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How to use intestinal ultrasonography in patients with Crohn disease: its role in the assessment of disease activity and disease monitoring in the era of the treat-to-target strategy

REVIEW ARTICLE

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Intestinal ultrasonography (IUS) is one of the primary noninvasive, cross-sectional imaging modalities for the diagnosis and monitoring of Crohn disease (CD). IUS is highly accessible and convenient, particularly for patients, making it an ideal tool for frequent and repeated assessments of CD, which is especially prevalent in younger populations. This review examines the current role of IUS in assessing disease activity and complications, including the use of various scoring systems, compares its utility with magnetic resonance enterography, and discusses its role in evaluating transmural response and healing during treatment monitoring, as well as its limitations.

Keywords: Intestinal ultrasound; Inflammatory bowel diseases; Crohn disease/diagnostic imaging; Magnetic resonance imaging; Transmural healing/response

Key points: Intestinal ultrasound is a useful non-invasive primary imaging tool for the assessment of disease activity, complication, and monitoring during the treatment period. Intestinal ultrasound can be used alternatively or together with magnetic resonance enterography to assess disease activity and treatment response depending on the disease location and phenotype. We need to consider the proper use and limitations of intestinal ultrasound when using it as a frequent disease monitoring tool.

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Introduction

Cross-sectional imaging techniques, such as computed tomography (CT), magnetic resonance enterography (MRE), and intestinal ultrasonography (IUS), have been recommended as complementary tools to endoscopy for evaluating both mural and extramural disease in inflammatory bowel disease (IBD), particularly Crohn disease (CD) [1]. These imaging modalities are receiving increasing attention for their utility in assessing transmural healing (TH), which has emerged as an important adjunct

to endoscopic remission, as outlined in the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) II guideline [2]. Since IBD frequently arises in younger individuals and requires repeated examinations over a prolonged disease course, these noninvasive imaging techniques are valuable for comprehensive and repeated monitoring of the small bowel—an area often beyond the reach of endoscopy. CT and magnetic resonance imaging (MRI) currently serve as the standards for small bowel assessment and demonstrate similar diagnostic performance [3,4]; however, MRI is preferred over CT to avoid cumulative radiation exposure from repeated scans. IUS presents another radiation-free alternative to MRI, and is generally the most well-tolerated and readily accepted by patients, as it does not require contrast media administration or injection, bowel preparation, or mandatory fasting [5]. This review discusses the current role of IUS in evaluating disease activity (including several scoring systems and complications), compares IUS with MRE, and considers its use in assessing transmural response and healing during treatment monitoring, as well as its limitations in the assessment of IBD, with a particular focus on CD.

Performance of IUS

Preparation

IUS generally does not require special preparation or fasting. Although fasting for at least 4 hours is recommended to reduce the amount of food and air in the bowel lumen, this may not substantially improve bowel wall visibility except in male patients [6]. Prolonged fasting (6–8 hours) reduces intraluminal fluid and air, prevents gaseous distention of the bowel [7], and can result in complete collapse of the bowel with minimal intraluminal fluid and decreased peristalsis. Therefore, fasting for more than 6 hours is recommended when assessing bowel motility [5]. Oral fluid intake approximately 30 minutes before IUS may help reduce air content and distend bowel loops, thus enhancing visibility of the bowel wall layers. However, this practice is not typically required before IUS, as there is ongoing debate regarding whether the benefits outweigh the additional burden [5,8,9]. Filling the bladder can improve visualization of the sigmoid colon and rectum, and also elevates the pelvic ileum from the deep pelvis, thereby facilitating evaluation by shortening beam penetration distance and enabling the use of graded compression.

Imaging Technique

A transducer frequency of at least 5 MHz is required to discriminate individual wall layers and accurately measure wall thickness [5]. Mid-frequency transducers (5–10 MHz or 7–13 MHz) provide an optimal balance between resolution and depth penetration [5,10], offering a penetration depth of approximately 8–10 cm with sufficient resolution to differentiate the various bowel wall layers. Low-frequency transducers (1–6 MHz) are used to examine deeper bowel segments, such as the pelvic ileum and rectum, or in obese patients. For detailed bowel examinations, a high-resolution mid-frequency transducer is generally preferred. Examiners may switch to a lower-frequency convex transducer or a higher-frequency linear transducer as needed, depending on the depth and location of the target bowel segment. Graded compression is an effective technique for managing gas-distended bowels; the examiner uses the transducer to displace air away from the region of interest (ROI), thereby shortening the distance between the transducer and the bowel loop and isolating the target segment for optimal visualization [8].

Scanning Method

Baseline IUS scanning in IBD requires a thorough evaluation of both the small and large bowels. The ileocolic (IC) region serves as an optimal starting point, as the IC valve, cecum, and terminal ileum (TI) are typically located in the right iliac fossa, with the right iliopsoas muscle acting as a key landmark. If direct identification of the IC valve proves challenging, the ascending colon can be used as an alternative landmark since it is readily visible in the right flank due to its large caliber and distinct haustrations. The examiner first locates the ascending colon in the transverse plane and then traces it downward to locate the IC valve, where the TI merges with the colon. Depending on the location of the patient's disease or examiner preference, either the colon or the small bowel may be traced first, starting from the IC region. For large bowel assessment, the examiner initially identifies the cecum by placing the transducer below the IC valve. The ascending, transverse, descending, and sigmoid colons—each situated at the periphery of the abdomen—are then sequentially traced. Useful landmarks include the ascending colon at the right flank, the descending colon at the left flank, and the proximal sigmoid colon over the left psoas muscle. The transverse colon's location may vary due to a redundant mesocolon, necessitating a broad sweep from the epigastrium downward to the lower abdomen. The colonic flexures are situated high in the abdomen and may be visualized intercostally; thus, deep inspiration can help lower the splenic flexure from the intercostal to the subcostal region. The rectum is scanned posterior to the distended bladder using a lower-frequency transducer, although visualization may be difficult if the bladder is collapsed. Following the completion of colon scanning, small bowel assessment begins by returning the probe to the right iliac fossa and identifying the TI, with the right psoas muscle serving as the landmark. The examiner traces proximally along the TI as far as possible. Complete tracing of the small bowel is challenging; therefore,

a systematic scan of all four abdominal quadrants is performed using parallel, overlapping lanes, both cranially and caudally, to cover the entire small bowel [5]. The pelvic ileum is especially difficult to evaluate due to restricted compression and limited beam penetration; stronger compression, a lower-frequency probe, and adequate bladder filling may facilitate visualization.

Imaging Parameters for Active Inflammation

The primary IUS features of disease activity are bowel wall thickness (BWT), increased bowel wall vascularity (Doppler signal), loss of bowel wall stratification (BWS), and mesenteric inflammatory fat (Table 1) [11–13].

