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# Phenotypic Identification and Classification of Functional Defecatory Disorders Using High-Resolution Anorectal Manometry

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**Podcast interview: www.gastro.org/gastropodcast. Also available on iTunes; see editorial on page 263.**

**BACKGROUND & AIMS:** Disordered defecation is attributed to pelvic floor dyssynergia. However, clinical observations indicate a spectrum of anorectal dysfunctions. The extent to which these disorders are distinct or overlap is unclear; anorectal manometry might be used in diagnosis, but healthy persons also can have abnormal rectoanal pressure gradients during simulated evacuation. We aimed to characterize phenotypic variation in constipated patients through high-resolution anorectal manometry. **METHODS:** We evaluated anorectal pressures, measured with high-resolution anorectal manometry, and rectal balloon expulsion time in 62 healthy women and 295 women with chronic constipation. Phenotypes were characterized by principal components analysis of high-resolution anorectal manometry. **RESULTS:** Two healthy persons and 71 patients had prolonged (>180 s) rectal balloon expulsion time. A principal components logistic model discriminated healthy people from patients with prolonged balloon expulsion time with 75% sensitivity and a specificity of 75%. Four phenotypes discriminated healthy people from patients with abnormal balloon expulsion times; 2 phenotypes discriminated healthy people from those with constipation but normal balloon expulsion time. Phenotypes were characterized based on high anal pressure at rest and during evacuation (high anal), low rectal pressure alone (low rectal) or low rectal pressure with impaired anal relaxation during evacuation (hybrid), and a short anal high-pressure zone. Symptoms were not useful for predicting which patients had prolonged balloon expulsion times. **CONCLUSIONS: Principal components analysis of rectoanal pressures identified 3 phenotypes (high anal, low rectal, and hybrid) that can discriminate among patients with normal and abnormal balloon expulsion time. These phenotypes might be useful to classify patients and increase our understanding of the pathogenesis of defecatory disorders.**

*Keywords:* Anorectal Test; Dyssynergic Defecation; Anismus; Pelvic Floor Dysfunction.

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Although symptoms and results of a digital rectal examination may suggest a defecatory disorder (DD), anorectal tests are necessary to confirm the diagnosis.[1–3] Diagnostic guidelines recommend anorectal manometry and a rectal balloon expulsion test (BET), which should be supplemented by barium or magnetic resonance defecography when necessary.[1,4] Currently, a negative rectoanal pressure gradient (ie, anal pressure greater than rectal pressure) measured by manometry or impaired rectal evacuation during defecography or rectal BET are considered indicative of DD.[5,6]

However, several questions exist about the use of anorectal manometry to diagnose DD and identify clinical phenotypes. First, the utility of an negative rectoanal pressure gradient (ie, anal pressure is greater than rectal pressure) as a marker of DD is unclear because this gradient among healthy persons and constipated patients with and without a defecatory disorder overlap considerably.[6] Although high-resolution manometry (HRM) increasingly is used to evaluate anorectal functions in clinical practice, all 30 asymptomatic women younger than 50 years in one study had greater anal pressures than rectal pressures during simulated evacuation.[7] Rectoanal dyssynergia does not predict an abnormal rectal BET in healthy people.[8]

Second, investigators in one study suggested that anorectal pressures during simulated evacuation are useful for classifying patients with DD into 3 types: dyssynergia (type 1), impaired rectal propulsion with paradoxic contraction (type 2), and increased intrarectal pressure with-

*Abbreviations used in this paper:* BET, balloon expulsion test; BMI, body mass index; DD, defecatory disorder; GC, geometric center; HRM, high-resolution manometry; PC, principal component; ROC, receiver operating characteristic.


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out anal relaxation (type 3).[9] Because all participants in that study had symptoms of DD, it is unclear whether these patterns can discriminate among healthy people, constipated patients without DD, and constipated patients with DD. Moreover, because these subtypes were defined a priori through pattern recognition by an expert rather than by formal analysis (eg, factor or principal components [PCs] analysis), it is unclear whether these subtypes are distinct or uncorrelated to each other. Also, this classification is based on the impaired rectoanal gradient during simulated evacuation, but it does not incorporate other features of DD (eg, high anal resting pressure).[4] Finally, clinical observations suggest that not all patients with DD can be classified into 1 of these 3 types.

Therefore, the aims of this study were to use anorectal parameters to discriminate among healthy people with normal balloon expulsion, constipated patients with normal balloon expulsion, and persons with abnormal balloon expulsion using a PC analysis that integrated original HRM variables into phenotypes. Similar approaches have been used to identify symptom phenotypes in irritable bowel syndrome,[10] colonic motor disturbances in chronic constipation,[11] and phenotypes incorporating anorectal manometry and magnetic resonance proctography in DD.[4] However, the present study was limited to anorectal manometry, which is used more widely than magnetic resonance proctography to diagnose DD. The aims of this study were as follows: (1) to evaluate the utility of anorectal HRM for diagnosing DD, (2) to assess whether anorectal HRM can identify phenotypes and facilitate the classification of DD, and (3) to evaluate the utility of symptoms for predicting abnormal balloon expulsion.

