BMJ Open Gastroenterology

Provocative tests of anal sphincter function correlate with symptoms and subtypes of faecal incontinence

Alexander O'Connor ,[1,2] Donghua Liao,[3] Matthew Davenport,[1,2] Abhiram Sharma,[1,2] Dipesh H Vasant ,[1,4] Niels Klarskov,[5,6] Asbjørn Mohr Drewes,[3] Edward Kiff,[2] John McLaughlin ,[1,7] Karen Telford[1,2]

To cite: O'Connor A, Liao D, Davenport M, *et al*. Provocative tests of anal sphincter function correlate with symptoms and subtypes of faecal incontinence. *BMJ Open Gastroenterol* 2025;**12**:e001600. doi:10.1136/bmjgast-2024-001600

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjgast-2024-001600).

Received 19 September 2024
Accepted 15 January 2025

For numbered affiliations see end of article.

Correspondence to
Dr Alexander O'Connor; alexander.oconnor@manchester.ac.uk

ABSTRACT

Objectives High-resolution anorectal manometry (HRAM) is the established investigation in faecal incontinence (FI). However, provocative tests (functional lumen imaging probe (FLIP) and anal acoustic reflectometry (AAR)) have been proposed as alternatives. This study uniquely explores all three methods in correlation with FI symptoms and subtypes.

Methods This was a prospective observational study of patients with FI attending a tertiary pelvic floor unit between August 2022 and January 2024. Patients underwent HRAM, FLIP and AAR with the order randomised. FI severity was assessed with the Vaizey score and quality-of-life with the Manchester Health Questionnaire.

Results 40 patients (39 women, median age: 62 (range: 38–85)) were recruited with 27 (67.5%) reporting urge FI, 8 (20%) mixed and 5 (12.5%) passive incontinence. FLIP squeeze measurements correlated with the Vaizey score, including incremental squeeze pressure at 40 mL (r_s=−0.412; p=0.008) and 50 mL (r_s=−0.414; p=0.009) and the pressure-diameter volume loop at 50 mL (r_s=−0.402; p=0.011). Incremental squeeze opening pressure with AAR correlated with the Vaizey score (r_s=−0.339; p=0.032). There was no correlation between symptom severity and HRAM parameters, or any parameter and quality-of-life scores. Resting parameters with all three modalities were lower in passive FI: mean resting pressure (HRAM; p=0.010), yield pressure (FLIP; p=0.031) and opening pressure (AAR; p=0.006). With FLIP, there was a trend towards reduced squeeze function in the urge group (pressure-diameter volume loop at 50 mL; p=0.295).

Conclusions FLIP and AAR correlate better with FI symptoms compared with HRAM. Therefore, these provocative tests could be used to guide the management of FI in prospective studies.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ High-resolution anorectal manometry (HRAM) is a standard investigation of faecal incontinence (FI), although conflicting reports exist about its correlation with symptom severity. Recently, provocative tests of anal sphincter function (functional lumen imaging probe (FLIP) and anal acoustic reflectometry (AAR)) have been proposed as complementary tools in the assessment of FI.

WHAT THIS STUDY ADDS

⇒ Both FLIP and AAR correlate with patient-reported FI symptom severity, unlike HRAM. All three modalities at rest can identify differences between the known FI subtypes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The provocative tests of anal sphincter function may be complementary to HRAM in the investigation of FI. With further research, these tools may become established in the investigation and management of FI.

INTRODUCTION

High-resolution anorectal manometry (HRAM) is the current diagnostic tool of choice to investigate the function of the continence mechanism, and it is now widely available in most specialist institutions.[1 2] In the investigation of faecal incontinence (FI), it has demonstrated reduced resting and squeeze pressures compared with continent controls.[3–5] However, HRAM parameters have only a weak correlation with FI symptom severity scores,[6] with a wide variability in measurements and overlap between FI and continent controls.[7] FI is typically classified into the clinical subtypes of urge (the inability to defer defecation), passive (faecal soiling without conscious awareness) or mixed FI. Urge and passive incontinence are typically associated with external and internal anal sphincter dysfunction, respectively.[8] However, there are discordant reports of the differences in HRAM parameters between these subtypes.[8] As a result, there are conflicting recommendations about its clinical utility in routine practice to guide treatment decisions, making the development of a tool that correlates with FI symptom severity and subtypes a desirable ambition.[9–11] While

HRAM relies on the use of a fixed diameter catheter, dynamic provocative tests of the anal sphincter have been proposed as complementary or alternative tools to measure its function.[12] Both functional lumen imaging probe (FLIP) and anal acoustic reflectometry (AAR) measure the resistance of the anal canal during volume-controlled distension of highly compliant bags.[12 13] Resistance to distension has been proposed as the main determinant of sphincter function.[14 15] Therefore, these tools provide unique insights into the properties of the sphincter muscle by assessing its length-tension relationship.[16]

Results with AAR can distinguish continent and incontinent patients while also differentiating between the known FI subtypes of urge, passive and mixed incontinence.[17 18] While AAR is not yet commercially available, limiting generalisability of its findings, FLIP has been studied in several units worldwide. When compared with HRAM, FLIP is better able to discriminate between those with and without FI symptoms, with authors suggesting it may be a more specific test.[19 20] Data from FLIP can also be processed in post-acquisition analysis, and additional novel parameters can be generated that correlate with the degree of anal sphincter injury[16] and the severity of FI.[21]

We hypothesise that these dynamic, provocative tests of anal sphincter function may better correlate with FI symptoms and may be able to identify differences in sphincter function between the known clinical subtypes of FI. This study, therefore, aims to explore the results of each modality (HRAM, FLIP and AAR) in their correlation with patient-reported FI symptom severity and to explore if differences can be identified between the known FI subtypes of urge, passive and mixed.

METHODS

Study design

This prospective observational study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines[22] (online supplemental file 1). Favourable approval from the local research ethics committee was received. Consecutive patients with FI attending for HRAM for suspected anal sphincter dysfunction between August 2022 and January 2024 were prospectively identified and invited to take part in the study. Patients were excluded if they were under the age of 18 as this was a study of adult patients with FI. Those who lacked cognitive capacity were excluded as they were unable to provide informed consent. Patients who were pregnant were excluded. Patients with a diagnosis of active inflammatory bowel disease or a history of anorectal cancer were excluded as these conditions may be the cause of FI, and there was a risk of iatrogenic injury with the insertion of the measurement catheters. All patients provided written informed consent.

