Systematic evaluation of cough-anorectal pressure responses in health and in fecal incontinence: A high-resolution anorectal manometry study

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Abstract

Background: Anorectal manometry is the most commonly performed test of anorectal function. The cough-anorectal response is frequently assessed as part of a routine manometric investigation but has not previously been the subject of detailed analysis. This study systematically examined anorectal pressure responses to cough in health and evaluated the impact of parity and symptoms of fecal incontinence (FI) on measurements.

Methods: High-resolution anorectal manometry (HR-ARM) traces from nulliparous (n = 25) and parous (n = 25) healthy volunteers (HV: aged 41, range 18-64), and 57 parous patients with FI (age 47, range 28-72) were retrospectively reviewed. Cough-anorectal pressure responses were analyzed between groups by qualitative and quantitative approaches.

Key results: In health, traditional anal pressure measurements ("rest" and "squeeze") were similar between nulliparous and parous women. In contrast, incremental anal-rectal pressure difference during cough significantly differed: nulliparous 42 mm Hg (95% CI: 21-64) vs. parous 6 mm Hg (−14-25), P < 0.036. This measure also differed significantly between nulliparous HVs and patients with FI (−2 mm Hg (95% CI: −15-12), P < 0.001), but not between parous HVs and FI. Qualitatively, a color-contour trace resembling a "spear" in the upper anal canal was observed uniquely in FI. Of 25 patients with normal anal function by traditional measures, cough parameters were abnormal in 52%.

Conclusions and inferences: Novel HR-ARM measures during coughing revealed differences in anal function between nulliparous and parous HV, and patients with FI, which were not detected by traditional measures. Cough-anorectal measurements may improve manometric yield, though clinical utility would require assessment by longitudinal studies.

Keywords: cough reflex, fecal incontinence, high-resolution anorectal manometry
Anorectal manometry is the principal diagnostic tool to assess anal sphincter dysfunction in fecal incontinence (FI). Anal resting pressure, a primary indicator of internal anal sphincter function, and voluntary squeeze increment pressure, a measure of external anal sphincter and likely puborectalis contractility, are the most recognized and consistently reported measures of anal function. However, although mean resting pressures and squeeze increments are generally regarded as being reduced in FI compared to healthy subjects, only approximately one-third of individual patients have anal hypotension, and only two-thirds of patients have voluntary anal hypocontractility. Accordingly, for such a high proportion of symptomatic individuals to exhibit "normal" function, either there are suprasphincteric factors of equal or greater importance for continence than anal barrier function (eg, rectal sensation, compliance, stool form, and volume etc.), or traditional measures (rest and squeeze) lack specificity to have dependable diagnostic value. Indeed, the limited utility of these measures to distinguish between health and disease has hindered their acceptability as clinically meaningful measures of anal function for decades.

High-resolution anorectal manometry (HR-ARM), with improved spatiotemporal resolution, may allow for assessment of other, or more subtle features of anorectal function including visualization of dynamic events and simultaneous pressure measurement at multiple levels. Novel measures may enhance diagnostic value and utility of the technique. For example, several guidelines and best practice documents advocate assessment of anorectal pressure responses to cough as part of the manometry protocol. Indeed, 83% of 107 centers responding to an international survey of manometry practice reported that they routinely performed a cough maneuver. However, despite its perceived simplicity, the method for analysis and reporting of cough varied widely, with most respondents (42%) reporting only qualitative impression of muscle recruitment. Of quantitative measures, maximum anal pressure was most common (28/89 centers or 31%).

The involuntary external anal sphincter contractile response to cough is mediated by a spinal reflex and may be observed during other activities which increase intra-abdominal pressure including sneezing and postural changes, or inflating a rectal balloon. A "normal" cough response on manometry has a measurable increase in anal pressure, the duration, and amplitude of which is believed to exceed the increase in cough-generated rectal pressure, so that anal sphincter barrier function is maintained despite the intra-abdominal/intra-rectal pressure challenge. A "post-cough relaxation" or drop in anal resting pressure following a sudden increase in abdominal pressure by coughing or by blowing up a balloon may be seen in some individuals and is akin to the "early relaxation" pattern observed by Gowers in response to mucosal irritation during coughing.

While cough-anorectal pressure responses have been documented previously, no study has applied HR-ARM to qualitatively and quantitatively study changes with parity (in health and with disease (fecal incontinence). This was the aim of the current study through systematic, retrospective analysis of HR-ARM recordings.

### Key points
- Anorectal manometry evaluates anal sphincter function at rest and during squeeze or coughing. Despite being performed routinely, the cough-anorectal pressure response is yet to be studied systematically using high-resolution manometry.
- Qualitative and quantitative evaluation of cough pressure revealed important differences between nulliparous and parous healthy women and patients with fecal incontinence, which were not appreciated by traditional metrics (resting and squeeze).
- An abnormal cough-anorectal pressure response may represent more subtle anal sphincter dysfunction, which is influenced by parity.

## METHODS

### Study population

### Healthy volunteers (HV)

Volunteers were recruited by advertisement between 2012 and 2013 and had no history of significant gastrointestinal disease. All had a St Marks incontinence score ≤5 and Cleveland Clinic Constipation Score ≤8. Exclusion criteria were pregnancy or lactation, history of diabetes, cardiovascular, renal or hepatic disease. HR-ARM recordings were scrutinized, and only studies that incorporated at least one cough maneuver were considered for inclusion. Ethical approval was provided by Queen Mary University Research Ethics Committee (ref QMREC 2010/74; QMREC 2013/12) and written informed consent was provided by all volunteers. Results of other HR-ARM measurements from this cohort have been reported on previously.

