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ORIGINAL ARTICLE

Gastroenterology: Inflammatory Bowel Disease

Noninvasive monitoring with bowel ultrasound (NIMBUS) in paediatric inflammatory bowel disease: Feasibility in a single centre

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Abstract

Objectives: Bowel ultrasound (BUS) is increasingly utilised for monitoring inflammatory bowel disease (IBD), a condition with stringent treatment targets to prevent complications. This study assessed the feasibility of BUS in paediatric IBD and its correlation with established monitoring markers.

Methods: A prospective study was conducted at a specialist paediatric IBD centre, including children aged 2–18 years with IBD diagnosed via modified Porto criteria. BUS parameters were based on paediatric ultrasound scoring systems, with imaging performed by a single paediatric radiologist. Biomarker data (faecal calprotectin, C-Reactive Protein, Erythrocyte Sedimentation Rate, White Cell Count, Ferritin and Albumin), and paediatric disease activity indices were recorded at time of BUS and again after a median follow-up of 2.8 months (interquartile range 1.8–4.1). Treatment changes were recorded, and ultrasound findings were correlated with clinical outcomes and inflammatory markers.

Results: Forty patients were included, 27 with ulcerative colitis (UC) or UC-type IBD-unclassified. BUS was feasible, with 98% retention ($n = 39$) and 96.5% measurable parameters (301/312). Poor-quality imaging occurred in 10.3%. In UC, bowel wall thickness (BWT, rho = 0.503, $p = 0.039$) and loss of haustration (rho = 0.490, $p = 0.039$) correlated with faecal calprotectin; no correlations were found for Crohn's disease or the total cohort. Activity index scores did not correlate with BUS parameters.

Conclusions: BUS shows potential as a noninvasive tool for assessing IBD activity in paediatric patients, especially in colitis where BWT correlates with calprotectin. However, image acquisition challenges highlight the need for expertise. Further studies across diverse cohorts are necessary to establish BUS's utility in paediatric IBD monitoring.

Trial Registration: Clinicaltrials.gov (21/12/2022): NCT05673278, https://clinicaltrials.gov/study/NCT05673278, IRAS ID: 8497/OCT/2022, Date of first enrolment: 01/05/2023.

KEYWORDS

child health, Crohn's disease, imaging, ulcerative colitis

1 | INTRODUCTION

Inflammatory bowel disease (IBD)—traditionally categorised as ulcerative colitis, Crohn's disease and IBD-unclassified—is a spectrum of chronic, immune-mediated inflammatory conditions primarily affecting the gastrointestinal tract.[1] Incidence of these conditions continues to rise within the paediatric population in global and national cohorts.[2,3] Treatment in IBD aims to bring about the suppression of inflammation, leading to mucosal (or transmural) and histological healing, with the lowest pharmaceutical burden.[4,5] Disease can be monitored through clinical response, three-dimensional imaging and faecal and serum biomarkers; however, the gold standard test is ileocolonoscopy and tissue biopsy.[6]

Existing monitoring tests are not without side effects/risk/harm. Endoscopic procedures carry the risks of general anaesthetic as well as local trauma and perforation; in addition to being expensive and carrying long waiting lists.[7] In clinical practice, the frequent use of endoscopy is not advocated for these reasons and practical management therefore involves the synthesis of clinical symptoms with inflammatory markers. This is not without difficulty however, as patient reporting of symptoms has not been demonstrated to correlate with gastrointestinal inflammation.[8] Amongst biomarkers, faecal calprotectin (FCP) is a highly sensitive marker of gastrointestinal inflammation and is well established for use in monitoring disease activity.[9]

Bowel ultrasound (BUS) is a noninvasive tool which can be used in IBD for disease monitoring and, despite increasing utilisation in the adult population, is underutilised in children.[10] Ultrasound is quick, reliable, non-radiating, accurate, inexpensive and acceptable to patients.[11] BUS also offers the opportunity for patient and family involvement in disease monitoring through the real-time visualisation of inflammation.[12] While potential advantages of BUS are numerous there remains ongoing need for assessment and standardisation of use, especially within the paediatric population.[13]