All patients with FI were seen by a consultant colorectal surgeon with an interest in pelvic floor disease who elicited a clinical history and performed a physical examination before making a referral for HRAM. After recruitment to the study, demographic and clinical data were recorded including age, gender, medical, surgical and obstetric history, and the nature of FI including the presence of post defecatory faecal leakage. Symptoms of concomitant obstructed defecation included any of the patient perceived difficulty in evacuation, regular digitation a sensation of incomplete emptying or excessive straining.[23] Urge FI was defined as an inability to defer defecation with an awareness of a call to stool. Passive FI was defined as faecal soiling without conscious awareness, while mixed FI was defined as a combination of both.

These three investigations have never been compared with each other before making a formal power calculation impossible. However, previous work with AAR alone demonstrated differences between the known subgroups of FI with a cohort of 50 patients.[24] It was therefore hypothesised that a sample of 40 patients measured with all three modalities may reveal differences between FI subtypes and identify correlations with symptom severity scores.

FI symptom severity

The severity of FI was quantified using patient-reported symptom severity questionnaires. These included the Vaizey score[25] and Manchester Health Questionnaire (MHQ).[26] The Vaizey score is a validated FI-specific patient-reported symptom severity questionnaire with a score of 0 indicating no FI symptoms and a maximum score of 24 indicating the most severe FI symptoms. The MHQ assesses the impact of FI on a patient's quality of life over nine domains. An overall score is generated between 0, representing no impact, and 900 reflecting the most severe impact on quality of life. The MHQ was developed from the established King's Health Questionnaire used to assess the quality of life impact from urinary incontinence.[27] The final five question 'symptom severity' domain was developed from the most cited problems associated with incontinence symptoms in patients. The questions were then adapted in the development of the MHQ to assess FI symptoms. These cause the greatest concern to patients and thus may reflect a subjective assessment of incontinence symptom severity. The results of the Vaizey score, total MHQ score and the symptom severity domain of the MHQ were used to quantify FI symptom severity and their impact on quality-of-life.

High-resolution anorectal manometry

HRAM was performed by an experienced gastrointestinal physiologist. The HRAM catheter used was a water-perfused catheter incorporating 10 circumferential pressor sensors at 0.8 cm intervals with an external diameter of 14 Fr (4.667 mm) (Mui Scientific, Ontario, Canada). Prior to the test, pressure was zeroed at the anal verge with the patient in the left lateral position. A digital rectal examination was performed, and patients were asked to 'squeeze' and 'push' to confirm

their understanding of these instructions. HRAM was then performed according to the standardised London protocol.[11] Mean resting pressure (MRP), maximum squeeze pressure (MSP) and incremental squeeze pressure (ISP) were recorded in mm Hg. The anal canal length was also calculated and defined as the length over which anal canal pressure exceeded rectal pressure by >5 mm Hg, recorded in cm.[28]

Anal acoustic reflectometry

AAR uses a highly compliant polyurethane bag of negligible cross-sectional area (CSA) (collapsed CSA: 0.4 mm^2) and 7 cm in length inserted into the anal canal (online supplemental figure 1). Using a digital signal processor (ED-1932; Knowles Electronics, Illinois, USA), sound waves are transmitted into the bag, and the reflected acoustic impulses are recorded and used to calculate the CSA along the length of the anal canal. The point of minimum CSA is identified and used to calculate measurements of anal canal function (online supplemental figure 2). Pressure is constantly recorded by a transducer (SX30D, Sensym sensor systems).

The technique of an AAR measurement and the observed parameters have been described previously.[29 30] Briefly, at rest, 10 cycles of inflation and deflation are performed. During each cycle, the bag is simultaneously inflated and deflated over 14 s manually using a handheld syringe filled with air. Following this, and after a minimum of 30 s, voluntary squeeze function is assessed, and the patient is asked to squeeze while the bag is inflated over seven seconds, a process repeated five times.

Using the minimum CSA and pressure data, various parameters can be calculated with their clinical significance having been reported previously (figure 1).[12 31] At rest, five parameters can be calculated at the point of minimum CSA: opening pressure (Op, cmH_2O), opening elastance (Oe, cmH_2O/mm^2), closing pressure (Cp, cmH_2O), closing elastance (Ce, cmH_2O/mm^2) and hysteresis (Hys, %). Op is the pressure at which the anal canal just starts to open at rest while Oe reflects the resistance to further distension after opening. Cp and Ce are the pressure the anal canal closes and the resistance, respectively, while Hys reflects the amount of energy dissipated during one cycle of opening and closing. Except for Hys, all parameters have been observed to be lower in patients with FI.[12] Two similar parameters are calculated during the voluntary contraction: squeeze opening

