bowel disease

#### Review

Ther Adv Gastroenterol

2018, Vol. 11: 1–13 DOI: 10.1177/ 1756284818816956

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**Current perspectives on the diagnosis** 

and management of functional anorectal

disorders in patients with inflammatory

**Abstract:** Despite advances in inflammatory bowel disease (IBD) therapies, a significant proportion of patients with quiescent disease experience persistent, debilitating symptoms of faecal incontinence (FI), urgency and defaecatory disorders due to anorectal dysfunction. Such symptoms are often underreported or misdiagnosed and can lead to potentially premature treatment 'escalation' and under-utilisation of pelvic floor investigations. In this review article, we consider putative pathophysiological post-inflammatory changes resulting in altered anorectal sensitivity, motility and neuromuscular coordination and how this may drive symptoms in quiescent IBD. Finally, we discuss a pragmatic approach to investigating and managing anorectal dysfunction and highlight areas for future research for this often-neglected group of patients.

*Keywords:* functional anorectal disorders, inflammatory bowel disease, faecal incontinence, dyssynergic defaecation, biofeedback therapy, anorectal dysfunction

Received: 23 September 2018; revised manuscript accepted: 13 November 2018.

#### Introduction

Inflammatory bowel diseases (IBD) are chronic disorders of the gastrointestinal tract associated with debilitating symptoms due to immunemediated enteric inflammation. Unfortunately, despite therapeutic advances, IBD remains incurable and affects approximately 250,000 adults in the United Kingdom (UK), 2 million in Europe and 1.5 million in North America.<sup>1,2</sup> As a result, many patients experience intermittent flares of intestinal inflammation in an unpredictable relapsing-remitting pattern, with recognizable symptoms of increased bowel frequency, bleeding and urgency.

While advances in the therapeutic armamentarium for IBD in recent decades have increased the likelihood of achieving disease remission and mucosal healing,<sup>3</sup> a significant proportion of patients still present with refractory gastrointestinal symptoms.<sup>4,5</sup> In this context, there can be considerable overlap between symptoms in active IBD and overlapping coexisting functional gastrointestinal disorders in patients with quiescent disease. This association has been noted to be as high as 33% in patients with ulcerative colitis (UC) and in 42-57% with Crohn's disease (CD).6,7 This poses a significant challenge for clinicians, as failure to positively recognize functional disorders in patients without objective evidence of active inflammation, can lead to repeatedly negative and often invasive investigations, increased healthcare utilisation, futile and potentially hazardous escalation of IBD therapies, and patient dissatisfaction due to refractory symptoms. Moreover, recent studies have highlighted that functional anorectal disorders, in particular defaecation disorders<sup>8,9</sup> and faecal incontinence (FI),<sup>10</sup> are understandably a significant cause of ongoing suffering for patients with IBD. While associations between anorectal dysfunction with fistulating disease and ileo-anal pouch surgery are well documented, there is otherwise minimal literature in this field.<sup>11,12</sup> The purpose of this review article is therefore to provide a current perspective on an approach to the diagnosis and management of these devastating, but often overlooked and

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Abnormal anorectal or pelvic floor structures	<ul> <li>Post-inflammatory changes, sphincter and pelvic surgeries, fistulae</li> <li>Haemorrhoidectomy,</li> <li>Obstetric injury,</li> <li>Trauma,</li> <li>Neuropathy secondary to spinal surgery, diabetes mellitus, multiple sclerosis, spinal cord injury, stroke</li> </ul>
Abnormal anorectal/pelvic floor sensorimotor function	<ul> <li>Post-inflammatory changes resulting in:</li> <li>Anorectal dysmotility</li> <li>Altered anorectal sensitivity</li> <li>Reduced anorectal compliance</li> <li>Impaired anorectal neuromuscular coordination</li> <li>Anal sphincter weakness</li> </ul>
Altered stool characteristics	Medications, bile salt malabsorption (e.g. ileal Crohn's, cholecystectomy), infection, laxatives, metabolic disorders, food intolerances, small intestinal bacterial overgrowth, functional bowel disorders and other coexisting pathological causes of chronic diarrhoea (e.g. Coeliac disease and pancreatic insufficiency).
Miscellaneous	Physical mobility, cognitive function
IBD, inflammatory bowel disease	

Table 1. Pathophysiological mechanisms of anorectal dysfunction in patients with quiescent IBD.

notoriously difficult to treat group of functional disorders that affect patients with IBD.