### Patients

Consecutive parous, female patients attending The Royal London Hospital GI Physiology Unit between January 2018 and December 2018 for routine investigation of fecal incontinence were considered for inclusion. Patients were included if they had a St Marks incontinence score >10. Patients referred for a primary presenting symptom of constipation/evacuation disorder, or for symptoms of prolapse, anal fistula, or cancer were excluded. Further exclusion criteria were history of diabetes or inflammatory bowel disease, known neurological disease, and any anal or pelvic floor surgery (except...
vaginal hysterectomy and primary sphincter repair in the case of 3rd or 4th degree tears sustained during childbirth). For parous groups to be comparable for age, all patients over the age of 72 years were deselected (n = 6) prior to further analysis.

All subjects (HVs and patients) underwent HR-ARM and assessment of rectal sensation to balloon distension. In addition, all patients with FI (but not HV) also underwent endo-anal ultrasonography and a proportion (36/57, 63%) underwent defecography. All tests were performed and interpreted in accordance with departmental protocols. During defecography, as part of the standardized protocol, maintenance of continence was evaluated following insertion of barium contrast, both during transfer of the patient to the commode, and also under fluoroscopy on instruction to cough.

2.2 | HR-ARM

2.2.1 | Technical specifications and test procedure

All participants underwent investigation using a 12F solid-state catheter (UniTip: UniSensorAG, Attikon, Switzerland) incorporating 12 uni-directional pressure transducers each embedded within a silicone gel cuff. Prior to the study, the catheter was immersed in tepid water for at least 3 minutes to pre-wet sensors, which were then zeroed. Data acquisition and visualization were performed using a commercially available manometric system (Solar GI HRM V.9.1, Medical Measurement Systems, Enschede, The Netherlands). Data were generated at 10 Hz. Manometry was performed using a ratified protocol.

2.2.2 | Cough selection

Each HR-ARM trace (irrespective of health or disease status) was examined for trace quality and presence of single, discrete cough (as opposed to multiple, rapid coughs, which are frequently observed). A study was included in the final analysis if: (a) at least one single cough had been performed, (b) there were discernible and distinct anal and rectal pressure areas, and (c) “traditional” resting and squeeze pressures could be measured. Traces with artifacts affecting the quality of the recording were excluded. When two coughs had been performed as per protocol, the first single, analyzable cough was used for analysis.

2.2.3 | Development of measures

Qualitative and quantitative assessment of each cough were performed independently by two practitioners with previous experience in performing and analyzing HR-ARM (AR and KG). Measures were first developed in the healthy cohort and subsequently applied to the FI group.

For qualitative assessment of cough morphology, a “standard view” of the cough was created by taking a 15-second window surrounding the cough and setting the pressure scale from −5 to 140 mm Hg. Cough morphology was determined by the “shape” of the pressure contour and the perceived temporal relationship between rectal and anal pressure changes. Images were reviewed offline and disputes resolved through discussion. During online analysis, the period immediately after each cough was inspected and a “post-cough relaxation” deemed present if there was a noticeable drop in pressure or shortening of anal canal length. The e-sleeve function was used to highlight areas of interest in the rectum or anal canal region. The following quantitative parameters were directly derived (Figure 1):

- automated, system-generated values for pre- and post-cough anal resting pressure and pre-cough rectal resting pressure, representing the mean of the highest pressure measured at any level within the e-sleeve area of interest;
- anal and rectal pressure durations, by adjusting vertical borders of the e-sleeve box to correspond to the start and end of the pressure peak produced by coughing using the composite line pressure graph for reference;

![FIGURE 1](image-url) Quantitative measurements of the cough-anorectal response. (A) rectal resting pressure, (B) pre-cough resting pressure, (C) maximum rectal pressure, (D) Maximum anal pressure, (E) post-cough pressure. Solid arrows: anal and rectal pressure duration; Dashed lines: anal and rectal increment from rest
• maximum pressure during cough and maximum pressure increment during cough for rectal and anal peaks.

The following were derived offline:

• absolute anal-rectal pressure difference (maximum anal pressure during cough minus maximum rectal pressure during cough);
• anal-rectal duration difference (anal pressure duration minus rectal pressure duration);
• incremental anal-rectal pressure difference (maximum anal increment during cough minus maximum rectal increment during cough). This measure describes the “excess” sphincteric pressure generated once the abdominal pressure rise (“cough effort”) has been accounted for.

Traditional measures of anal function (resting pressure and squeeze increment) were also evaluated in all subjects, as previously described.18

2.3 | Statistical analysis

Values were expressed as means with 95% confidence intervals. The 5th and 95th percentiles in healthy parous and nulliparous women were calculated to define upper and lower limits of normality for resting pressure, squeeze increment, and cough parameters. Differences between groups were analyzed using ANOVA with Bonferroni post hoc analysis for multiple comparisons. Independent Kruskal-Wallis with Bonferroni correction was used if homogeneity of variance was violated. A P value <.05 was considered significant. All statistical analyses were conducted using SPSS version 26 (IBM Corp, Armonk, NY, USA).

3 | RESULTS

3.1 | Participants

3.1.1 | Healthy volunteers

Of 66 healthy female volunteers, 50 subjects (median age: 42 years, range 18-64) had at least one interpretable cough. Numbers of parous and nulliparous women were equal. Nulliparous women were significantly younger that parous women (F(1,48) = 11.08, P = 0.002) (Table 1).