It is possible to measure several parameters using BUS. Bowel wall thickness appears to have the most clinical utility in relation to gastrointestinal inflammation.[14] Systematic review of paediatric studies suggests that the most important parameters for the assessment of inflammation are bowel wall thickness and colour doppler flow, indicating hyperaemia. Evidence for accuracy and value to clinical practice are still required.[13]

Given the advantages of BUS there is potential for the integration of ultrasound into routine follow up for children and young adults with IBD. However, despite a growing body of work, integration of BUS into practice, particularly within the United Kingdom, is lacking. Other contributions to this may be the uncertain relationship between ultrasound and reliably utilised markers such as faecal calprotectin and disease activity scores. Furthermore, there is concern regarding the feasibility of performing scans in the paediatric population and uptake amongst colleagues in paediatric gastroenterology and radiology alike.[15]

What is Known

- Treatment aims in inflammatory bowel disease increasingly target mucosal or transmural healing.
- Ultrasound is increasingly used in clinical and research settings to characterise inflammation.
- Feasibility of implementation in the paediatric population and how ultrasound findings relate to established biochemical disease markers is uncertain.

What is New

- Several previously described ultrasound parameters were measurable within a paediatric cohort.
- Bowel wall thickness (BWT) correlates with faecal calprotectin in paediatric ulcerative colitis.
- Correlation of ultrasound parameters was not demonstrated in the total cohort or in Crohn's-type disease.
- Feasibility data support future prospective BUS studies in this population.

The primary objective of this study was to prospectively examine the feasibility and utility of BUS in a paediatric IBD cohort and to inform future, randomised studies in this area. Secondary aims were to examine the relationship between measurable ultrasound parameters and established noninvasive monitoring modalities such as disease activity scores, faecal calprotectin and serum biochemical markers (white cell count (WCC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Ferritin, Albumin). Correlation between ultrasound parameters and clinically relevant outcomes at follow-up (i.e., treatment escalation and FCP) were also evaluated.

2 | METHODS

This was a longitudinal prospective feasibility study carried out in a single specialist paediatric gastroenterology centre (Noah's Ark Children's Hospital for Wales, Cardiff). The study protocol, including methodology and statistical plan have been published previously in full.[16] The study was undertaken between 01 May 2023 and 23 July 2024.

Children aged 2–18 years with a modified Porto criteria diagnosis of IBD were eligible for inclusion.[17]

Patients without IBD and those with IBD who previously undergone IBD-related surgery were excluded. Patients were identified by the clinical team from in- and outpatient lists, endoscopy and infusion schedules and from the locally held paediatric IBD database. All families gave informed consent, those under 16 years of age could provide assent and all could withdraw at any time. Participants were consecutively collected.

Recruited participants continued to have standard clinical care as per ESPGHAN/ECCO guidance.[17–20] This care included ad hoc measurement of inflammatory (WCC, CRP and ESR) and nutritional (Albumin, Ferritin) blood tests as well as stool samples for faecal calprotectin. Anthropometric measures [height, weight, body mass index (BMI)], medications, disease activity scores were also collected in this manner. At enrolment the most recent blood and stool tests (up to 3 months before study entry) were included. No blood samples or stool samples were obtained for the purpose of the study, with a 3-month period allowing for capture of most routine monitoring. Disease activity scores (Paediatric Ulcerative Colitis Activity Index (PUCAI), Paediatric Crohn's Disease Activity Index (PCDAI)] were recorded at recruitment, at time of ultrasound and over course of clinical follow-up, as were anthropometric measures (height, weight and BMI).[21]