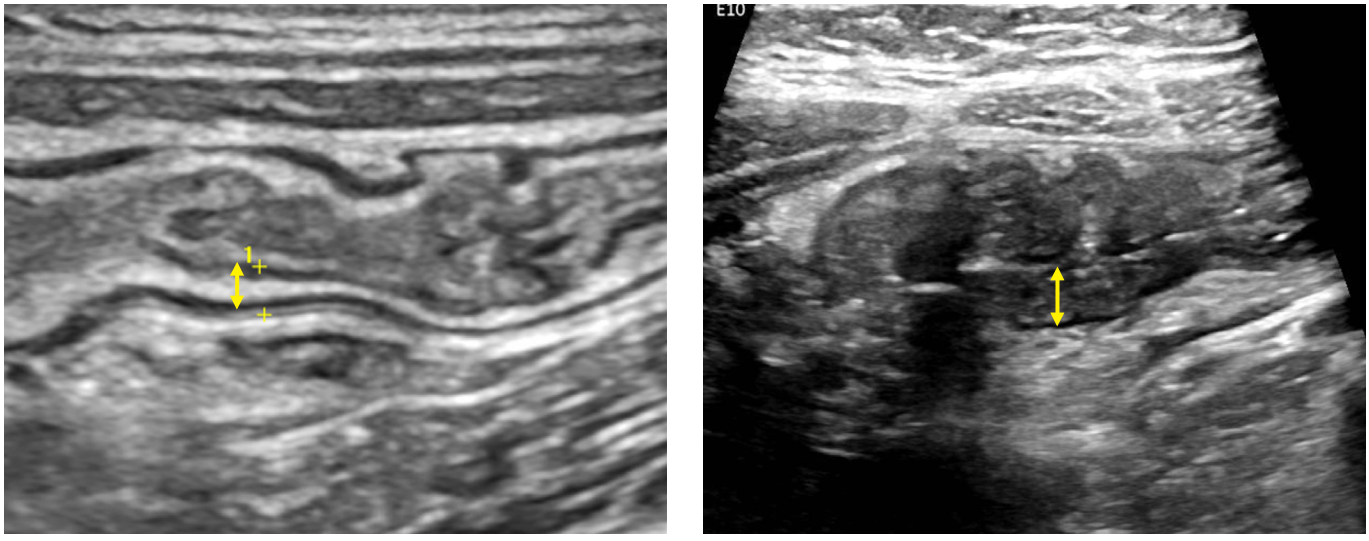
(1) BWT is the most essential transmural feature to assess. It is the simplest and most reproducible parameter, with a cut-off value >3 mm commonly used to indicate active inflammation [12,14,15]. The normal bowel wall appears as five alternating hyper- and hypoechoic layers: hyperechoic innermost mucosa, hypoechoic outer mucosa (muscularis mucosae), hyperechoic submucosa, hypoechoic proper muscle, and a hyperechoic serosal line. Because the innermost hyperechoic mucosa and the outermost hyperechoic serosa are often poorly visualized, the bowel wall typically appears as three layers on IUS: the inner hypoechoic layer (outer mucosa), the middle hyperechoic layer (submucosa), and the outer hypoechoic layer (proper muscle). BWT should be measured perpendicularly to the wall, between two clearly defined hypoechoic lines—from the serosa-muscle interface (outer edge of the outer hypoechoic line) to the mucosa-lumen interface (inner edge of the inner hypoechoic line) (Fig. 1). The segment most affected should be chosen, and the average of four separate BWT measurements—two each in transverse and longitudinal views—should be used [13,16]. Numerous studies have found that BWT correlates well with the degree of inflammation in both CD and ulcerative colitis [17,18]. Nevertheless, BWT may yield false positives and negatives. Bowel wall thickening is not specific to CD, as it can occur in infectious, neoplastic, and other inflammatory diseases. Chronic inflammation due to submucosal fat deposition and/or muscular hypertrophy can also result in persistent thickening [19]. False negatives are possible in patients with obesity, those with anorectal lesions, or bowel disease with only superficial mucosal lesions. [14] Therefore, comprehensive consideration of IUS parameters, including BWT, is mandatory to determine the presence of active inflammation (Fig. 2).

(2) Color Doppler signal (CDS) is one of the most important parameters for evaluating disease activity (Fig. 3). To maximize sensitivity for detecting low-velocity vascular flow in the bowel wall, Doppler parameters should be carefully optimized: set the wall filter to the lowest level, adjust the velocity scale to approximately 4–7 m/s, set color sensitivity to high, and increase the gain until flash artifacts appear, then reduce it until artifacts disappear. CDS should be assessed at sites showing pathological BWT ≥3 mm, including the site with the greatest BWT, and scored semi-quantitatively using systems such as the modified Limberg score (Table 1) [12,20,21], although some interobserver variability exists. Color Doppler flow is considered present when color pixels persist throughout the observation period and/or reappear in the same location. Lack of

