

Validation of the London Classification for Rectal Hyposensitivity in an Anorectal Manometry Database of 2540 Patients With Functional Defecatory Disorder

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Background/Aims

Rectal hyposensitivity (RH), as defined by the London Classification, has been linked to sensory dysfunction caused by diabetes mellitus and Parkinson's disease (PD); however, its clinical interpretation has not been sufficiently validated. In this study, we aim to explore the correlations between rectal sensory thresholds and the clinical characteristics of patients with functional defecatory disorders.

Methods

We reviewed data from patients who underwent high-resolution anorectal manometry and acquired their clinical characteristics using a standardized questionnaire. The associations between RH based on either 1 (borderline RH) or 2 (RH) abnormal rectal sensory thresholds and patients' clinical and demographic characteristics were analyzed using linear and logistic regression models in the overall sex-stratified populations.

Results

We enrolled 2540 patients, of whom 1046 (41.2%) were men. Overall, 150 (5.9%) patients were diagnosed with RH, whereas 422 (16.6%) had borderline RH. Multivariate linear regression analysis revealed that the Cleveland Clinic Constipation Score (CCCS) increased linearly with the increase in the number of abnormal rectal sensory thresholds (effect per threshold: 0.900 [standard deviation: 0.188]). Upon stratification by sex, borderline RH was positively associated with diabetes mellitus, PD, and CCCS (adjusted odds ratio [aOR] = 2.11, 95% confidence interval [1.08, 4.15]; aOR = 1.49 [1.03, 2.14]; aOR = 1.03 [1.01, 1.05], respectively) in women. However, RH was positively associated with only the CCCS.

Conclusions

Defining RH based on 1 or more abnormal sensory thresholds showed better clinical correlation with patient characteristics. However, further prospective studies are needed to validate these findings before proposing revisions to the current London classification criteria.

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Key Words

Anorectal manometry; Constipation; Defecatory disorder; Rectal hyposensitivity

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Introduction

Rectal hyposensitivity (RH) is a disorder characterized by diminished perception of rectal distension and is often linked with sensory dysfunction in diseases such as diabetes mellitus (DM) or Parkinson's disease (PD).¹⁻³ RH is also associated with other conditions such as obesity, hypermobility syndrome, and opioid use, underscoring its effect in the pathophysiology of functional gastrointestinal disease.⁴⁻⁶ However, the clinical interpretation of RH remains incompletely elucidated due to the limited availability of large-scale real-world studies.

Based on the recently proposed London classification, patients are diagnosed with RH when 2 or more of their 3 rectal sensory tests exceed the upper limit of normal (ULN).⁷ In contrast, when only 1 of the 3 sensory tests exceeded the ULN, the diagnosis is considered inconclusive and designated as borderline RH. However, the London classification criteria were based on expert opinion rather than clinical evidence, and the clinical implications of the 3 rectal sensory tests have yet to be established. Additionally, the abovementioned RH diagnosis threshold has yet to be fully validated.

To validate this threshold, several limitations in the current body of literature should first be addressed. First, previous studies included a notably small proportion of male participants; in the 2 most recent studies, men accounted for only 14.6% and 8.2% of the respective study populations.^{8,9} This underrepresentation of men could lead to biased estimation of the prevalence and characteristics of RH in the general population. Moreover, previous studies have also observed sex-based differences in RH prevalence. For instance, a recent systematic review and meta-analysis on anal motor and rectal sensory dysfunction in male and female patients undergoing anorectal manometry for symptoms of fecal incontinence (FI) reported a pooled RH prevalence of 19% (95% CI, 15–23%) in men and 7% (95% CI, 5–9%) in women.¹⁰ Second, some known etiological factors, such as DM or PD, were either not accounted for or occurred too infrequently to permit meaningful analysis. Therefore, the current classification of RH and borderline RH as well as its component sensory thresholds requires validation with relevant data acquired from a large patient cohort. Thus, we conducted the present study to examine the associations between abnormal rectal sensory thresholds and the clinical and demographic characteristics of patients with functional defecatory disorder, aiming to address the abovementioned research gaps.