# Pathophysiology of functional anorectal disorders in IBD

Given the complexity of the normal continence and defecatory mechanism, it is unsurprising that disruption of one or more mechanism as a consequence of IBD can lead to either evacuatory dysfunction or FI and multiple factors are involved in its pathogenesis.<sup>13</sup> The pathophysiologic mechanisms of persistent defaecatory symptoms in patients with quiescent IBD can be categorized under four broad groups which often overlap (Table 1). When assessing the symptomatic patient with quiescent IBD, it is therefore important for the clinician to be both holistic and mechanistic in the approach to understand which combination of these factors could be driving their patient's individual symptoms. It is clearly important to be thorough in excluding structural abnormalities and to consider other potentially treatable causes of altered stool characteristics. The approach to investigation and management of chronic diarrhoea has been reviewed elsewhere in recently published guidelines.14 The next section of this paper will review the current understanding of the key pathophysiological processes which can result in abnormal sensorimotor function of the anorectum and pelvic floor in IBD patients.

### Anorectal motor function

Several studies have demonstrated that IBD has an impact on the motor function of different parts of the gastrointestinal tract. Current understanding is that inflammation-induced neuroplastic changes in the enteric neural circuitry (including the myenteric plexus) contribute to disrupted motility in active and quiescent IBD.15-<sup>17</sup> Predictably, based on the differing distributions of inflammation, the patterns of dysmotility induced by UC and CD vary, with the small bowel being more commonly implicated in CD with antroduodenal manometry demonstrating significantly impaired contractility in up to 74% of patients with quiescent disease.<sup>18-20</sup> By contrast, colonic changes including motor or sensory are more commonly seen in patients with UC, even after resolution of the inflammation. This might be related to a persistent subclinical inflammation associated with increased colonic paracellular permeability which may drive symptoms.<sup>21</sup> Indeed studies using manometry, scintigraphy and barostats have demonstrated decreased contractility and reduced colonic tone postprandially, and in quiescent UC, a reduction in the number of high amplitude propagated contractions but increase in the low amplitude propulsive activity compared with controls.<sup>22</sup> Moreover, studies in both UC and CD patients have consistently demonstrated lower anal pressure, poor rectal distensibility, reduced compliance together

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History

with enhanced perception.22 While the exact mechanism for reduced anal sphincter pressures remains unclear, a recent study evaluating anorectal motor-evoked potentials to magnetic stimulation in FI patients demonstrated prolonged nerve conduction, suggesting neuropathy in spino-anal and spino-rectal pathways contributes to the pathogenesis of FI.<sup>23</sup> Unfortunately, this technique has not been applied in an IBDspecific population with FI to date.

Anorectal sensitivity and compliance: visceral hypersensitivity, an exaggerated perception of stimuli encompassing both allodynia and hyperalgesia, is one of the main hallmarks of functional gastrointestinal disorders.<sup>24</sup> IBD patients with active or inactive disease have been shown to have continuous release of inflammatory mediators which can give rise to sensorimotor alterations in the gut, and development of visceral hypersensitivity. These neuroplastic changes occur both centrally or peripherally in afferent nociceptive pathways from the viscera to the brain and is termed central sensitisation<sup>25</sup> This response to mucosal injury has been demonstrated in healthy humans in preclinical models<sup>26</sup> and interestingly, studies using rectal distension in IBD patients have similarly demonstrated increased sensitivity to standardised stimuli in patients with quiescent CD27,28 and UC.29-31

The exact mechanisms of altered sensitivity in the absence of active inflammation are unclear. However, alterations in gut microflora, gut permeability, immune activation, increased mucosal serotonin availability and abnormalities of enteric nerve structure and function have been postulated in recent literature where it is suggested that one in three patients with IBD in remission, still have persistent abnormalities of sensation, motility and gut microbiota.32

#### Identifying patients with functional anorectal disorders in the IBD clinic

A major challenge in diagnosing functional disorders in IBD patients is that these often present with similar symptoms to those experienced by patients with active inflammation including urgency, frequency, FI, constipation and evacuatory disturbance.33 This underpins the need for a systematic approach to assessment of such symptoms, and should include the aspects described in the following sections.

