Gender differences in chronic constipation on anorectal motility

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Abstract

Background: The epidemiology of chronic constipation (CC) skews toward female predominance, yet men make up an important component of those suffering from CC. We sought to determine whether there are sex-specific differences in symptoms and physiologic parameters on anorectal manometry (ARM).

Methods: We performed a case–control analysis of sequential men and age-matched women (2:1 ratio) presenting for ARM as part of the evaluation of CC. We collected physiologic parameters derived from 3D high-resolution ARM in addition to the ROME III constipation module and the Pelvic Floor Distress Inventory 20 (PFDI-20) questionnaires. We analyzed univariate, sex-specific differences in ARM physiologic parameters and PFDI-20 parameters and adjusted for putative confounders using multivariate logistic regression.

Key Results: Our study enrolled 80 men and 165 age-matched women. Men had a higher median sphincter resting pressure (81.2 vs 75.2 mm Hg, \(P = .01\)) and mean squeeze pressure (257.0 vs 170.5 mm Hg, \(P < .0001\)) than women. Although men reported significantly less severe straining and incomplete evacuation, they had greater mean rectoanal pressure differential (−106.7 vs −71.1 mm Hg, \(P < .0001\)), smaller mean defecation index (0.17 vs 0.27, \(P = .03\)) and higher volume threshold for urgency (115.2 vs. 103.4 mL, \(P = .03\)). However, women were more likely to have abnormal balloon expulsion time (BET) than men (52.7% vs 35.0%, \(P = .01\)). After multivariate analysis, male gender was the only independent predictor of a normal BET (OR: 0.48, 95% CI: 0.27–0.86, \(P = .01\)).

Conclusions & Inferences: Men and women with CC differ with regard to symptom severity and physiologic parameters derived from ARM suggesting differences in their pathophysiology.

KEYWORDS
anal sphincter, anorectal disorders, anorectal manometry, chronic constipation, dyssynergic defecation, gender

INTRODUCTION

Constipation affects nearly 15%–20% of the population and is one of the most common diagnoses in clinical practice.1 Between 14.9% and 52.9% of patients with CC have a defecation disorder,2 characterized by paradoxical contraction or inadequate relaxation of the pelvic...
floor muscles and/or inadequate propulsive forces during attempted defecation. Dyssynergic defecation (DD), as defined by the Rome III Criteria, is a subcategory of functional defecatory disorders characterized by paradoxical contraction or inadequate relaxation of the pelvic floor muscle or inadequate propulsive forces during attempted defecation. The diagnosis of DD can be determined by two abnormal tests of the pelvic floor on attempted defecation (i.e., impaired evacuation on balloon expulsion or defecography, and inappropriate relaxation of the anal sphincter on manometry, electromyography, or imaging). The diagnosis of DD is most commonly made in clinical practice through anorectal manometry (ARM) by simultaneously assessing intrarectal pressure and anal sphincter relaxation during simulated defecation and with timed balloon expulsion of a 50-cc balloon while seated on a bedside commode to enhance the specificity of diagnosing DD. Diagnosing DD in patients with refractory CC is particularly important as these patients respond better to anorectal biofeedback than to laxatives. Therefore, ARM is currently recommended as an early step in the workup of patients who have failed conservative measures. High-resolution ARM (HR-ARM) and high-definition ARM (HD-ARM) are the latest technology for the assessment of anorectal function with closely spaced pressure sensors that traverse the anal canal and an additional pressure sensor in the rectum. Both catheters measure circumferential pressures and provide spatiotemporal mapping of anorectal pressures; however, only HD-ARM provides a three-dimensional pressure profile. Several studies have evaluated the normal values for healthy women with HR-ARM and HD-ARM, however; few studies have evaluated normal values in men. Therefore, most normal anorectal manometry parameters in clinical practice have been extrapolated from women. While gender is known to affect some ARM parameters, to date no studies have evaluated differences between men and women with chronic constipation (CC). Furthermore, symptom presentation has never been examined between men and women with DD. Thus, we sought to evaluate differences between men and age-matched women with constipation with regard to: (i) anorectal manometry parameters, (ii) symptom correlation with ARM findings. We hypothesized that men with constipation would have a unique presentation of altered anorectal physiology and symptoms compared to age-matched, female controls.