Materials and Methods

Study Population

We retrospectively analyzed a prospectively collected database of patients who underwent high-resolution anorectal manometry (HRAM) at the motility clinic of a tertiary university hospital between August 2012 and August 2021. The indications for HRAM included complaints of functional defecatory disorder, namely constipation and FI. Before undergoing anorectal manometry, the patients were required to complete a standardized bowel symptom questionnaire. The questionnaire included data requisite for the scoring systems for symptom severity, such as the Rome IV core criteria for functional constipation (FC) and Cleveland Clinic Constipation Score (CCCS).^{11,12} The questionnaire also included demographic data pertaining to the surgical and obstetric history as well as the presence of known etiologic factors of RH.¹ All patients with a complete, non-erratic HRAM dataset and questionnaire were included in the analysis.

The study protocol was approved by the Institutional Review Board of Asan Medical Center (IRB No. 2021-1416), which waived the requirement of obtaining informed consent from the participants.

High-resolution Anorectal Manometry and Rectal Sensory Testing

Rectal sensory testing was conducted as part of comprehensive HRAM, which was performed by an experienced registered nurse, with recordings approved by a gastroenterologist. Patients were required to stop medications, including opioids, that may confound the HRAM results before testing. Bowel preparations were not routinely performed. HRAM was performed using a solid-state high-resolution probe (16.7-Fr outer diameter; Diversatek, Milwaukee, WI, USA). A latex balloon tied to the end of the catheter was inserted inside the rectum and inflated with a hand-held syringe using simple ramp distension at a rate of 10 mL/second, up to a total volume of 240 mL. The thresholds for the first constant sensation volume (FCSV), desire to defecate volume (DDV), and urge perception volume (UPV) were recorded.

We used previously published dataset of 54 asymptomatic healthy participants (27 men, aged 20–67 years) who underwent evaluation of rectal sensation using a high-resolution manometry probe at our motility clinic to define the ULN of the 3 abovementioned rectal sensory thresholds. Hyposensitivity in each threshold

category was defined as 1 threshold higher than the respective ULN, which was 30 mL for FCSV, 160 mL for DDV, and 230 mL for UPV, corresponding to 2 standard deviations above the mean value.¹³

Outcomes

The primary analysis assessed the association of RH, borderline RH, and each abnormally elevated rectal sensory threshold with each component of the Rome IV criteria for FC and the CCCS. The secondary analysis investigated constipation severity according to the CCCS, adjusted for demographics (as detailed in Table 1) using multivariate linear regression. Additionally, we performed a sex-stratified sub-analysis.

Statistical Methods

Continuous variables are presented as medians and interquartile range, whereas categorical variables are presented as numbers and percentages. The rectal sensory thresholds were analyzed as binary variables (above the threshold or not). The diagnoses of RH and borderline RH were also counted as binary variables. For each binary outcome, the analysis of variance, Kruskal–Wallis test, or chi-squared test for univariable analyses, whereas logistic regression models were used in the multivariable analyses. Patient characteristics with a P -value < 0.05 in the univariable analyses of any 5 outcomes were included in the multivariable analyses. All statistical analyses were performed using R statistical software, version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

This study enrolled 2540 patients, of whom 1046 (41.2%) were men. Notably, 150 (5.9%) and 422 (16.6%) patients were diagnosed with RH and borderline RH, respectively, based on the London classification. Variables such as sex, age, height, weight, marital status, and concomitant irritable bowel syndrome (IBS) differed significantly among patients with different numbers of abnormal rectal sensory thresholds (all $P < 0.05$) (Table 1).

Symptoms Associated with Constipation

The proportions of patients who reported symptoms from the CCCS and Rome IV criteria, stratified according to the number of abnormal rectal sensory thresholds, are shown in Figure. Significant differences were noted in the frequencies of symptoms, including bowel movements, painful evacuation effort, and assistance for defecation in the CCCS ($P = 0.010$, $P = 0.019$, $P < 0.001$,

respectively). In the Rome IV criteria, significant differences were observed for straining and anorectal obstruction symptoms ($P = 0.010$, $P = 0.002$, respectively). Overall, there was a tendency toward increasing symptom frequency with an increase in the number of abnormal rectal sensory thresholds.