### In addition to an IBD-focused clinical history, particularly when objective evidence of active inflammation and structural pathology is lacking, screening questions for diagnostic features of functional disorders and risk factors for pelvic floor dysfunction should be sought.

This should include a detailed obstetric history in women, in particular related to complications during vaginal deliveries, and to anal sphincter surgeries (e.g. haemorrhoidectomy and sphincterotomy) in both sexes.34

A careful review of medications related to the symptoms is also important. In particular the distribution of previous inflammatory disease can be an important cue, for example in patients with distal colitis or proctitis whose inflammation has previously been confined to the rectum with inability to tolerate rectal therapies such as foam or liquid enemas can be a clue to underlying rectal hypersensitivity.35

It is also important to ask screening questions for positive features of coexisting functional bowel disorders such as irritable bowel syndrome (IBS) including the characteristics of stools, associated bloating and abdominal pain associated with defaecation.<sup>36</sup> Furthermore, while patients often report an increase in frequency of defaecation, a common pitfall in clinical practice is the failure to characterise this in more detail. For example, for some, the frequent urge to visit the toilet may not result in passage of a bowel motion and can be misinterpreted as diarrhoea. It is therefore important to screen for defaecation disorders by eliciting a history of incomplete emptying, the need to strain to pass stools and it is important to understand the stool consistency to interpret whether there are any features to suggest overflow diarrhoea and faecal impaction. The need to use rectal digital manoeuvres to help evacuate stool is an important clinical feature in suspected defaectory disorders and has been shown to be a predictive of outcomes to pelvic floor biofeedback therapy for evacuatory disorders.37,38

Clinicians must proactively screen for FI, as studies have shown that FI affects up to 74% of IBD patients,<sup>39,40</sup> but is often underreported due to fear of embarrassment.<sup>41</sup> FI is one of the most embarrassing symptoms suffered by patients with IBD and can be socially debilitating and isolating, impacting heavily on the quality of life of the patients.<sup>40</sup> Moreover, poor bowel control and the need for urgent toilet access have been reported to be amongst the top 10 concerns of people with IBD.42 When taking a history, clinicians must recognize the three different subtypes of FI. These are: (a) passive incontinence (the involuntary discharge of stool or gas without awareness); (b) urge incontinence (the discharge of faecal matter in spite of active attempts to retain bowel contents); and (c) faecal seepage (the leakage of stool following an otherwise normal evacuation). In this context, use of validated diagnostic questionnaires may be helpful.43 Indeed, an IBD-specific FI validated assessment tool has recently been developed to address this concern and helps assess and approach a potentially embarrassing problem sensitively both in clinical practice as well as in research.<sup>43</sup> In addition to diagnostic questionnaires, patient reported outcome measures have become increasingly common in clinical care and can be helpful in understanding the thoughts, perceptions, opinions and attitudes of patients regarding their disease and its treatment.44 A quality of life assessment can also help clinicians understand the impact of symptoms on healthcare utilisation and the patients' lives. 40,45

### Physical examination

A detailed history should be followed by a thorough physical examination including a neurological examination. The importance of examining the perineum and the anorectum cannot be over emphasised.<sup>46</sup> A detailed inspection looking for stoma bags, scars suggestive of previous surgical interventions including; cholecystectomy, IBD surgeries, evidence of external hemorrhoids or rectal prolapse can be helpful. Asking the patients to cough and strain may help identify apparent perineal descent or rectal prolapse.

Testing of perianal sensation and anocutaneous reflexes assessing neural integrity for continence, should follow a visual inspection. A digital rectal examination testing the resting sphincter tone, strength of puborectalis sling and anal sphincter squeeze provides valuable insight.<sup>46</sup> It also gives clue on any impacted stools, altered stool consistency.<sup>29</sup> Assessing a push and bearing down manoeuvre during digital rectal examination is useful in assessing for evacuatory disorders by eliciting changes in abdominal muscle tightening, perineal descent and contraction or relaxation of

anal sphincter and puborectalis and can therefore be helpful in selecting patients for physiological testing.<sup>46,47</sup>