Table 1. Intestinal ultrasound parameters for active inflammation

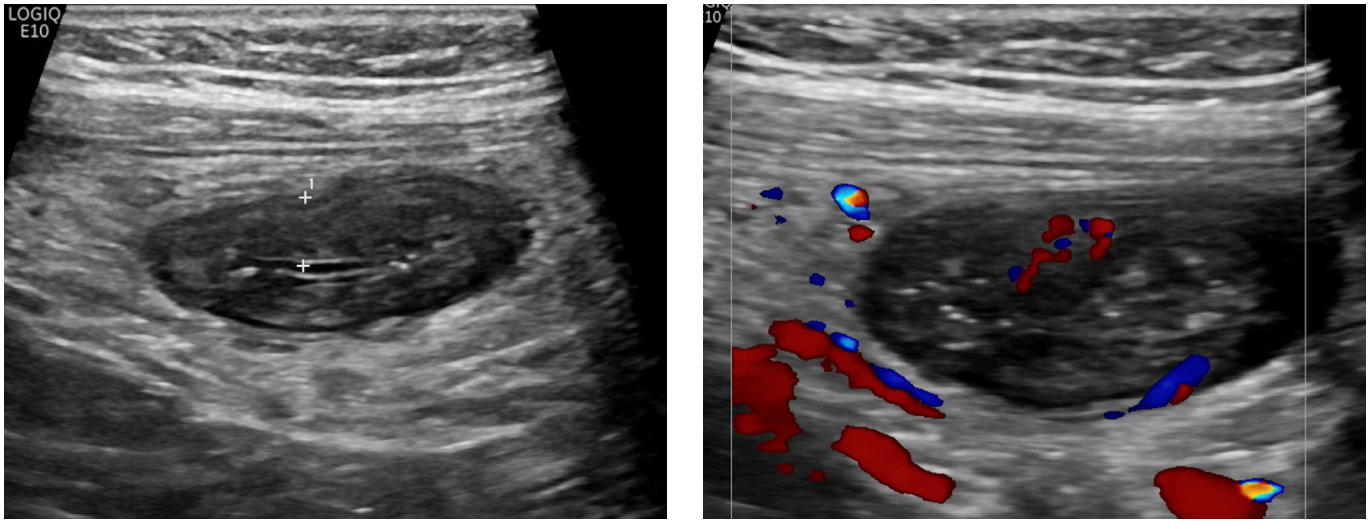
Parameter	Definition	Cut-off
Bowel wall thickening	- Distance between mucosa-lumen interface and the serosa-muscle layer interface - Average of two or more separate measurements in the longitudinal and transverse planes	Most reliable marker Active: BWT >3 mm
Bowel wall flow	- Vascular signals detected by color Doppler - Modified Limberg score 0: Absent 1: Small spots within the wall 2: Long stretches within the wall 3: Long stretches extending into the mesentery	Color Doppler imaging with a low-velocity setting Active: grade ≥2
Loss of bowel wall stratification	- Hypoechoic submucosal layer leading to disrupted mural layers secondary to inflammation and edema - Assessment of submucosal thickening/prominence	Active: present Focal loss (<3 cm), extensive (≥3 cm)
Mesenteric fat wrapping/ stranding	Presence of a hyperechoic area surrounding the pathologic intestinal wall, indicating mesenteric inflammatory fat	Binary outcome (presence/absence) Active: present
Ulcer	Focal depression in mucosal layer	
Loss of intestinal motility	Helpful in areas suspicious for stenosis and/or stricture with proximal dilatation	
Others	Loss of colonic haustration, ascites, lymphadenopathy, presence of complication (abscess, fistula, stenosis, etc.)	

BWT, bowel wall thickness.



A B

Fig. 1. Measurement of bowel wall thickness.
A. Normal bowel wall is measured between the mucosa-lumen interface (inner hypoechoic line) and the muscle–serosa interface (outer hypoechoic line). B. In pathologic bowel wall, bowel wall thickening is associated with loss of bowel wall stratification; therefore, the measurement is made between the innermost and outermost hypoechoic lines.



A B

Fig. 2. Ultrasonographic parameters of active inflammation.
Diffuse bowel wall thickening (A, >3 mm) with loss of bowel wall stratification and increased Doppler signal (B, modified Limberg score grade 2) indicate active inflammation.

detectable vascularity in a thickened bowel wall may result from technical or patient-related factors, such as device insensitivity (suboptimal Doppler parameters), high body mass index, or a penetration depth >40 mm [5,15].

(3) Decreased echogenicity in the normally hyperechoic submucosal layer results in loss of BWS, a sign that reflects more severe inflammation, longitudinal ulceration, and poor prognosis [22,23]. This can be assessed using binary (present/absent) or categorical (present/uncertain/absent) methods, though expert consensus recommends scoring as present, focal (<3 cm), or extensive (>3 cm) [12].

(4) Mesenteric inflammatory fat indicates changes in echogenicity (often hyperechoic) and hypertrophy of mesenteric fat surrounding an affected bowel segment ("fat wrapping"), producing a mass

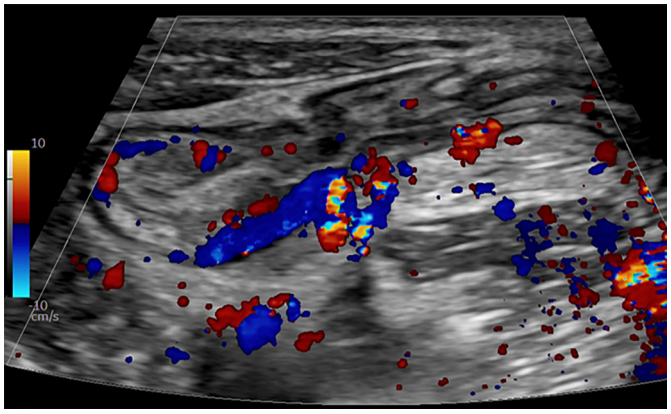


Fig. 3. **A case of active inflammation in the terminal ileum.** The color Doppler signal is markedly increased, with a Limberg score of grade 3 (long stretches extending into the mesentery).

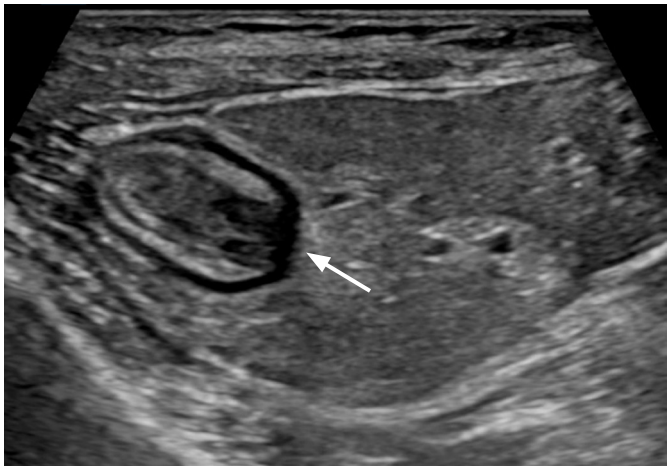


Fig. 4. **Mesenteric fat stranding and wrapping.** This refers to mesenteric inflammatory fat that appears as changes in echogenicity and hypertrophy of mesenteric fat surrounding a pathologic bowel segment. The involved bowel loop shows bowel wall thickening with ulceration (arrow) along the mesenteric border, indicating active inflammation.

effect on adjacent bowel loops (Fig. 4). It typically appears along the mesenteric border, but may also be circumferential [24]. Also termed fibrofatty proliferation or creeping fat, it is highly correlated with disease activity, although less so than bowel wall thickening. It can also appear in chronic inflammation, reflecting a mesenteric adipose tissue response to inflammatory stimuli and promoting fibromuscular proliferation of the intestine [25].

Other parameters include ulceration, loss of bowel motility, serosal margin spiculation, lymphadenopathy (>10 mm in short axis), and loss of colonic haustration. However, these findings are less well validated in terms of interobserver agreement and are not specific to IBD.