Association Between Symptom Severity and Rectal Hyposensitivity

The results of multivariate linear regression analysis for constipation severity according to the CCCS, adjusted for the demographics, are listed in Table 1. The severity of constipation increased linearly with the increase in the number of abnormal rectal sensory thresholds, with the adjusted effect per abnormal threshold being equal to 0.9 (standard deviation = 0.188) (Table 2).

Variables Associated with Rectal Hyposensitivity, Stratified by Sex

The baseline characteristics of patients stratified by sex are presented in Supplementary Table. In the sex-stratified sub-analysis, univariate analysis revealed that body mass index (BMI), PD, DM, diagnosis of FC by Rome IV, CCCS, and educational status were significantly associated with RH in women (all $P < 0.05$). In the subsequent multivariate analysis, RH based on 1 or more abnormal sensory thresholds was positively associated with PD, DM, and the CCCS and inversely associated with higher educational status ($P = 0.030$, $P = 0.032$, $P = 0.012$, and $P = 0.024$, respectively), whereas RH identified by the London classification was associated only with the CCCS and education status ($P = 0.029$ and $P = 0.045$, respectively) (Table 3).

In contrast, univariate analysis in men showed that age, hemorrhoid surgery, spinal surgery, diagnosis of IBS, CCCS, educational status, and stress were significantly associated with RH (all $P < 0.05$). Multivariate analysis in men showed that RH based on 1 or more abnormal sensory thresholds was positively associated with age and the CCCS and inversely associated with concomitant IBS and a small amount of stress ($P = 0.005$, $P < 0.001$, $P = 0.017$, and $P = 0.047$, respectively). RH based on the London classification was associated with a different set of factors, showing a positive association with the CCCS and negative association with hemorrhoid surgery and concomitant IBS ($P = 0.001$, $P = 0.024$, $P = 0.028$).

Variables Associated With Individual Sensory Thresholds, Stratified by Sex

Multivariable analysis between each variable and individual

Table 1. Demographic and Baseline Clinical Data of Patients Stratified by the Number of Abnormally Elevated Rectal Sensory Thresholds