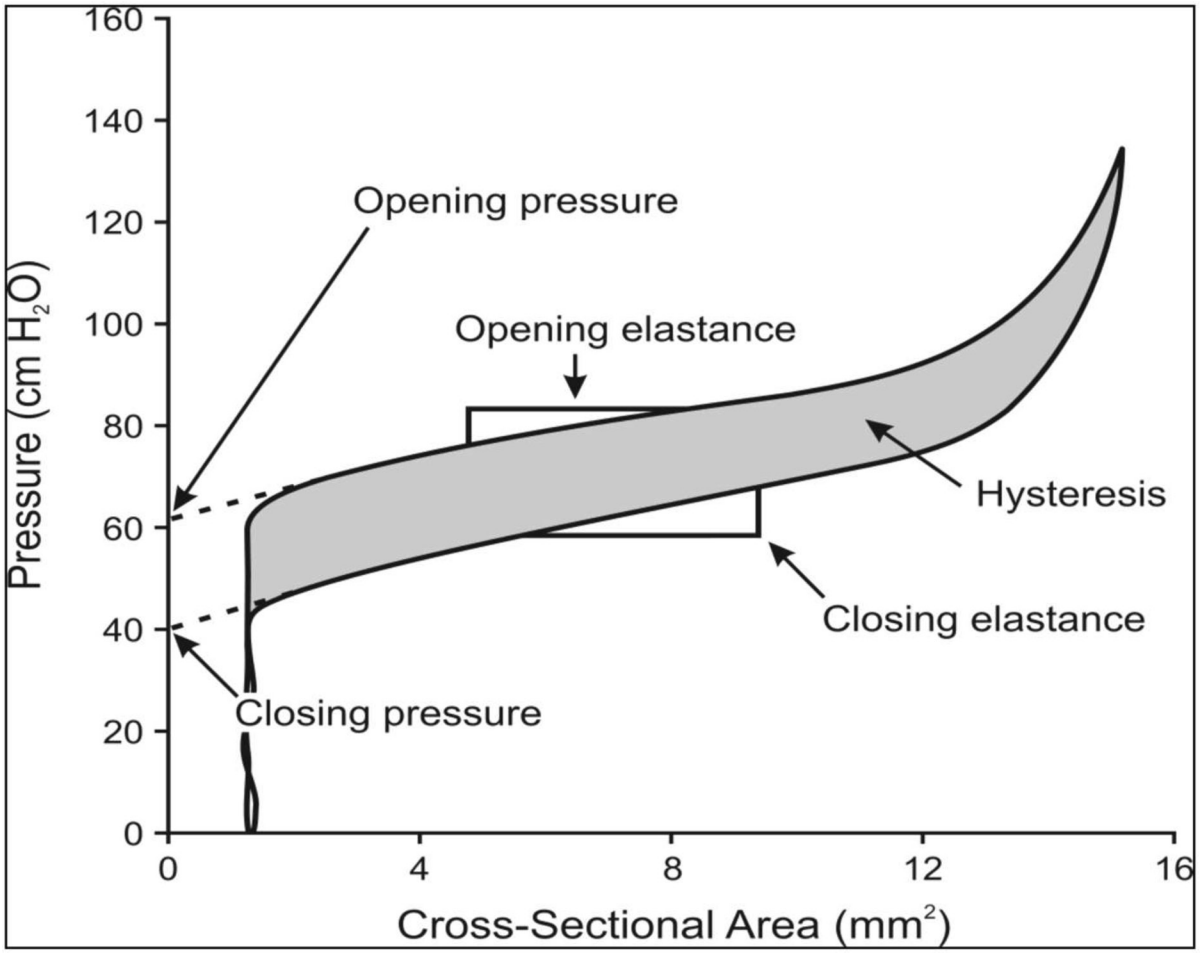

Figure 1 Graph of cross-sectional area and pressure at the high-pressure zone produced by one cycle of inflation and deflation of the polyurethane bag with anal acoustic reflectometry. The calculated physiological parameters are highlighted on the graph. (Reproduced with permission from Mitchell *et al*[31] Wolters Kluwer Health. Publishing License No 5380741033645).

pressure (SqOp, cmH_2O) and squeeze opening elastance (SqOe, cmH_2O/mm^2). Incremental squeeze opening pressure (IncSqOp, cmH_2O) is calculated as SqOp–Op and reflects the maximum pressure observed during squeeze above Op measured at rest.

Functional lumen imaging probe

The EndoFLIP system (Medtronic, Minnesota, USA) uses a highly compliant bag 12 cm in length that fills with a conductive solution to a maximum diameter of 25 mm while an electrical current passes through it (online supplemental figure 1). Using the electrical impedance measured between 16 pairs of detection electrodes, the diameter (and CSA) of the bag at 5 mm intervals can be calculated along a length of 8 cm. In combination with a solid-state pressure transducer, FLIP generates diameter, CSA and pressure measurements as the bag inflates and deflates inside the anal canal.

The measurement protocol used, termed the 'ramp' distension protocol, has previously been described.[21 32 33] Briefly, at a rate of 40 mL/min, the bag is filled twice to 10 mL to ensure it is unfolded. It is then filled to 20, 30, 40 and 50 mL. Each distension is followed by 30 s of iso-volumetric recording at rest before the subject is asked to squeeze for 10 s. Between each filling volume, the bag is emptied and, after a 10 s pause, is then reinflated to the next volume. Geometric and pressure data are displayed on the EndoFLIP display (online supplemental figure 3). Data are also sampled at 10 Hz and were downloaded for post-acquisition analysis using a customised MATLAB subroutine[32] (R2022a, Mathworks, Natick, Massachusetts, USA).

Parameters were calculated at the area of minimum CSA, including the yield pressure, Cp, pressure-strain elastic modulus (Ep) and Distensibility Index (DI) (minimum CSA/bag pressure) during rest and voluntary squeeze, which have been described previously.[12 21 33 34] Like measurements obtained with AAR, yield pressure reflects the pressure at which the narrowest part of the anal canal starts, and continues, to increase in diameter while the Cp reflects the pressure observed when the anal canal closes again. Ep is a measure of the resistance to distension and can be observed during the opening or closing of the anal canal. Incremental squeeze bag pressure was calculated as maximum bag pressure during squeeze minus the bag pressure during rest. The pressure-diameter volume loop area was also calculated during the voluntary squeeze. Using a graph of minimum bag diameter vs pressure, the change in both parameters from rest, to maximum voluntary squeeze (decrease in minimum diameter and increase in pressure), and back to rest again can be plotted at each bag volume. The area contained by this loop can be calculated, and recorded in mm*mm Hg, to quantify the voluntary squeeze function (figure 2). For example, a larger loop area indicates a greater increase in pressure and/or a greater decrease in the minimum bag diameter which indicates a greater squeeze function.

Order of investigations and randomisation

Patients underwent HRAM as part of their routine investigations for FI first. Following recruitment and informed consent, patients were measured within 1 week with AAR and FLIP. The order of AAR and FLIP was randomised