Disease Activity and Severity Assessment: Scoring Systems

Active inflammation can be defined either qualitatively using predetermined criteria or quantitatively with scoring indices—both approaches incorporate combinations of IUS parameters. Multiple criteria and scoring systems exist to assess disease activity, but none have achieved full validation or global acceptance. A representative qualitative criterion is "BWT ≥3 mm and at least one additional abnormal IUS feature among increased Doppler signal, loss of wall layering, mesenteric inflammatory fat, loss of haustral marking, or complications." De Voogd et al. [20] reported an area under the curve (AUC) of 0.939 for diagnosing active inflammation in pregnant CD patients using these criteria. You et al. [26] examined the correlation between fecal calprotectin (FC) and IUS-assessed activity using the same criteria, finding an AUC of 0.756 for FC ≥250 μg/g. The diagnostic performance of the IUS criteria in this study was lower than that reported by De Voogd et al. [20], possibly due to differing definitions of "active inflammation." Specifically, De Voogd et al. [20] defined active inflammation using both FC level and a clinical activity index, thereby expanding the spectrum of cases considered as active inflammation. Previous meta-analyses have summarized various activity scoring systems from different study groups [11,27]. In this review, recent IUS scoring systems are summarized in Table 2, which provides quantitative measures of disease activity and severity (Fig. 5) [21,28–33].

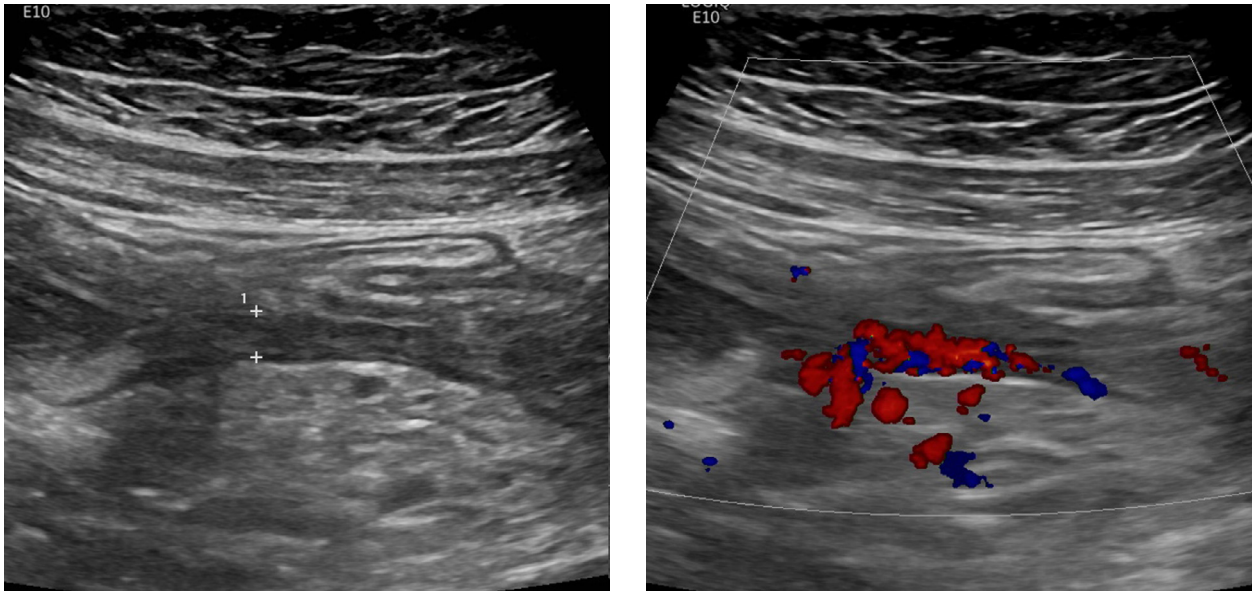
Ripolles et al. [28] developed a simplified ultrasonography (US) score based on BWT and CDS grades, reporting an AUC of 0.923 for diagnosing endoscopically active disease (simplified endoscopic activity score of Crohn disease [SES-CD] >3) with a cut-off value of 5.5. A subsequent validation study demonstrated an AUC of 0.979 for diagnosing active disease (SES-CD >2) with a cut-off of 3.1 [32]. Novak et al. [29] introduced a simple sonographic score defined by the equation: (0.0563×BWT1)+(2.0047×BWT2)+(3.0881×BWT3)+(1.0204×Doppler1)+(1.5460×Doppler2). This scoring system achieved AUCs of 0.866 and 0.836 for diagnosing moderate-to-severe endoscopic scores in the development and validation cohorts, respectively [29]. The International Bowel Ultrasound (IBUS) group in Europe develope the IBUS Segmental Activity Score (SAS) system, which incorporates four key parameters: BWT, CDS, BWS, and mesenteric fat, as determined by an 11-expert consensus Delphi process [21]. The International Bowel Ultrasound Segmental Activity Score (IBUS-SAS) score is calculated as follows: 4×BWT+15×mesenteric fat score+7×bowel wall flow score+4×BWS score. In validation, this system showed an AUC of 0.895 for diagnosing active disease (SES-CD ≥3) with a cut-off of 48.7 [33]. The IBUS-SAS score demonstrated strong positive correlation with endoscopic activity (SES-CD), the Crohn's Disease Activity Index, and inflammatory biomarkers, and showed excellent

Table 2. Criteria and scoring system for disease activity in Crohn disease using IUS

Type of activity assessment	Definition	Cut-off	Diagnostic performance of disease activity	Development/ validation study
Qualitative criteria of active inflammation	BWT ≥3 mm and ≥1 for abnormal IUS features[a]	NA	AUC 0.939[b]	De Voogd (2022) [20]
Quantitative scoring of disease activity	Simplified US score: BWT (mm)+color Doppler grade[c]	5.5	AUC 0.923 (for SES-CD >3)	Ripolles (2021) [28]
		3.1	AUC 0.979 (for SES-CD >2)	Ripolles (2024) [32]
	Simple sonographic score: (0.0563×BWT1)+(2.0047×BWT2)+(3.0881×BWT3)+(1.0204×Doppler1)+(1.5460×Doppler2)	NR	Development cohort: AUC 0.866 Validation cohort: AUC 0.836 (for ≥moderate endoscopic score)	Novak (2017) [29]
	Simple ultrasound score for Crohn disease (SUS-CD): bowel wall thickness (score 0–3), color Doppler score[d] (score 0–2)	1	AUC 0.92 (for SES-CD >2)	Saevik (2021) [30]
		2.5	AUC 0.835 (for SES-CD ≥3)	Wang (2023) [33]
	Intestinal bowel ultrasound-segmental activity score (IBUS-SAS): 4×BWT+15×mesenteric fat score+7×bowel wall flow score+4×bowel wall stratification score	NR	–	Novak (2021) [21]
		48.7	AUC 0.895 (for SES-CD ≥3)	Wang (2023) [33]
	Bowel ultrasound score (BUSS)=0.75×BWT+1.65×BWF[e]	3.52	AUC 0.864 (for SES-CD >2)	Allocca (2022) [34]

IUS, intestinal ultrasonography; BWT, bowel wall thickness; NA, not applicable; AUC, area under the curve; SES-CD, simplified endoscopic activity score for Crohn disease; NR, not reported.

