

Transabdominal Intestinal Ultrasound for the Assessment of Ileal Disease Activity in Crohn's Disease

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Abstract

Background and study aims: Transabdominal intestinal ultrasonography (IUS) is increasingly used to assess transmural inflammatory activity in Crohn's disease (CD). This study evaluated the diagnostic performance of IUS for detecting ileal inflammatory activity in CD by comparing individual ultrasonographic parameters and composite activity scores with ileocolonoscopy.

Patients and methods: This single-center retrospective study included patients with CD with ileal involvement who underwent ileocolonoscopy and transabdominal IUS within a 7-day interval. Ileal endoscopic activity was assessed using the Simple Endoscopic Score for Crohn's Disease (SES-CD), with a score ≥ 3 indicating active disease. Ultrasonographic evaluation included bowel wall thickness (BWT), color Doppler signal (CDS), their combined assessment, and composite scores: International Bowel Ultrasound Segmental Activity Score (IBUS-SAS), Simple Ultrasound Score for Crohn's Disease (SUS-CD), and Bowel Ultrasound Score (BUSS). Endoscopic findings served as the reference standard.

Results: Fifty patients were analyzed. Increased BWT and the presence of CDS were significantly associated with higher ileal SES-CD scores. When evaluated individually, BWT and CDS demonstrated moderate sensitivity and high specificity for endoscopically active disease. Among composite scores, SUS-CD showed the highest sensitivity and overall accuracy, whereas IBUS-SAS and BUSS demonstrated high-specificity profiles. ROC analysis identified an optimal BWT cut-off of 3.69 mm, providing improved specificity compared with the conventional 3-mm threshold.

Conclusion: Transabdominal intestinal ultrasound shows high specificity for detecting ileal inflammation in Crohn's disease. Individual ultrasonographic parameters and composite ultrasound activity scores may serve as useful noninvasive adjuncts to endoscopic assessment of ileal disease activity. (*Acta gastroenterol belg.*, 2026, 89, 465-473).

Keywords: Transmural inflammation; bowel wall thickness; color doppler signal; IBUS-SAS.

Introduction

Ileocolonoscopy is the gold standard method for the diagnosis and follow-up of Crohn's disease (CD) (1). Endoscopic evaluation plays a key role in establishing diagnosis, determining disease severity, monitoring treatment response, detecting complications, and screening for dysplasia. In recent years, endoscopic remission has been accepted as one of the most important therapeutic targets in Crohn's disease, highlighting the central role of mucosal assessment in routine clinical practice (2).

However, ileocolonoscopy is invasive, requires bowel preparation, may necessitate sedation, and is

associated with patient discomfort, high cost, and limited repeatability. These limitations restrict its frequent use during follow-up and have led to increasing interest in non-invasive, easily accessible, and radiation-free imaging modalities for assessing disease activity (3).

Transabdominal intestinal ultrasonography (IUS) is increasingly used for the diagnosis and follow-up of inflammatory bowel disease (IBD) (4, 5). It allows real-time evaluation of the bowel wall and surrounding structures and has gained importance as a practical tool for monitoring disease activity in Crohn's disease (6). The most commonly described ultrasonographic findings associated with active CD are increased bowel wall thickness and color Doppler signal reflecting mural hypervascularity (7, 8). Additional features, such as disruption of bowel wall stratification and inflammatory changes in the mesenteric fat, have also been associated with active transmural inflammation (7, 9).

Several studies have evaluated the concordance between IUS findings and endoscopic activity in patients with Crohn's disease, particularly those with ileal involvement (10–12). Although IUS can detect active disease with reasonable diagnostic accuracy when endoscopic findings are accepted as the reference standard, reported sensitivity and specificity vary, particularly in patients with mild or limited mucosal disease (13, 14).

Traditionally, most studies have focused on single ultrasonographic parameters, particularly bowel wall thickness, using predefined cut-off values to define pathological involvement (12,15). Although this approach is simple and clinically practical, it may not fully reflect the complexity of transmural inflammation. Composite intestinal ultrasound activity scores have therefore been developed to integrate multiple ultrasonographic features into standardized numerical indices (16,17).