#### Investigations to exclude active inflammation

Laboratory biochemical tests. By definition, patients with quiescent disease will have undergone investigations to exclude active inflammation. These initial tests would include inflammatory markers as part of a standard blood profile with C-reactive protein. Another helpful, more recent advance as a non-invasive biomarker, is faecal calprotectin, a small calcium-binding protein, which is elevated in the presence of active intestinal inflammation.<sup>48</sup> A cutoff value of  $\leq 250 \,\mu g/g$ has been shown to be predictive endoscopic remission in CD with a sensitivity of 94% and specificity of 62%. Similarly, a faecal calprotectin level  $>250 \,\mu\text{g/g}$  has a sensitivity of 71% and a specificity of 100% for active mucosal disease in UC.49 When comparing the ability to differentiate between functional disorders and IBD a cutoff of  $<100 \,\mu\text{g/g}$  appears to provide optimal differentiation.50

Furthermore, all patients with diarrhoea and a suspected flare should have stool samples cultured to exclude infection.

*Endoscopic evaluation.* Endoscopic evaluation is an integral aspect of assessment of mucosal inflammation and other pathology and indeed confirmation of mucosal or histological healing.<sup>51,52</sup>

*Imaging.* Depending on the disease phenotype, particularly in patients with small bowel CD, enterography or video capsule enteroscopy may be indicated to exclude small bowel inflammation.<sup>52</sup> Similarly, in patients with penetrating disease and clinical findings suggestive of fistulation, structural pelvic imaging may be necessary.

# Investigations to exclude other treatable causes of chronic diarrhoea

A heterogenous group of other conditions which can cause altered stool consistency can coexist in patients with quiescent IBD (summarised in Table 1). As the symptoms of these conditions can mimic those of active inflammation, conditions such as coeliac disease and exocrine pancreatic insufficiency can be effectively screened for non-invasively and other conditions such as bile 
 Table 2. Important tests to evaluate anorectal function.

	Test	Indication
Test for anal structure	Endoanal ultrasound	To evaluate morphological integrity of anal sphincters.
Tests for anorectal sensorimotor function	Anorectal manometry Anorectal sensory testing	Anal sphincter strength Ano-rectal coordination during simulated defecation Assess rectal compliance Recto-anal inhibitory reflex Assess rectal sensitivity
Tests for evacuation	Balloon expulsion test	Evacuatory function
	Defaecating proctogram/ magnetic resonance imaging Proctogram	Identify structural or functional obstructive features in patients with evacuatory disorders.

salt malabsorption and small intestinal bacterial overgrowth<sup>53</sup> should be considered, particularly in patients with risk factors including ileal CD, as per recently published guidelines.<sup>14</sup>

# The role of anorectal manometry in the IBD patient

Anorectal manometry (ARM) is the most important test to assess anorectal function and detect motor abnormalities of sphincter function and anorectal coordination. It is indicated in patients presenting with FI and chronic refractory constipation and suspected evacuatory dysfunction. ARM enables assessment of rectal sensation, reflexes, and compliance.54 It uses manometric equipment to measure the resting tone of the anal canal, voluntary function during squeeze, and reflex recto-anal coordination during rectal distension. In addition, it allows assessment for dyssynergic patterns and recto-anal coordination during simulated defecation ('push').55 It is therefore a useful test to confirm physiological abnormalities to select patients for biofeedback therapy. In a normal ARM, bearing down would produce increased rectal pressures simultaneously with anal relaxation.

Another potential indication for ARM would be during the preoperative work up for IBD patients with stomas who are under consideration for reconstructive bowel surgery. In these patients, ARM can be performed on the 'out of circuit', defunctioned anorectum. The physiological findings can be useful to assess the anorectal pressures as a predictor of post re-anastomosis functional anorectal disorders and inform the need for preoperative pelvic floor physiotherapy or biofeedback therapy (discussed in detail below) or alternative management strategies to mitigate these risks preoperatively.<sup>56</sup>

Other important tests for evaluation of anorectal function are summarised in Table 2.<sup>55</sup>

# Diagnosing functional defaecation disorders in IBD patients

Functional defaecation disorders (FDDs) are an important, but often under-recognised cause of refractory defaecatory symptoms in patients with IBD.<sup>9</sup> The pathophysiological abnormality in FDDs is a dyssynergic pattern of defecation secondary to the inability to coordinate the abdominal and pelvic floor muscles to evacuate stools.

