Original paper

# Association between intestinal ultrasound parameters and clinical disease activity in paediatric Crohn's disease

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### Abstract

**Introduction:** Assessing disease activity in paediatric Crohn's disease (CD) remains challenging because endoscopy, although the reference standard, is invasive and unsuitable for repeated monitoring. Intestinal ultrasound (IUS) has emerged as a noninvasive tool for real-time assessment of transmural inflammation, but its relationship with clinical and biochemical markers is not fully established.
**Aim of the research:** This study evaluated associations between IUS parameters, clinical disease activity, and inflammatory biomarkers in paediatric CD.
**Material and methods:** In this retrospective cohort study, 58 children with confirmed CD (6–17 years) underwent standardised IUS. Bowel wall thickness (BWT), bowel wall stratification (BWS), and Doppler vascularity were assessed. Clinical activity was measured using the Paediatric Crohn's Disease Activity Index (PCDAI), while inflammatory markers included C-reactive protein (CRP) and faecal calprotectin. Statistical analyses included Spearman correlations, Mann–Whitney *U* tests, and ROC analysis.
**Results:** Mean BWT was 5.54 ±1.93 mm, and mean PCDAI was 27.88 ±16.21. BWT correlated moderately with PCDAI ($r = 0.450$, $p = 0.010$), whereas BWS and Doppler vascularity showed no significant associations. BWT > 4 mm demonstrated the best diagnostic accuracy for active disease (AUC = 0.752). No significant correlations were found between ultrasound parameters and CRP or faecal calprotectin. Elevated faecal calprotectin (> 1000 µg/g) was associated with severe disease activity. The number of patients included in individual analyses varied due to incomplete data availability.
**Conclusions:** BWT is the ultrasound parameter most strongly associated with clinical activity in paediatric CD. IUS should complement, rather than replace, biochemical and clinical assessment in multimodal disease monitoring.

## Introduction

Crohn's disease (CD) is a chronic inflammatory condition of the gastrointestinal tract, with a relapsing and remitting course, often diagnosed during childhood or adolescence. In paediatric patients, the disease may significantly interfere with growth, nutritional status, and overall development, which makes regular and reliable assessment of disease activity particularly important [1, 2]. In everyday clinical practice, disease activity is typically evaluated using a combination of clinical indices, endoscopic findings, imaging, and laboratory markers such as C-reactive protein (CRP) and faecal calprotectin [3]. Although these markers are useful and widely available, they do not always reflect the full extent of intestinal inflammation, especially its transmural component, which is characteristic of CD [4]. Endoscopy remains the reference method for assessing mucosal inflammation, but its invasive nature and the need for sedation in children limit its use in repeated monitoring [5]. Imaging techniques such as magnetic resonance enterography provide a broader assessment of the bowel wall and surrounding tissues, but their routine use may be restricted by availability and practical considerations [6]. Intestinal ultrasound (IUS) has become an increasingly used tool in the assessment of inflammatory bowel disease, particularly in paediatric patients [7]. It is noninvasive, does not involve radiation, and can be repeated as often as needed. Importantly, it allows direct evaluation of bowel wall thickness, preservation of mural stratification, vascularity on Doppler imaging, and inflammatory changes in the surrounding mesentery [8, 9]. These features make it a promising method for assessing current disease activity and monitoring patients over time [10]. Despite its growing use, the relationship between ultrasound findings, biochemical markers, and



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clinical disease activity in children with CD is still not fully clear. In addition, the potential role of intestinal ultrasound in predicting disease relapse remains an area of ongoing interest [11].

## Aim of the research

The aim of this study was to evaluate the association between selected intestinal ultrasound parameters and markers of inflammation, including CRP and faecal calprotectin, as well as clinical disease activity assessed using the Paediatric Crohn's Disease Activity Index (PCDAI). We also aimed to explore whether ultrasound findings are useful in identifying patients at increased risk of disease relapse.

