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Delphi consensus survey: the opinions of patients living with refractory ulcerative proctitis and the health care professionals who care for them

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ABSTRACT

Background Refractory ulcerative proctitis presents a huge clinical challenge not only for the patients living with this chronic, progressive condition but also for the professionals who care for them. Currently, there is limited research and evidence-based guidance, resulting in many patients living with the symptomatic burden of disease and reduced quality of life. The aim of this study was to establish a consensus on the thoughts and opinions related to refractory proctitis disease burden and best practice for management.

Methods A three-round Delphi consensus survey was conducted among patients living with refractory proctitis and the healthcare experts with knowledge on this disease from the UK. A brainstorming stage involving a focus group where the participants came up with an initial list of statements was completed. Following this, there were three rounds of Delphi surveys in which the participants were asked to rank the importance of the statements and provide any additional comments or clarifications. Calculation of mean scores, analysis of comments and revisions were performed to produce a final list of statements.

Results In total, 14 statements were suggested by the focus group at the initial brainstorming stage. Following completion of three Delphi survey rounds, all 14 statements reached consensus following appropriate revision.

Conclusions We established consensus on the thoughts and opinions related to refractory proctitis from both the experts who manage this disease and the patients living with it. This represents the first step towards developing clinical research data and ultimately the evidence needed for best practice management guidance of this condition.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Refractory ulcerative proctitis presents a huge clinical challenge and there is currently limited research and evidence-based guidance on this chronic, progressive condition.

WHAT THIS STUDY ADDS

⇒ A list of consensual statements on the thoughts and opinions related to refractory proctitis from both the experts who manage this disease and the patients living with it.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These statements represents the first step towards developing clinical research data and ultimately the evidence needed for best practice management guidance of this condition.

INTRODUCTION

Ulcerative colitis (UC) has a prevalence of 1 in 125 (0.8%).[1] It is unclear at any one time how many patients with UC have ulcerative proctitis where inflammation is confined to the anatomical region of the rectum.[2] Refractory ulcerative proctitis is a prevalent problem and there is a large unmet need within IBD research on this chronic, progressive condition.

A ratio of 4.2:3.7:2.2[3] for extensive colitis (E3), left-sided colitis (E2) and proctitis (E1) has been reported, respectively, with the highest prevalence of ulcerative proctitis identified at 33%.[4] In a recent prospective European population-based inception cohort, 31% (93/300) of patients with UC have E1 at diagnosis, with 24% progressing to E2 and 14% progressing to E3 at the end of 7-year follow-up.[5] The pooled frequency of UC extension rates are 22.8%, more specifically 17.8% at 5 years and 31% at 10 years, or 17.8% (95% CI 11.2 to 27.3) from E1 to E3, 27.5% (95% CI 7.6 to 45.6) from E2 to E3 and 20.8% (95% CI 11.4 to 26.8) from E1 to E2. Controlling the disease in limited proctitis is essential to preventing disease extension and any possible risks that may result from extension, such as a more severe clinical course and an increased risk of colorectal cancer.[6]

In patients whose disease does not progress and remains confined to the rectum, ulcerative proctitis is still often responsible for distressing symptoms such as tenesmus, urgency, faecal incontinence, proximal constipation and rectal bleeding, leading to a reduced quality of life.[7] A third (31%) of patients with ulcerative proctitis have refractory disease.[8] Refractory disease is defined as active proctitis which fails rectal and oral therapy with aminosalicylates (5-ASA) and corticosteroids.[9] 5-ASA suppositories are the first-line treatment in patients with refractory disease, followed by immunomodulators and/or biological therapies.[10] Treatment of refractory proctitis remains challenging because these patients are systematically excluded from randomised controlled trials with drugs with new modes of action.[8] In the absence of controlled data, recommendations for the management of ulcerative proctitis are therefore extrapolated from data in more extended UC or from small real-world evidence.

Effective and timely management of patients with ulcerative proctitis is therefore important not only to control symptoms and improve quality of life, but also potentially to delay or prevent proximal extension of inflammation and improve outcomes.[8] To develop management strategies and improve health outcomes for patients living with refractory ulcerative proctitis, agreement is needed on the current knowledge and opinions on the condition.

Aims

This study aimed to explore and better understand the opinions of healthcare professionals caring for, and patients living with, ulcerative proctitis. In order to do this, we recruited a small group of healthcare professionals and patients from around the UK to contribute initial thoughts on clinical and research needs in this area of IBD care by taking part in a focus group. We used the statements generated from the focus group work to develop a Delphi survey of key statements, this was then opened to a wider group of patients and healthcare professionals who met the inclusion criteria.