As with other functional gastrointestinal disorders, Rome IV has provided a set of diagnostic criteria for identification of FDDs.<sup>57</sup> However, in quiescent IBD, pelvic floor dyssynergia is more complex, in that it often presents with a mixed picture of symptoms including increased stool frequency, defaecatory urgency, and FI, rather than purely constipation and defaecatory difficulties.<sup>58</sup> Thus, FDDs pose a diagnostic challenge in the setting of IBD and it is important to consider this as a possibility when IBD patients in remission present with such symptoms. The use of two tests including ARM plus a balloon expulsion test or defecography is mandatory to make this diagnosis.<sup>57</sup> The balloon expulsion test is a useful screening test for FDDs whereby the patient is asked to expel a balloon filled with 50 ml of water within 1 min.<sup>57</sup>

### Management of functional anorectal disorders in quiescent IBD

When symptomatic IBD patients are in remission, a wide spectrum of diseases, can mimic or even coexist with IBD. It therefore becomes important for clinicians to explore the possibilities listed in Table 1 to differentiate the symptoms of refractory IBD from those secondary to other mimicking conditions, especially when there is poor response to standard IBD therapies.

Once active disease is ruled out, the management needs to be individualised for each patient and should target specific symptoms with the aim of improving quality of life. Strategies should include supportive and specific measures and must take into consideration patient's symptoms, underlying pathophysiology, age, comorbid conditions, patient's concerns and expectations.

### Supportive treatment

#### General measures for FI in quiescent IBD

Patients should be asked to maintain a food and symptom diary to identify any specific agents which trigger a looser consistency of stools.<sup>59</sup> Various studies have identified common factors, which include lactose and fructose in diet, and caffeinated drinks enhancing gastrocolic/gastroileal reflexes.60-62 Brisk physical exercise immediately after meals or immediately after waking up, may precipitate FI.63 Fibre supplements such as psyllium husk have traditionally been advocated as stool-bulking agent to reduce watery stools and have shown to have modest improvement in a single case-controlled study.64 However, fibre supplements have a potential to worsen diarrhoea by increasing colonic fermentation of the unabsorbable fibre. Another important consideration for improvement of functional gut symptoms is the restriction of the poorly absorbed, short chain carbohydrates, fermentable, oligo, di, monosaccharides and polyols (FODMAPs) from the diet. A study from Australia with 52 CD and 20 UC patients showed improvement in overall abdominal symptoms including abdominal pain, bloating, wind and diarrhoea in 50% who adhered to this diet.65

#### Constipation-predominant symptoms

The mainstay of treatment for constipation would include avoidance of constipating medications including opiates, addition of adequate fibre (up to 25 g per day), regular fluid intake and exercise. However, it has been shown that these lifestyle modifications may actually be part of strongly held beliefs rather than being evidence based.<sup>66</sup> Timed toilet training, use of effective straining methods and utlising the mechanisms that stimulate colon activity such as after waking and after a meal are some measures that might prove to be helpful.67 A systematic review by Rao and colleagues has shown that fibre is beneficial for mild to moderate constipation and constipation-predominant IBS. However, they did not find much benefit from a FODMAP-restricted diet in this subset of patients.<sup>68</sup> Further studies are needed to establish their role in patients with constipationpredominant symptoms.

# Pharmacotherapy for functional anorectal disorders in the IBD patient

Faecal incontinence. It is important to understand that if the symptoms are driven by a functional bowel disorder such as IBS, they do not respond to IBD-specific treatments such as mesalazine and this has been shown in a randomised controlled study.<sup>69</sup> The antidiarrhoeal agents loperamide, diphenoxylate and atropine sulfate have been shown to be effective in controlling stool frequency, consistency, urgency, and FI in patients with chronic diarrhoea<sup>70</sup> In refractory cases, other treatment options include clonidine, which has been shown to increase colonic and rectal compliance, and reduces tone, pain, gas sensation and rectal urgency.71 The use of centrally acting neuromodulators for functional gastrointestinal disorders is currently topical, being strongly advocated in a Rome Foundation working party report.72,73 Interestingly, there is moderate evidence for the efficacy of tricyclic antidepressants in IBD patients with residual symptoms, despite controlled inflammation.74 This approach can be helpful in addressing the rectal hypersensitivity and may improve urgency and incontinence symptoms.75