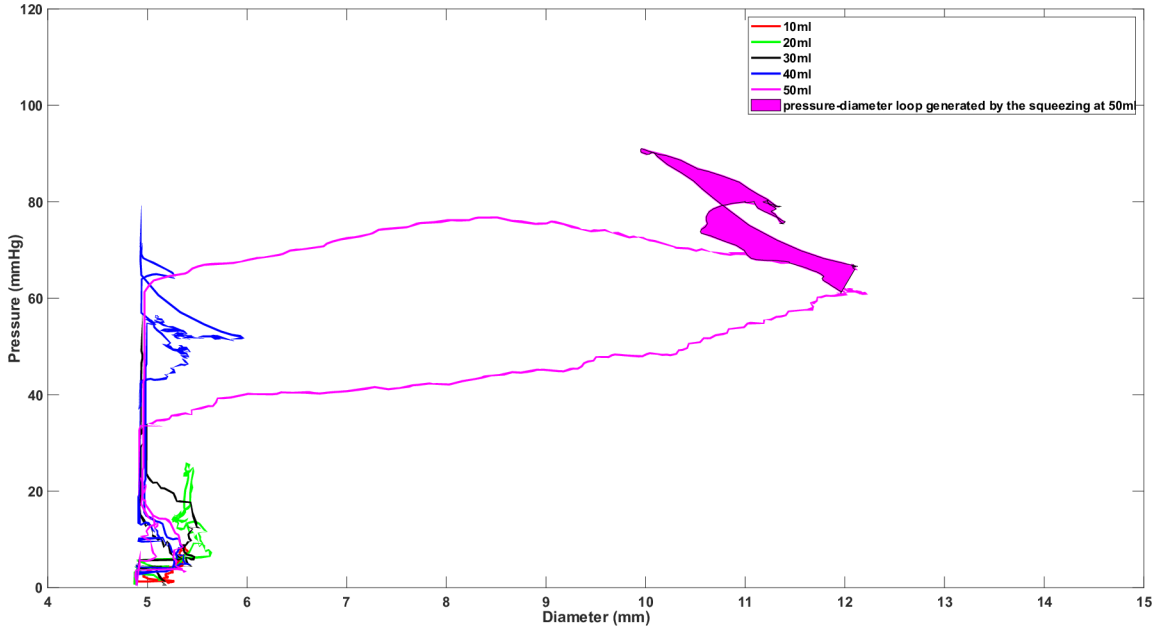

Figure 2 Minimum diameter vs pressure graph for one FLIP measurement with a measurement from 0 mL to 50 mL and then back to 0 mL indicated by the magenta line. During inflation of the FLIP bag at rest, the minimum measured diameter increases to the greatest value (12 mm). After 30 s of iso-volumetric recording, the patient is asked to squeeze for 10 s and the subsequent decrease in diameter and increase in pressure from maximum squeeze back to rest used to calculate the pressure-diameter volume loop indicated by the shaded area. FLIP, functional lumen imaging probe.

and conducted by a statistician using a computer-generated model. There was a minimum of 2 min rest between investigations, and no bowel preparation was required before any measurement.

Statistical analysis

Statistical analysis was performed using SPSS V.29.0 (IBM, New York, USA). Data are presented as median (IQR) unless otherwise stated. The Kruskal-Wallis test and the Mann-Whitney U test were used to compare independent samples. Correlation analyses were conducted with Spearman's rank order correlation coefficient (0.90–1.0: very strong correlation, 0.70–0.89: strong correlation, 0.40–0.69: moderate correlation, 0.10–0.39: weak correlation, 0.00–0.10: negligible correlation).[35] Statistical significance was considered at the $p<0.05$ level.

RESULTS

40 patients with FI (39 (98%) women, median age: 62 (range: 38–85)) were recruited consecutively and measured with AAR and FLIP following HRAM. Two additional patients were approached and declined to participate. All included patients completed measurements with all three modalities except one who could not tolerate the 50 mL bag volume with FLIP, therefore, for this patient, only data recorded until the end of 40 mL distension were analysed. FLIP data obtained at the 30 mL bag volume were not analysed, given the anal canal remained closed in most patients at rest (29/40, 74%).

Baseline demographics and symptomatology of the included patients are presented in table 1. All patients suffered with FI with the majority (27, 67.5%) reporting urge FI. Of the female patients (n=39), 38 (97%) were parous and all reported at least one vaginal delivery with most (33/38, 87%) describing a history of obstetric trauma (episiotomy or perineal tear).

Table 1 Patient demographics

Parameter	Patients (n=40)
Age, median (range)	62 (38–85)
Female, n (%)	39 (98)
Bowel symptom history, n (%)	
Obstructive defaecation syndrome	16 (40)
Faecal incontinence	40 (100)
Urge faecal incontinence*	27 (67.5)
Passive faecal incontinence*	5 (12.5)
Mixed faecal incontinence*	8 (20)
Post defecatory faecal leakage	22 (55)
Urinary incontinence, n (%)	13 (33)
Obstetric history, n (%)	
Parous†	38/39 (97)
Vaginal delivery‡	38/38 (100)
Caesarean section‡	6/38 (16)
Forceps use§	11/38 (29)
Ventouse use§	6/38 (16)
Episiotomies or perineal tear§	33/38 (87)
Previous gynaecological surgery, n (%)†	20/39 (51)
Hysterectomy	14
Sterilisation	3
Anterior repair	3
Other	4
Previous pelvic floor interventions, n (%)	19 (48)
Percutaneous tibial nerve stimulation	10
Transvaginal rectocele repair	6
Other	5
Previous abdominal surgery, n (%)	12 (30)
Cholecystectomy	6
Appendicectomy	5
Other	2

*Percentage calculated from patients with faecal incontinence.
†Females only.
‡Percentage calculated from parous females only.
§Percentage calculated from females with vaginal deliveries only.

Correlation of HRAM, FLIP and AAR with FI symptom severity

Resting function

There was no correlation between patient-reported symptom severity scores and any measured parameter at rest, including MRP with HRAM ($r_s=0.160$), Op with AAR ($r_s=0.169$) and yield pressure with FLIP ($r_s=0.200$) ($p>0.05$ for all) (online supplemental table 1).

Voluntary squeeze function

Several parameters measured with FLIP demonstrated a correlation with the Vaizey score including the incremental increase in FLIP bag pressure during squeeze at 40 mL ($r_s=-0.412$; $p=0.008$) and 50 mL ($r_s=-0.414$; $p=0.009$) bag volumes. Only the incremental squeeze bag pressure at 40 mL demonstrated a correlation with the quality-of-life measure MHQ ($r_s=-0.337$; $p=0.033$). The pressure-diameter volume loop at 50 mL bag volume also showed a correlation with the Vaizey score ($r_s=-0.402$; $p=0.011$). There was, however, no correlation with squeeze DI and symptom severity scores ($p>0.05$ for all).

With AAR, IncSqOp demonstrated a correlation with the Vaizey score ($r_s=-0.339$; $p=0.032$) (table 2).

There was no correlation with HRAM measurements of voluntary squeeze function and patient-reported FI symptom severity ($p>0.05$).

Comparison between FI subtypes

Of the 40 included patients, 27 (67.5%) reported isolated urge FI, 8 (20%) mixed symptoms and 5 (12.5%) isolated passive incontinence (table 1). There was no significant difference between the three groups in age ($p=0.123$ (Kruskal-Wallis test)).