A single bowel ultrasound was undertaken for each participant after recruitment; all scans were performed by a single paediatric radiologist (AE) skilled in BUS. The radiologist was blinded to all clinical information. All scans were performed using a Canon Aplio i700 (with 14 MHz and curvilinear 5–8 MHz probes). A global assessment of the bowel was initiated before segmental measurement of predefined criteria relating to IBD activity using high-frequency linear probe. This method is outlined in the study protocol and per *Dollinger and Kayal*.[22] The parameters measured are outlined in Table 1, alongside how each variable was scored.[23] Ultrasound parameters were assessed in predefined bowel segments (the sigmoid colon, descending colon, transverse colon, ascending colon, caecum and terminal ileum) with the score recorded for each participant at the most affected segment. Parameters included were identified from existing studies and scoring systems, to assess feasibility of a range of variables.[11,24,25] Resultant scan quality and barriers to achieving adequate images were documented. Ultrasound quality was allocated a rank by the single paediatric radiologist, with 'A' indicating good quality, 'B' denoting satisfactory quality and 'C' indicating poor quality. Scan findings were not shared with the clinical team and a standard operating procedure was devised, should serious or unexpected findings have been identified on ultrasound imaging. Ultrasound images demonstrating measurable parameters were recorded anonymously for all patients.

Medical records could be reviewed up to 12 months following ultrasound imaging. Blood and stool results as well as disease activity indices and anthropometry were recorded. Adverse events, treatment escalation, admissions and complications were recorded. Treatment escalation was defined as either the initiation of rescue therapy, in the form of exclusive enteral nutrition, steroid therapy or increase of dose or frequency of administered biologic treatment. Primary feasibility metrics were recorded for individual participants including loss to follow-up, ultrasound parameters measurable, scan quality and barriers to adequate quality imaging. A STROBE checklist was completed and can be accessed as a Supporting Information file: STROBE Checklist.

TABLE 1 Bowel ultrasound (BUS) scoring system used for the assessment of intestinal inflammation.

Ultrasound parameter	Score description
Bowel wall thickness	0: ≤2 mm
	1: >2 mm
	2: >3 mm
	3: >4 mm
Colour Doppler signal	0: Absent
	1: Small spots (single vessels) visible within the wall
	2: Long stretches visible within the wall
	3: Long stretches visible extending into the mesentery
Loss of wall layer stratification	0: Preserved
	1: Not preserved
Loss of haustration	0: Preserved
	1: Not preserved
Fat wrapping	0: Present
	1: Absent
Motility in the terminal ileum	0: Preserved
	1: Not preserved
Lymphadenopathy	0: Absent
	1: Present
Abscess/stricture	0: Absent
	1: Present
Total Ultrasound Score (/12)	Sum of all parameters
Image study quality	A: Good
	B: Adequate (Specify reason)
	C: Poor (Specify reason)

Note: Features measured at site of maximal activity or wall thickness. Total ultrasound score reported as a sum of these parameters; maximal score 12.

2.1 | ETHICS STATEMENT

NHS Research Ethics Committee (23/WA/0028, 24 March 2023) granted Health and Care Research Wales and Heath Research Authority approval. The study was sponsored by Cardiff and Vale University Health Board. All families gave informed consent, those under 16 years of age could provide assent and all could withdraw at any time. No payments or any other benefits were made to participants (Declaration of Helsinki requirement).

2.2 | Statistical analysis

All data were reported as means with standard deviation (SD), medians with interquartile range (IQR) or frequencies within the total cohort. Primary feasibility metrics, for recruitment, retention and follow up are reported as frequencies and assessed against traffic light criteria previously defined in the contemporary literature and study protocol.[16,26] Sample size considerations were undertaken, as outlined in the published protocol, with the aim of demonstrating feasibility. Comparable works, at the time of study design included numbers of participants ranging from 9 to 50. A target recruitment figure of 50 individuals was defined.[16,27]

Shapiro–wilk test was undertaken to assess for normality of distribution. Spearman's rank (rho) was calculated to correlate individual ultrasound parameters, as well as total ultrasound score with paired activity indices, calprotectin, CRP, ESR, Albumin and Ferritin. Receiver operating characteristic (ROC) analyses were undertaken to evaluate the sensitivity and specificity of total ultrasound score, as well as bowel wall thickness (BWT) in predicting increase in treatment and elevated faecal calprotectin at follow up. Elevated calprotectin, where analysed as a binary outcome, was defined as 250 µg/g being 'positive' and less than 250 µg/g being 'negative'.[28] A $p \leq 0.05$ was considered statistically significant. All analyses were two-sided. Data were analysed using SPSS Statistics for Windows, Version 29.0.2.0 (IBM Corp.).