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Among these, the International Bowel Ultrasound Segmental Activity Score (IBUS-SAS) has been proposed and validated, and its diagnostic performance has been increasingly evaluated against endoscopic reference standards (11, 16, 18). IBUS-SAS incorporates bowel wall thickness, color Doppler signal, bowel wall stratification, and inflammatory mesenteric fat, thereby providing a broader assessment of transmural inflammatory activity. In contrast, simpler composite scores such as the Simple Ultrasound Score for Crohn's Disease (SUS-CD) and the Bowel Ultrasound Score (BUSS) rely mainly on bowel wall thickness and Doppler activity and may be easier to apply in routine practice. Data directly comparing these composite ultrasound scores with individual ultrasonographic parameters in ileal disease activity remain limited.

Therefore, this study aimed to evaluate the diagnostic performance of transabdominal intestinal ultrasonography in detecting ileal inflammatory activity in patients with Crohn's disease. We compared endoscopic findings assessed using the Simple Endoscopic Score for Crohn's Disease (SES-CD) with individual ultrasonographic parameters and composite ultrasound activity scores, including IBUS-SAS, SUS-CD, and BUSS.

Materials and Methods

Study Design and Patient Population

This single-center observational study was conducted at a tertiary referral hospital. This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Istanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, Turkey (approval number: 83088843-604.01.01-24048). The requirement for informed consent for participation was waived by the Ethics Committee owing to the retrospective design of the study. To ensure patient confidentiality, all collected data were pseudonymized before analysis, and access to the study dataset was restricted to the investigators.

At our tertiary referral center, patients with an established diagnosis of Crohn's disease are monitored using IUS as an adjunct to endoscopic evaluation during routine clinical follow-up. Patients were considered for inclusion when both ileocolonoscopy and transabdominal IUS had been performed as part of the same clinical disease activity assessment. IUS was performed on a separate day within 7 days after ileocolonoscopy.

Patients were eligible if they had a confirmed diagnosis of Crohn's disease based on clinical, endoscopic, radiologic, and histopathological findings, if ileal involvement could be adequately assessed by both ileocolonoscopy and intestinal ultrasonography, and if no treatment modification occurred between the two examinations. Patients with isolated colonic

disease without ileal involvement, inadequate bowel preparation, incomplete ultrasonographic examinations, missing key clinical or imaging data, or extensive small bowel resection precluding meaningful ileal assessment were excluded. Patients with prior ileocecal resection were included, provided that reliable evaluation of the neoterminal ileum by both ileocolonoscopy and transabdominal intestinal ultrasonography was technically feasible.

Although data from 57 patients were initially reviewed, seven patients were excluded because of unsuccessful terminal ileum intubation during ileocolonoscopy. After applying the inclusion and exclusion criteria, 50 patients constituted the final study cohort.

Endoscopic Assessment

Ileocolonoscopy was performed as part of the routine clinical evaluation using standard endoscopic techniques. The terminal ileum was intubated whenever technically feasible, and endoscopic disease activity was assessed by experienced endoscopists who were not involved in the ultrasonographic evaluation.

The endoscopic severity of ileal disease was graded using the Simple Endoscopic Score for Crohn's Disease (SES-CD). An ileal SES-CD value of ≥ 3 was considered indicative of active disease, in accordance with commonly accepted thresholds (19).

In patients with a history of ileocecal resection, postoperative recurrence was evaluated using the Rutgeerts score, based on findings at the ileocolonic anastomosis and neoterminal ileum. Endoscopic postoperative recurrence was defined as a Rutgeerts score of ≥ 2 (20).

Ultrasonographic Assessment and Ultrasound-Based Activity Scores

Transabdominal intestinal ultrasonography was performed in the gastroenterology outpatient clinic using a Hitachi HI VISION Preirus ultrasound system equipped with a 13–6 MHz linear probe and a 5–2 MHz convex probe. No special patient preparations were required.

All intestinal ultrasound examinations were performed by a single gastroenterologist certified by the International Bowel Ultrasound Group (IBUS) and with more than 5 years of experience in intestinal ultrasound. Ileocolonoscopy assessments and SES-CD scoring were performed by different operators. Because IUS was performed in a routine clinical setting, formal blinding to endoscopic findings could not be fully ensured. The IUS variables analyzed in this study were obtained from the ultrasonography reports generated at the time of the original examinations, and no retrospective image re-evaluation was performed for study purposes. The terminal ileum or neoterminal ileum

and colonic segments were systematically evaluated whenever feasible. Bowel wall thickness (BWT) was measured at the site of maximal mural thickening using the mean of two longitudinal and two cross-sectional measurements. Color Doppler signal activity, bowel wall stratification, and inflammatory changes in the surrounding mesenteric fat were recorded as part of a standardized ultrasonographic evaluation (18).