Table 2 Correlation matrix between voluntary squeeze measurements of anal sphincter function and faecal incontinence symptom severity measures

	Symptom severity measure		
Voluntary squeeze parameter (n=40)	**Vaizey score**	**MHQ total**	**MHQ severity**
High-resolution anorectal manometry			
Maximum squeeze pressure, mm Hg	r_s=−0.136	r_s=−0.167	r_s=−0.043
Incremental squeeze pressure, mm Hg	r_s=−0.211	r_s=−0.291	r_s=−0.149
Anal acoustic reflectometry			
Squeeze opening pressure, cmH_2O	r_s=−0.175	r_s=−0.139	r_s=−0.150
Inc. Squeeze opening pressure, cmH_2O	**r_s=−0.339**†	r_s=−0.287	r_s=−0.249
Squeeze opening elastance, cmH_2O/mm^2	r_s=0.197	r_s=0.021	r_s=0.062
Functional lumen imaging probe			
Squeeze DI at 40 mL, mm^2/mm Hg	r_s=0.006	r_s=0.045	r_s=0.026
*Squeeze DI at 50 mL, mm^2/mm Hg	r_s=0.070	r_s=−0.022	r_s=−0.036
Incremental squeeze bag pressure at 40 mL, mm Hg	**r_s=−0.412**†	**r_s=−0.337**†	r_s=−0.299
*Incremental squeeze bag pressure at 50 mL, mm Hg	**r_s=−0.414**†	r_s=−0.265	r_s=−0.261
Pressure-diameter volume loop at 40 mL, mm*mm Hg	**r_s=−0.376**†	r_s=−0.290	r_s=−0.293
*Pressure-diameter volume loop at 50 mL, mm*mm Hg	**r_s=−0.402**†	r_s=−0.175	r_s=−0.188

Significance at p<0.05 level (two-tailed).
*Measurements from 39 participants used for analysis.
†p<0.05.
DI, Distensibility Index; MHQ, Manchester Health Questionnaire.

Table 3 Comparison of parameters measured at rest between the known faecal incontinence subtypes

	Faecal incontinence subtype			
Resting parameter	**Urge (n=27)**	**Mixed (n=8)**	**Passive (n=5)**	**P value***
High-resolution anorectal manometry				
Mean resting pressure, mm Hg	49.0 (35–63)	37.5 (30.0–58.9)	26.0 (17.0–30.0)	**0.010**
Anal canal length, cm	2.7 (2.3–3.2)	2.7 (2.5–3.3)	2.7 (1.8–4.7)	0.941
Anal acoustic reflectometry				
Opening pressure, cmH_2O	53.7 (38.7–73.5)	40.2 (26.6–48.2)	26.1 (23.3–36.3)	**0.006**
Opening elastance, cmH_2O/mm^2	2.0 (1.5–2.5)	1.3 (1.1–1.4)	1.4 (1.1–2.0)	**0.023**
Closing pressure, cmH_2O	36.6 (25.0–51.2)	25.8 (16.6–35.1)	15.7 (12.6–24.2)	**0.011**
Closing elastance, cmH_2O/mm^2	1.7 (1.4–2.3)	1.1 (0.8–1.2)	1.1 (0.8–1.5)	**0.005**
Hysteresis, %	28.6 (26.5–34.2)	34.0 (27.5–34.5)	35.6 (29.3–43.3)	0.150
Functional lumen imaging probe				
Yield pressure, mm Hg	24.0 (17.0–43.2)	21.3 (11.3–35.8)	13.1 (11.1–18.5)	**0.031**
Opening Ep, kPa	3.5 (2.3–4.9)	2.7 (2.3–4.2)	1.9 (1.5–3.0)	0.080
Closing pressure, mm Hg	19.0 (10.6–23.2)	13.2 (7.1–20.0)	12.0 (10.0–14.5)	0.204
Closing Ep, kPa	2.4 (1.7–3.9)	1.9 (1.0–2.4)	1.2 (1.0–1.9)	**0.017**
DI at 40 mL, mm^2/mm Hg	1.1 (0.6–3.1)	2.0 (1.6–2.7)	4.3 (2.4–5.2)	**0.020**
†DI at 50 mL, mm^2/mm Hg	2.4 (1.4–4.7)	3.6 (2.5–4.8)	5.8 (3.6–6.6)	0.088

Significance at p<0.05 level.
*Kruskal-Wallis test.
†Measurements from 26 patients with urge faecal incontinence.
DI, Distensibility Index; Ep, pressure-strain elastic modulus.

Resting function

The parameters measured at rest between the three subgroups of FI using the three modalities are presented in table 3. Between the urge, mixed and passive groups, there were differences in measurements of MRP (49.0 vs 37.5 vs 26.0 mm Hg; p=0.010), Op (53.7 vs 40.2 vs 26.1 cmH_2O; p=0.006) and yield pressure (24.0 vs 21.3 vs 13.1 mm Hg; p=0.031). The greatest values of each were observed in the urge cohort, and the lowest in the passive group indicating the weakest resting function. The DI at 40 mL bag volume was different between the groups with the greatest values, indicating greater compliance of the anal canal, in the passive subgroup compared with the mixed and urge cohorts (4.3 vs 2.0 vs 1.1 mm^2/mm Hg; p=0.020).

The two measurements of resistance to distension with AAR (Oe and Ce) were both different between the three groups (p=0.023 and p=0.005 respectively). The lowest values, indicating the least resistance to distension, were observed in the passive and mixed cohorts compared with the urge group (Oe: 1.4 vs 1.3 vs 2.0 cmH_2O; Ce: 1.1 vs 1.1 vs 1.7 cmH_2O). With FLIP, the closing Ep, which also represents the resistance of the anal canal, demonstrated the same reduced measurements in the passive and mixed cohorts compared with the urge group (1.2 vs 1.9 vs 2.4 kPa; p=0.017). The same trend with the opening Ep (1.9 vs 2.7 vs 3.5 kPa) did not reach statistical significance (p=0.08).