[a]IUS features: loss of wall stratification, increased color Doppler signal, fat wrapping, loss of haustral markings, or complications such as inflammatory infiltrates, abscess, fistula, or stenosis. [b]Reference: fecal calprotectin ≥250 μg/g or fecal calprotectin ≥100 μg/g+Harvey-Bradshaw Index≥4. [c]Modified Limberg scale: absent (grade 0), 1–2 points/cm^2 (grade 1), 3–5 points/cm^2 (grade 2), >5 points and vessels outside the intestinal wall (grade 3). [d]Color Doppler score: no or single vessel (score 0), 2–5 vessels/cm^2 (score 1), >5 vessels/cm^2 (score 2). [e]Bowel wall flow (BWF): 0=absence; 1=presence of blood signals on color Doppler.



A B

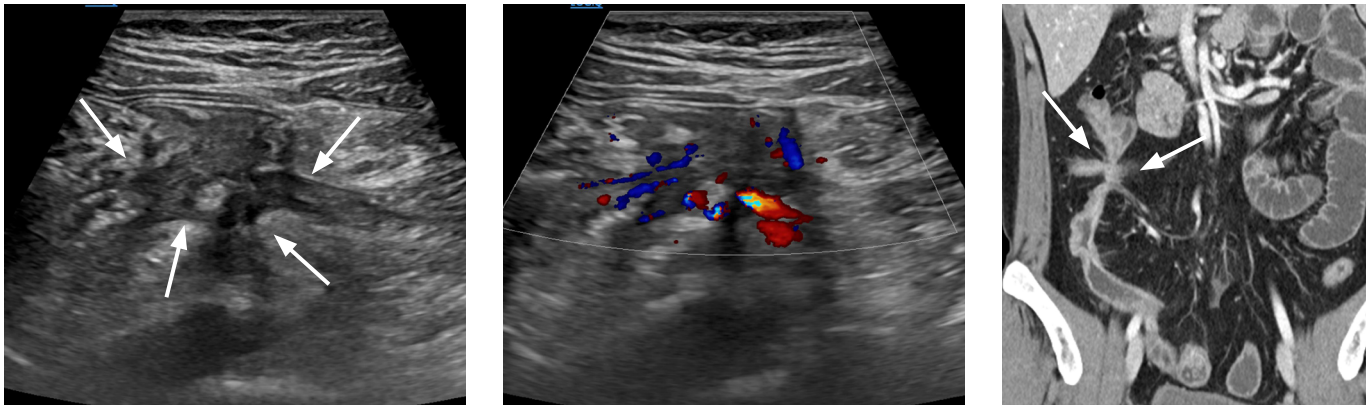
Fig. 5. Quantitative scoring of disease activity using intestinal ultrasonography parameters.
Bowel wall thickening (4.5 mm) with loss of bowel wall stratification (A) and increased Doppler signal (modified Limberg score 3, B) indicate active inflammation. The Simple Ultrasound Score for Crohn's Disease score is 3 (bowel wall thickness score 1+Crohn disease score 2), exceeding the cut-off of 1. The International Bowel Ultrasound Segmental Activity Score is 66 (4×4.5+15×1+7×3+4×3), exceeding the cut-off of 48.7. The Bowel Ultrasound Score is 5.025 (0.75×4.5+1.65×1), exceeding the cut-off of 3.52—all indicating active inflammation.

interobserver agreement. The Simple Ultrasound Score for Crohn's Disease (SUS-CD) was developed through multiple linear regression analysis using SES-CD as the dependent variable and is calculated as the sum of BWT (score 0–3) and color Doppler score (score 0–2). SUS-CD demonstrated an AUC of 0.92 for predicting endoscopic activity (SES-CD >2) with a cut-off of SUS-CD ≥1, and an AUC of 0.88 for predicting moderate endoscopic activity (SES-CD >7) with a cut-off of SUS-CD ≥3 [30]. In external validation, SUS-CD showed an AUC of 0.835 for diagnosing endoscopic activity (SES-CD ≥3) with a cut-off of 2.5, and significant correlation with other activity indices [33]. The Bowel Ultrasound Score (BUSS) was derived from another prospective study and is calculated as: 0.75×BWT+1.65×bowel wall flow. This score was assessed for its ability to diagnose active inflammation and its responsiveness to treatment; BUSS ≥3.52 yielded an AUC of 0.864 for diagnosing endoscopic activity (SES-CD >2) [34]. Further discussion of this work will be presented in a later section.

Assessment of Complications

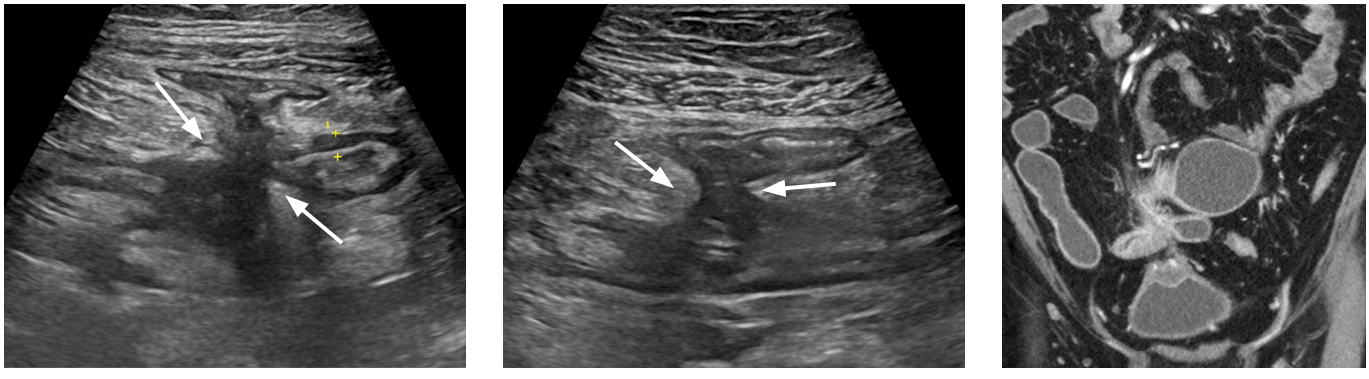
Transmural inflammation can lead to various penetrating complications, including penetrating disease, micro- or macroperforation, mesenteric inflammation, and stricturing disease.