3 | RESULTS

3.1 | Patient characteristics and feasibility metrics

Forty patients, median age 13.7 (IQR 11.0–14.8, range 6.0–16.6) were included. Baseline characteristics can be visualised in Table 2. Twenty-three individuals had ulcerative colitis (UC) or inflammatory bowel disease unclassified (IBDU) UC-type (57.5%). Twenty-eight

TABLE 2 Patient ($n = 40$) baseline enrolment characteristics.

Characteristics	Frequency (percentage, %) or median (25th–75th interquartile range)
Age, years	13.7 (11.0–14.9)
Sex	
Male	28 (70%)
Female	12 (30%)
Follow-up duration, months	2.8 (1.8–4.1)
Body mass index, *z*-scores (mean (standard deviation))	0.6 (1.3)
Weight *z*-score (mean (standard deviation))	0.6 (1.2)
Disease subtype	
UC (+IBDU-UC)	23 (57.5%)
Crohn's Disease	17 (42.5%)
Activity index score	
PUCAI	10 (5–20)
PCDAI	25 (15–30)
Treatment	
Steroids	11 (27.5%)
Biologic	
ADA	1 (2.5%)
IFX	24 (60%)
USTE	1 (2.5%)
VEDO	6 (15%)
Dual therapy (ADA+UST)	1 (2.5%)
N	
Immunomodulator/other	7 (15%) 1 (2.5%)
6-MP	12 (30%)
AZA	4 (10%)
Mesalazine	1 (2.5%)
EEN	7 (17.5%)
Treatment escalation	
Commence IFX	1 (2.5%)
Increase biologic dose/ schedule	4 (10%)
Class switch	2 (5%)
Start immunomodulator	1 (2.5%)
Biochemical markers	
CRP, mg/L	0 (0–2)
ESR mm/h	4 (2–8)

TABLE 2 (Continued)

Characteristics	Frequency (percentage, %) or median (25th–75th interquartile range)
WCC × 10^9/L	7.4 (5.9–8.9)
FCP μg/g	108 (41.3–1144.8)
Raised FCP (>250 μg/g)	14 (35%)
Ferritin μg/L	26.0 (15.3–69.8)
Albumin g/L	41 (38.0–43.0)

Note: Anthropometry *z*-scores calculated using UK-WHO growth charts (Royal College of Paediatrics and Child Health. UK-WHO Growth Charts: Fact Sheets and Data Tables. RCPCH; 2009. Available from: https://www.rcpch.ac.uk/resources/uk-who-growth-charts).

Abbreviations: 6-MP, 6-mercaptopurine; ADA, adalimumab; AZA, azathioprine; CRP, C-reactive protein; EEN, exclusive enteral nutrition; ESR, erythrocyte sedimentation rate; FCP, faecal calprotectin; IFX, infliximab; PCDAI, paediatric Crohn's disease activity index; PUCAI, paediatric ulcerative colitis activity index; UC, ulcerative colitis; USTE, ustekinumab; VEDO, vedolizumab; WCC, white cell count.

patients were male (70%). The median time from FCP result to BUS was 5.3 weeks (IQR 2.4–9.1).

A full summary of feasibility outcomes can be seen in Table 3. A total of 103 patients were approached by the study team either in person or via postal invite for inclusion in the study, with 40 individuals being recruited (38.8%). One patient was lost to follow-up and did not undergo ultrasound scan, therefore $n = 39$ patients were 'retained' until study closure (98%). Participants were recruited over 15 months. The initial target of 50 participants was not achieved due to time constraints related to the tenure of the research team. Of all ultrasound parameters collected across the 39 ultrasound studies ($n = 312$), 301 were able to be visualised and recorded (96.5%). In total, imaging was of 'poor quality' in four cases (10.3%). Qualitative data were collected in this group and in three cases superficial adipose tissue contributed to lack of ultrasound penetration and in one case there was 'significant gaseous distension'. Overall study recruitment, retention and imaging metrics were fulfilled per the predefined feasibility metrics.