Ultrasound-based disease activity was assessed using composite activity scores. IBUS-SAS was calculated using BWT, color Doppler signal (CDS), bowel wall stratification (BWS), and inflammatory mesenteric fat (i-fat), according to previously described methodologies (11, 18): $\text{IBUS-SAS} = (4 \times \text{BWT}) + (15 \times \text{i-fat}) + (7 \times \text{CDS}) + (4 \times \text{BWS})$. For the dichotomous diagnostic performance analysis, an IBUS-SAS value of ≥ 25.2 was used to define ultrasonographic activity, based on previously reported validation data against endoscopic disease activity (11).

SUS-CD and BUSS were also calculated using BWT and CDS variables and evaluated for diagnostic performance. SUS-CD was calculated as the sum of categorized BWT and CDS scores: BWT was scored as 0 for <3.0 mm, 1 for 3.0–4.9 mm, 2 for 5.0–7.9 mm, and 3 for ≥ 8.0 mm; CDS was scored as 0 for absent, 1 for mild-to-moderate, and 2 for marked Doppler signal. A segmental SUS-CD value of ≥ 1 was used to define ultrasonographic activity (14). BUSS was calculated as $0.75 \times \text{BWT} + 1.65 \times \text{bowel wall flow (BWF)}$, where BWF was defined as any color Doppler signal. A BUSS value of >3.52 was used as the cut-off for ultrasonographic activity (21).

Individual ultrasonographic parameters were also evaluated. Increased BWT (≥ 3 mm) and any positive CDS (≥ 1) were analyzed individually and in combination and subsequently compared with endoscopic disease activity (10, 22).

Clinical and Laboratory Variables

Demographic and clinical data, including age, sex, disease duration, disease location and behavior according to the Montreal classification, history of ileocecal resection, and current medical treatment, were obtained from medical records (23). Clinical disease activity was assessed using the Crohn's Disease Activity Index (CDAI), and patients with a CDAI score of <150 were considered to be in clinical remission (24). Laboratory parameters routinely measured at the time of ultrasonographic evaluation, including C-reactive protein (CRP), were recorded.

Statistical Analysis

Statistical analyses were performed using SPSS software (version 20; IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range), as

appropriate, and categorical variables as frequencies and percentages. The distribution of continuous variables was assessed using the Shapiro–Wilk test.

Group comparisons were performed using Student's t-test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Associations between continuous variables were assessed using Pearson's or Spearman's correlation coefficients, depending on data distribution.

The diagnostic performance of IUS for detecting active ileal disease was evaluated using endoscopic activity as the reference standard. Sensitivity, specificity, positive and negative predictive values, accuracy, and likelihood ratios were calculated for individual ultrasonographic parameters and composite activity scores. Receiver operating characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) was calculated. Optimal cut-off values were determined using the Youden index. A two-sided p value <0.05 was considered statistically significant.

Results

Patient Characteristics

The study population comprised 50 patients with Crohn's disease. The mean age was 39.7 ± 13.7 years, and 30 patients (60.0%) were male. Based on clinical disease activity assessment, 28 patients (56.0%) were in clinical remission (CDAI <150). Additional demographic, clinical, disease-related, and treatment characteristics of the study population are presented in Table 1.

Endoscopic and Ultrasonographic Findings

The median SES-CD score of the study population was 4.0 (IQR: 7). Based on ileal endoscopic assessment, 36 patients had endoscopically active disease (SES-CD ≥ 3), while the remaining patients had inactive disease.

Transabdominal intestinal ultrasonography revealed increased bowel wall thickness (BWT ≥ 3 mm) in 27 patients, whereas 23 patients had a mean ileal wall thickness <3 mm. Color Doppler signal activity was absent in 34 patients, whereas 16 patients demonstrated Doppler activity ≥ 1 .

Patients with increased bowel wall thickness (≥ 3 mm) had significantly higher endoscopic disease activity than those with wall thickness <3 mm (SES-CD: 5.0 ± 2.98 vs. 1.73 ± 1.86 ; $p < 0.001$). Similarly, Doppler activity was associated with significantly higher SES-CD scores than Doppler-negative examinations (5.56 ± 3.30 vs. 2.52 ± 2.31 ; $p < 0.001$) (Table 2).

The diagnostic performance of individual ultrasonographic parameters for detecting endoscopically active ileal disease was evaluated. Increased bowel wall thickness (≥ 3 mm) demonstrated a sensitivity of 67.0%, specificity of 79.0%, and accuracy

Table 1. — Demographic, clinical, disease-related and treatment characteristics of the study population (n = 50).