2 METHODS

2.1 Subjects

Men and women with CC referred to Beth Israel Deaconess Medical Center’s Gastrointestinal Motility Laboratory for ARM from December 2012 to January 2016 were considered for study enrollment. The institutional review board of Beth Israel Deaconess Medical Center approved the retrospective review of data. A total of 245 patients (80 men and 165 age-matched women) were consecutively recruited for this study. All patients completed the Rome III integrative questionnaire and the Pelvic Floor Distress Inventory (PFDI-20). Patients younger than 18 years were excluded, and those with a history of fecal incontinence or major anorectal or colonic surgery. Relevant data were collected on each patient, including age, gender, and IBS subtype.

2.2 Equipment (Three-dimensional, high-resolution anorectal manometry)

Anal pressures were assessed using the 3D high-resolution probe (HD-ARM). The probe is 6.4 cm in length and has an outer diameter of 10.75 mm. It has 256 pressure sensors that are arranged in 16 rows, and each row has 16 circumferentially oriented sensors. The probe has a central lumen for inflation and a Luer lock at one end through which a balloon is attached. The balloon is composed of non-latex, clear thermoplastic elastomer (3.3-cm long, with a capacity of up to 400 mL) and disposable sheath. The probe is attached to an amplifier and recorder system, and the manometric and topographic images are displayed on a computer monitor by using specialized software.

2.3 Procedure

Patients were instructed to fast for approximately four hours prior to ARM. There were also instructed to use two fleet enemas prior to anorectal manometry. Patients were asked to lie in the left lateral decubitus position with knees and hips flexed. Before commencing the study, a digital rectal examination was performed to ascertain that the patient understood the commands such as squeeze and push. The probe was inserted and assessment of anorectal pressure was performed after a resting period of 5 minutes in the following order (Fig. 1): at rest (20 seconds), during three attempts of squeeze (20 seconds each), and in three attempts of simulated defecation. A fourth simulated defecation was attempted after inflation the balloon with 60 mL of air. Afterward, the patients were assessed for the rectoanal inhibitory anal reflex (RAIR). Rectal sensation thresholds were measured through progressive inflation of the intrarectal balloon with 10–20–mL increments until the patient reports first sensation and thereafter with 20-mL increments until the patient reported desire to defecate and or severe urgency (maximum of 250 mL reached).
2.4 | Balloon expulsion test

All patients underwent a timed balloon expulsion test (BET) following ARM. The BET was performed by inserting standard single-use anorectal balloon expulsion catheter (Mui Scientific, Mississauga, ON, Canada) followed by inflating non-latex 400-mL volume balloon with 50 mL of warm water while the patient was in the left lateral decubitus position. The patient was then asked to sit on a commode in privacy and expel the balloon. A maximum of 5 minutes was allowed to evacuate the balloon.

2.5 | Anorectal manometry analysis

Analysis of the manometric data was performed independently by two of the authors (MZ, WH) using ManoView analysis software (Medtronic, Minneapolis, MN, USA). Discrepancies in the results were resolved by a third author (JN, KS). Anal, intrarectal, and maximal squeeze pressures were assessed at rest and with squeeze. The maximum intrarectal pressure and anal sphincter relaxation during simulated bear down maneuvers were used to assess the presence of dyssynergia. Adequate rectal propulsion was defined as an intrarectal pressure of >40 mm Hg during simulated defecation. Adequate anal relaxation was defined as >20% relaxation during simulated defecation. The combination of intrarectal pressure and anal relaxation allowed dyssynergic patterns of defecation to be identified as per Rao (Fig. 2).