METHODS

Between January 2022 and June 2022, a three-round Delphi survey[11] was undertaken to establish a consensus of opinions related to refractory proctitis disease burden and its management in National Health Service (NHS)-based healthcare in the UK.

For the panellist selection, gastroenterologists (consultants and specialist trainees) and IBD nurse specialists working within the NHS were approached through the British Society of Gastroenterology (BSG) IBD section and the BSG IBD Clinical Research Group. Patients living with proctitis were invited to take part through their previous enrolment in the NIHR IBD BioResource study, or through response to a national advertisement on the NIHR Nottingham Biomedical Research Centre Website and social media. Participants were asked to confirm that they met the inclusion criteria (table 1) and then complete an online valid informed consent process via Microsoft forms.

Table 1 Inclusion and exclusion criteria

Inclusion	Exclusion
► Able to give valid informed consent ► Aged 18 years or above ► One of the following roles – NHS gastroenterology consultant or specialist trainees – NHS IBD nurse specialist – Patient under the care of the NHS for proctitis	► Unable to communicate in verbal and written English ► Unable to access the internet

IBD, Inflammatory bowel disease; NHS, National Health Service.

A focus group was initially formed (group authorship, see Collaborators section) in which the participants were asked to contribute their thoughts on the clinical and research needs in this area of IBD. Following this, the research team analysed and refined the statements, paying careful attention to preserve the original wording used by the focus group participants to produce initial statements for the Delphi survey. Each survey round was online for 6 weeks and reminder emails were sent approximately every 10 days after the initial invitation. In the first round, participants were asked to rank the importance of items by rating each item on a 10 point Likert rating scale[12] (1–10) from 1: strongly disagree to 10: strongly agree. They were also asked to provide recommendations regarding any additions and/or subtractions to the list of proposed items. Only those participants who completed round 1 of the survey were invited to round 2. In the second round, all ambiguous items or proposals driven by comments of the first round and concerning exclusion, aggregation or retention of items, together with any new items identified from the first round, were included in the second survey. Items that did not reach a consensual mean score of at least 7 out of 10 were excluded from further rounds for consideration. Following the second round, a ranking of item importance was made to rationalise the number of items and model this according to the Consolidated Standards of Reporting Trials Statement and TIDieR Checklist[13] for consistency. Synthesis of comments and further additions and deletions were made until there was final majority agreement. Three rounds were completed.

RESULTS

A flowchart detailing the Delphi process is shown in figure 1.

The composition of participants in each stage of the Delphi survey rounds can be found in table 2. A total of