Variable	Value
Age, years, mean $\pm$ SD	39.7 $\pm$ 13.7 (18–78)
<40 years, n (%)	26 (52.0)
$\geq$ 40 years, n (%)	24 (48.0)
Sex, n (%)	
Male	30 (60.0)
Female	20 (40.0)
Disease duration, months, median (IQR)	36 (97)
New diagnosis (<2 years), n (%)	17 (34.0)
Disease behavior (Montreal), n (%)	
Inflammatory (B1)	36 (72.0)
Stricturing (B2)	4 (8.0)
Penetrating (B3)	10 (20.0)
Perianal disease, n (%)	
Yes	7 (14.0)
No	43 (86.0)
CDAI, median (IQR)	129.5 (159)
Clinical remission (CDAI <150), n (%)	28 (56.0)
CRP, mg/L, median (IQR)	3.6 (16.6)
History of ileocecal resection, n (%)	
Yes	14 (28.0)
No	36 (72.0)
Treatment modality, n (%)	
Anti-TNF or other biological monotherapy ¹	5 (10.0)
Biological therapy combined with azathioprine	11 (22.0)
Azathioprine monotherapy	15 (30.0)
Mesalazine ^{2,3}	20 (40.0)
Systemic corticosteroids ²	4 (8.0)
Budesonide ²	5 (10.0)
Without medical treatment	4 (8.0)
CDAI, Crohn's Disease Activity Index; CRP, C-reactive protein; IQR, interquartile range; SD, standard deviation.	
1 All patients in this group received anti-TNF agents, except for one patient who was treated with ustekinumab.	
2 Some patients received more than one treatment modality at the time of assessment.	
3 The relatively frequent use of mesalazine reflects real-world prescribing practices during the study period and should be interpreted descriptively.	

of 70.0%. Color Doppler signal activity showed lower sensitivity (42%) but higher specificity (93%), with an accuracy of 56%.

Composite ultrasound activity scores and combined ultrasonographic parameters were also evaluated using predefined thresholds. For IBUS-SAS $\geq$ 25.2, SUS-CD $\geq$ 1, BUSS $>$ 3.52, and combined BWT $\geq$ 3 mm + CDS positivity, sensitivities were 48.1%, 69.4%, 41.7%, and 40.0%, respectively, while specificities were 86.6%, 78.6%, 92.9%, and 93.3%, respectively. The diagnostic performance characteristics of all ultrasonographic parameters and composite assessments are summarized in Table 3.

ROC curve analysis demonstrated significant discriminatory performance of bowel wall thickness for detecting endoscopically active ileal disease, with an area under the curve (AUC) of 0.793 (95% CI: 0.666–0.919; $p = 0.001$) (Figure 1). Using the Youden index,

the optimal BWT cut-off was 3.69 mm, corresponding to a sensitivity of 61%, specificity of 93%, and accuracy of 70%.

According to ileal SES-CD evaluations, 18 patients had aphthous ileitis defined as ulcers $<$ 0.5 cm, while 18 had ileal ulcers $\geq$ 0.5 cm. When the mean bowel wall thickness was compared between the two groups, patients with ulcers $\geq$ 0.5 cm had significantly greater wall thickness than those with aphthous ileitis (4.58 ± 1.88 mm vs. 3.03 ± 1.40 mm; $p = 0.018$). When bowel wall thickness was categorized using the conventional predefined threshold of $\geq$ 3 mm and the ROC-derived threshold of $\geq$ 3.69 mm, a higher proportion of patients with ulcers $\geq$ 0.5 cm had bowel wall thicknesses above these thresholds compared with the aphthous ileitis group; however, these differences did not reach statistical significance. Doppler signal activity was detected in 6 patients (33%) in the aphthous ileitis group

Table 2. — Comparison of endoscopic disease activity according to ultrasonographic findings.

Ultrasonographic finding	SES-CD (mean $\pm$ SD)	p value
Bowel wall thickness <3 mm $\geq$ 3 mm	1.73 $\pm$ 1.86 5.00 $\pm$ 2.98	<0.001
Doppler activity Absent Present	2.52 $\pm$ 2.31 5.56 $\pm$ 3.30	<0.001

SES-CD, Simple Endoscopic Score for Crohn's Disease; SD, standard deviation.

Table 3. — Diagnostic performance of ultrasonographic parameters and ultrasound activity scores for detecting endoscopically active ileal disease.