2.6 | Symptom assessments

Patients completed the PFDI-20 questionnaire and the Rome III Constipation Module prior to undergoing ARM. The PFDI measures symptom severity and evaluates the quality of life in all forms of pelvic floor disorders including pelvic organ prolapse, urinary incontinence, and colorectal dysfunction. The short form of version of the PFDI has a total of 20 questions and three subscales (six questions evaluating Urinary distress inventory, six questions evaluating Pelvic Organ Prolapse Distress Inventory, and eight questions evaluating Colorectal-Anal Distress Inventory). Each question, if answered by yes, is scored from not at all (least distress) to quite a bit (greatest distress). Pelvic Floor Distress Inventory 20 has been previously validated and widely used for many years. We used the four questions pertaining to constipation as individual parameters for analysis: (i) Do you usually experience pressure in the lower abdomen?; (ii) Do you feel need to strain too hard to have a bowel movement?; (iii) Do you feel you have not completely emptied your bowels at the end of a bowel movement?; and (iv) Do you usually have pain when you pass your stool?. The Rome III Constipation Module consists of 17 questions assessing constipation-related symptoms and is used to classify respondents as having functional constipation (FC) or irritable bowel syndrome with constipation (IBS-C).

2.7 | Statistical analysis

Continuous variables were summarized using means and standard deviations for normally distributed data and medians and inter-quartile ranges for non-normal data, while categorical variables were expressed as proportions. We compared baseline characteristics and ARM results of male and age-matched female patients. For the discrete outcomes, univariate comparisons were made using the Fisher’s exact test or chi-squared test and continuous outcomes were compared using a t-test.
or Wilcoxon rank-sum test, for non-normally and normally distributed data, respectively. We used multivariate logistic regression to estimate the association between demographics, constipation parameters from the PFDI, and ARM parameters and the odds of delayed balloon expulsion. Covariates were selected for the multivariate model based on clinical experience.

3 | RESULTS

3.1 | Demographic features and clinical characteristics of the study population

Two hundred and forty-five consecutive patients—80 men and 165 age-matched women—referred for ARM for constipation were included in the study. Thirty-five patients met Rome III criteria for FC (28 women [17.0%], 7 men [8.8%]), 98 patients met Rome III criteria for IBS-C (71 women [43.0%], 27 men [33.8%]), and 112 patients (66 women [40.0%], 46 men [57.5%]) did not meet the Rome III criteria for IBS-C or FC (Table 1). A greater, but non-significant, proportion of women met Rome III criteria for FC (17.0% women, 8.8% men, \( P = 0.12 \)) and IBS-C (43% women, 33.8% men, \( P = 0.21 \)).

Based on responses to the constipation-specific PFDI-20 question, women reported significantly more severe straining during defecation and incomplete evacuation compared to men (3.09 vs 2.47, \( P = 0.003 \) for straining; 3.14 vs 2.76, \( P = 0.04 \) for incomplete evacuation) (Table 2). In contrast, abdominal pain/discomfort severity and severity of pain with defecation were not significantly different between men and women.

3.2 | Anorectal manometry results

Median resting anal pressure was higher in men compared to women (81.2 vs 75.2 mm Hg, \( P = 0.01 \)) as was the mean squeeze pressure (257.0 vs 170.5 mm Hg, \( P < 0.0001 \)) (Table 3). During simulated defecation, the mean rectoanal pressure gradient, both with and without inflated intrarectal balloon, was significantly more negative (i.e., anal > rectal pressure) in men compared to women (\( P < 0.0001, P = 0.004 \), respectively).