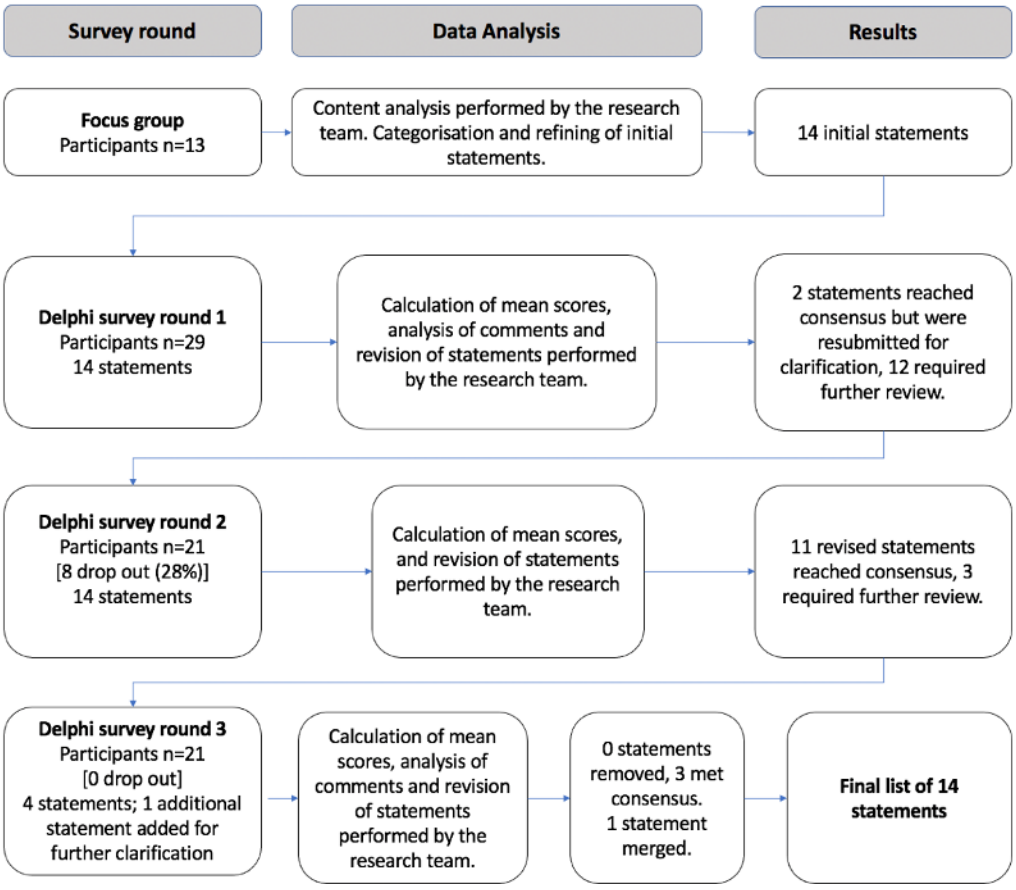

Figure 1 Flowchart of the Delphi process.

29 participants completed the Delphi survey round 1 and ranked the 14 initial statements.

Scores from the statements were categorised as being from medical professionals, specialist IBD nurses or patients with a consensual mean score provided for the whole group. Mean scores were calculated and following analysis of comments, the statements were revised. The first round consensus was reached on 2 statements (14%) which were resubmitted for further clarification with 12 (86%) requiring further review.

The second Delphi round response rate was 72% (21 of 29 participants; accounting for dropout of 3 medics, 2 nurses and 3 patient participants) and included 14 revised statements for review. Following the calculation of mean scores and revision of statements, a total of 11 statements (79%) reached consensus with only 3 (21%) requiring further review.

The total response rate for the third Delphi round was 100% (21 out of 21 participants). In this round, four statements were included, including the three statements from the previous round that did not reach consensus and a further statement added for clarification. Here, the participants were asked to rank the statements in order of importance. Following data analysis, 3 statements met consensus (75%), 1 statement was merged and 0 statements were excluded to produce a final list of 14 statements that met the criteria for consensual agreement. The 14 statements achieving consensus are available in table 3 with detailed agreement scores provided for each category of participation.

DISCUSSION

This is the first study of its kind to provide a list of consensual statements on the opinions and needs of those caring for and living with refractory ulcerative proctitis. A wide variety of both healthcare professionals and patients with an understanding of the condition participated in this

Table 2 The composition of participants in each Delphi survey round

	Medical professionals (M)	Registered nursing professionals (N)	Patients living with IBD (P)
Delphi survey round 1 (=29)	16	6	7
Delphi survey round 2 (=21)	13	4	4
Delphi survey round 3 (=21)	13	4	4

Table 3 Final statements with levels of agreement

	Final statements	Level of agreement (%)
1	In patients who are compliant to both rectal and oral therapy over an 8-week period, mesalazine-refractory proctitis is still an existing clinical problem.	WG: 0.78 M: 0.82 N: 0.9 P: 0.53
2	Present patient reported outcomes do not capture the symptom burden appropriately in proctitis. Disability, faecal incontinence, urgency, constipation and health-related quality of life are not captured.	WG: 0.83 M: 0.8 N: 0.9 P: 0.83
3	Constipation is a common problem in symptomatic refractory proctitis, and efforts should be made to treat it independently of inflammatory disease.	WG: 0.76 M: 0.8 N: 0.65 P: 0.75
4	A multidisciplinary team approach should be highly considered and at the appropriate time, a surgical option should also be considered in refractory inflammatory disease, though the type of surgical intervention is as yet unclear.	WG: 0.79 M: 0.84 N: 0.83 P: 0.6
5	Patient age and comorbidities should be factored into the decision-making process for therapies in refractory proctitis.	WG: 0.84 M: 0.91 N: 0.75 P: 0.7
6	Drug costs should not play a major role in the decision-making process regarding therapies for refractory proctitis.	WG: 0.79 M: 0.76 N: 0.93 P: 0.73
7	In the treatment of refractory inflammatory disease, patients prefer oral or systemic therapies rather than topical therapy.	WG:0.7 M: 0.66 N: 0.8 P: 0.78
8	Research investigating the role of thiopurines to treat inflammatory disease in mesalazine-refractory proctitis is limited.	WG: 0.73 M: 0.74 N: 0.9 P: 0.57
9	Low-dose topical or oral steroid therapy (5 mg prednisolone tablets or suppositories, or budesonide) may be considered to treat symptoms from inflammatory disease in select situations.	WG: 0.84 M: 0.9 N: 0.83 P: 0.83
10	Present evidence does not provide any clarity regarding the use and sequencing of biological agents and small molecules to treat inflammatory disease from refractory proctitis.	WG: 0.77 M: 0.81 N: 0.78 P: 0.63
11	Combination treatment with immunomodulators and any biological agents should be considered to treat refractory inflammatory disease in proctitis.	WG: 0.8 M: 0.83 N: 0.95 P: 0.55
12	After excluding other differential diagnoses, inflammatory disease may be treated with second-line or third-line biological treatments and small molecules.	WG: 0.83 M: 0.87 N: 1.0 P: 0.6
13	The role of off-licence topical therapies such as acetarsol or tacrolimus is unclear in the treatment of active inflammatory disease. More research is needed.	WG: 0.8 M: 0.84 N: 0.83 P: 0.65
14	Further research should be focused on refractory proctitis.	WG: 0.92 M: 0.94 N: 1.0 P: 0.75