Variables	No. of abnormal rectal sensory thresholds			P-value
	0 (n = 1968)	1 (n = 422)	≥ 2 (n = 150)	
Sex				< 0.001
Men	768 (39.0)	197 (46.7)	81 (54.0)	
Women	1200 (61.0)	225 (53.3)	69 (46.0)	
Age (yr)	63.0 [51.0, 72.0]	65.0 [57.0, 73.0]	67.0 [49.0, 74.0]	< 0.001
Height (cm)	161.9 [156.0, 168.0]	162.2 [156.0, 170.0]	165.0 [160.0, 171.0]	< 0.001
Weight (kg)	59.0 [52.0, 66.0]	61.0 [53.5, 68.0]	63.0 [54.0, 72.0]	< 0.001
BMI (kg/m ²)	22.6 [20.4, 24.9]	23.0 [20.9, 25.3]	22.8 [20.8, 25.6]	0.102
Smoking				0.409
Never smoker	1656 (84.1)	353 (83.6)	125 (83.3)	
Active smoker	153 (7.8)	32 (7.6)	17 (11.3)	
Past smoker	159 (8.1)	37 (8.8)	8 (5.3)	
Marital status				0.010
Married	1416 (72.0)	334 (79.1)	109 (72.7)	
Currently not married	552 (28.0)	88 (20.9)	41 (27.3)	
Presenting symptom				< 0.001
Constipation only	1087 (55.2)	182 (43.1)	77 (51.3)	
Fecal incontinence only	274 (13.9)	48 (11.4)	13 (8.7)	
Constipation + fecal incontinence	607 (30.8)	192 (45.5)	60 (40.0)	
Etiologic factors				
Parkinson's disease	56 (2.8)	20 (4.7)	7 (4.7)	0.079
Diabetes mellitus	286 (14.5)	72 (17.1)	26 (17.3)	0.310
Pseudo-obstruction	61 (3.1)	13 (3.1)	4 (2.7)	> 0.999
Other neurologic disorders	12 (100.0)	1 (100.0)	0 (0.0)	
Parity ^a				0.986
Nulliparous	269 (22.4)	50 (22.2)	16 (23.2)	
Parous	931 (77.6)	175 (77.8)	53 (76.8)	
No. of vaginal deliveries ^a				0.218
1	131 (10.9)	20 (8.9)	7 (10.1)	
2	332 (27.7)	56 (24.9)	14 (20.3)	
3	182 (15.2)	33 (14.7)	11 (15.9)	
≥ 4	148 (12.3)	38 (16.9)	16 (23.2)	
Cesarean section ^a				0.650
Yes	150 (12.5)	24 (10.7)	7 (10.1)	
No	1050 (87.5)	201 (89.3)	62 (89.9)	
Menopause ^a				0.330
Not in menopause	395 (32.9)	64 (28.4)	25 (36.2)	
In menopause	805 (67.1)	161 (71.6)	44 (63.8)	
Surgical history				
Abdominal bowel surgery	157 (8.0)	29 (6.9)	11 (7.3)	0.729
Pelvic surgery, including hysterectomy ^a	187 (15.6)	44 (19.6)	10 (14.5)	0.308
Hemorrhoid surgery	322 (16.4)	82 (19.4)	17 (11.3)	0.063
Spinal surgery	165 (8.4)	39 (9.2)	19 (12.7)	0.190
Concomitant IBS				0.033
Without IBS	1592 (80.9)	362 (85.8)	101 (84.9)	
With IBS	376 (19.1)	60 (14.2)	22 (14.7)	
Rome IV functional constipation				0.242
Without FC diagnosis	1044 (53.0)	209 (49.5)	54 (45.4)	
With FC diagnosis	924 (47.0)	213 (50.5)	78 (52.0)	

^aAmong women.

BMI, body mass index; IBS, irritable bowel syndrome; FC, functional constipation.