Ultrasonographic parameter	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	LR+	LR-
BWT $\geq$ 3 mm	67.0	79.0	70.0	89.0	48.0	3.19	0.42
CDS $\geq$ 1	42.0	93.0	56.0	94.0	38.0	6.00	0.62
IBUS-SAS $\geq$ 25.2	48.1	86.6	60.0	89.4	42.1	3.59	0.60
BWT $\geq$ 3 mm + CDS $\geq$ 1	40.0	93.3	58.0	93.3	37.8	6.00	0.64
SUS-CD $\geq$ 1	69.4	78.6	72.0	89.3	50.0	3.24	0.39
BUSS $>$ 3.52	41.7	92.9	56.0	93.8	38.2	5.83	0.63

PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR-, negative likelihood ratio; IBUS-SAS, International Bowel Ultrasound-Segmental Activity Score; SUS-CD, Simple Ultrasound Score for Crohn's Disease; BUSS, Bowel Ultrasound Score; BWT, bowel wall thickness; CDS, Color Doppler signal.

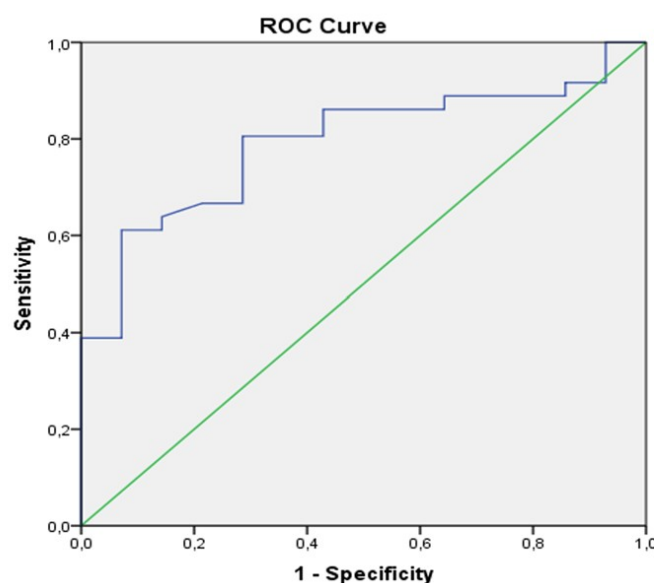


Figure 1. — Receiver operating characteristic (ROC) curve analysis of bowel wall thickness for the detection of endoscopically active ileal Crohn's disease.

and 8 patients (44%) in the group with ulcers $\geq$ 0.5 cm, with no statistically significant difference between the groups ($p = 0.732$) (Table 4).

Associations between intestinal ultrasonography findings and laboratory and clinical disease activity were also evaluated. BWT $\geq$ 3 mm was more frequent in patients with elevated CRP levels than in those with lower CRP levels (72.4% vs. 46.4%), although this difference did not reach statistical significance ($p =$

0.084). In contrast, color Doppler signal positivity was significantly more common in patients with elevated CRP levels (55.2% vs. 17.0%; $p = 0.008$).

No significant association was observed between clinical disease activity assessed using CDAI and ultrasonographic findings. The prevalence of increased BWT ($p = 0.516$) and Doppler signal positivity ($p = 0.122$) did not differ significantly between patients with clinical remission and those with active disease.

Table 4. — Comparison of ultrasonographic findings between aphthous ileitis and ileal ulcers ≥ 0.5 cm.

Ultrasonographic parameter	Aphthous ileitis (n=18)	Ileal ulcer ≥ 0.5 cm (n=18)	p value
Mean bowel wall thickness (mm), mean $\pm$ SD	3.03 $\pm$ 1.40	4.58 $\pm$ 1.88	0.018
Bowel wall thickness ≥ 3 mm, n (%)	9 (50%)	15 (83.3%)	0.077
Bowel wall thickness ≥ 3.69 mm, n (%)	8 (44%)	14 (78%)	0.087
Doppler activity positivity, n (%)	6 (33%)	8 (44%)	0.732

SD, standard deviation.

Among patients with endoscopically active ileal disease, disease duration did not differ significantly between patients with and without color Doppler signal activity (56.4 $\pm$ 54.9 months vs. 65.1 $\pm$ 75.0 months; $p = 0.885$). Likewise, although mean disease duration was numerically longer in patients with BWT ≥ 3 mm than in those with BWT < 3 mm, this difference was not statistically significant (73.0 $\pm$ 71.1 vs. 39.5 $\pm$ 42.3 months; $p = 0.143$).