3.2 | Intestinal ultrasound scores, bowel wall thickness and markers of inflammation

3.2.1 | Total cohort

A summary of ultrasound scores across the cohort can be visualised in Supporting Information S1: Table 1. For the total cohort no significant correlation was demonstrated between BWT and FCP (rho = 0.239, $p = 0.18$). Activity index score also did not correlate with BWT (rho = 0.005, $p = 0.977$). There was no significant correlation between recent FCP and total intestinal ultrasound score (rho = 0.058, $p = 0.747$) or between contemporary activity index score and total intestinal ultrasound score (rho = 0.082, $p = 0.623$). No correlations were demonstrated between total ultrasound score or individual ultrasound parameters and anthropometric measures (BMI) or biochemical markers (WCC, Albumin, Ferritin). A summary of these results can be visualised in Table 4 and Supporting Information S1: Table 2.

3.3 | Ulcerative colitis

Significant associations were noted between faecal calprotectin and two ultrasound parameters: bowel wall thickness (rho = 0.503, $p = 0.039$) and loss of normal haustration pattern (rho = 0.490, $p = 0.039$). Faecal calprotectin was also negatively associated with intra-abdominal lymphadenopathy (rho = –0.550, $p = 0.022$). No correlations were demonstrated between total ultrasound score or individual parameters and anthropometric measures (BMI), biochemical markers (WCC, CRP, Albumin, Ferritin) or contemporary activity indices. These results are summarised in Table 4.

3.4 | Crohn's disease

No significant correlations were identified between faecal calprotectin, PCDAI, anthropometric measures (BMI), biochemical markers (WCC, CRP, Albumin, Ferritin) and either total ultrasound score or individual ultrasound parameters. These results are summarised in Table 4.

3.5 | Predicting disease behaviour

A summary of treatment changes can be visualised in Table 2. Receiver operating characteristic (ROC) testing was undertaken to assess the predictive power of total ultrasound score and BWT on treatment escalation at follow up across the total, UC and CD cohorts. Data are included in Supporting Information S1: Table 3. No significant predictive power was identified in this analysis.

4 | DISCUSSION

Our study demonstrated the feasibility of obtaining measures of intestinal inflammation using ultrasound in a paediatric cohort. We report the feasibility of measuring criteria defined within reported paediatric ultrasound scoring systems.[11,25] Importantly, the key feasibility metrics were achieved. Recruitment targets

TABLE 3 A summary of measures evaluated to assess feasibility of the NIMBUS study.

Feasibility measure	Total achieved (percentage, %)	Total approached/ attempted to measure	Traffic light outcome	Traffic light criteria
Recruitment rate, participants	40 (38.8)	103	AMBER	>60% Green, 30%–60% Amber, <30% Red
Retention rate, participants	39 (98)	40	GREEN	>80% Green, 70%–80% Amber, <70% Red
Total ultrasound parameters	301 (96.5)	312	GREEN	>80% Green, 70%–80% Amber, <70% Red
Bowel wall thickness	38 (97.4)	39	GREEN	>80% Green, 70%–80% Amber, <70% Red
Colour Doppler	38 (97.4)	39	GREEN	>80% Green, 70%–80% Amber, <70% Red
Bowel wall Stratification	37 (94.9)	39	GREEN	>80% Green, 70%–80% Amber, <70% Red
Colonic Haustration	39 (100)	39	GREEN	>80% Green, 70%–80% Amber, <70% Red
Fat wrapping	37 (94.9)	39	GREEN	>80% Green, 70%–80% Amber, <70% Red
Terminal Ileal motility	36 (92.3)	39	GREEN	>80% Green, 70%–80% Amber, <70% Red
Lymphadenopathy	38 (97.4)	39	GREEN	>80% Green, 70%–80% Amber, <70% Red
Abscess	38 (97.4)	39	GREEN	>80% Green, 70%–80% Amber, <70% Red