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

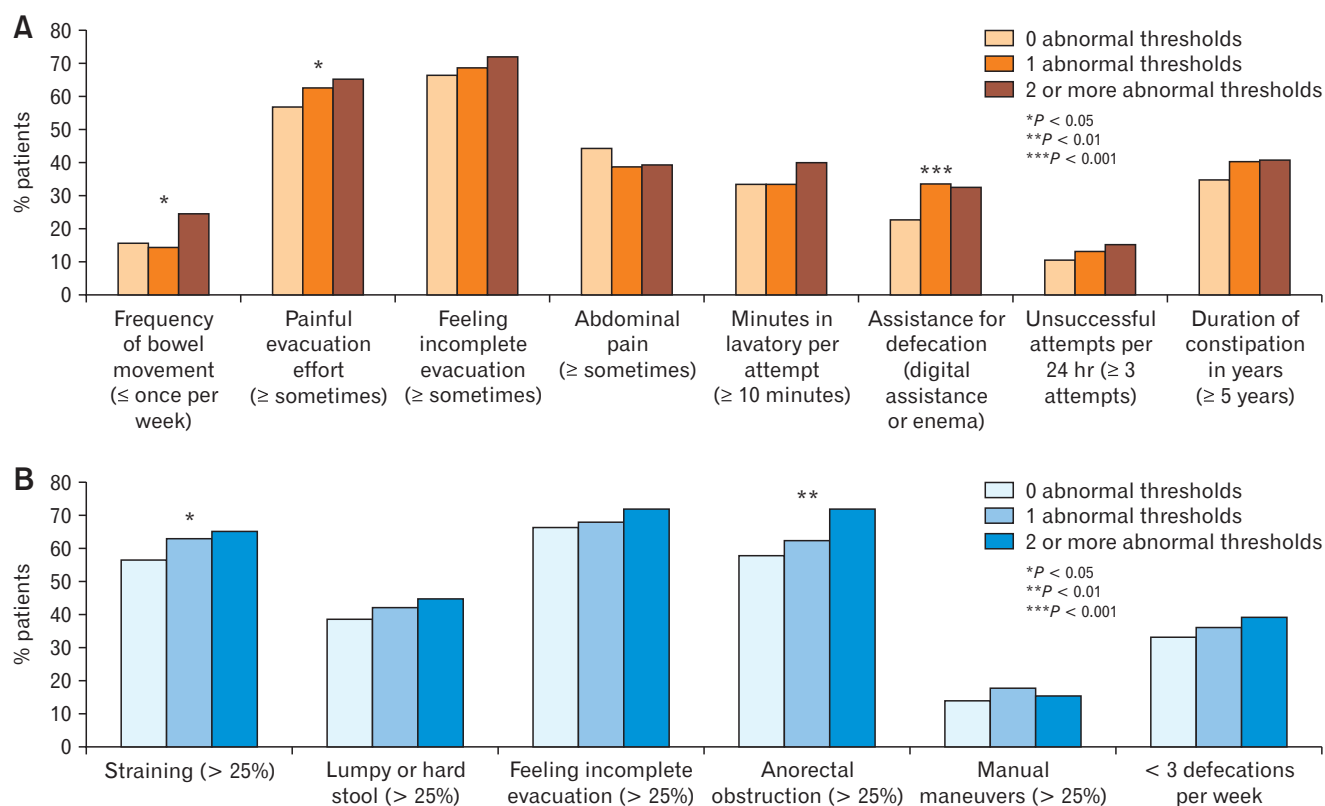


Figure. Symptoms associated with constipation stratified according to the number of abnormal rectal sensory thresholds. (A) Proportions of patients with a Cleveland Clinic Constipation Score of 2 or higher. (B) Proportions of patients satisfying each Rome IV criterion for functional constipation.

Table 2. Association Between the Cleveland Clinic Constipation Score and the Number of Abnormal Rectal Sensory Thresholds

Variable	Number of abnormal rectal sensory thresholds			Effect per an abnormal rectal sensory threshold (SD) ^a	P-value
	0 (n = 1968)	1 (n = 422)	$\geq$ 2 (n = 150)		
CCCS	11.2 (6.2)	12.1 (6.1)	13.4 (6.0)	0.900 (0.188)	$<$ 0.001

^aEstimated mean difference in the Cleveland Clinic Constipation Score (CCCS) per increase in the number of abnormal rectal sensory threshold, assuming a linear effect of number of thresholds, with 2 or more as a single group, adjusted for sex, age, height, weight, body mass index, history of Parkinson's disease and diabetes mellitus, spinal surgery, hemorrhoid surgery, presenting symptoms, concomitant diagnosis of irritable bowel syndrome, and functional constipation by the Rome IV criteria, and educational status.

Data are presented as mean (SD).

sensory threshold revealed that different variables were associated with each sensory threshold, and these associations were further differentiated according to sex. In women, the FCSV was associated with DM, diagnosis of FC by the Rome IV criteria, CCCS, and educational status ($P = 0.006$, $P = 0.014$, $P = 0.005$, $P = 0.006$, respectively). Notably, in women, the DDV was associated with BMI, PD, and diagnosis of FC by Rome IV ($P = 0.029$, $P = 0.038$, $P = 0.003$, respectively), whereas the UPV was associated with PD only ($P = 0.020$).

In men, the FCSV was associated with age and the CCCS ($P < 0.001$, $P = 0.003$, respectively). Moreover, in men, the DDV was associated with hemorrhoid surgery, CCCS, and education status ($P = 0.005$, $P = 0.011$, $P = 0.031$, respectively), whereas the UPV was associated with spinal surgery and CCCS ($P = 0.040$, $P = 0.003$, respectively).