*Constipation.* Patients presenting with constipation or FDDs may benefit from use of laxatives. This is often a difficult discussion to have with patients suffering with frequency, FI and urgency in the context of overflow type diarrhoea and an abdominal X-ray can therefore be useful to objectively demonstrate proximal constipation particularly in the setting of distal colitis. Another useful strategy in quiescent UC patients maintained on 5-aminosalicylates could be switching to the olsalazine preparation. Olsalazine has been shown to increase orocaecal transit and may be beneficial due to its favourable side-effect profile in this context which includes diarrhoea<sup>76,77</sup> Newer drugs including the intestinal secretagogues linaclotide, lubiprostone, plecanatide and serotonergic enterokinetic agents such as prucalopride may also benefit IBD patients with constipation/FDDs although more studies are needed to confirm their efficacy in this subset of patients.<sup>78–80</sup>

Neuromuscular training/biofeedback therapy. Biofeedback therapy (BFT), a well-tolerated, effective instrument-based technique, has been shown to improve physiological function, symptoms and quality of life in patients with functional anorectal disorders.<sup>81</sup> BFT is based on the principles of 'operant conditioning', whereby a new behavior (i.e. improved perception of anorectal sensation and coordination) is learned during a process of repeated reinforcement and instant feedback. During BFT, the patient's awareness of their physiological response is augmented during neuromuscular training.

BFT is effective in achieving the following goals: (1) improving anal sphincter muscle strength; (2) improving the coordination between the abdominal, gluteal, and anal sphincter muscles during voluntary squeeze and following rectal perception; and (3) enhancing anorectal sensory perception.<sup>70</sup> Each goal requires a specific method of training and the treatment protocol therefore needs to be adapted for each patient based on their underlying symptoms and their manometry findings. Training is performed under direct supervision of the therapist with continuous assessment by visual, auditory or verbal feedback during exercises, followed by objective feedback using a probe inserted in the anal canal to display physiological traces on a monitor. Patients typically attend 4-6, 60 minute sessions, although the optimal number of sessions is unknown.81

Biofeedback therapy for faecal incontinence. Due to its efficacy in patients with FI,<sup>10,82</sup> BFT has been assigned a grade A recommendation by international neurogastroenterology and motility societies.<sup>81</sup> BFT exercises for FI are structured

for gradual strengthening and endurance of the anal musculature and improvement of rectal sensation. This is achieved using modified Kegel exercises in the sitting or lying position with the probe in situ.81 During these anal sphincter exercises the patient is educated about the changes in manometric pressure traces on the display screen. The patient is usually advised to practice for 20 min 2-3 times per day at home, and there is emerging evidence that the amount of in-home practice is predictive of a positive outcome.82 Another important aspect of BFT for FI is urge resistance training. The principles of urge resistance training are to desensitise the rectum to sensations of balloon inflation. This is achieved by increasing balloon distension in slow increments with larger volumes until a strong urge is experienced. When the strong urge is experienced the patient is taught deep breathing techniques to help them relax and counteract the urge sensation.<sup>81</sup> Sensory retraining is also another aspect to BFT in FI patients with impaired rectal sensation. This is achieved using balloon inflation to determine the patients' sensory threshold and teaching them to squeeze the anal sphincter whenever they feel a sensation.<sup>81</sup> The aim is for the patient to respond to lower volumes of distension. Patients are encouraged to squeeze at home whenever they feel the sensation in the anorectum with a view to preventing accidents.

Biofeedback therapy for functional defaecation disorders. Similarly, BFT has been shown to be effective in FDDs, whereby during training, patients learn how to coordinate the defaecatory movement consisting of an abdominal push effort (diaphragmatic and rectus muscle training) synchronised with anal relaxation.<sup>81</sup> During sessions, using the display of their manometry tracings and diagrams of normal anorectal manometry traces, patients are taught how to correct their dyssynergia. Patients are often subsequently trained on a commode and practice expulsion of a simulated stool, using a 50 ml water filled balloon in the rectum, to improve evacuatory function. Sensory retraining, particularly in patients with hyposensitivity, can be helpful. This can be performed by repeated inflations and deflations of the inflated rectal balloon with a view to resetting the sensory threshold to a lower value.81

Biofeedback therapy in patients with inflammatory bowel disease. Emerging evidence suggests that pelvic floor BFT may also have a role in treating anorectal dysfunction in patients with quiescent IBD,<sup>33,83</sup> but there are very few studies in the literature that have investigated this, and none that have prospectively defined the magnitude of the clinical problem. Due to the complex overlap between symptoms of FI and FDDs in patients with anorectal dysfunction in quiescent IBD, the approach to BFT needs to be tailored to the individual patients' symptoms and physiological findings and would likely involve a combination of the approaches in FI and FDDs (described above).