## Material and methods

### Study design and participants

This retrospective study included 58 paediatric patients aged 6–17 years. Inclusion criteria were age between 6 and 17 years and a diagnosis of CD documented in the medical records (e.g. discharge summaries or imaging reports). Exclusion criteria included ulcerative colitis, other inflammatory bowel diseases, significant comorbidities, and incomplete medical records.

Diagnosis of CD was established based on standard clinical, endoscopic, histopathological, and radiological criteria. All patient data were obtained from routine clinical assessments recorded in their medical history.

### Ultrasound examination

Each patient underwent a single standardised intestinal ultrasound examination according to the clinical protocol at our centre. The examination was performed by an experienced operator. Bowel wall thickness (BWT) was measured in the most affected bowel segment and recorded as the maximal thickness (mm). Bowel wall vascularity was evaluated using Power Doppler imaging. Vascularisation was graded on a binary scale: 0 – no relevant increase in intramural vascularity, no hyperaemia; 1 – increased intramural vascularity, hyperaemia of the bowel wall. Mesenteric inflammatory features were assessed, including increased mesenteric echogenicity, thickened mesenteric fat, and the presence of enlarged mesenteric lymph nodes.

### Clinical and laboratory assessment

Disease activity was evaluated using the PCDAI. Laboratory markers of inflammation included serum C-reactive protein (CRP) and faecal calprotectin, which were collected within one week of the ultrasound examination to ensure temporal correlation. These markers were used to compare biochemical inflammation with ultrasound findings and clinical disease activity.

### Statistical analysis

Continuous data were summarised as medians with interquartile ranges, and categorical data as counts and percentages. The relationship between bowel wall thickness and PCDAI was tested with Spearman's correlation. Differences in PCDAI between patients with and without Doppler signal or with preserved versus disrupted mural layers were assessed using the Mann–Whitney *U* test. To evaluate the ability of bowel wall thickness to identify active disease (PCDAI > 10), receiver operating characteristic (ROC) curves and area under the curve (AUC) analyses were conducted. Statistical significance was defined as $p < 0.05$.

## Results

A total of 58 patients were included in the analysis. The mean BWT was 5.54 ±1.93 mm, while the mean PCDAI score was 27.88 ±16.21, indicating overall moderate disease activity. Laboratory markers demonstrated substantial variability, particularly faecal calprotectin (mean 1939.70 ±1981.45 µg/g) and CRP (mean 4.92 ±10.48 mg/l), reflecting heterogeneity in inflammatory burden. Due to the retrospective design of the study, data availability varied across patients, and not all clinical, laboratory, and ultrasonographic parameters were available for every patient (Table 1).

**Table 1.** Baseline characteristics of the study population

| Variable | *N* | Mean ± SD | Median (IQR) | Range |
|---|---|---|---|---|
| Bowel wall thickness (BWT) [mm] | 35 | 5.54 ±1.93 | 5.00 (3.00) | 2.0–10.0 |
| PCDAI score | 46 | 27.88 ±16.21 | 25.00 (21.88) | 5.0–70.0 |
| C-reactive protein (CRP) [mg/l] | 53 | 4.92 ±10.48 | 1.33 (4.43) | 0.06–58.90 |
| Erythrocyte sedimentation rate (ESR) [mm/h] | 42 | 25.95 ±29.20 | 14.00 (27.75) | 1.0–120.0 |
| Faecal calprotectin [µg/g] | 51 | 1939.7 ±1981.5 | 1220.0 (1866.0) | 7.6–8000.0 |

*Continuous variables are presented as mean ± standard deviation (SD) and median (interquartile range, IQR). Sample sizes differ between variables due to incomplete data availability (retrospective study).*

### Sex-related differences in clinical features and disease course

The study group consisted of 58 paediatric patients diagnosed with Crohn's disease, including 31 (53.4%) boys and 27 (46.6%) girls. Severe disease activity was observed in 18 (58.1%) boys and 12 (44.4%) girls ($p = 0.287$), indicating a non-significant trend toward a more severe clinical course in males. Elevated faecal calprotectin levels (> 1000 µg/g) were more frequent in boys (20/31; 64.5%) compared to girls (14/27; 51.9%) ($p = 0.331$, ns). Hospitalisation during disease was required in 19 (61.3%) boys and 13 (48.1%) girls ($p = 0.312$, ns). These findings suggest sex-related differences in disease severity, although none reached statistical significance.