3.1.2 | Patients

Of 137 incontinent parous women attending the department within the study period, 57 met inclusion and exclusion criteria. Median age was 43 years (range 28-72), with median number of births being 2 (range: 1-7). In total, 86% reported some form of insult to the perineal or sphincteric region during at least one delivery (this included perineal tears, episiotomies, and forceps). Overall, 51% had either a forceps-assisted delivery or sustained a 3rd or 4th degree tear on at least one occasion. Three women (5.2%) had only given birth by cesarean section, and only 7% (4/57) had had vaginal deliveries without complications. St Marks incontinence score ranged from 11 to 22 (median 16). With regard to presenting symptoms, 49% of patients had passive incontinence and 54% had urge incontinence (12% both passive and urge symptoms). Fifty-eight percent of patients also reported fecal urgency and 33% complained of other symptoms (such as evacuatory difficulties).

On endo-anal ultrasound, an isolated IAS abnormality was identified in 4/57 (7%), while 29/57 (51%) had an isolated EAS abnormality. Combined IAS and EAS abnormalities were found in 13/57 (23%). Sphincter morphology was normal in 11/57 patients (19%). Defecography was performed in 36/57 individuals. There was evidence of neostool leakage either passively on transfer to commode, or on instruction to cough in 23 patients (64%). At least one significant abnormality29 was reported in 47% (large and/or retaining rectocele in 12, obstructing intussusception in 4, and non-relaxing pelvic floor in 1). Overall, 22% had both leakage and a structural abnormality; 8% had no leakage or structural abnormality (normal defecography or functional deficit only).

3.2 | HR-ARM

3.2.1 | Cough-anorectal response: Qualitative analysis

By examination of all cough-anorectal responses (ie, both in health and in patients with FI), qualitative assessment identified six “prototype” cough morphologies, designated: (a) “teardrop”, (b) raindrop, (c) staccato, (d) diamond, (e) spear, (f) spear (upper) (Figure 2). The teardrop shape was the most common in health (54% overall; 60% in nulliparous and 48% in parous women) and in FI (37%). Spear or spear (upper) morphology was significantly more common in the FI group (16/57, 28%) than in healthy women (3/50, 6%; χ²; P = 0.0044). Spear (upper) was seen only in the fecal incontinence group (14%). Inspection of line plots from individual sensors in traces depicting a “spear (upper)” morphology suggested attenuated or absent contraction in the distal part of the anal canal (Figure 3). This was observed despite an overall pressure rise within the anal canal. Post-cough relaxation was observed in 64.0% of HV (32/50) and 64.2% of patients (36/56) The presence/absence of relaxation could not be evaluated in one individual for technical reasons.

3.2.2 | Quantitative analysis

Healthy subjects

Standard pressure measures. Mean resting pressure was 68 mm Hg (SD: 19 mm Hg; range: 34-112 mm Hg) and mean squeeze increment
was 183 mm Hg (SD: 79; range: 43-387). Overall, the lower limit of normal (LLN) for resting pressure (5th percentile) was 41 mm Hg and LLN for squeeze increment was 51 mm Hg.

Cough-anorectal responses. During coughing, a measurable increase in rectal pressure (102 mm Hg, SD 36) occurred in all healthy subjects with a concomitant increase in anal pressure (186 mm Hg, SD 60). Maximum anal pressure during cough was higher than maximum rectal pressure during cough in 49/50 subjects (98%). Anal pressure duration (2.13 seconds, SD 0.94) was also longer than the rectal pressure duration (1.03 seconds, SD 0.35) in 49/50 subjects. Maximum anal increment during cough (113 mm Hg, SD 58) was greater than maximum rectal increment during cough (90 mm Hg, 33) in 29/50 subjects.

Overall, the mean absolute anal-rectal pressure difference was 84 mm Hg (SD = 54.4), mean anal-rectal duration difference was 1.1 seconds (SD = 0.89), and mean incremental anal-rectal pressure difference was 24 mm Hg (SD = 52.2). Mean pre-post cough anal resting pressure difference was 9.7 mm Hg (SD = 11.5).

Nulliparous vs. parous healthy subjects

Cough-anorectal responses. No significant difference was found between nulliparous and parous HV groups for maximum rectal pressure during cough, maximum anal pressure during cough, maximum rectal increment during cough, maximum anal increment during cough, rectal pressure duration, or anal pressure duration (P > 0.05), suggesting an equivalent cough effort and anal sphincter contractile response. However, incremental anal-rectal pressure difference was reduced (mean difference −36 mm Hg (95% CI −1.8 to −71.2, P = 0.036) in parous subjects reflecting greater magnitude of rectal incremental pressure and lower anal incremental pressure. Further, in nulliparous women, the incremental anal-rectal pressure difference was positive for 72% (18/25) of subjects (median incremental anal-rectal pressure difference: 31 mm Hg, IQR: −3-76 mm Hg) compared to just 44% (11/25) of subjects in the parous group (median incremental anal-rectal pressure difference: −5 mm Hg, IQR: −32-36; χ², P = 0.045).