were achieved despite falling within the predefined 'amber' category. All patients receiving a mailed invitation to participate were included in this calculation which culminated in a lower total recruitment percentage (38.8%); however, recruitment was good with 40 patients—from an initial target of 50—enrolled. Research team tenure was the limiting factor in recruitment. Data outlining the number of patients approached face to face were not recorded, however it is anticipated that the recruitment percentage would have been higher for this method. Most patients were 'retained' until the end of the study, and this was attributed a 'green' feasibility outcome. This is likely related to study methodology, wherein follow-up data were collected from the electronic hospital records as further visits or scan appointments were not required. It is possible that with a study model in which several ultrasound scans are performed over a longer duration that participation—and therefore participant retention—may drop off. It is not clear how acceptable repeated ultrasound measures would be in the paediatric cohort, however all recruited patients tolerated scans at a single timepoint. As this was a feasibility study, no formal power calculation was performed. A target of 50 participants was set based on established guidance suggesting that 24–50 participants is appropriate for feasibility work to inform future trial design, though this may restrict the ability to draw definitive statistical inference.[29]

Green traffic light criteria were achieved for all the included ultrasound parameters suggesting that it is possible to reliably visualise the selected markers within a paediatric cohort. While the included parameters were able to be recorded for most of the cohort (96.5%) it is important to note that imaging quality was poor for 10.3%. This was mostly attributable to variable participant body composition. However, it does suggest that the ultrasound user must negotiate these hurdles to measure all parameters, or that there remains a subgroup of individuals for whom BUS is less feasible, and 3D imaging such as MRI may be more appropriate. In our study, all scans were obtained by a single paediatric radiologist skilled in BUS, who was able to obtain these measurements despite these barriers to image quality. These challenges are amplified in the paediatric cohort where compliance with imaging may be difficult to achieve particularly with younger individuals.[30] Historical barriers to uptake of ultrasound have included a lack of training opportunities and reliance on established modalities.[13] The compounding of these factors can account for variable ultrasound uptake by paediatric gastroenterologists. With inter-rater reliability yet to be established in paediatric BUS, even amongst professionals experienced in BUS, this must be established before widespread bedside use.[10] The research, education and collaboration initiatives from the International Bowel Ultrasound group (IBUS) demonstrate the efforts to overcome barriers to routine use.[31]

The most important findings were the correlations between maximal bowel wall thickness (rho = 0.503, $p = 0.039$) and loss of normal haustration pattern (rho = 0.490, $p = 0.039$) with faecal calprotectin within the ulcerative colitis group. BWT has been previously reported to be the most important ultrasound measure for the assessment of IBD activity[32]; leading to its inclusion in two paediatric BUS scoring systems for

TABLE 4 Results of Spearman's correlation coefficient calculations for individual ultrasound parameters and associations with faecal calprotectin and activity index scores at time of ultrasound in total IBD, UC and CD.