(1) Sinuses and fistulas: These are inflammatory tracts that appear as linear regions of altered echogenicity originating from the serosal surface of the intestine, and they may contain air or debris. Fistulas are tracts that communicate between two different epithelialized structures, while sinus tracts are blind-ending structures with a cross-sectional lumen diameter of less than 2 cm, a distinguishing feature from abscesses (Figs. 6, 7) [35,36]. These penetrating tracts typically show increased Doppler signal in the wall, and the affected



A B C

Fig. 6. Assessment of complication: fistula.
Ultrasonography show complex enteroenteric and enterocolic fistulae (A, arrows) with increased Doppler signal (B, Limberg score grade 3) between the ascending colon and multiple ileal loops, corresponding to the computed tomography image (C, arrows).



A B C

Fig. 7. Assessment of complication: fistula.
A, B. Enteroenteric fistulae are observed with active inflammation between different ileal loops (arrows). This lesion correlated with computed tomography images (C).

bowel loops may appear tethered or angulated [37].

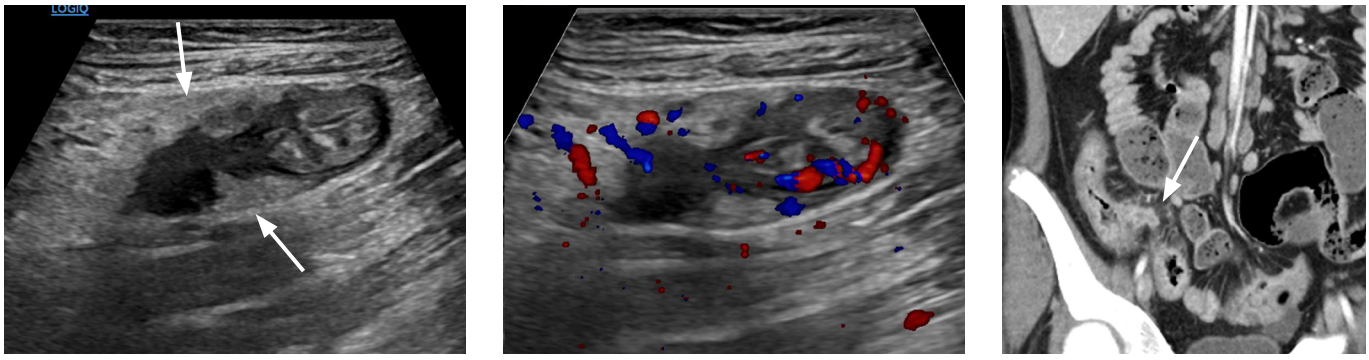
(2) Inflammatory infiltrates and abscesses: These refer to acute suppurative inflammations of the soft tissues adjacent to an inflamed bowel segment. Inflammatory infiltrates present as hypoechoic, poorly organized collections without a discernible wall, often associated with increased CDS. Abscesses, on the other hand, are organized fluid collections that may have variable internal echogenicity, containing debris, septations, or nondependent echogenic gas, and are typically located adjacent to actively inflamed bowel loops (Fig. 8). Abscesses may demonstrate peripheral hyperemia with absent central blood flow. Inflammatory infiltrates and abscesses generally arise from focal bowel wall perforations, indicating severe transmural inflammation or deep ulceration. IUS offers diagnostic capability comparable to other cross-sectional imaging modalities, such as CT and MRI, for detecting penetrating disease and abscesses [38,39]. However, its performance is highly dependent on disease location; thus, magnetic resonance (MR) is preferred over IUS for certain anatomical areas such as the deep pelvis or left hypochondrium, and for evaluation of complex penetrating disease [40].

(3) Stenosis: The definition of stenosis is heterogeneous among different US studies [41,42]. Nonetheless, stenosis is generally defined by meeting at least two of the following three criteria: luminal narrowing (<10 mm or not otherwise specified), bowel wall thickening at the site of narrowing (≥3–4 mm), and pre-stenotic or proximal dilation (≥25 or ≥30 mm) (Table 3) [15,43]. Some studies have also incorporated motility assessment, considering findings such as poor fluid flow (to-and-fro movement) or increased peristalsis in the proximal fluid-filled bowel segment [44–46]. There is a need for a standardized definition to clarify whether morphological criteria, motility assessment, or both should be prioritized. Cross-sectional imaging, including IUS, is valuable for diagnosing and characterizing stricturing disease (Figs. 9, 10, Video clip 1). Stenoses typically contain both inflammatory and fibrotic components; determining the dominant component within a stenosis is essential for guiding management decisions. According to a recent meta-analysis, the diagnostic accuracy of IUS for stenosis varies, with sensitivity ranging from 68%–100% and specificity from 86%–100%, depending on the reference standard (endoscopy with or without histology, or CT) [42]. Small intestine contrast ultrasonography (SICUS), which involves oral contrast administration, demonstrated higher sensitivity for detecting stenosis compared to conventional IUS (89%–97% vs. 74%–81%) [43,47,48], as oral contrast helps reveal ileal stenosis and pre-stenotic dilation.

Table 3. Assessment of complications using IUS

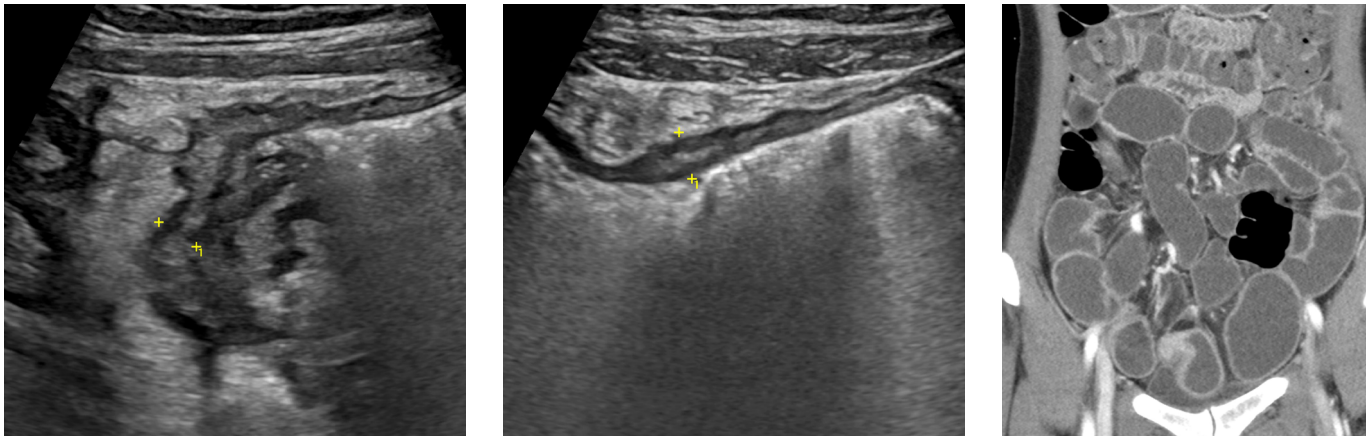
Complications	IUS findings
Penetrating tracts Sinus Fistula	- Blind-ending linear structures (sinus) - Linear tracts communicating between two distinct epithelialized structures (fistula)
Inflammatory infiltrates	- Hypoechoic, poorly organized collection without a discernible wall - Associated hyperemia showing increased Doppler signal
Abscesses	- Organized fluid collections with variable internal echogenicity containing internal debris, septations, or echogenic gas - Located adjacent to actively inflamed bowel segments
Stenosis	Presence of at least two of the following three components: - Luminal narrowing: <10 mm - Bowel wall thickening at the narrowing point: ≥3 mm or ≥4 mm - Pre-stenotic or proximal dilatation: ≥25 mm or ≥30 mm

IUS, intestinal ultrasonography.