No significant differences were present between men and women in mean volume of first sensation and desire to defecate, however, the maximal tolerable volume was significantly higher in men compared to

| Table 1 | Demographic features and clinical characteristics of the study population |
|---------|-----------------|-----------------|---------|
| Number  | Male            | Female          | P-value |
|         | 80              | 165             | -       |
| Age (SD)| 46.2 (16.8)     | 46.4 (15.2)     | NS      |
| Patients with functional constipation | 7 (8.8%)      | 28 (17.0%)      | .12     |
| Patients with IBS | 27 (33.8%) | 71 (43.0%) | .21 |
| No Rome III diagnosis | 46 (57.5%) | 66 (40.0%) | .01 |

Bold values indicate statistical significance at \( P < 0.05 \).
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3.3 | Balloon expulsion testing

Significantly more women had a prolonged BET using >1 minute and >2 minute as the upper limit of normal compared to men (63.6% vs 48.8%, \( P = .03 \) and 52.7% vs 35.0%, \( P = .01 \), respectively) (Table 3).

3.4 | Dyssynergic defecation subtypes

A dyssynergic pattern of defecation was present in the majority of men (98%) and women (94%) (Table S1). The majority of women demonstrated type II dyssynergia (64.2%), followed by type I (17.6%), type IV (10.3%), and lastly type III (2.4%). Similarly, among men, the type II pattern was found to be the most common (76.3%) followed by type I (12.5%) and type IV (5.0%). No male subject demonstrated type III dyssynergia (Table S1).

3.5 | Dyssynergic defecation subtypes combined with balloon test

The combination of a dyssynergic pattern of defecation during simulated defecation and prolonged BET may predict response to biofeedback therapy.25–27 Our results showed that women were significantly more likely than men to have both a dyssynergic pattern of defecation and a prolonged BET (≥2 minutes) (52.1% vs 37.3%, \( P = .04 \)) (Table 3). Only one woman showed a normal pattern of simulated defecation with a prolonged BET. The majority of the women with abnormal BET showed Type 2 DD (52.8%), followed by Type 1 (62.1%), Type 4 (52.9%), and lastly Type 3 (25.0%) (Table S2). The majority of male patients with prolonged BET were found to have a Type 2 (39.3%) pattern of dyssynergia, followed by both Type 4 (50.0%) and Type 1 (20.0%).

3.6 | Predictors of normal BET

After multivariable adjustment for confounders, male gender was the only independent predictor of a normal balloon expulsion test (OR: 0.48, 95% CI: 0.27-0.86, \( P = .01 \)) (Table 4). Age, presence of DD by

### TABLE 2  Symptom differences among gender and chronic constipation types

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean PFDI score for lower abdominal pressure</td>
<td>2.09 (1.59)</td>
<td>2.21 (1.57)</td>
<td>.59</td>
</tr>
<tr>
<td>Mean PFDI score for straining</td>
<td>2.47 (1.58)</td>
<td>3.09 (1.27)</td>
<td>.003</td>
</tr>
<tr>
<td>Mean PFDI score for incomplete evacuation</td>
<td>2.76 (1.47)</td>
<td>3.14 (1.14)</td>
<td>.04</td>
</tr>
<tr>
<td>Mean PFDI score for painful defecation</td>
<td>1.13 (1.53)</td>
<td>1.57 (1.65)</td>
<td>.08</td>
</tr>
</tbody>
</table>