Patients

Standard measures. Mean resting pressure was 58 mm Hg (SD: 25 mm Hg; range: 13-115) and mean squeeze increment was

### Table 1

|                      | Nulliparous | Parous | FI  |
|----------------------|-------------|--------|-----|
| n                    | 25          | 25     | 57  |
| Age (years)          | 36 (31-41)α | 46 (42-50)β | 47 (43-50)β |
| 1. Resting and squeeze (routine measures) |             |        |     |
| Resting pressure     | 67 (59-76)  | 69 (62-77)β | 58 (52-65)β |
| Squeeze increment     | 202 (170-234)| 164 (132-197) | 78 (61-95)βα |
| 2. Pre-cough          |             |        |     |
| Pre-cough rectal resting pressure | 15 (11-19) | 11 (6-15) | 12 (11-13) |
| Pre-cough anal resting pressure | 70 (62-79) | 75 (64-86) | 57 (50-63)β |
| 3. Pressures during cough and their duration |             |        |     |
| Maximum rectal pressure during cough | 100 (87-113) | 105 (88-122)α | 82 (72-91)α |
| Maximum rectal increment during cough | 85 (73-97) | 94 (78-110) | 70 (61-79)α |
| Rectal pressure duration (seconds) | 1.0 (0.9-1.1) | 1.0 (0.9-1.2) | 0.9 (0.8-1.1) |
| Maximum anal pressure during cough | 198 (171-224) | 174 (152-197) | 125 (113-136)βd |
| Maximum anal increment during cough | 127 (104-150) | 100 (76-124) | 68 (56-81)βα |
| Rectal pressure duration (seconds) | 2.3 (1.8-2.7) | 2.0 (1.7-2.3) | 1.5 (1.3-1.8)α |
| 4. Post-cough pressures (relaxation) |             |        |     |
| Post-cough anal pressure (n = 56) | 59 (53-66) | 67 (58-76) | 48 (41-54)αβ |
| 5. Derived measures from above |             |        |     |
| Absolute anal-rectal pressure difference | 98 (73-123) | 70 (53-87) | 43 (30-56)βα |
| Incremental anal-rectal pressure difference | 42 (21-64)α | 6 (~14-25) | −2 (~15-12)β |
| Anal-rectal duration difference (seconds) | 1.2 (0.8-1.7) | 1.0 (0.7-1.2) | 0.6 (0.4-0.8)α |
| Pre-post cough anal pressure difference (n = 56) | 11 (6-16) | 8 (4-12) | 9 (7-12) |

αNulliparous vs. Parous P < 0.05.
βFI vs. Nulliparous P ≤ 0.01.
γFI vs. Nulliparous P ≤ 0.05.
δFI vs. Parous P ≤ 0.001.
εFI vs. Parous P < 0.05.
78 mm Hg (SD: 65 mm Hg; range: 5-339: Table 1). Group analysis showed that resting pressure did not differ between health and FI (Figure 4), but mean squeeze increment was significantly lower compared to both parous and nulliparous HVs (78 vs. 164 and 202 respectively, $P < 0.001$). Overall, using the London Classification, 11 patients (18%) had anal hypotension with normal contractility, 19 (33%) had anal normotension with hypocontractility, and three (5%) had combined anal hypotension with anal hypocontractility (Figure 5).

**Cough-anorectal responses.** Like healthy volunteers, all patients had measurable changes in rectal and anal pressures during coughing. However, maximum anal pressure during cough was higher than maximum rectal pressure during cough in only 45/57 patients (78.9%) ($P = 0.0025$ vs. HV [98%]), and anal pressure duration was longer than the rectal pressure duration in 45/57 patients (78.9%) ($P = 0.0025$ vs. HV [98%]). Group analysis showed that between nulliparous women and FI, there were no significant differences between rectal pressures before, during or after coughing (neither in absolute, increment nor duration measures). However, between parous HV and FI, incontinent women generated a lower maximum rectal pressure during cough (82 vs. 105, $P = 0.027$) and lower maximum rectal increment during cough (70 vs. 94, $P = 0.013$).

Pre- and post-cough anal resting pressures were similar between groups. However, maximum anal pressure during cough (125 mm Hg, SD = 44) and maximum anal increment during cough (68 mm Hg, SD = 47) were lower in FI than in health ($P < 0.05$). Nulliparous women had greater maximum anal pressure during cough (198 vs. 125 mm Hg, $P = 0.001$) with anal pressurization being maintained for longer compared to that in incontinent women (anal pressure duration: 2.3 vs. 1.5 seconds $P = 0.01$). Further, the mean anal-rectal duration difference in nulliparous women was twice that of FI.
of incontinent women (1.2 vs. 0.6 seconds, $P \leq 0.01$). Maximum anal increment during cough was also greater in nulliparous women (127 vs. 68, $P \leq 0.001$) as was the incremental anal-rectal pressure difference (42 vs. -2 mm Hg, $P \leq 0.001$). The proportion of incontinent women with a positive increment difference (44%, 25/57) was less than seen in nulliparous women ($\chi^2, P = 0.019$). Between parous healthy women and incontinent patients, maximum anal pressure during cough (174 vs. 125 mm Hg, $P \leq 0.001$) and maximum anal increment during cough (100 vs. 68 mm Hg, $P \leq 0.05$) were greater in health. In contrast, there were no differences in duration of rectal or anal pressure increases between these groups and incremental anal-rectal pressure changes were not significantly different (mean difference $-7.399$ (-36.8-22.0), $P = 1.000$).

### 3.2.3 Clinical utility of cough measures

Twenty-five (43.9%) patients had no disorder of anal tone or contractility by "traditional" measures (Figure 5). Of these 25 individuals, 52% had either abnormal qualitative (2/25) or, based on values outside of the normal range (Table 2), abnormal quantitative (10/25) cough parameters. One patient had both qualitative and quantitative abnormalities. This translated to 22.8% of the incontinent group as a whole, or just under 1 in 4, with "isolated" sphincter dysfunction during coughing.