M, medical professionals; N, nurse practitioners; P, patients; WG, whole group.

three-stage Delphi survey. It became apparent from the focus group that refractory proctitis presents a large clinical disease burden to both patients and the professionals who care for them. Despite full compliance with both oral and rectal mesalazine therapies, a third of patients still suffer from refractory disease.[8] The symptom burden these patients experience is felt to not be adequately reported resulting in limited knowledge on the matter.

When posed with the idea that current clinical and research tools are effective at measuring symptom burden in proctitis, it was felt that while rectal bleeding is well captured in scoring systems such as the MAYO score and the Simple Clinical Colitis Activity Index,[14 15] additional symptoms such as urgency and rectal discomfort are often excluded. Additionally, patient participants highlighted that other parameters of living with proctitis that were important to them, such as toilet tracking, fear of going out and incontinence during sexual intercourse were often overlooked as burdensome, contributing significantly to a reduced quality of life. There was disparity in patient and healthcare professionals opinions and what was deemed to be of importance, this perhaps represents the difference of opinions in what is important to patients regarding 'living well' with IBD. At present, there are no existing clinical scores for the assessment of proctitis alone, and thus it is felt that current reported outcomes do not capture the symptom burden appropriately in patients living with proctitis alone. Consensually, constipation was found to be a common issue in symptomatic refractory proctitis as emphasised in previous studies, which detailed how proximal constipation should always be considered in refractory cases.[16 17] The participants agreed that management of faecal stasis should be prioritised and treated independently of existing IBD.

A long-term study on the natural disease course of UC has found that 40% of patients underwent a colectomy within 50 years of diagnosis; however, despite being considered curative, surgery is associated with significant risks.[18 19] An initial statement mentioning that in patients with refractory proctitis, a colectomy should be considered, was felt to be extreme with many participants requiring further clarification. It was agreed that for a select number of patients who have exhausted all treatment options, surgery may be warranted, which could lead to an improved quality of life. However, the consensus was that we should be encouraging a multidisciplinary team approach and holistic discussions with patients outlining all medical and surgical options alongside risks and proposed benefits. Although the type of surgical intervention is as yet unclear, it was felt that in a select group of well-counselled patients with refractory disease, a surgical intervention such as a subtotal colectomy and end ileotomy, is a viable option and appropriate discussions should be had.[10 20] Nevertheless, after a subtotal colectomy, the diseased segment is left in situ so residual symptoms might persist.

Consensus was agreed that patient's age and comorbidities should be considered, with drug cost being less relevant, in regard to the decision-making process for therapies in refractory proctitis. It was felt that the associated poor quality of life, including lost days of work, social isolation and the mental health burden associated with this condition, is far more important than therapy costs, as they have the potential to significantly improve patient outcomes. In one study, a significant number of participants (43.9%) reported absenteeism as a result of IBD, with persistent abdominal pain, fatigue and difficulty participating in social activities being strong precipitators.[21] Additionally, therapies should be offered on an individualised patient basis with the age and comorbidities of patients taken into account.