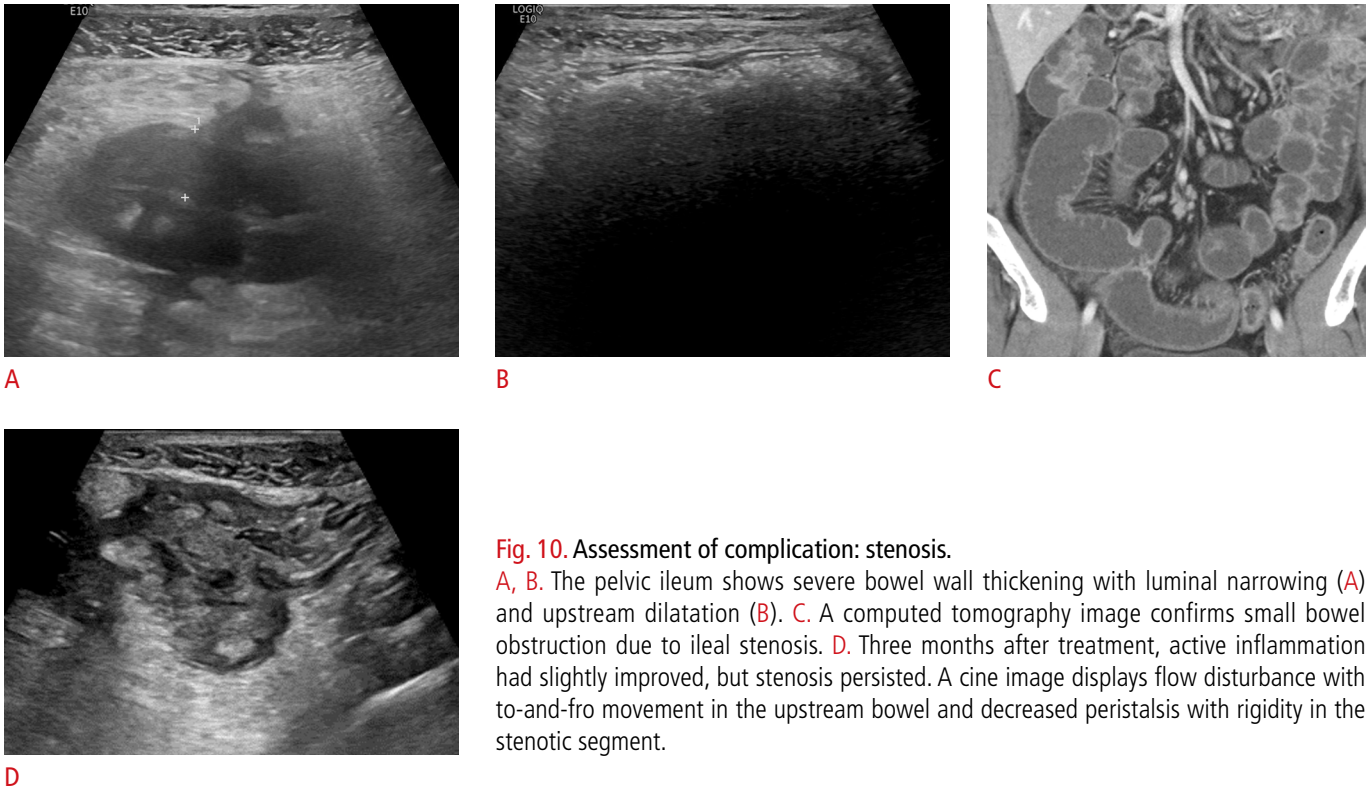
A B C

Fig. 8. Assessment of complication: abscess.
An abscess is associated with a focal wall defect at the mesenteric border of the distal ileum (A, arrows; B), and computed tomography images show diffuse active inflammation in the distal ileum and penetrating disease with abscess formation (C, arrow).



A B C

Fig. 9. Assessment of complication: stenosis.
A. Severe luminal narrowing is associated with marked bowel wall thickening and loss of wall stratification, indicating stenosis with active inflammation in the distal ileum. B. The upstream ileum is dilated with fluid and gas and shows bowel wall thickening, and the posterior bowel wall is obscured by bowel gas shadowing. C. A computed tomography image confirms small bowel obstruction due to ileal stenosis with active inflammation.



A B C D

Fig. 10. Assessment of complication: stenosis.
A, B. The pelvic ileum shows severe bowel wall thickening with luminal narrowing (A) and upstream dilatation (B). C. A computed tomography image confirms small bowel obstruction due to ileal stenosis. D. Three months after treatment, active inflammation had slightly improved, but stenosis persisted. A cine image displays flow disturbance with to-and-fro movement in the upstream bowel and decreased peristalsis with rigidity in the stenotic segment.

Although the presence of pre-stenotic dilation can confirm stenosis when using oral contrast, its absence on IUS does not exclude the diagnosis. SICUS also demonstrated an excellent detection rate for other CD-related complications, such as inflammatory masses, fistulas, and abscesses, in a previous prospective study [47], and showed improved diagnostic accuracy compared to IUS in a meta-analysis [43]. However, the METRIC study, which directly compared SICUS and IUS, found that both modalities had nearly identical diagnostic performance for small bowel disease extent (sensitivity/specificity for IUS and SICUS: 72%/86%) and colon disease extent

(IUS: 13%/82%; SICUS: 17%/92%) [49]. Given that SICUS requires the additional step of oral contrast administration and is more time-consuming, it is not widely used despite its modestly higher sensitivity for complications [50].