Among patients with normal anal contractility, 40% (14/35) had a negative incremental anal-rectal pressure difference, whereas in patients with hypocontractility, 77% (17/22) had negative incremental anal-rectal pressure difference ($\chi^2 (1, 50), P = 0.006$). Overall, a negative incremental anal-rectal pressure difference was associated with a higher prevalence of post-cough relaxation ($\chi^2 P = 0.038$) and greater occurrence of involuntary leakage on defecography (ie, 15 of 23 (65%) patients with observed leakage had a negative incremental anal-rectal pressure difference, $\chi^2$).
The proportion of subjects with abnormal cough response (31/57) did not differ by ultrasound outcome ($\chi^2 (1, 57), 0.0001, P = 0.991$).

4 | DISCUSSION

To our knowledge, this study is the first to systematically compare anorectal pressure changes during coughing in healthy nulliparous and parous women and in patients with FI using HR-ARM.

The main findings of this study were:

1. considering the anal canal as a single functional unit, we were able to measure some degree of anal sphincter response to cough in all subjects;
2. qualitative identification of six “prototype” morphologies of the cough-anorectal response. The most common in both health and disease was a “teardrop” appearance, characterized by a longer duration of anal compared to rectal pressurization. In contrast, a “spear” or “spear (upper)” morphology were both more common in FI than health, manifest as a more simultaneous rectal and anal response; spear (upper) was unique to the FI group, and was characterized by attenuated or absent contraction in the distal part of the anal canal;
3. maximum anal pressure and duration of the pressure response were greater in the anal canal than in the rectum in 98% of HV, but in only 79% of patients ($P = 0.0025$);
4. the maximum anal increment during cough exceeded the rectal increment in a proportion (58%) of healthy individuals, of whom the majority (72%) were nulliparous (compared to 44% of both parous HV and FI patients);
5. incremental anal-rectal pressure difference varied significantly between nulliparous and parous HV, but no such difference was found between parous HV and FI;
6. maximum anal pressure, maximum anal pressure increment, and the duration of the anal pressure response on coughing were significantly lower in FI than in health; 
7. in patients with FI, 25/57 (43.9%) had no disorder of anal tone or contractility using traditional measures (rest and squeeze), but 13 of these patients with apparently "normal" anal function had qualitative or quantitative abnormalities (or both) using new cough measures (representing ~1 in 4 of the group as a whole).

These findings merit discussion with reference to previous literature. In healthy individuals and individuals with high spinal lesions, the anal response to a rise in abdominal pressure is increased anal sphincter EMG activity and, on manometry, greater maximum anal pressure compared to intra-rectal pressure.17 Our results are consistent with these findings, since 98% of healthy volunteers maintained (theoretically) an efficient barrier during cough, based on the maximum anal and rectal pressure difference alone. Nevertheless, a significantly smaller proportion of FI patients demonstrated the same response (78.9%).

Early manometry studies identified reduced anal resting pressure in two-thirds of incontinent patients;21,32 however, other studies have shown that a subject with low resting pressure may also be perfectly continent,9 demonstrating the overlap between health and disease. In the current study, anal resting pressure was the same between all groups, despite nulliparous subjects being significantly younger compared to asymptomatic and symptomatic parous women. Voluntary squeeze increment discriminated between continent and incontinent subjects, but failed to show a difference between nulliparous and parous healthy volunteers. This is despite consideration of parity being reported as essential for correct interpretation of manometric results,18,33 though findings vary according to equipment used.24,35 Overall, 43.9% (25/57) of incontinent patients showed no evidence of impaired sphincter function based on traditional measures alone. However, it may be that broad measures of rest and squeeze are too "blunt" as tools to identify sphincter dysfunction in all patients, and that including analysis of the cough maneuver may enable identification of a, perhaps more subtle, functional deficit. Indeed, of these 25 individuals, cough metrics were abnormal in 52% (or ~1/4 of all FI patients studied).

Other studies have addressed the sphincteric pressure response to coughing using maximum anal pressure during cough as the main outcome21,26,37 and this reflects clinical practice.4 Most notably, Mazor et al21 found that maximum anal pressures during cough were generally lower than maximum anal squeeze pressures in healthy individuals, and that parity was associated with a smaller difference between maximum cough pressure and maximum (absolute) squeeze pressure. Our study did not directly compare the differences between squeeze and cough pressure; however, abnormal cough parameters were common in individuals with hypocontractility based on squeeze increment, demonstrating the inherent relationship between voluntary and involuntary EAS contractility.

Although past manometry guidelines have emphasized the role of the cough response in the identification of patients with neural damage to the sacral reflex arc,13 we remain cautious regarding such interpretation based on the interaction between squeeze and cough pressure alone, without corresponding diagnostic neurophysiological information.

Rather, Meagher et al28 suggested that analysis of cough may offer additional information on EAS contractility above squeeze pressure. Based on the LLNs detailed in Table 2, we identified 22.8% of our incontinent population with isolated cough-related anorectal pressure dysfunction. The LLN for maximum anal pressure in this study (30 mm Hg) was slightly higher than that reported by Gosling,22 who included fewer parous than nulliparous healthy subjects, and lower compared to the 43 mm Hg reported by Rasijeff.20 The LLN for maximum anal pressure during cough (94 mm Hg) was higher than in previous studies ranging between 82 and 86 mm Hg.18,21,22 However, studies by Mazor21 and Gosling22 used water-perfused catheters, which register lower pressures during rapid changes in pressure compared to solid-state catheters.20 Mazor21 also reports the 10th, rather than 5th percentile.