In patients with a history of ileocecal resection ($n = 14$), postoperative endoscopic disease activity was assessed using the Rutgeerts score. IUS findings according to postoperative endoscopic recurrence status (Rutgeerts $< i2$ vs. $\geq i2$) are summarized in Supplementary Table 1. In this subgroup, BWT ≥ 3 mm had a sensitivity of 70%, specificity of 75%, and accuracy of 71% for detecting endoscopic recurrence. The corresponding positive and negative predictive values were 88% and 50%, respectively. Ileal color Doppler signal activity showed lower sensitivity (30%) but specificity of 100% and accuracy of 50%, with positive and negative predictive values of 100% and 36%, respectively.

Discussion

In this study, we assessed the diagnostic performance of transabdominal intestinal ultrasonography for the evaluation of ileal disease activity in Crohn's disease, using ileocolonoscopy as the reference standard. We found that increased bowel wall thickness and color Doppler signal activity were significantly associated with endoscopic ileal disease activity. In addition to these individual ultrasonographic parameters, IBUS-SAS, SUS-CD, and BUSS were evaluated as composite ultrasound activity scores. Overall, these scores showed broadly comparable diagnostic patterns, with higher specificity and positive predictive values than sensitivity. The combined assessment of bowel wall thickness and Doppler activity yielded comparable results, supporting the ability of intestinal ultrasonography to reliably identify endoscopic inflammation when ultrasonographic activity is present. Taken together, these findings underscore the value of intestinal ultrasonography as a practical, noninvasive approach for identifying clinically meaningful ileal disease activity.

The comparison of composite ultrasound scores with simpler ultrasonographic approaches raises an important

practical point. IBUS-SAS incorporates BWS and i-fat in addition to BWT and CDS, and therefore provides a broader representation of transmural inflammatory activity (18). However, in our cohort, simpler BWT- and CDS-based approaches showed diagnostic performance comparable to IBUS-SAS. SUS-CD had the highest sensitivity and overall accuracy among the composite scores, whereas BUSS showed a high specificity and high PPV profile similar to the combined BWT + CDS assessment. This finding is also consistent with the development of SUS-CD, in which BWS and fatty wrapping were not retained in the final simplified score because they did not add substantial diagnostic value beyond BWT and CDS and showed lower interobserver reliability (14). These observations suggest that in a small ileal cohort, such as ours, BWT and CDS may capture much of the clinically relevant ultrasound information needed to identify endoscopically active disease. Nevertheless, more comprehensive scores, such as IBUS-SAS, may still have value when a standardized and reproducible description of transmural inflammatory activity is needed, particularly for follow-up assessments and comparisons across studies.

Crohn's disease is characterized by transmural involvement of the intestinal wall, whereas endoscopic assessment primarily reflects mucosal disease activity. Although mucosal healing is currently regarded as a central therapeutic target, it does not necessarily indicate the resolution of inflammation across the entire bowel wall (25). Previous studies have shown that only a limited proportion of patients who achieve endoscopic remission also exhibit normalization of bowel wall thickness, highlighting the dissociation between mucosal and transmural healing (8, 25). Yzet et al. evaluated patients with endoscopic healing and reported that IUS-assessed transmural healing, defined as bowel wall thickness < 3 mm without color Doppler signal, was associated with a lower risk of Crohn's disease relapse and CD-related hospitalization during follow-up (26). Importantly, even among patients with complete endoscopic healing, the absence of transmural healing was associated with a higher risk of relapse, suggesting that transmural assessment may provide prognostic information beyond mucosal evaluation (26). Conversely, a normal bowel wall appearance on cross-sectional imaging does not reliably exclude the presence of mild or superficial mucosal inflammation,

particularly in the early stages of the disease or in patients with aphthous ileitis (8, 22, 27).

This pathophysiological distinction provides an important framework for interpreting our findings. The incomplete concordance observed between intestinal ultrasonography and endoscopic activity should therefore not be interpreted as a shortcoming of ultrasonography, but rather as a consequence of the different inflammatory compartments evaluated by these modalities. In routine clinical practice, ileocolonoscopy and intestinal ultrasonography should be viewed as complementary tools; endoscopy offers detailed information on mucosal integrity, whereas ultrasonography captures transmural inflammatory changes, such as bowel wall thickening and mural hypervascularity (10, 27). Accordingly, intestinal ultrasonography may provide clinically relevant information that is not fully captured by mucosal assessment alone (25, 28).