## Materials and Methods

### *Study Subjects*

Between August 2010 and September 2011 there were 670 women referred for anorectal HRM to our institution who completed questionnaires and 655 patients authorized review of their medical records for research (Supplementary Figure 1). Because our objectives were to better understand the utility of anorectal manometry and a rectal balloon expulsion test in women presenting with primary constipation, 360 patients with other conditions were excluded, providing 295 patients who had Rome III symptom criteria for functional constipation or constipation-predominant irritable bowel syndrome for this analysis (Supplementary Figure 1). Although patients who had major anorectal procedures or colonic surgery were excluded, patients who had undergone other abdominal surgeries (eg, right hemicolectomy, 1 patient; and appendectomy, cholecystectomy, and hysterectomy, 93 patients) were included. Permission to review these studies was obtained from the Mayo Clinic Institutional Review Board. Also, 62 healthy, asymptomatic women were recruited for this study through public advertisement.

All participants had a clinical interview and physical examination. In healthy participants, exclusion criteria were significant cardiovascular, respiratory, neurologic, psychiatric, or endocrine disease, irritable bowel syndrome as assessed by a validated bowel disease questionnaire,[12] medications (with the exception of oral contraceptives or thyroid supplementation), and abdominal surgery (other than appendectomy, cholecystectomy, or hysterectomy).

### *Procedures*

**Anorectal manometry.** Anal pressures were assessed by an HRM catheter (4.2-mm outer diameter; Sierra Scientific Instruments, Los Angeles, CA), which has 10 circumferential sensors: 8 sensors at 6-mm intervals along the anal canal and 2 sensors in the rectal balloon. At each level, 36 circumferentially oriented, pressure-sensing elements detect pressure using proprietary pressure transduction technology (TactArray; Pressure Profile Systems, Inc, Los Angeles, California) over 2.5 mm. Then, these 36 sector pressures are averaged to obtain a single value. The response characteristics of each sensing element are such that they can record pressure transients in excesses of 6000 mm Hg/s and are accurate to within 1 mm Hg of atmospheric pressure for measurements obtained for at least the final 5 minutes of the study, immediately before thermal recalibration. The data-acquisition frequency is 35 Hz for each sensor.

Each study contained, in the following chronologic order, an assessment of anorectal pressures at rest, during squeeze (3 attempts), and in simulated evacuation with an empty rectal balloon. Thereafter, the rectoanal inhibitory reflex and rectal sensation were evaluated simultaneously by progressively distending the rectal balloon until patients reported severe urgency, in 20-mL increments from 0 to 200 mL, and thereafter in 40-mL increments, until a maximum volume of 400 mL. The data were analyzed as described elsewhere.[7]

**Rectal BET.** A 4-cm–long latex balloon filled with 50 mL of warm water, tied to 2-mm diameter plastic tubing, was inserted into the rectum, with the study participant lying in the left lateral decubitus position. The participant then was asked to sit on a commode and expel the balloon in privacy. The BET was noted. The balloon was removed if participants could not expel the balloon within 3 minutes.[13]

**Colonic transit.** Colonic transit was assessed with established scintigraphic techniques in 114 patients.[14] Colonic transit was summarized as the colonic geometric center (GC), which is the weighted average of counts in the different colonic regions. A higher GC reflects faster colonic transit. Based on the 10th percentile value for healthy participants in our laboratory, delayed colonic transit was defined by a GC value for 24 hours of less than 1.5.

### *Statistical Analysis*

Because only 2 healthy women had a prolonged BET, healthy women and patients with a prolonged BET were combined for analysis, providing 3 groups: healthy women with a normal BET (<180 sec) (the reference group), DD with normal BET, and DD or healthy women with a prolonged BET. Univariate associations between variables and subject group status were assessed by the Fisher exact test for bowel symptoms categorized as significant or as not according to Rome II criteria, and by the Kruskal–Wallis rank test for anorectal manometry variables.

The next step was to discriminate among these 3 groups using a logistic regression discriminant analysis of anorectal variables (ie, anal resting and squeeze pressures, length of anal high-pressure zone, anal squeeze duration, and rectal and anal pressures and anal relaxation during simulated evacuation). However, correlations among anorectal parameters (eg, between anal resting and squeeze pressure) can limit the interpretation of this analysis. Hence, a PC analysis was used to transform anorectal variables into uncorrelated factors as described later. In essence,