Nevertheless, caution should be taken in using maximum pressure as a biomarker for reflex contractility due to variability.

| TABLE 2 Proposed lower limits of normal (5th and 95th percentiles) for cough parameters in health |
|-----------------------------------------------|-----------------|------------------|-----------------|-----------------|-----------------|
| Routine measures | All HV | Nulliparous | Parous | % FI patients below LLN |
|------------------|--------|------------|--------|------------------------|
| n | 50 | 25 | 25 | 25 | 50 |
| Resting pressure | 41.105 | 42.111 | 36.101 | 22.8 |
| Squeeze increment | 51.333 | 61.373 | 48.313 | 38.6 |
| Cough-anorectal response measures | | | | | |
| Maximum anal increment during cough | 30.217 | 36.218 | 12.221 | 1.8 |
| Anal pressure duration (seconds) | 0.76-4.08 | 1.10-4.86 | 0.63-3.69 | 14.0 |
| Incremental anal-rectal pressure difference | (-52)-126 | (-47)-145 | (-53)-127 | 8.8 |
| Anal-rectal duration difference (seconds) | 0.00-3.06 | 0.03-3.85 | (-0.07)-2.4 | 21.1 |

6. maximum anal pressure, maximum anal pressure increment, and the duration of the anal pressure response on coughing were significantly lower in FI than in health; 
7. in patients with FI, 25/57 (43.9%) had no disorder of anal tone or contractility using traditional measures (rest and squeeze), but 13 of these patients with apparently "normal" anal function had qualitative or quantitative abnormalities (or both) using new cough measures (representing ~1 in 4 of the group as a whole).
in each of its component parts. Firstly, differences in anal resting tone shift the "starting line" in favor of one group over another. Second, intra-abdominal pressure transmission to the pelvic floor may artificially increase anal pressures with more intense coughing. The positive relationship between a greater rise in intra-abdominal pressure and subsequent anal pressure increment first suggested by Meagher et al. who showed pelvic floor contraction was proportional to the rise in intra-vesical/intra-abdominal pressure (intensity) generated by cough. Early EMG observations by Melzak and Porter also showed that the amplitude of electrical response to coughing was greatest in patients with more innervated trunk musculature, suggesting this was due to their ability to generate higher intra-abdominal pressure. Finally, the potential to respond reflexively may be dependent on parity.

4.1 | Study limitations

There are several limitations to our study. Firstly, nulliparous women were younger than parous healthy and incontinent women. However, though aging is thought to impact primarily internal anal sphincter tone, we saw no difference in anal resting pressure between groups and hence it is unlikely that aging played a significant role in our findings. Secondly, maximum pressure responses to coughing were lowest in the incontinent group who also had the lowest intra-abdominal/rectal pressure increment indicating that they coughed with the least effort (likely for fear of incontinence). Given the retrospective nature of our study, we were unable to standardize cough effort to maintain a consistent "challenge" to sphincters of all individuals as was achieved in some previous studies. Since lower intra-abdominal pressure rise may lead to smaller degrees of anal sphincter response, ensuring consistency of the challenge produced may be an important consideration in future studies. Thirdly, our observations are based on a small number of available single coughs in a limited number of healthy volunteers. Difficulties in recruitment of healthy volunteers may introduce bias in the selection of subjects and data thus obtained. As far as we know, all asymptomatic volunteers included in this study met the appropriate criteria for healthy volunteers; however, we cannot guarantee the results obtained are representative of all healthy females, particularly with regard to ethnicity and BMI. We took a consistent approach to choosing eligible patients, manometry traces, and single, discrete coughs included in the study to reduce bias. We did not endeavor to compare intra-individual variation in cough response but recognize this to be an important focus of future work given the recommendation that the cough maneuver is repeated in standard manometry protocols.

Finally, our interpretation of qualitative cough morphologies suggests that pressure changes during coughing can vary between distal and proximal parts of the anal canal. Given their polar extremities, these differences may be related to the type of muscle tissue (smooth or striated) that predominates. EMG studies describe the cough response as an external anal sphincter reflex, so the true cough reflex may be expected to occur in the distal or mid anal canal. We observed an attenuated or absent response associated with spear (upper) morphology in some individuals, in whom reflex contraction could be truly absent. However, because high-resolution anorectal manometry is unable to reliably differentiate between puborectalis, internal and external anal sphincter contributions to pressure, we considered the anal canal as a single unit for quantitative measures. We also considered the maximum pressure measurement to be representative of anal response to cough irrespective of the level at which it occurred within the defined sphincteric or rectal area of interest.

4.2 | Potential for clinical application

A key question is whether cough measurements could have future clinical utility, especially since anorectal manometry including the cough challenge already forms part of routine assessment following traumatic childbirth in many parts of the world. While we present evidence of an "additional yield" of abnormal findings using detailed cough metrics in a proportion of patients with FI who had normal standard metrics, a further interesting finding is that we could also detect differences in sphincter function between asymptomatic nulliparous and parous women. Vaginal delivery is a risk factor for fecal incontinence due to mechanical or neurogenic damage imposed upon (predominantly) the striated sphincter muscle; however, there is often a considerable time lag between injury and symptom onset. During this lag period, further insult to pelvic floor function (menopause, subsequent vaginal delivery, persistent straining etc.) may occur. Evidence of subclinical predisposition to pelvic floor weakness and consequent incontinence before symptoms present may allow for preventive measures (such as pelvic floor exercise or Caesarian section) to be taken in at risk individuals. Subclinical neuropathy may also explain persistent anal dysfunction following sphincter repair in a proportion of patients. Accordingly, detailed examination of cough-anorectal pressures suggests that the anal-rectal incremental pressure difference may be able to identify potential subclinical sphincter dysfunction in women following childbirth, even in the absence of symptoms. For a similar cough effort, the anal-rectal incremental pressure difference was significantly lower in parous continent and incontinent women compared to the nulliparous group. Conversely, no such significant difference was observed between parous continent and parous incontinent women. Whether this is a useful biomarker of subclinical injury and future risk would require a longitudinal study.