Voluntary squeeze function

The squeeze DI at 40 mL bag volume was greater in the mixed (1.4 mm^2/mm Hg) and passive (1.3 mm^2/mm Hg) groups compared with the urge cohort (0.5 mm^2/mm Hg) (p=0.046). However, when considering the incremental DI values there was a trend towards reduced squeeze function in the urge FI group (−0.4 mm^2/mm Hg) compared with the passive cohort (−2.6 mm^2/mm Hg) although these results did not reach statistical significance (p=0.251). There was no difference in the pressure-diameter volume loop measurements between the groups (p>0.05). However, the pressure-diameter volume loop at 50 mL bag volume suggests that those in the urge cohort (6.1 mm*mm Hg) may have the poorest voluntary squeeze function compared with the mixed (19.2 mm*mm Hg) or passive (23.1 mm*mm Hg) groups (p=0.295). There was a difference in SqOp measured with AAR (p=0.024) between the three groups, although there was no difference in IncSqOp (p=0.678) (online supplemental table 2).

There were no differences in HRAM measurements of voluntary squeeze function between the FI subtypes (p>0.05 for all) (online supplemental table 2).

DISCUSSION

This prospective study is the first to our knowledge to compare all three modalities of HRAM, FLIP and AAR in the same patients with FI. It aimed to investigate the role of FLIP and AAR, two provocative tests of anal sphincter function, compared with HRAM in the assessment of FI symptoms and subtypes. We prospectively recruited 40 patients, and the results suggest AAR and FLIP may have a unique ability to correlate with symptom severity, a finding not replicated with HRAM. We also found that all three modalities were able to identify differences between the known FI subgroups of urge, passive and mixed. While deficiencies in any component of the continence mechanism can lead to FI, anal sphincter dysfunction is still considered a principal cause.[36] HRAM is the current investigation of choice to assess anal sphincter function using a fixed diameter catheter to measure pressures at rest, and during the voluntary squeeze.[2] The results of HRAM do not always correlate with FI symptom severity.[6] Therefore, clinicians often rely on a clinical history and physical examination alone in guiding treatment decisions making it a desirable ambition to develop a more sensitive test. Resistance to distension has been proposed as the main determinant of sphincter function[15] leading to the development of dynamic provocative tests of anal sphincter distensibility including AAR and FLIP.[12] FLIP and AAR measure the distensibility of a sphincter during volume-controlled distension thereby assessing the length-tension relationship of the muscle.[12] Both tools have demonstrated clinical utility in the investigation and management of FI[12 13 37] and are considered equally acceptable to patients compared with HRAM.[38] This study suggests they may also have a unique ability to correlate with symptom severity.

Patient-reported symptom severity scores are routinely used to quantify symptoms of FI and their impact on quality of life.[39] During the assessment of the voluntary squeeze, measurements with AAR and FLIP demonstrated a correlation with the Vaizey score, a finding not replicated with HRAM. In the largest reported series of AAR measurements of 100 women with FI, significant correlations with the resting parameters of Op, Oe and Ce and the Vaizey score were reported.[17] In the same study, no such correlation was observed with conventional anal manometry. Later work with FLIP has suggested it is a more specific test to diagnose anal sphincter 'weakness' as 44% of patients with normal DI results, but abnormal MSP measurements, had no sphincter lesion or neuropathy that could explain the abnormal anal sphincter function (MSP) identified with HRAM.[19] In our study, the strongest correlations observed with any measured parameter and the Vaizey score were the incremental squeeze bag pressures at 40 mL and 50 mL. The incremental squeeze bag pressure at 40 mL also demonstrated a unique correlation with MHQ, a measure of the impact of FI on quality of life. This suggests squeeze function measured with FLIP may be clinically relevant in the investigation of FI, and a more useful objective tool to assess disease severity. However, various factors influence the impact of FI on quality-of-life including personal circumstances, relationships and employment status which could explain the limited correlation with

measurements of sphincter function and quality-of-life assessments. Despite this, in measuring the sphincter at increasing bag volumes, FLIP is uniquely able to increase the length of the muscle allowing measurement of its length-tension function.[40] This reflects an ideal measurement of the function of any muscle and is not possible with HRAM which relies on fixed diameter catheters.

Conflicting data have been presented relating to correlations between FI severity and HRAM results. In the largest reported series of 351 female patients with FI, there was only a weak correlation between MRP and the FI severity index, with no correlation observed with MSP.[41] Indeed, Heitmann *et al* in a series of 246 patients with FI undergoing investigation with HRAM and 3D-EAUS concluded these investigations are not strong predictors of FI severity.[6] In our study, there was no correlation with the Vaizey score and MRP, ISP or MSP with HRAM. These findings suggest an overall weak or absent correlation between measurements of anal sphincter function with HRAM and FI symptom severity.

FI is commonly described according to the subtypes of urge and passive incontinence, which are typically associated with external and internal sphincter dysfunction respectively.[42 43] Mixed FI (both urge and passive) is also encountered in clinical practice and is considered a distinct subtype.[8] When subsequently investigated with manometry, squeeze pressure is commonly reduced in urge FI, while resting pressure is typically reduced in the passive subtype.[8] Previous work with AAR and FLIP has revealed differences in sphincter function at rest, with the weakest function observed in the passive subtype.[17 44] In this study, measurements at rest obtained with HRAM (MRP), AAR (Op, Cp) and FLIP (yield pressure, DI) were all different between the FI subtypes. The lowest values for all measurements were observed in the passive FI group, indicating internal sphincter dysfunction. When considering the squeeze function, there were no differences in HRAM measurements between the subtypes. With AAR and FLIP, a consistent trend towards reduced voluntary squeeze function was observed in the urge group compared with the passive FI cohort, which may suggest external sphincter dysfunction. These results support the assumption that urge and passive FI are predominantly associated with external and internal sphincter dysfunction, respectively. However, this is likely an oversimplification of a complex and multifactorial condition. The results of this study suggest that all three techniques may be useful in identifying differences between FI subtypes, and that FLIP and AAR appear also to suggest weaker striated muscle function in the urge cohort, consistent with our understanding of the pathophysiology of urge FI.[8]

Given FLIP is commercially available and in use in several international units, further work is now required to develop and standardise the FLIP measurement protocol and observed parameters.[33] This should coincide with the generation of a set of normal cut-off values to guide clinicians. In doing so, the clinical utility of FLIP can be further explored against the established investigation of HRAM in further prospective studies of diagnostic accuracy reported using the STARD guidelines.[45] These should seek to assess the diagnostic accuracy of FLIP against HRAM in the diagnosis of FI compared with continent controls, and to establish its ability to predict FI subtypes based on its unique provocative measurements of sphincter function.