		Total IBD		UC		CD	
Ultrasound measure		**Faecal calprotectin**	**Disease Activity Score**	**Faecal calprotectin**	**Disease Activity Score**	**Faecal calprotectin**	**Disease Activity Score**
Bowel wall thickness	Correlation coefficient	0.239	0.005	**0.503***	0.321	−0.123	−0.238
	Sig. (2-tailed)	0.18	0.977	0.039	0.155	0.649	0.357
	N	33	38	17	21	16	17
Colour Doppler Signal	Correlation coefficient	0.083	0.07	0.208	0.244	−0.125	−0.296
	Sig. (2-tailed)	0.647	0.678	0.423	0.286	0.645	0.248
	N	33	38	17	21	16	17
Loss of bowel wall stratification	Correlation coefficient	0.039	0.256	0	0.103	0.16	0.388
	Sig. (2-tailed)	0.831	0.126	1	0.657	0.568	0.138
	N	32	37	17	21	15	16
Loss of Haustration	Correlation coefficient	0.119	0.041	**0.490***	0.27	−0.335	−0.319
	Sig. (2-tailed)	0.504	0.805	0.039	0.224	0.205	0.212
	N	34	39	18	22	16	17
Fat wrapping	Correlation coefficient	−0.216	0.107	−0.255	−0.3	−0.157	0.317
	Sig. (2-tailed)	0.235	0.529	0.322	0.187	0.576	0.232
	N	32	37	17	21	15	16
Terminal ileal motility	Correlation coefficient	−0.132	0.096	−0.351	−0.048	0.094	0.166
	Sig. (2-tailed)	0.478	0.579	0.182	0.841	0.738	0.539
	N	31	36	16	20	15	16
Lymphadenopathy	Correlation coefficient	−0.125	−0.068	**−0.550***	−0.315	0.44	0.244
	Sig. (2-tailed)	0.487	0.685	0.022	0.165	0.088	0.346
	N	33	38	17	21	16	17
Abscess or stricture	Correlation coefficient	.	.	.	.	.	.
	Sig. (2-tailed)	.	.	.	.	.	.
	N	33	38	17	21	16	17
Total Ultrasound Score	Correlation coefficient	0.058	0.082	0.136	0.144	−0.011	0.037
	Sig. (2-tailed)	0.747	0.623	0.604	0.533	0.969	0.888
	N	33	38	17	21	16	17

Note: All correlation coefficients are Spearman's coefficients (rho). *N* = number of analysis points were both parameter and FCP and AI are present. Total IBD number *n* = 39, UC *n* = 27 and CD *n* = 12. Statistically significant results highlighted in **bold.**

UC.[11,25] It has also been included in all attempts to standardise BUS scoring in adult Crohn's disease, yielding utility in the large and small bowel.[23] BWT has been demonstrated to be useful in the detection of endoscopic inflammation, though in the same cohort was not found to correlate with FCP.[33]

Of particular interest is the lack of correlation between BWT and faecal calprotectin in the total cohort

and within the participants with Crohn's disease. It is important to note that there was vast heterogeneity in time elapsed between FCP sampling and BUS, which may affect the general interpretation of these findings. This aside, rationale for this finding could be twofold, pertaining to ultrasonographic findings or to faecal calprotectin measurement. The pattern of inflammation in active ulcerative colitis is that of continuous prominent thickening of the mucosal layer whereas CD patients may have noncontinuous submucosal enlargement.[34] As a result, BWT may be greater over a larger area in patients with UC and therefore this may be more readily measurable. The greater ease by which colonic disease and thickness can be detected through ultrasound has led to earlier advancement in standardisation of these techniques in UC over Crohn's disease.[23] Detection of Crohn's disease lesions may be feasible in the adult cohort and, while some work has yielded positive results of BUS for detection of inflammation in paediatric CD, our findings may suggest that this is more difficult to reproduce in this group.[24]

Regarding FCP measurement, recent data suggest a topographical effect of disease location on FCP level. In their work evaluating the variation of FCP level in a cohort with heterogenous distribution of disease along the gastrointestinal tract, Ukashi et al. demonstrated that FCP levels significantly diminished in those with proximal disease. Moreover, they noted that patients with colonic disease had a significantly higher FCP level than those with even extensive small bowel involvement.[35] This potential differential gradient in faecal calprotectin, compounded with the possible barriers to bowel wall assessment within the small bowel may explain the lack of correlation in the total and Crohn's disease groups.