Table 3. Multivariate Analysis of Association Between Rectal Hyposensitivity Based on 1 or 2 Thresholds, Individual Binary Sensory Thresholds, and Patient Characteristics, Stratified by Sex

Levels	RH based on 1 or more sensory thresholds		RH based on 2 or more sensory thresholds		FCSV		DDV		UPV	
	aOR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value	aOR (95% CI)	P-value
Female patients										
BMI (kg/m ²)	1.02 (0.99, 1.06)	0.213	1.00 (0.94, 1.07)	0.962	1.02 (0.97, 1.06)	0.451	1.06 (1.01, 1.11)	0.029	1.03 (0.98, 1.08)	0.290
PD	Reference		Reference		Reference		Reference		Reference	
	2.11 (1.08, 4.15)	0.030	0.94 (0.22, 4.01)	0.930	1.90 (0.84, 4.28)	0.120	2.36 (1.05, 5.29)	0.038	2.51 (1.16, 5.45)	0.020
DM	Reference		Reference		Reference		Reference		Reference	
	1.49 (1.03, 2.14)	0.032	1.55 (0.80, 3.00)	0.190	1.81 (1.18, 2.76)	0.006	1.16 (0.69, 1.95)	0.562	0.99 (0.59, 1.67)	0.981
FC	Reference		Reference		Reference		Reference		Reference	
	0.97 (0.72, 1.30)	0.833	1.02 (0.59, 1.78)	0.931	0.63 (0.43, 0.91)	0.014	1.92 (1.25, 2.95)	0.003	1.31 (0.89, 1.95)	0.175
CCCS	1.03 (1.01, 1.05)	0.012	1.05 (1.00, 1.10)	0.029	1.04 (1.01, 1.07)	0.005	1.00 (0.97, 1.03)	0.981	1.02 (0.99, 1.06)	0.153
Education status	Reference		Reference		Reference		Reference		Reference	
	0.70 (0.51, 0.95)	0.024	0.51 (0.26, 0.99)	0.045	0.55 (0.36, 0.84)	0.006	0.87 (0.57, 1.34)	0.538	0.81 (0.54, 1.22)	0.319
Male patients										
Age (yr)	1.15 (1.04, 1.27)	0.005	1.00 (0.86, 1.16)	0.988	1.32 (1.16, 1.51)	<.001	0.97 (0.86, 1.10)	0.659	0.99 (0.88, 1.10)	0.828
Hemorrhoid surgery	Reference		Reference		Reference		Reference		Reference	
	0.91 (0.63, 1.30)	0.605	0.43 (0.21, 0.90)	0.024	1.07 (0.71, 1.61)	0.759	0.41 (0.22, 0.76)	0.005	0.66 (0.41, 1.07)	0.093
Spinal surgery	Reference		Reference		Reference		Reference		Reference	
	1.13 (0.70, 1.83)	0.613	1.39 (0.66, 2.91)	0.384	1.05 (0.60, 1.85)	0.861	1.26 (0.66, 2.42)	0.483	1.76 (1.03, 3.00)	0.040
IBS	Reference		Reference		Reference		Reference		Reference	
	0.61 (0.41, 0.92)	0.017	0.44 (0.21, 0.91)	0.028	0.65 (0.40, 1.06)	0.083	0.72 (0.42, 1.24)	0.232	0.67 (0.41, 1.09)	0.108
CCCS	1.04 (1.02, 1.07)	<.001	1.07 (1.03, 1.12)	0.001	1.05 (1.01, 1.08)	0.003	1.04 (1.01, 1.08)	0.011	1.05 (1.02, 1.08)	0.003
Education status	Reference		Reference		Reference		Reference		Reference	
	0.93 (0.69, 1.24)	0.614	0.80 (0.48, 1.31)	0.372	1.32 (0.94, 1.85)	0.113	0.62 (0.40, 0.96)	0.031	0.83 (0.57, 1.19)	0.310
Stress status	Reference		Reference		Reference		Reference		Reference	
	0.66 (0.43, 0.99)	0.047	0.81 (0.42, 1.59)	0.546	0.87 (0.53, 1.41)	0.568	0.62 (0.35, 1.09)	0.096	0.68 (0.41, 1.12)	0.133
	0.91 (0.60, 1.38)	0.670	0.72 (0.36, 1.45)	0.356	1.02 (0.62, 1.68)	0.939	0.70 (0.40, 1.24)	0.222	0.77 (0.46, 1.28)	0.310
Overwhelming	1.23 (0.74, 2.04)	0.427	1.46 (0.67, 3.17)	0.342	1.51 (0.83, 2.73)	0.174	1.23 (0.64, 2.36)	0.540	1.08 (0.59, 1.99)	0.796