Despite our findings, this study did have limitations principally in its relatively small sample size of only 40 patients leaving only five patients in the passive FI cohort. This may impact the results due to the heterogeneity of the included patients with various FI aetiologies, comorbidities and previous surgical procedures identified. 16 (40%) reported a symptom of obstructive defaecation syndrome which may have contributed to their FI, however, all included patients had suspected anal sphincter dysfunction and underwent all three tests making each their own control to overcome this limitation. Although the order of the investigations was randomised, patients may have felt fatigued by the end of the study which may have influenced their squeeze effort. In this study, and in our unit, water-perfused HRAM is used rather than solid-state devices which have superior 3D pressure topography which may be better able to correlate with symptom severity.[46] The correlations with AAR and FLIP parameters and symptom severity, while significant and clinically relevant, were predominantly moderate in strength suggesting the results should be interpreted with caution and further work is required with larger series. In addition, AAR is not yet commercially available and the measurements with FLIP were only produced in post-acquisition analysis. This currently limits the generalisability of the findings. Finally, in recent years, two distinct FLIP measurement protocols termed the ‘stepwise’ and ‘ramp’ techniques have emerged from different specialist centres risking a lack of standardisation that could limit the adoption of this novel test.[33]

CONCLUSION

This prospective study has explored the role of FLIP, AAR and HRAM in the investigation of FI in 40 patients. It has demonstrated that FLIP and AAR better correlate with patient-reported symptoms and that all three modalities were able to identify differences between the subgroups of urge, passive and mixed FI. While FI is multifactorial, anal sphincter dysfunction remains a leading cause. Therefore, future work should continue to explore these novel tests of anal sphincter distensibility in further prospective studies.

Author affiliations
[1]Faculty of Biology, Medicine and Health, The University of Manchester and Manchester Academic Health Sciences Centre Manchester, Manchester, UK
[2]Department of Colorectal Surgery, Manchester University NHS Foundation Trust, Manchester, UK
[3]Mech-Sense, Department of Gastroenterology, Aalborg University Hospital, Aalborg, Denmark
[4]Neurogastroenterology Unit, Gastroenterology, Manchester University NHS Foundation Trust, Manchester, UK

[5]Department of Obstetrics and Gynecology, Herlevand Gentofte University Hospital, Herlev, Denmark
[6]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark
[7]Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester, UK

Acknowledgements The authors wish to acknowledge The Royal College of Surgeons of England for their support in the production of this manuscript.

Contributors AO'C, DL, EK, NK, AS and KT designed the study. AO'C and DL undertook data acquisition. AO'C, DL, MD, AS and KT were involved in the data analysis and interpretation. AO'C, EK, MD, AS and DHV assisted in drafting the initial manuscript. AMD, AS, DHV, JM, NK, EK and KT supervised the project and the preparation of the manuscript. All authors provided critical revision of the manuscript, were involved in intellectual discussion, approved the final version of the manuscript and agree to be accountable for all aspects of the work. AO'C is the guarantor author.

Funding AOC received funding from The Royal College of Surgeons of England (Award/Grant number is not applicable)

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Greater Manchester West, Ref: 19/NW/0633. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data presented in this manuscript are available from the corresponding author on reasonable request.

ORCID iDs
Alexander O'Connor http://orcid.org/0000-0002-3964-9152
Dipesh H Vasant http://orcid.org/0000-0002-2329-0616
John McLaughlin http://orcid.org/0000-0001-6158-5135

REFERENCES

1 Lee TH, Bharucha AE. How to Perform and Interpret a High-resolution Anorectal Manometry Test. *J Neurogastroenterol Motil* 2015;22:46–59.
2 Carrington EV, Heinrich H, Knowles CH, *et al*. Methods of anorectal manometry vary widely in clinical practice: Results from an international survey. *Neurogastroenterol Motil* 2017;29:e13016.
3 Zifan A, Ledgerwood-Lee M, Mittal RK. A Predictive Model to Identify Patients With Fecal Incontinence Based on High-Definition Anorectal Manometry. *Clin Gastroenterol Hepatol* 2016;14:1788–96.
4 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.
5 Vitton V, Ben Hadj Amor W, Baumstarck K, *et al*. Water-perfused manometry vs three-dimensional high-resolution manometry: a comparative study on a large patient population with anorectal disorders. *Colorectal Dis* 2013;15:e726–31.
6 Heitmann PT, Rabbitt P, Schloithe AC, *et al*. The relationships between the results of contemporary tests of anorectal structure and sensorimotor function and the severity of fecal incontinence. *Neurogastroenterol Motil* 2020;32:e13946.
7 Bharucha AE, Fletcher JG, Harper CM, *et al*. Relationship between symptoms and disordered continence mechanisms in women with idiopathic faecal incontinence. *Gut* 2005;54:546–55.
8 Desprez C, Turmel N, Chesnel C, *et al*. Comparison of clinical and paraclinical characteristics of patients with urge, mixed, and passive fecal incontinence: a systematic literature review. *Int J Colorectal Dis* 2021;36:633–44.
9 Paquette IM, Varma MG, Kaiser AM, *et al*. The American Society of Colon and Rectal Surgeons' Clinical Practice Guideline for the Treatment of Fecal Incontinence. *Diseases of the Colon & Rectum* 2015;58:623–36.
10 Assmann SL, Keszthelyi D, Kleijnen J, *et al*. Guideline for the diagnosis and treatment of Faecal Incontinence-A UEG/ESCP/ESNM/ESPCG collaboration. *United European Gastroenterol J* 2022;10:251–86.
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:e13679.
12 O'Connor A, Byrne CM, Vasant DH, *et al*. Current and future perspectives on the utility of provocative tests of anal sphincter function: A state-of-the-art summary. *Neurogastroenterol Motil* 2023;35:e14496.
13 Zifan A, Sun C, Gourcerol G, *et al*. Endoflip vs high-definition manometry in the assessment of fecal incontinence: A data-driven unsupervised comparison. *Neurogastroenterol Motil* 2018;30:e13462.
14 Harris LD, Winans CS, Pope CE. Determination of yield pressures: a method for measuring anal sphincter competence. *Gastroenterology* 1966;50:754–60.
15 HARRIS LD, POPE CE 2nd. "SQUEEZE" VS. RESISTANCE: AN EVALUATION OF THE MECHANISM OF SPHINCTER COMPETENCE. *J Clin Invest* 1964;43:2272–8.
16 Zifan A, Mittal RK, Kunkel DC, *et al*. Loop analysis of the anal sphincter complex in fecal incontinent patients using functional luminal imaging probe. *Am J Physiol Gastrointest Liver Physiol* 2020;318:G66–76.
17 Hornung BR, Mitchell PJ, Carlson GL, *et al*. Comparative study of anal acoustic reflectometry and anal manometry in the assessment of faecal incontinence. *Br J Surg* 2012;99:1718–24.
18 Mitchell PJ, Klarskov N, Telford KJ, *et al*. Viscoelastic assessment of anal canal function using acoustic reflectometry: a clinically useful technique. *Dis Colon Rectum* 2012;55:211–7.
19 Leroi AM, Melchior C, Charpentier C, *et al*. The diagnostic value of the functional lumen imaging probe versus high-resolution anorectal manometry in patients with fecal incontinence. *Neurogastroenterology Motil* 2018;30:e13291.
20 Gourcerol G, Granier S, Bridoux V, *et al*. Do endoflip assessments of anal sphincter distensibility provide more information on patients with fecal incontinence than high-resolution anal manometry? *Neurogastroenterology Motil* 2016;28:399–409.
21 Haas S, Faaborg P, Liao D, *et al*. Anal sphincter dysfunction in patients treated with primary radiotherapy for anal cancer: a study with the functional lumen imaging probe. *Acta Oncol* 2018;57:465–72.
22 von Elm E, Altman DG, Egger M, *et al*. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;61:344–9.
23 Horrocks EJ, Chadi SA, Stevens NJ, *et al*. Factors Associated With Efficacy of Percutaneous Tibial Nerve Stimulation for Fecal Incontinence, Based on Post-Hoc Analysis of Data From a Randomized Trial. *Clin Gastroenterol Hepatol* 2017;15:1915–21.
24 Mitchell PJ. *Investigation of the Anal Sphincter Mechanism and Faecal Incontinence Using Acoustic Reflectometry*. The University of Manchester, 2010.
25 Vaizey CJ, Carapeti E, Cahill JA, *et al*. Prospective comparison of faecal incontinence grading systems. *Gut* 1999;44:77–80.
26 Bug GJ, Kiff ES, Hosker G. A new condition-specific health-related quality of life questionnaire for the assessment of women with anal incontinence. *BJOG* 2001;108:1057–67.
27 Kelleher CJ, Cardozo LD, Khullar V, *et al*. A new questionnaire to assess the quality of life of urinary incontinent women. *Br J Obstet Gynaecol* 1997;104:1374–9.
28 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;26:625–35.