|                      | Median resting anal pressure (mm Hg) | 81.2 (24.1) | 75.2 (26.3) | .01          |
| Mean squeeze pressure (mm Hg) | 257.0 (92.4) | 280.0 (2249) | <.0001       |
| Mean volume needed for RAIR (mL) | 31.1 (23.0) | 28.0 (2249) | .31          |
| Mean rectoanal pressure differential (mm Hg) | −106.7 (49.5) | −71.1 (41.2) | <.0001       |
| Mean rectoanal pressure differential with inflated balloon (mm Hg) | −11.0 (48.3) | 13.3 (67.1) | .004         |
| Median defecatory index | 0.17 (0.27) | 0.27 (0.37) | .30          |
| Median defecatory index w/inflated balloon | 1.01 (0.62) | 1.57 (1.27) | .0002        |
| Mean percent anal relaxation with defecation | 6.6 (21.2) | 6.0 (20.3) | .81          |
| Mean percent anal relaxation with defecation (balloon inflated) | −5.3 (23.3) | −9.3 (34.9) | .35          |
| Number of patients with impaired anal relaxation (≤20%) | 54 (70.1%) | 110 (78.6%) | .19          |
| Mean volume of first sensation (mL) | 35.1 (21.0) | 30.7 (16.5) | .08          |
| Mean volume for desire to defecate (mL) | 78.8 (30.2) | 76.0 (32.7) | .52          |
| Mean volume for urgency (mL) | 115.2 (36.4) | 103.4 (33.5) | .03          |
| Number with prolonged balloon expulsion (1 minute) | 39 (48.8%) | 105 (63.6%) | .03          |
| Number with prolonged balloon expulsion (2 minutes) | 28 (35.0%) | 87 (52.7%) | .01          |
| Any dyssynergic defecation type | 75 (93.8%) | 162 (98.2%) | .24          |
| Meeting criteria for biofeedback (both by ARM + prolonged BET ≥2 minutes) | 28 (37.3%) | 86 (52.1%) | .04          |

Bold values indicate statistical significance at \( P < 0.05 \).
<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds of prolonged BET (±2 minutes)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>0.48 (0.27-0.86)</td>
<td>.01</td>
</tr>
<tr>
<td>Age</td>
<td>1.00 (0.98-1.01)</td>
<td>.72</td>
</tr>
<tr>
<td>Any dyssynergia (types 1-4)</td>
<td>0.52 (0.15-1.77)</td>
<td>.30</td>
</tr>
<tr>
<td>Mean resting anal pressure</td>
<td>1.00 (1.00-1.00)</td>
<td>.60</td>
</tr>
<tr>
<td>High level of painful defecation</td>
<td>1.33 (0.68-2.60)</td>
<td>.41</td>
</tr>
<tr>
<td>High level of incomplete evacuation</td>
<td>0.56 (0.28-1.11)</td>
<td>.10</td>
</tr>
<tr>
<td>High level of straining</td>
<td>1.16 (0.60-2.25)</td>
<td>.66</td>
</tr>
<tr>
<td>High level of lower abdominal pain/pressure</td>
<td>1.21 (0.69-2.13)</td>
<td>.51</td>
</tr>
<tr>
<td>IBS-C</td>
<td>0.91 (0.50-1.67)</td>
<td>.76</td>
</tr>
<tr>
<td>Functional constipation</td>
<td>0.70 (0.31-1.59)</td>
<td>.40</td>
</tr>
</tbody>
</table>

ARM, resting pressure, Rome diagnosis, and constipation symptom severity were not associated with abnormal BET.

### 3.7 | Anorectal manometry in irritable bowel syndrome-constipation

Men fulfilling the Rome III Criteria for IBS-C had higher median resting anal pressures and mean squeeze pressures compared to men who did not fulfill the criteria for IBS-C (86.1 vs 75.9 mm Hg, P=.002, 286.2 vs 242.1 mm Hg, P=.04, respectively) (Table S3). In contrast, other parameters were similar in men who did and did not fulfill Rome III criteria for IBS-C. Women fulfilling Rome III Criteria for IBS-C were more likely to report more severe incomplete and painful evacuation (P=.006 for incomplete evacuation, 0.05 for painful defecation) while women fulfilling Rome III Criteria for IBS-C were more likely to complain of lower abdominal pain/pressure (P<.0001). Men and women were similar in terms of severity of abdominal pain and painful defecation. However, women with CC were more likely to report more severe symptoms of incomplete evacuation and painful evacuation (Table 2).

### 4 | DISCUSSION

Current guidelines recommend ARM and BET be performed in patients with CC who fail to respond to laxatives to exclude DD. However, previous studies of ARM in constipated subjects have focused primarily on women rather than men, with only two studies to date including both men and women with CC. In one of these studies, 67 men were compared to 340 women, and in the second, only 36 men were compared to 209 women.