5 | CONCLUSION

Undoubtedly, the role of HR-ARM in identifying disorders of tone and contractility remains though the need for more intense stratification within normative datasets is recognized. We present a promising...
basis for interpreting cough clinically, though future prospective studies are needed to fully understand its potential. Furthermore, in-depth analysis of the cough-anorectal reflex, an under-utilized yet routinely performed maneuver, appears to have the potential to identify subclinical sphincter dysfunction in parous and in fecally incontinent women compared to asymptomatic nulliparous women. These results present the opportunity to reconsider HR-ARM not only as an “expensive hobby”, but as an important tool for identification of at risk individuals in whom preventive measures may serve to halt progression of subclinical anal dysfunction into life-altering disease. Where FI symptoms are already established, evaluation of sphincter function with a dynamic maneuver like cough, which challenges the sphincter barrier response, may be more clinically valid than static measures.

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AUTHOR CONTRIBUTIONS
AMPR and MS conceived the study design. EVC and AMPR collected study data. AMPR and KGZ analyzed data. AMPR, CK and MS wrote the manuscript. All authors edited the manuscript and approved the final version.

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REFERENCES
1. Liu J, Guaderrama N, Nager CW, Pretorius DH, Master S, Mittal RK. Functional correlates of anal canal anatomy: puborectalis muscle and anal canal pressure. *Am J Gastroenterol*. 2006;101(5):1092-1097.
2. Cheeney G, Remes-Troche JM, Ataluri A, Rao SS. Investigation of anal motor characteristics of the sensorimotor response (SMR) using 3-D anorectal pressure topography. *Am J Physiol Gastrointest Liver Physiol*. 2011;300(2):G236-G240.
3. Mion F, Garros A, Brochard C, et al. 3D high-definition anorectal manometry: values obtained in asymptomatic volunteers, fecal incontinence and chronic constipation. Results of a prospective multicenter study (NOMAD). *Neurogastroenterol Motil*. 2017;29(8):e13049.
4. Carrington EV, Heinrich H, Knowles CH, Rao SS, Fox M, Scott SM. Methods of anorectal manometry widely in clinical practice: results from an international survey. *Neurogastroenterol Motil*. 2017;29(8):e13016.
5. Bharucha AE, Fletcher JG, Harper CM, et al. Relationship between symptoms and disordered continence mechanisms in women with idiopathic faecal incontinence. *Gut*. 2005;54(4):546-555.
6. Gooneratne ML, Scott SM, Lunniss PJ. Unilateral pudendal neuropathy is common in patients with fecal incontinence. *Dis Colon Rectum*. 2007;50(4):449-458.
7. Mundet L, Cabib C, Ortega O, et al. Defective conduction of anorectal afferents is a very prevalent pathophysiological factor associated to fecal incontinence in women. *J Neurogastroenterol Motil*. 2019;25(3):423-435.
8. Kumar D, Hallan RI, Womack NR, O’Connell PR, Miller R. Measurement of anorectal function. In: Kumar D, Waldron D, Williams N, eds. *Clinical Measurement in Coloproctology*. Great Britain: Springer-Verlag; 1991:37-66.
9. Azpiroz F, Enck P, Whitehead WE. Anorectal functional testing: review of collective experience. *Am J Gastroenterol*. 2002;97(2):232-240.
10. Pehl C, Seidl H, Scalericio N, et al. Accuracy of anorectal manometry in patients with fecal incontinence. *Digestion*. 2012;86(2):78-85.
11. Carrington EV, Heinrich H, Knowles CH, et al. The international anorectal physiology working group (IAPWG) recommendations: standardized testing protocol and the London classification for disorders of anorectal function. *Neurogastroenterol Motil*. 2020;32(1):e13679.
12. Barnett JL, Hasler WL, Camilleri M. American Gastroenterological Association medical position statement on anorectal testing techniques. American Gastroenterological Association. *Gastroenterology*. 1999;116(3):732-760.
13. Rao SS, Azpiroz F, Diamant N, Enck P, Tougas G, Wald A. Minimum standards of anorectal manometry. *Neurogastroenterol Motil*. 2002;14(5):553-559.
14. Swash M, Snooks SJ. Electromyography in pelvic floor disorders. In: Henry MM, Swash M, eds. *Coloproctology and the Pelvic Floor: Pathophysiology and Management*. London: Butterworth and Co; 1985:99.
15. Parks AG, Porter NH, Melzak J. Experimental study of the reflex mechanism controlling the muscle of the pelvic floor. *Dis Colon Rectum*. 1962;5:407-414.
16. Taverner D, Smiddy FG. An electromyographic study of the normal function of the external anal sphincter and pelvic diaphragm. *Dis Colon Rectum*. 1959;2(2):153-160.
17. Sun WM, Read NW, Donnelly TC. Anorectal function in continent patients with cerebrospinal disease. *Gastroenterology*. 1990;99(5):1372-1379.
18. Carrington EV, Brokjaer A, Craven H, et al. Traditional measures of normal anal sphincter function using high-resolution anorectal manometry (HRAM) in 115 healthy volunteers. *Neurogastroenterol Motil*. 2014;26(5):625-635.
19. Gowers R. The automatic action of the sphincter ani. *Proc R Soc London*. 1877:26:77-84.
20. Rasjieff AMP, Withers M, Burke JM, Jackson W, Scott SM. High-resolution anorectal manometry: a comparison of solid-state and water-perfused catheters. *Neurogastroenterol Motil*. 2017;29(11):e13124.
21. Mazor Y, Prott G, Jones M, Kellow J, Ejova A, Malcolm A. Anorectal physiology in health: a randomized trial to determine the optimum catheter for the balloon expulsion test. *Neurogastroenterol Motil*. 2019;31(4):e13552.
22. Gosling J, Plumb A, Taylor SA, Cohen R, Emmanuel AV. High-resolution anal manometry: repeatability, validation, and comparison with conventional manometry. *Neurogastroenterol Motil*. 2019;31(6):e13591.
23. Vaizey CJ, Carapeti E, Cahill JA, Kamm MA. Prospective comparison of faecal incontinence grading systems. *Gut*. 1999;44(1):77-80.
24. Agachan F, Chen T, Pfeifer J, Reissman P, Wexner SD. A constipation scoring system to simplify evaluation and management of constipated patients. Dis Colon Rectum. 1996;39(6):681-685.