### Age at diagnosis and disease severity

Most patients (36/58; 62.1%) were diagnosed between the ages of 10 and 15 years. Early diagnosis (< 10 years) was observed in 14 (24.1%) patients, while 8 (13.8%) patients were diagnosed after the age of 15 years. Among patients with severe disease, 11/30 (36.7%) were diagnosed before the age of 10 years, compared to 3/28 (10.7%) in the mild/moderate group ($p = 0.041$). No statistically significant association was observed between age at diagnosis and the need for surgical treatment ($p = 0.518$).

### Calprotectin levels and disease activity

Elevated faecal calprotectin (> 1000 µg/g) was found in 34/58 patients (58.6%). Among these patients, 25/34 (73.5%) presented with severe disease activity. In contrast, among patients with calprotectin ≤ 1000 µg/g (24/58; 41.4%), only 5/24 (20.8%) had severe disease ($p < 0.001$). This demonstrates a strong association between elevated calprotectin levels and disease severity.

### Ultrasound findings

Assessment of bowel wall stratification (BWS) was available in 56 patients, with preserved stratification observed in 45 (80.36%) cases and disrupted stratification in 11 (19.64%) cases. Doppler evaluation was performed in 40 patients, of whom 30 (75.0%) demonstrated increased vascularity, while 10 (25.0%) had absent vascular signal (Table 2).

**Table 2.** Ultrasound characteristics of bowel inflammation

| Parameter | *N* (%) |
|---|---|
| Bowel wall stratification (BWS) | |
| Preserved | 45 (80.4) |
| Disrupted | 11 (19.6) |
| Colour Doppler vascularity | |
| Increased vascularity | 30 (75.0) |
| Absent vascularity | 10 (25.0) |

*Sample sizes differ between variables due to incomplete data availability (retrospective study).*

### Correlation between ultrasound parameters and clinical activity (PCDAI)

Among the analysed ultrasound parameters, BWT showed a statistically significant moderate positive correlation with PCDAI (Spearman $r = 0.450$, $p = 0.010$), indicating that increasing bowel wall thickness is associated with higher clinical disease activity. In contrast, BWS ($r = 0.082$, $p = 0.589$) and Doppler signal ($r = 0.250$, $p = 0.154$) did not demonstrate significant correlations with PCDAI.

### Diagnostic performance for active disease (PCDAI-based definition)

Using predefined thresholds (BWT > 4 mm, disrupted BWS, and positive Doppler signal) as indicators of active disease, BWT demonstrated the highest diagnostic performance, with sensitivity of 0.541, specificity of 0.857, positive predictive value (PPV) of 0.870, and a statistically significant association with disease activity (Fisher's exact test $p = 0.005$). The area under the ROC curve (AUC) for BWT was 0.752, indicating acceptable discriminative ability. In comparison, BWS showed limited diagnostic utility (sensitivity 0.216, specificity 0.857, AUC = 0.529, $p = 0.729$), while Doppler signal demonstrated moderate but non-significant performance (sensitivity 0.595, specificity 0.619, AUC = 0.600, $p = 0.172$) (Table 3).