29 Heywood NA, Nicholson JE, Sharma A, *et al*. Continuous vs stepwise anal acoustic reflectometry: An improved technique for physiological measurement of anal sphincter function? *Neurourol Urodyn* 2020;39:447–54.
30 Heywood NA, Sharma A, Kiff ES, *et al*. Placement of a fine-bore rectal balloon catheter in the anal canal does not affect anal sphincter pressures: improving our understanding of physiological function with anal acoustic reflectometry. *Colorectal Dis* 2020;22:1626–31.
31 Mitchell PJ, Klarskov N, Telford KJ, *et al*. Anal acoustic reflectometry: a new reproducible technique providing physiological assessment of anal sphincter function. *Dis Colon Rectum* 2011;54:1122–8.
32 Haas S, Liao D, Gregersen H, *et al*. Increased yield pressure in the anal canal during sacral nerve stimulation: a pilot study with the functional lumen imaging probe. *Neurogastroenterol Motil* 2017;29.
33 O'Connor A, Liao D, Drewes AM, *et al*. A comparison of function lumen imaging probe measurements of anal sphincter function in fecal incontinence. *Neurogastroenterol Motil* 2024;36:e14791.
34 Faaborg PM, Haas S, Liao D, *et al*. Long-term anorectal function in rectal cancer patients treated with chemoradiotherapy and endorectal brachytherapy. *Colorectal Dis* 2021;23:2311–9.
35 Schober P, Boer C, Schwarte LA. Correlation Coefficients: Appropriate Use and Interpretation. *Anesth Analg* 2018;126:1763–8.
36 Rasijeff AMP, García-Zermeño K, Di Tanna G-L, *et al*. Systematic review and meta-analysis of anal motor and rectal sensory dysfunction in male and female patients undergoing anorectal manometry for symptoms of faecal incontinence. *Colorectal Dis* 2022;24:562–76.
37 Desprez C, Roman S, Leroi AM, *et al*. The use of impedance planimetry (Endoscopic Functional Lumen Imaging Probe, EndoFLIP®) in the gastrointestinal tract: A systematic review. *Neurogastroenterol Motil* 2020;32:e13980.
38 Byrne C, Vasant D, Kiff E, *et al*. PWE-59 patient acceptance of anorectal physiology diagnostics: how important is the catheter? Abstracts of the BSG Annual Meeting, 8–12 November 2021; November 2021:A172–3.
39 Vaizey CJ. Faecal incontinence: standardizing outcome measures. *Colorectal Dis* 2014;16:156–8.
40 Tuttle LJ, Zifan A, Sun C, *et al*. Measuring length-tension function of the anal sphincters and puborectalis muscle using the functional luminal imaging probe. *Am J Physiol Gastrointest Liver Physiol* 2018;315:G781–7.
41 Bordeianou L, Lee KY, Rockwood T, *et al*. Anal resting pressures at manometry correlate with the Fecal Incontinence Severity Index and with presence of sphincter defects on ultrasound. *Dis Colon Rectum* 2008;51:1010–4.
42 Abrams P, Andersson KE, Birder L, *et al*. Fourth International Consultation on Incontinence Recommendations of the International Scientific Committee: Evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. *Neurourol Urodyn* 2010;29:213–40.
43 Rao SSC, American College of Gastroenterology Practice Parameters Committee. Diagnosis and management of fecal incontinence. American College of Gastroenterology Practice Parameters Committee. *Am J Gastroenterol* 2004;99:1585–604.
44 Desprez C, Gourcerol G, Savoye-Collet C, *et al*. Relationship between anal functional lumen imaging probe (EndoFLIP®) results and the clinical presentation of faecal incontinence. *Colorectal Dis* 2022;24:1379–89.
45 Bossuyt PM, Reitsma JB, Bruns DE, *et al*. n.d. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. *BMJ*351:h5527.
46 Bharucha AE, Basilisco G, Malcolm A, *et al*. Review of the indications, methods, and clinical utility of anorectal manometry and the rectal balloon expulsion test. *Neurogastroenterol Motil* 2022;34:e14335.