To the best of our knowledge, our current study includes the largest cohort of men with CC presenting for ARM. We found sex-based differences in pelvic floor pathophysiology and rectal symptoms in patients with CC. Specifically, we found that men with CC were significantly less likely to have DD by BET, ARM, and the combination of BET and a dyssynergic pattern on ARM compared to age-matched women with CC. Similar to prior studies on healthy men, men with CC had significantly higher resting and squeeze pressures, a more negative rectoanal pressure differential gradient, and smaller defecatory index. After multivariate adjustment for potential confounders, male gender was the only predictor of a normal BET.

Similar to previous studies, we found the vast majority of patients with CC demonstrated an abnormal defecatory pattern on ARM during simulated defecation. Our results correspond to previous data that show fewer men with constipation had a prolonged BET. In our study, we found that male gender is the only predictor of a normal balloon expulsion test after controlling for confounders. Therefore, we presume that different manometric parameters and/or patterns between men and women might be considered to diagnose DD rather than using one definition across both groups. Because a prolonged BET is less common in men, an abnormal BET may be more important in the diagnosis of DD in men than women. Although our study did not look at response to biofeedback, we could speculate that the presence of a prolonged BET could be more relevant in men than in women and perhaps could be suggestive of a subset of male patients that would derive greater benefit from biofeedback.

We observed that women have more severe constipation symptoms than men, specifically incomplete evacuation and painful defecation. However, no differences in painful defecation and lower abdominal pressure were seen between the two groups. Similar results were seen in a previous study which found that women reported feelings of incomplete evacuation, infrequent bowel movements, straining, and abdominal fullness more commonly than men, although these differences were not significant.

Some of the physiologic differences observed in our data may be related to baseline anatomic differences between the sexes. It is known that men have a greater skeletal muscle mass and a longer anal sphincter compared to women documented by ARM, MR imaging, and 3D-EUS. Additionally, increased anterolateral abdominal wall musculature in men compared to women may allow for increased abdominal pressure during defecation. Women may also have altered anorectal parameters secondary to hormonal changes associated with menopause and childbirth.

We acknowledge several limitations which could affect the interpretation of the results. Firstly, this study employed a cross-sectional design, and causation cannot be clearly ascertained. Specifically, we are unable to determine with certainty whether sex was the driver of the physiologic and symptomatic changes seen in our population or a reflection of the changes seen in our specific population. Along these lines, we should also note the inherent referral bias to a tertiary care center, which may have led to a greater rate of diagnosing DD in our study population and thus our findings may not be representative of constipated patients in the community. However, those patients with severe CC who seek care at tertiary centers and undergo ARM reflect those who are most likely to seek care and potentially have the most severe disease burden. Additionally, we used specific questions from the PFDI-20 which were applicable to constipation to define symptom...
severity. We acknowledge that the instrument as a whole was validated in women, but the individual questions used in our study do not reflect an overall construct but rather specific symptoms and are relevant to men as well. Lastly, we lack some data related to the concomitant confounders that may affect anorectal function such as obstetric history, structural disease, and psychiatric comorbidities. Nevertheless, our study benefitted from a relatively large sample size, particularly the large number of male patients, utilization of 3D high-resolution ARM, and the assessment of symptom severity using validated questionnaires.

In conclusion, this is the largest comprehensive study of men with CC using HD-ARM. Our data suggest that there are significant physiologic and symptomatic differences between the sexes. We also propose that the clinical interpretation of ARM could benefit from sex-specific standards in order to prioritize the referral of appropriate patients for pelvic biofeedback therapy.

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DISCLOSURE

No competing interest declared.

AUTHOR CONTRIBUTION

AL planned and designed the research study; WH contributed to data collection, MZ analyzed the manometric data; JN and KS solved the discrepancies in the manometric data; KS conducted the statistical analysis; MZ, JN, AL, KS, BK drafted the manuscript; all authors approved the final version of the article, including the authorship list.

REFERENCES


SUPPORTING INFORMATION

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