### Correlation between ultrasound parameters and laboratory markers

No significant correlations were observed between BWT and laboratory markers, including CRP

**Table 3.** Diagnostic performance of ultrasound parameters for active disease (defined by PCDAI)

| Parameter | Sensitivity | Specificity | PPV | NPV | AUC | Spearman's *r* | *P*-value |
|---|---|---|---|---|---|---|---|
| BWT > 4 mm | 0.541 | 0.857 | 0.870 | 0.514 | 0.752 | 0.450 | 0.010 |
| Disrupted BWS | 0.216 | 0.857 | 0.727 | 0.383 | 0.529 | 0.082 | 0.589 |
| Increased Doppler vascularity | 0.595 | 0.619 | 0.733 | 0.464 | 0.600 | 0.250 | 0.154 |

*Active disease was defined as a Paediatric Crohn's Disease Activity Index (PCDAI) score > 10. BWT > 4 mm, disrupted stratification, and increased Doppler vascularity were considered positive ultrasound findings. Diagnostic performance metrics and Spearman's correlation coefficients were calculated using complete-case analysis: n = 32 for BWT, n = 46 for BWS, and n = 33 for Doppler vascularity.*

($r$ = 0.037, $p$ = 0.836), erythrocyte sedimentation rate (ESR) ($r$ = −0.220, $p$ = 0.261), and faecal calprotectin ($r$ = 0.113, $p$ = 0.544). BWS demonstrated a weak but statistically significant positive correlation with CRP ($r$ = 0.275, $p$ = 0.049), while no associations were found with ESR ($r$ = 0.143, $p$ = 0.365) or faecal calprotectin ($r$ = 0.003, $p$ = 0.981). Similarly, Doppler signal showed no significant correlations with CRP ($r$ = 0.256, $p$ = 0.116), ESR ($r$ = 0.239, $p$ = 0.196), or faecal calprotectin ($r$ = 0.154, $p$ = 0.364).

## Discussion and conclusions

In our cohort of 58 paediatric CD patients (median age ≈ 15 years, 58.6% male), the demographic profile was similar to that reported in other paediatric series. For example, van Wassenaer *et al.* found a median age of 15 years and a roughly equal sex distribution in a large prospective paediatric IUS study. Our patients exhibited substantial disease activity (median PCDAI 25 [IQR 21,88]). The mean BWT on ultrasound was 5.54 mm (median 5.0 mm, range: 2–11 mm), indicating that many patients had active intestinal inflammation. In contrast, van Wassenaer *et al*. defined BWT thresholds of 2–3 mm (TI) and 1.6–2.0 mm (colon) as low activity, and > 3.7 mm (TI) or > 2.7 mm (colon) as high activity. They reported odds ratios of 11.5 for high BWT in the ileum and 8.6 in the colon predicting active disease [4]. Similarly, Riahinezhad *et al*. observed that ileal wall thickness increased significantly with higher disease activity – from a mean of 2.12 mm in mild disease to 4.49 mm in severe disease ($p$ = 0.005) [12]. Our mean BWT of 5.54 mm is even higher than those means, consistent with a predominance of moderate-to-severe cases. We found a significant correlation between BWT and the PCDAI (Spearman's rho = 0.450), and a threshold of BWT > 4 mm had modest sensitivity (59.1%) and poor specificity (30%) for identifying active disease (PCDAI > 10) in ROC analysis. This discrepancy may reflect differences in study design: van Wassenaer *et al*. and Riahinezhad *et al*. correlated IUS with objective endpoints (endoscopic scores or PCDAI stages), whereas our retrospective analysis relied on routine PCDAI assessment [4, 12].

We also examined two qualitative IUS parameters: mural stratification and Doppler vascularity. In our series, 80.36% of patients had preserved wall stratification, and 19.64% had disrupted stratification. Loss of stratification is generally interpreted as an indicator of chronic or severe inflammation. Increased Doppler flow (Limberg grade ≥ 1) was observed in 75% of patients, reflecting active inflammation. Prior work supports a link between vascularity and activity: Riahinezhad *et al*. found that the frequency of colour Doppler signal increased significantly in higher PCDAI categories [12]. We also did not observe a significant difference in PCDAI between patients with versus without detectable Doppler signal ($p$ = 0.154). Thus, while the presence of Doppler flow suggests inflammation, it did not effectively stratify disease activity in our cohort. This may be due to the small sample or the fact that Doppler sensitivity can be operator dependent.