This Delphi survey found that patients prefer oral or systemic therapies as opposed to topical therapies for the treatment of refractory inflammatory disease. When posed with a statement that anti-TNFs, ustekinumab, tofacitinib, vedolizumab or filgotinib should be equally used for patients with refractory proctitis, the general consensus was that there is currently not enough real-life evidence to support this assertion. This problem exists because all licencing trials for the afore-mentioned drugs exclude proctitis from their inclusion criteria, resulting in a lack of evidence-based guidance and a real clinical dilemma for those caring for these patients.[22–24]

Agreement was reached that in patients with refractory proctitis, combination treatment with both biological agents and immunomodulators should be considered. It is essential that any clinician excludes other differentials prior to advanced therapies, such as acute infection, irritable bowel syndrome or Crohn's disease, as these diagnoses may present with similar symptoms which mimic refractory disease. Furthermore, assuming that the symptoms described by a patient are due to active inflammatory disease, with proximal constipation being appropriately managed, then second-line or third-line biological treatments and small molecules could be warranted. Additionally, in select scenarios when the risks and benefits have been appropriately counselled to a patient, a low-dose topical or steroid therapy, such as 5 mg prednisolone tablets or suppositories, could be considered to treat troublesome symptoms in proctitis. For purposes of clarification, we included a dosage for prednisolone, which should not detract from the guidance for prescribing.

An additional area that was felt to have unclear clinical guidance included the role of thiopurines in the treatment of mesalazine-refractory proctitis and the use of off-licence topical therapies such as acetarsol or tacrolimus. The 2019 BSG IBD guidelines state that if the diagnosis is correct and standard therapy fails, then thiopurine therapy should be added in for proctitis, with escalation to biologics if no response is seen.[25] One study found that azathioprine was more effective at achieving steroid-free clinical and endoscopic remission after 6 months compared with oral 5-ASAs in corticosteroid-dependent UC.[17] For off-licence topical therapies, a Cochrane review on tacrolimus inducing remission in

corticosteroid-refractory UC highlighted the fact that further research including clinical trials are warranted to create real evidence-based guidance on the use of these drugs.[26] However, a recent retrospective analysis on the efficacy of acetarsol suppositories found that two out of three patients with refractory proctitis responded well to acetarsol.[27] The results of this study would be highly beneficial in furthering our understanding and creating practical guidance on the treatment of refractory proctitis.

From the Delphi survey, it was felt that there is not enough clarity surrounding the use of small molecules and sequencing of biological agents for the treatment of proctitis. Evidence-based guidance advising on the use of biological sequencing exists for UC, but there is no current guidance on their role in proctitis or extensive disease. Additionally, the source of these recommendations come from licencing trials which exclude proctitis from their inclusion criteria.[28 29]

While formal clinical guidelines are still required, these statements could be considered and used by practitioners in real clinical practice to act as a basis for the management of refractory proctitis, especially in patients with poor disease control. As an example, combination treatment with immunomodulators and biological agents should be considered to treat refractory inflammatory disease in proctitis. A limitation to this study is the small sample size of the Delphi survey participants and further work could focus on validating these statements in a prospective study with a larger sample size of participants with a broader scope of knowledge on the condition.

Refractory proctitis is an under-researched area, as most clinical trials exclude this specific patient group, resulting in a dearth of evidenced-based data and guidance for the medical professionals who care for them. Ultimately, the thoughts from the Delphi survey confirmed this opinion and consensus was met that further research should be focused on this disease.

CONCLUSION

In conclusion, we achieved a consensus on 14 statements by means of the Delphi methodology on the opinions and needs of patients living with refractory ulcerative proctitis, and the healthcare professionals who care for them. We hope this statement will guide funders on potential themed calls. This is the first step towards more clinical research and ultimately guidance aimed at this specific patient group with ulcerative proctitis.

Twitter Shellie Radford @Shellie_Jean

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Collaborators Focus group collaborators: Dr Christian Selinger, Dr Christopher Lamb, Ms Rachel Linger, Dr Matthew Brookes, Professor Ailsa Hart, Dr Daniel Gaya, Dr Jonathan Segal, Dr Stuart Bloom, Dr Ian Arnott, Dr Philip Smith, Miss Madhoor Ramdeen, Ms Helen Steed, Mrs Pearl Avery, Dr Shahida Din, Mr John Appleton, Mr John Anneh, P Adams, Ms B Kussel, Dr Jonathan Macdonald, Mrs Susan Ritchie, Ms Victoria Fletcher, Dr Anjan Dhar, Mr Mario Guslandi, Mr J Butterworth, Dr Philip Oppong, Dr N Sharma, Ms S. Andrews, Ms Deborah Morris.

Contributors All authors contributed equally to the manuscript. MK undertook manuscript generation and management of collaborator comments. SR undertook study design, protocol generation and management of participant recruitment and data, leading on data analysis. GWM had initial study concept, study design, data analysis and overall study and manuscript review.

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