Bowel wall thickness is one of the most consistently reported ultrasonographic markers of inflammatory activity in Crohn's disease and has traditionally been interpreted using predefined cut-off values. A threshold of 3 mm has been widely adopted as an indicator of pathological bowel wall thickening, providing a reasonable balance between sensitivity and specificity (15, 22). However, this dichotomous approach may oversimplify the relationship between mural thickening and inflammatory burden, particularly in patients with mild or early disease.

Several investigators have suggested that bowel wall thickness should be interpreted as a continuous variable rather than solely as a categorical parameter. Fraquelli et al. reported that increasing bowel wall thickness was associated with progressively higher specificity for active disease, whereas lower cut-off values were associated with greater sensitivity but reduced specificity (22). Similarly, Calabrese et al. demonstrated that greater degrees of mural thickening were more strongly associated with clinically relevant and endoscopically active disease, supporting a graded interpretation of bowel wall thickness (27).

In the present study, ROC analysis identified an optimal bowel wall thickness cut-off of 3.69 mm for the detection of endoscopically active ileal disease, yielding higher specificity than the conventional 3 mm threshold, albeit with reduced sensitivity. This finding aligns with previous reports suggesting that higher cut-off values may be more suitable when the aim is to confirm active disease rather than exclude it (22, 27). In a recent point-of-care intestinal ultrasound study, Nagarajan et al. reported that a bowel wall thickness threshold of 3.4 mm achieved excellent diagnostic performance for endoscopic disease activity, with both high sensitivity and specificity and an area under the curve of 0.96 (29). Together, these findings suggest that slightly higher cut-off values may be preferable when the aim is to confirm clinically relevant disease activity rather than exclude

mild inflammation. However, because the 3.69-mm threshold was derived from ROC analysis within our cohort, it should be interpreted as an exploratory finding and requires external validation before being applied in routine clinical practice.

Importantly, the analysis of ileal ulcer morphology further supports this concept. Patients with ulcers ≥ 0.5 cm exhibited significantly greater mean bowel wall thickness than those with aphthous ileitis, whereas categorical comparisons using fixed cut-off values did not consistently reach statistical significance. These observations indicate that subtle increases in mural thickness may convey clinically meaningful information that is not fully captured by dichotomous classification alone.

The relatively lower sensitivities observed for several ultrasound-based assessments, particularly IBUS-SAS, BUSS, CDS, and the combined BWT + CDS approach, compared with some previous studies may be explained by several methodological and disease-related factors. First, our analysis focused specifically on ileal disease activity, whereas ultrasound activity scores have generally been developed or evaluated across multiple bowel segments rather than for isolated ileal assessment alone (14, 18). Consistent with this interpretation, Freitas et al. reported limited diagnostic performance of segmental SUS-CD and IBUS-SAS in terminal ileal Crohn's disease, suggesting that the performance of composite ultrasound scores may differ when applied specifically to the terminal ileum (30). Second, endoscopic activity in our study was defined as an ileal SES-CD score of ≥ 3 , which may include patients with mild and superficial mucosal lesions. Because IUS primarily reflects transmural inflammation, aphthous or limited mucosal lesions may not always be accompanied by sufficient bowel wall thickening, Doppler hypervascularity, or other transmural changes to meet ultrasound-based activity thresholds (25). This interpretation is supported by our finding that patients with ulcers ≥ 0.5 cm had significantly greater bowel wall thickness than those with aphthous ileitis. Third, combined ultrasonographic definitions, such as BWT + CDS positivity, represent more stringent criteria and are therefore expected to increase specificity and positive predictive value at the expense of sensitivity (10, 22). Accordingly, the diagnostic pattern observed in our study suggests that IUS may be more useful for confirming clinically relevant ileal inflammation than for excluding mild endoscopic activity.

When interpreting the IBUS-SAS results, the selected cut-off should also be considered. We used the previously reported threshold of ≥ 25.2 because it was proposed in validation work comparing IBUS-SAS with endoscopic disease activity (11). However, different thresholds have been reported in subsequent cohorts; for example, Qin et al. reported a higher threshold of 46.5, indicating that the optimal cut-off may vary according to patient population, reference standard,

disease severity, and the level of analysis (31). Therefore, our IBUS-SAS findings should be interpreted in relation to this predefined threshold rather than as supporting a single cut-off applicable across all clinical settings.