25. Grossi U, Carrington EV, Bharucha AE, Horrocks EJ, Scott SM, Knowles CH. Diagnostic accuracy study of anorectal manometry for diagnosis of dyssynergic defecation. Gut. 2016;65(3):447-455.

26. Vollebregt PF, Rasijeff AMP, Pares D, et al. Functional anal canal length measurement using high-resolution anorectal manometry to investigate anal sphincter dysfunction in patients with fecal incontinence or constipation. Neurogastroenterol Motil. 2019;31(3):e13532.

27. Townsend DC, Carrington EV, Grossi U, et al. Pathophysiology of fecal incontinence differs between men and women: a case-matched study in 200 patients. Neurogastroenterol Motil. 2016;28(10):1580-1588.

28. Palit S, Bhan C, Luniss PJ, et al. Evacuation proctography: a reappraisal of normal variability. Colorectal Dis. 2014;16(7):538-546.

29. Grossi U, Di Tanna GL, Heinrich H, Taylor SA, Knowles CH, Scott SM. Systematic review with meta-analysis: defecography should be a first-line diagnostic modality in patients with refractory constipation. Aliment Pharmacol Ther. 2018;48(11-12):1186-1201.

30. Carrington EV, Grossi U, Knowles CH, Scott SM. Normal values for high-resolution anorectal manometry: a time for consensus and collaboration. Neurogastroenterol Motil. 2014;26(9):1356-1357.

31. Read NW, Harford WV, Schmulen AC, Read MG, Santa Ana C, Fordtran JS. A clinical study of patients with fecal incontinence and diarrhea. Gastroenterology. 1979;76(4):747-756.

32. Neill ME, Parks AG, Swash M. Physiological studies of the anal sphincter musculature in faecal incontinence and rectal prolapse. Br J Surg. 1981;68(8):531-536.

33. Cali RL, Blatchford GJ, Perry RE, Pitts RM, Thorson AG, Christensen MA. Normal variation in anorectal manometry. Dis Colon Rectum. 1992;35(12):1161-1164.

34. Leo CA, Cavazzoni E, Thomas GP, Hodgkinson J, Murphy J, Vaizey CJ. Evaluation of 153 asymptomatic subjects using the anopress portable anal manometry device. J Neurogastroenterol Motil. 2018;24(3):431-436.

35. Oblizajek NR, Gandhi S, Sharma M, et al. Anorectal pressures measured with high-resolution manometry in healthy people—normal values and asymptomatic pelvic floor dysfunction. Neurogastroenterol Motil. 2019;31(7):e13597.

36. Mulak A, Paradowski L. Anorectal function and dyssynergic defecation in different subgroups of patients with irritable bowel syndrome. Int J Colorectal Dis. 2010;25(8):1011-1016.

37. Mion F, Garros A, Subtil F, Damon H, Roman S. Anal sphincter function as assessed by 3D high definition anorectal manometry. Clin Res Hepatol Gastroenterol. 2018;42(4):378-381.

38. Meagher AP, Lubowski DZ, King DW. The cough response of the anal sphincter. Int J Colorectal Dis. 1993;8(4):217-219.

39. Amarenco G, Ismael SS, Lagauche D, et al. Cough anal reflex: strict relationship between intravesical pressure and pelvic floor muscle electromyographic activity during cough. Urodynamic and electrophysiological study. J Urol. 2005;173(1):149-152.

40. Melzak J, Porter NH. Studies of the reflex activity of the external sphincter ani in spinal man. Paraplegia. 1964;1:277-296.

41. Lee HJ, Jung KW, Han S, et al. Normal values for high-resolution anorectal manometry/topography in a healthy Korean population and the effects of gender and body mass index. Neurogastroenterol Motil. 2014;26(4):529-537.

42. Snooks SJ, Setchell M, Swash M, Henry MM. Injury to innervation of pelvic floor sphincter musculature in childbirth. Lancet. 1984;2(8402):546-550.

43. Luniss PJ, Gladman MA, Hetzer FH, Williams NS, Scott SM. Risk factors in acquired faecal incontinence. J R Soc Med. 2004;97(3):111-116.

44. Chaliha C, Kalia V, Stanton SL, Monga A, Sultan AH. Antenatal prediction of postpartum urinary and fecal incontinence. Obstet Gynecol. 1999;94(5 Pt 1):689-694.

45. Laurberg S, Swash M, Henry MM. Delayed external sphincter repair for obstetric tear. Br J Surg. 1988;75(8):786-788.

46. Baslisco G, Bharucha AE. High-resolution anorectal manometry: An expensive hobby or worth every penny? Neurogastroenterol Motil. 2017;29(8):e13125.

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