There are several advantages of ultrasound over FCP, most importantly that assessment is instantaneous and can be delivered at the point of care. Moreover, compliance with obtaining faecal samples can be variable within the paediatric and young adult cohorts, whereas ultrasound has been demonstrated to be acceptable to patients; within this study and the wider literature.[10,36] The correlation between BWT and FCP supports the use of ultrasound for quantifying inflammation in colitis. Utilisation of a single measurable parameter, in the form of BWT, could reduce study time as well as inter-user variability, with BWT having previously been noted to be the most reproducible measure within BUS.[37] The additional correlation demonstrated between loss of bowel wall haustration and faecal calprotectin in our study further indicates that distal, colonic disease was associated with elevated FCP. Moreover, there was a negative association between FCP and intrabdominal lymphadenopathy. Mesenteric lymphadenitis has been demonstrated to be associated with Crohn's disease to a greater extent than UC, which may account for this correlation.[38] Of note, only the terminal ileum was measured within the ultrasound scoring system and as a result, small bowel disease may not be reported. This, along with the small sample size, limits the interpretation of these findings. Moreover, variation in time from FCP measurement to BUS means these findings must be interpreted with trepidation.

Bowel wall thickness, total ultrasound score, or single BUS parameters were not found to be predictive for future disease behaviour. There are several reasons for this within the data. First, median follow up was undertaken over 2.8 months (IQR 1.8–4.1), which, in the mostly outpatient setting, may not have been an extended enough timeframe to capture incremental changes in treatment across the cohort. Furthermore, overall management was guided by established biomarkers and patient report of symptoms. Symptoms were generally reported as mild for the cohort [(median PUCAI 10 (IQR 5–20), median PCDAI 25 (IQR 15–30)] and the clinical team were blinded to ultrasound findings. As a result, treatment might not have been escalated. It is also recognised that subclinical inflammation may exist in the absence of abnormal blood or stool markers as well as in asymptomatic individuals.[4] As, in this study, endoscopic or histological confirmation of disease were not obtained, subclinical disease may not have been captured. This may account for the lack of correlation and treatment alteration.

The strengths of this study include the prospective recruitment of 40 patients within a single specialist paediatric gastroenterology centre. Ultrasound scans were undertaken by a single specialist paediatric radiologist skilled in BUS, reducing potential inter-user variability, particularly given the relatively small sample size. Interindividual reproducibility is not assessed using this methodology however, and future studies would include multiple paediatric sonographers of varying expertise. Every effort was made to ensure standardised care continued for each individual, with ultrasound being the only intervention as to not affect clinical outcomes at follow-up. Predefined feasibility metrics were achieved, although the recruited sample was small ($n = 40$). While every effort was made to position ultrasound within the normal clinical follow-up in our cohort, the variable time between blood and FCP measurements and ultrasound may have affected strength of measured correlations. The inclusion of a spectrum of IBD phenotypes including Crohn's-type and colitis diseases reflects real-world heterogeneity, however it might be, that BUS finds greater utility when examined in colitis. This differs from other contemporary work, wherein association has been reported between ultrasound measures and disease activity in Crohn's disease, which may be attributable our study methodology.[24]

For the purposes of assessing feasibility single ultrasound scans were undertaken, however the

implementation of serial studies intra-participant may allow for a better evaluation of BUS for monitoring. Further work may focus on the longer-term effect of chronic ultrasound or 3D imaging findings on IBD prognosis, through serial imaging, to explore these techniques' role in real-time monitoring and disease mapping. When implemented serially over time BUS may allow for intra-patient measurement of disease and prediction of response to specific treatments.[39,40] Future studies should also include a greater patient population and multiple blinded ultrasound operators. Exploration of ultrasound findings in the context of gold-standard monitoring tests, such as endoscopy, would also be of great benefit.

5 | CONCLUSION

In this study, we have demonstrated the feasibility of BUS in a paediatric IBD cohort. We report that contemporary bowel wall thickness and loss of haustration measurements performed with BUS may correlate with faecal calprotectin levels in paediatric ulcerative colitis. Significant correlations were not noted in those with Crohn's disease. However, small sample size and variable time from faecal calprotectin sampling to ultrasound may affect interpretation of these findings. Serial BUS in paediatric colitis requires investigation. Barriers to image acquisition and BUS uptake were identified.

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CONFLICT OF INTEREST STATEMENT

James J. Ashton is a senior advisory board member for Orchard Therapeutics. There are no other conflicting or competing interests for other named authors.

DATA AVAILABILITY STATEMENT

No additional data are available.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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