RH, rectal hyposensitivity; FCSV, first constant sensation volume; DDV, defecatory desire volume; UPV, urge perception volume; aOR, adjusted odds ratio; BMI, body mass index; PD, Parkinson's disease; DM, diabetes mellitus; FC, functional constipation; CCCS, Cleveland Clinic Constipation Score; IBS, irritable bowel syndrome.

Logistic regression analyses included patient characteristics with P-values < 0.05 in the univariable analyses of any outcome, which included age, BMI, active smoker, PD, DM, number of vaginal deliveries, previous hysterectomy, FC, CCCS, and educational status for women; and age, marital status, hemorrhoid surgery, spinal surgery, IBS, CCCS, education status, stress status, and sleeping status for men.

Discussion

In the present study, we investigated the prevalence and features of RH in patients diagnosed with functional defecatory disorder and found that RH based on the conventional London classification was present in 5.9% of patients, whereas RH based on 1 or more abnormally elevated thresholds was present in 22.5% of patients. Constipation severity, measured by the CCCS, bore a positive correlation with the number of abnormal rectal sensory thresholds. Compared with the conventional RH definition, defining RH on the basis of 1 or more elevated thresholds aligned more closely with patient symptoms and characteristics, such as PD and DM, which are associated with sensory dysfunction and are mechanistically linked to RH. Sex-stratified sub-analysis identified distinct variables associated with RH in men and women as well as in each sensory threshold. These findings suggest that each rectal sensory threshold may represent different underlying mechanisms of RH, suggesting the possibility of distinct phenotypes of the condition.

Several studies have investigated the prevalence and characteristics of RH in patients with constipation. An early investigation in patients with constipation (with or without FI) reported a prevalence rate of 24.4% (163 of 667 patients) when RH was defined as the presence of 1 or more elevated rectal sensory thresholds.¹⁴ Subsequent studies in similar patient populations reported RH prevalence rates of 13.6–17.0%, albeit by defining RH as the presence of 2 or more elevated rectal sensory thresholds.^{6,8,9,15} In contrast, our study identified a lower prevalence rate of RH (5.9%) when RH was defined as the presence of 2 or more elevated rectal sensory thresholds.

This discrepancy between the results of the previous and current studies may be attributed to several factors. While our cohort included a higher proportion of male participants (41.2%) compared to earlier studies (in which men accounted for 8.2–14.6% of the cohort) and RH reportedly occurs more frequently in men, the overall lower prevalence of RH may also reflect other contributing factors. Differences in catheter design and pressure-sensing technology among manufacturers could affect anorectal manometry results, further complicating comparisons across studies.¹⁶ Additionally, our study population may have had distinct baseline characteristics, as it was recruited from a single tertiary-care center, probably enrolling patients whose characteristics differed from those of previous studies.^{8,9} Geographic and cultural differences in constipation symptoms, along with variations in study methodology, may also have affected the differing results. These factors underscore the

need for further research to better understand the variability in RH prevalence across different populations and settings.

Compared with studies in other populations, recent studies in Korean patients with constipation indicate distinct pathophysiological characteristics, with a notable trend toward a higher greater male preponderance, at a women to men ratio of 1.92:1.^{17,18} Another factor would be the differences in the size of the pelvis and rectum as well as the results of anorectal manometry according to race or ethnicity.^{19–21} Therefore, direct comparison between the studies of different populations may not be feasible.