A recent systematic review and meta-analysis of the seven small studies available, has shown that most patients (up to 97% without ileo-anal pouch anastomosis) with persistent defaecatory symptoms and quiescent IBD have FDDs.<sup>9</sup> The majority of IBD patients with FDDs in these studies (70%) responded to BFT<sup>9</sup>. BFT therapy also appears to be effective in patients with FDDs after ileo-anal pouch anastamosis<sup>9,84</sup>

# Neuromodulation

Given that post-inflammatory neuroplastic changes and neuropathy appear to be implicated in the pathophysiology of anorectal dysfunction in IBD, neuromodulation remains an attractive therapeutic option in this field. Sacral nerve stimulation and percutaneous tibial nerve stimulation are two modalities that have impressive success rates in non-IBD patients<sup>85</sup> and have been tested in two very small studies in IBD patients with FI.<sup>86–88</sup> Whilst the data for sacral nerve stimulation appear promising, only five patients with CD were studied,<sup>86</sup> and therefore further research is needed to confirm efficacy.

Other non-invasive neurostimulation devices such as transcranial direct current stimulation,<sup>89</sup> vagus nerve stimulation<sup>90</sup> and repetitive magnetic stimulation<sup>91</sup> have all recently been piloted in FI/ IBD/functional gastrointestinal disorders studies and may also have future therapeutic potential for research studies in this field.

# Other miscellaneous therapies

Other therapies ranging from use of disposable anal plugs and sphincter bulking therapies are available. However, they have limited evidence to support their routine use.<sup>92,93</sup> Other methods, including myomectomy, botulinum toxin injection or surgery, have been used for management of FDDs with constipation-predominant symptoms and have been shown to be less effective than BFT.  $^{94}$ 

### Conclusion

Despite being in the era of improved biological therapies for IBD, a significant proportion of patients continue to suffer with persistent and debilitating symptoms of FI and defaecatory disorders in the absence of active inflammation, significantly impacting on their wellbeing and quality of life. Current lack of awareness amongst clinicians compounded by a failure to recognise anorectal dysfunction in IBD patients may lead to potentially premature treatment 'escalation' and prolonged, futile exposure to corticosteroid therapy with undesirable consequences and indeed under-utilisation of pelvic floor investigations.35 This situation may stem from the fact that many gastroenterologists receive minimal training opportunities in gastrointestinal motility95-97 as reflected in a recent survey on the utility of ARM and BFT.98

FI should be screened for sensitively in IBD clinics on a routine basis. In the absence of active inflammation, and other explanations for symptoms, defaecatory disorders and neuromuscular and perceptive anorectal changes are very common amongst quiescent IBD patients. Due to the differing pathophysiology outlined in this article, clinicians must recognise that defaecatory disorders present differently in IBD patients with coexisting frequency, urgency and FI symptoms, compared with non-IBD patients with a pure functional constipation symptom profile. Patients with IBD across the spectrum of anorectal dysfunction outlined in this article, should be recognised early, offered holistic care and anorectal function tests with referral to pelvic floor services for consideration of BFT if appropriate.

There is a great need for further research in this population to understand the proportion of patients affected by anorectal dysfunction with quiescent disease. BFT appears to be an effective treatment modality for both FDDs and FI in this context, but larger studies would be required to confirm this. Future areas for research include the need for neurophysiological studies to help understand more about the pathophysiology of anorectal dysfunction in IBD. There is also a need to develop specific diagnostic criteria/agreed guidelines for diagnosing FDD in IBD patients. Further mechanistic studies to see if neuromodulation can induce favourable neuroplastic changes in spino-anal and spino-rectal pathways to objectively improve anorectal function are urgently needed.

## Funding

This work was supported by a quality improvement project grant awarded to DHV by Dr Falk and Guts UK.

### **Conflict of interest statement**

The authors declare that there is no conflict of interest.

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