102° ± 42° and 103° ± 38°, respectively.

Univariate analysis

In the univariate analysis, two manometric variables were statistically associated with the response to BT: type IV was identified as a success factor (OR = 5.03 [1.02; 24.92]) (p = 0.03), and type II was identified as a failure factor (OR = 0.41 [0.17; 0.99]) (p = 0.05). No significant relationship was apparent between the muscular subtype and the response to BT (p = 0.52). For the demographic characteristics, the KESS score before BT (p = 0.03) was identified as a factor associated with the response to BT (OR = 0.9 [0.81; 0.99]) (Table 5).

Discussion

To our knowledge, this study is the first to demonstrate that the type of defecation disorder identified by HRM may predict the response to BT. Indeed, patients with type IV defecation disorders were significantly more likely to respond to BT, whereas patients with type II were less likely responders. Moreover, according to Grossi et al. study, these two types are the most observed disorders in symptomatic patients [21]. Type IV is

Table 5 Odds ratios

Parameters	p	OR [95% CI]
Type II	*0.05*	*0.41 [0.17; 0.99]*
Type IV	*0.03*	*5.03 [1.02; 24.92]*
Basal KESS score	*0.03*	*0.9 [0.81; 0.99]*
Degree of IAS defect	*0.05*	*1.47 [0.43; 5.03]*

characterized by ineffective rectal contraction without sphincter relaxation and type II by ineffective rectal contraction and paradoxical anal contraction. Thus, the discriminant parameter between the two types appears to be the anal contraction. Indeed, an ineffective rectal contraction (present in both types) does not appear to interfere with the therapeutic effect of BT. However, a paradoxical anal contraction seems to be the major factor influencing the response to BT. Indeed, it can be assumed that a paradoxical anal contraction is difficult to treat, maybe, as suggested by some authors, because it may be associated with a psychological disorder, such as anxiety, depression, and past of sexual abuse that can prevent the success of BT [22, 23].

Previous studies have tried to identify predictive factors of success for BT. The factors currently identified as predictors of success for OC patients include older age, stool consistency, and more than five BF sessions, high rectal pressure during straining, inability to evacuate the balloon inflated to 40 mL, absence of an increase in the anorectal angle during attempted defecation, and low defecation index (maximum rectal pressure/anal canal residual pressure) [10–13, 15, 16]. In our study, usual manometric values were not identified as predictive factors. In 2011, Shim et al. proposed a composite predictive response score for biofeedback, including stool consistency, laxative treatment duration, rectal pressure at strain, and evacuation time of the balloon inflated to 40 mL [10]. This strategy may be the most appropriate for predicting the response to BT, but this particular scoring system has not been widely used in the literature. The clinical response factors identified in the literature for FI patients are no history of associated constipation, more than six sessions of BT, female sex, older age, and severe anal incontinence. Predictive factors for BT failure are male sex, young age, and mild anal incontinence [12, 14]. In our study, another new clinical predictive factor of the response to BT was identified: the KESS score [17]. Indeed, a low KESS score was a predictive factor for success meaning that BT rather improve patients with less severe symptoms. This result suggests that a systematic completion of this standardized questionnaire during the first consultation may be proposed and could provide early guidance regarding the therapeutic strategy.

Despite its retrospective nature, that can be a limitation, our study has identified clinical and manometric predictive factors of success or failure for BT. These results appear to be informative, especially because of the high unexplained failure rate of BT (50%) [9]. Moreover, the available data regarding the efficacy of perineal rehabilitation is extensive but data often derived from heterogeneous population. In the literature, the success rate of BT, which is approximately 50%, is comparable between OC and FI [14, 15]. One criticism that could be made to our study is that our population was heterogeneous and comprised 49% of patients suffering from OC and 51% suffering from FI [10, 13, 15]. However, our objective was to evaluate the utility of HRM in the response to BT, which is an indicated treatment for both diseases. Furthermore, our sample size was similar to most of the studies that have investigated predictive factors and was also comparable in terms of mean age and sex ratio [10, 12, 13, 16]. BT has many advantages, including excellent tolerance and cost-effectiveness, but BT also has several disadvantages such as poor accessibility, length of time needed for treatment, and lack of acceptability [24]. Thus, the interest in identifying predictive factors of BT response to improve patient selection is particularly notable. Moreover, considerable heterogeneity exists in the practice of BT, even though no significant differences in terms of efficacy between the different types of perineal rehabilitation have been identified in the literature [8, 25]. In the present study, the same experienced operator performed BT in all patients that enabled the reproducibility of the technique between patients. The response rate to perineal rehabilitation in our study was 50.5%, which was comparable to the literature [9].

The evaluation of therapeutic efficacy in anorectal functional disorders and, more generally, in digestive functional diseases, is most often focused on the symptomatology described by the patient. Therefore, we performed a VAS analysis that is simple, reproducible, subjective, and widely used [10, 15]. We also collected severity scores for constipation (the KESS score) and anal incontinence (the Jorge and Wexner score) that are two validated scores largely used in the literature [17, 18].

Our results suggest that HRM may bring again a new interest in the study of anorectal functional disorders. Indeed, based on topographical assessments of pressure, HRM has demonstrated, these last years, that it enables the diagnosis of not only sphincter defects but also pelvic floor disorders such as internal rectal prolapse and perineal descent. Thus, HRM provides a kind of anorectal "functional imaging" and needs to be further evaluated [5, 8, 26].

Its role in the therapeutic strategy brings a real new stone to the building in the area of the investigation of anorectal functional disorders. However, now, further studies with larger and more homogeneous sample sizes are needed to confirm our results and to develop predictive scoring methods from clinical, manometric, and morphological data.

Compliance with ethical standards

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