Since the pressure sensors and balloons used for HRAM vary according to the manufacturer and the institution where the test is performed, the current guideline published by the International Anorectal Physiology Working Group agreed that no specific normal values could be proposed and recommended using the normal values from published data with identical protocols or from local studies of healthy volunteers.⁷ Therefore, we utilized the ULN defined by the analyses of 54 asymptomatic healthy participants (27 men, age: 20–67 years) from our motility clinic.¹³

Except for patients with constipation (with or without FI), our target population included patients whose primary complaint was FI. Although broadly referred to as functional defecatory disorder and generally considered as separate entities, the coexistence of symptoms in constipation and FI have been reported.⁶ Precluding patients with FI as their primary complaint might result in overlooking those with actual constipation symptoms.

Sex-specific analyses showed that different variables were associated with RH and borderline RH and the FCSV, DDV, and UPV in each sex. Mazon et al⁹ found a poor correlation between each perception threshold of the FCSV, UPV, and maximum tolerated volume, suggesting that each sensory threshold may represent distinct underlying mechanisms. Our study provides additional evidence supporting this notion, highlighting the role of the FCSV. As shown in Table 3, in women, the FCSV was significantly associated with DM, FC, and CCCS. This suggests that the FCSV may play a pivotal role in defining RH, particularly in female patients, and could be the most important variable for identifying sensory dysfunction in certain patient groups. However, this conclusion warrants further validation through additional studies to confirm its broader applicability and relevance. Moreover, as the clinical characteristics and phenotype of RH seem to differ significantly between men and women, interpreting the results of HRAM and formulating the diagnosis of RH based on sex might be necessary.

We acknowledge several limitations of our study. First, our study was conducted at a single tertiary referral center, which may

have introduced selection bias and limited the generalizability of our findings to other populations. Second, owing to the retrospective study design, we were unable to establish a cause–effect relationship between RH and the symptoms of constipation as well as the diagnosis of FC itself. It is unclear whether abnormal rectal sensation causes symptoms of constipation or if constipation itself or stool withholding behavior, pain, or trauma may cause abnormal rectal sensation.²² Further research is needed to clarify the mechanisms underlying this relationship. Third, although we controlled for variables such as age, BMI, and comorbidities in our analysis, there may be other factors beyond our control, which could have influenced our results. Fourth, while the maximum tolerable volume parameter is integrated into the London classification criteria, we substituted it with the UPV for comparable clinical significance. The main reason was concern regarding the risk of iatrogenic colorectal perforation, which could be related to excessive inflation of the balloon.^{23–25} Similarly, recent studies with HRAM have frequently used the UPV as a key measure, given the mounting evidence of urge sensation as one of the key factors in the pathophysiology of constipation.^{26,27}

While the London proposal for diagnosing rectal sensitivity disorders is based on balloon distension during anorectal manometry, future studies employing barostat protocols may provide more accurate measures of rectal sensitivity. Barostat studies, which offer finer control over distension and promote standardization, could offer further validation of the proposed definition of RH based on a single abnormal threshold. In addition to barostat testing, novel technologies such as the Fecobionics system have shown promise in evaluating defecatory function under more physiologic conditions, demonstrating that fecal consistency itself significantly alters defecatory parameters. Incorporating such tools could offer more nuanced insights into the mechanical and sensory contributors to RH.²⁸

In conclusion, this study provides valuable insights into the prevalence and characteristics of RH in patients with functional defecatory disorder. Our findings underscore the associations of RH with certain comorbidities, such as PD and DM, and highlight distinct sex-based differences in the variables associated with RH and rectal sensory thresholds. Moreover, our results suggest that each rectal sensory threshold may be linked to different pathophysiological mechanisms, indicating the potential for varied phenotypes of RH. Although this study raises the possibility that RH could be more accurately defined by one or more abnormal sensory thresholds rather than the current requirement of 2 or more thresholds per the London classification, the retrospective nature of the study and its limitations caution against drawing definitive conclu-

sions regarding the redefinition of RH. Future prospective studies with larger cohorts and better control of confounding variables are needed to further investigate the clinical implications of the different rectal sensory thresholds and ascertain whether a revision of the current classification criteria is warranted.

Supplementary Material

Note: To access the supplementary table mentioned in this article, visit the online version of *Journal of Neurogastroenterology and Motility* at <http://www.jnmjournal.org/>, and at <https://doi.org/10.5056/jnm24019>.

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