For biochemical markers, our patients had a median CRP of 1.33 mg/dl and a very high median faecal calprotectin (FC) of 1220 µg/g. These markers showed the patterns expected from prior studies: Plume *et al.* reported a moderate correlation between FC and PCDAI in children (rs ≈ 0.546), while CRP often lacks sensitivity, especially in isolated ileal disease [13]. In our data we observed no significant correlations between BWT and FC, but recent studies highlight the added value of combining them. Parihar *et al.* demonstrated that combining a BWT > 3 mm with FC > 250 µg/g yielded high sensitivity and specificity for predicting endoscopic severity (SES-CD). In the ileum, this combination reached 88.6% sensitivity and 78.9% specificity [14]. Paredes *et al.* also found that FC correlated significantly (though weakly, $r$ ≈ 0.50) with an ultrasound activity index in ileal Crohn's [15]. In line with these findings, the very high FC in our patients suggests marked intestinal inflammation; integrating IUS findings with FC could potentially improve accuracy in detecting active disease. Future analysis of our cohort might establish optimal FC cutoffs that align with our ultrasound features.

Overall, our findings underscore that intestinal ultrasound provides complementary information to clinical and laboratory indices. IUS is well-established as a non-invasive, safe, and patient-friendly tool for monitoring Crohn's disease. It can directly visualize transmural inflammation and complications that clinical scores or blood tests may miss [16]. Indeed, experts note that combining IUS with biomarkers like FC offers a "robust method" for assessing disease severity [14]. In practice, IUS may detect subclinical activity or healing that would otherwise be overlooked. In our study, however, IUS parameters alone had limited concordance with PCDAI. This suggests that IUS should be interpreted alongside other measures. As Dolinger and Kayal emphasize, IUS is most effective when used in conjunction with clinical judgement and ancillary tests [16].

This study has several limitations. Incomplete data availability resulted in varying sample sizes across individual analyses, potentially limiting the statistical power of some comparisons. Its retrospective nature and single-center scope may introduce selection bias. We lacked a concurrent gold-standard assessment (such as endoscopy or MRI) to definitively gauge mucosal healing; this limits our ability to determine the true accuracy of the ultrasound findings. Additionally, our analysis used routine clinical IUS exams rather than a standardized research protocol. We measured the thickest segment only and did not apply a formal scoring system (unlike the validated Pediatric Crohn's Disease IUS score). Ultrasound is inherently operator-

dependent, and we did not have data on interobserver reliability. Finally, the sample size ($n$ = 58) is relatively modest for subgroup analyses, which may explain why some comparisons lacked statistical power.

Future prospective studies are needed to validate these observations. We recommend using standardised IUS indices, such as the PCD-US score developed by van Wassenaer *et al.*, which combines BWT and mesenteric fat evaluation and has shown high accuracy for detecting paediatric CD activity [4]. Longitudinal studies should follow patients over time to see how IUS changes predict relapse or response. Correlating IUS not only with clinical indices but also with endoscopic and histologic outcomes will clarify its role in tight-control management. Standardisation of IUS training and reporting is also crucial. As noted in consensus statements, an ideal IUS activity index includes measures of wall thickness, vascularity, stratification, and fat changes [16]. Adhering to such guidelines can improve the reliability and comparability of future research.

## Conclusions

Our study highlights that intestinal ultrasound is a valuable adjunct in paediatric CD management, providing insights beyond traditional indices. However, in our cohort IUS markers had only limited correlation with the PCDAI and conventional lab markers. Thus, ultrasound should be used as part of a multimodal assessment. Consistent with other experts, we believe that combining ultrasound with faecal calprotectin and clinical evaluation "provides a robust method" to assess disease activity. Continued research and standardised protocols are needed to fully establish how best to integrate IUS into routine care for paediatric Crohn's disease.




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## Ethical approval

Not applicable.

## Conflict interest

The authors declare no conflict of interest.

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