In addition to the overall study population, the diagnostic performance of intestinal ultrasonography was evaluated in patients with a history of ileocecal resection. In this postoperative subgroup, ultrasonographic findings demonstrated a similar pattern, with increased bowel wall thickness showing moderate sensitivity and specificity for endoscopic recurrence, whereas color Doppler signal positivity was highly specific but had limited sensitivity. The high specificity and positive predictive value of Doppler signal positivity indicate that ultrasonographic evidence of transmural activity in this setting is highly suggestive of clinically relevant postoperative disease activity. These findings are consistent with those of previous studies identifying bowel wall thickening and Doppler hypervascularity as the most reliable ultrasonographic markers of postoperative recurrence (32, 33). Castiglione et al. reported that a bowel wall thickness threshold of ≥ 5 mm achieved high sensitivity and specificity for the detection of severe endoscopic recurrence, defined by a Rutgeerts score of ≥ 3 (32). Furthermore, review data have shown that intestinal ultrasonography demonstrates good overall diagnostic accuracy for recurrence, with a strong correlation with ileocolonoscopy findings (27). Taken together, intestinal ultrasonography appears to be a useful adjunctive tool in the postoperative follow-up of Crohn's disease, facilitating the identification of patients who may benefit from timely endoscopic reassessment.

In the present study, intestinal ultrasonography findings were only weakly associated with clinical disease activity assessed using the CDAI and serum CRP levels. This observation is consistent with previous reports demonstrating that clinical indices, laboratory markers, and imaging modalities capture different dimensions of disease activity in Crohn's disease (33, 34). The absence of a strong correlation between ultrasonographic findings and CDAI or CRP should not be interpreted as true discordance but rather as a reflection of the distinct biological aspects assessed by these tools.

While CDAI and CRP primarily reflect systemic and symptomatic manifestations of disease activity, intestinal ultrasonography provides direct information on localized transmural inflammatory changes in the intestine. In this context, ultrasonographic assessment may offer complementary insights, particularly in patients with ongoing transmural inflammation despite low clinical activity scores or normal laboratory parameters (10, 27). This complementary role underscores the value of intestinal ultrasonography as an adjunct to, rather than a replacement for, established clinical and laboratory markers.

We also explored the relationship between ultrasonographic findings and disease duration, an aspect that has received limited attention in the existing

literature (28). In our cohort, disease duration was not significantly associated with bowel wall thickness or Doppler signal activity. This suggests that transmural inflammatory activity detected by ultrasonography may be more closely related to current disease behavior than to disease chronicity, supporting the role of intestinal ultrasonography as a modality that reflects ongoing inflammatory burden rather than cumulative disease history (27).

Overall, the findings of this study highlight the utility of intestinal ultrasonography as a complementary tool in the assessment of ileal Crohn's disease activity. While ileocolonoscopy remains essential for evaluating mucosal inflammation, ultrasonography provides additional information on transmural disease involvement in a noninvasive and easily repeatable manner. In particular, increased bowel wall thickness and Doppler signal activity were strongly associated with endoscopic inflammation, supporting the role of ultrasonography in identifying patients who may benefit from close monitoring or targeted endoscopic reassessment. These observations support the integration of intestinal ultrasonography into routine clinical practice alongside endoscopic evaluation.

The present study has several limitations. First, this was a single-center observational study with a relatively limited sample size, which may restrict the generalizability of our findings. Second, intestinal ultrasonography was performed by a single operator; therefore, inter-observer variability could not be assessed. Additionally, intra-observer variability analysis was not performed, which represents a further limitation of our methodology. Because IUS was performed as part of routine clinical care in this retrospective study, formal blinding of the ultrasonographer to endoscopic findings could not be fully ensured. Third, ileocolonoscopy was used as the sole reference standard for disease activity, and no direct comparison with other cross-sectional imaging modalities such as magnetic resonance enterography was performed. In addition, the cross-sectional design of the study precludes the assessment of longitudinal changes in ultrasonographic findings over time or their predictive value for long-term outcomes. Finally, although postoperative patients were included, the number of resected cases was relatively small; therefore, subgroup analyses should be interpreted with caution.

Conclusion

In patients with ileal Crohn's disease, both individual ultrasonographic parameters and composite ultrasound activity scores demonstrated high specificity despite modest sensitivity, indicating that the presence of ultrasonographic activity reliably reflects endoscopic disease activity. These results suggest that intestinal ultrasonography may be particularly useful for confirming active disease and for follow-up assessment by providing

noninvasive information on inflammatory changes related to bowel wall involvement, which complements endoscopic evaluation.

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