Comparison with MR Enterography

Meta-analyses have shown that the diagnostic accuracy of IUS and MRE for detecting active inflammation is nearly identical [4,51]. Horsthuis et al. [4] reported per-patient sensitivities of 89.7% for IUS and 93% for MRE, specificities of 95.6% for IUS and 92.8% for MRE, and per-segment sensitivities of 73.5% for IUS and 70.4% for MRE, with specificities of 92.9% and 94%, respectively. A recent meta-analysis reported a summary AUC of 0.93 (0.91–0.95) for IUS and 0.94 (0.92–0.96) for MRE. However, in the multicenter METRIC trial, which directly compared IUS and MRE in the same patients, MRE showed significantly greater sensitivities than IUS for assessing the extent and presence of small bowel disease—a 10% advantage for extent and 5% for presence [52]. Another prospective study found that IUS and MRE had similar diagnostic accuracy for detecting active small bowel disease, but IUS was less accurate for determining the extent of disease (mean extent: IUS, 20±11 cm vs. MRE, 28±15 cm), and both modalities underestimated the true extent of inflammation compared with surgical resection [53]. The concordance between IUS and MRE was good for disease location (κ=0.81), strictures (κ=0.86), and abscesses (κ=0.88), but MRE was superior for detecting enteroenteric fistulae (κ=0.67). Therefore, MRE is preferred for the initial diagnostic workup to define disease distribution and phenotype, as its diagnostic accuracy exceeds that of IUS, particularly for small bowel involvement. MRE is also preferred for the evaluation of complications and perianal disease due to its consistent accuracy regardless of disease location or phenotype. IUS offers significant advantages from the patient's perspective: according to the METRIC study, patients were more willing to undergo IUS than MRE (99% vs. 91%), although they still preferred MRE over colonoscopy and ranked diagnostic accuracy as the most important attribute [54]. IUS plays an important role in close monitoring and frequent disease activity assessments, enabling point-of-care and real-time decision-making due to its minimal burden and convenience. Thus, IUS and MRE may be used alternately or together to assess treatment response and disease relapse, depending on disease location and phenotype. For extensive disease, complex phenotypes (penetrating and/or stricturing disease), or small bowel involvement in the deep pelvis, proximal ileum, or jejunum, MRE is preferred over IUS. Conversely, IUS is more suitable for short-segment, IC, colon-dominant, or non-complex inflammatory disease. It is especially useful for detailed evaluation of the bowel wall, including ulcerations. The comparison of IUS and MRE in terms of their characteristics and preferred clinical applications is summarized in Table 4.

Role of IUS in Disease Monitoring

Therapeutic response should be assessed by focusing on changes in key IUS features. For monitoring treatment response, BWT is the most critical parameter, followed by CDS grade, BWS, and mesenteric inflammatory fat among the various IUS indicators. Responses can be categorized into four groups: transmural remission or healing; transmural response (clear improvement in imaging features but with persistent signs of inflammation); stable disease; or progressive

Table 4. Comparison between intestinal ultrasonography and magnetic resonance enterography

	Intestinal ultrasonography	Magnetic resonance enterography
Advantages	Noninvasive, radiation-free No need for oral or IV contrast media Assessment of terminal ileum and colon Assessment of transmural and extramural activity Real-time assessment of bowel motility Possible to use Doppler technique	Radiation-free Assessment of small bowel Assessment of transmural and extramural activity Validated activity scores (MaRIA/CDMI) Assessment of complications, especially for complex fistula Assessment of deep-seated pelvic disease
Disadvantages	Operator-dependent Limited by gas-filled bowel or obesity Limited assessment of the proximal ileum, jejunum, transverse colon, and rectum Less validated scoring systems for disease activity	Time-consuming Requires bowel distention with oral contrast Requires IV contrast medium Requires frequent breath-holdings by patients
Preferred clinical situations	Short disease extent L2 and L3 disease (colon and ileocolic) Non-complex B1 phenotype (inflammatory) Evaluation of bowel wall layers and ulceration	Baseline study: disease extension, location, and behavior Long disease extent L1 and L3 disease (ileal and ileocolic) B2–3 phenotype (stricturing, penetrating, or complex) Presence of perianal disease

IV, intravenous; MaRIA, magnetic resonance index of activity; CDMI, Crohn disease magnetic resonance imaging index; L, disease location category; B, disease behavior category according to the Montreal classification.

disease (increased inflammatory parameters, new segments involved, CD-related complications, or a combination thereof) [36]. Transmural response is typically defined as a reduction in BWT of >25%, >2 mm, or >1 mm, along with at least a one-grade reduction in CDS. However, the definition of TH remains neither standardized nor validated. Most commonly, TH is defined as BWT ≤3 mm with normal CDS in both the small and large bowel [55–57]. However, various combinations of IUS parameters are used to define TH: several studies have defined TH as normalized BWT (≤3 mm) alone [58–60], while others have defined it as resolution of all inflammatory parameters [61,62]. The optimal timing for IUS response assessment is considered to be at baseline, week 14, and between weeks 26 and 52, depending on elevated FC, symptoms, or clinical suspicion of flare [57]. Response after steroids or biologics may be observed by 4 weeks; thus, early IUS assessment can be performed at weeks 4–8. According to a recent review, the TH rate ranged from 13% to 27% in early IUS assessments (1–4 months) and from 14% to 51% in later assessments (12–24 months) [63]. As indicated, response rates differ across studies based on treatment regimen, evaluation intervals, TH definition, disease duration, and histological characteristics of the involved segment. Several prospective studies have reported the responsiveness of IUS parameters for assessing transmural response and healing during treatment [20,61,64,65] (Table 5). In the TRUST trial, the four main IUS parameters—BWT, CDS, BWS, and mesenteric inflammatory fat—significantly improved at 3 and 12 months, in parallel with clinical and biochemical improvements. Notably, colonic lesions responded more rapidly than those in the ileum [64]. In the STARDUST trial, 46% of patients demonstrated an IUS response (25% reduction in BWT), and 24% achieved TH (normalization of all IUS parameters) at week 48, with greater responses seen in colonic disease and biologic-naïve patients [65]. Another prospective multicenter study monitoring various biologic therapies over 12 months found that 20%–30% of patients achieved TH at 12 months, and mean BWT improved significantly at both 3 and 12 months. Colonic involvement was associated with higher TH rates, while greater baseline BWT predicted a lower likelihood of achieving TH at both 3 and 12 months [61]. A previously mentioned prospective study assessed treatment response using a self-developed IUS scoring system, BUSS (Table 2). They reported that BUSS was responsive during treatment: a change in BUSS of less than −1.2 gave an AUC of 0.786 and 80% accuracy in detecting endoscopic response (SES-CD reduction ≥50% from baseline), and BUSS <3.52 (defined as TH) showed 78% accuracy for detecting endoscopic remission (SES-CD ≤2) [34]. Additionally, after 12 months of therapy, BUSS ≥3.52 was a significant predictor of worse outcomes, such as the need for steroids, therapy changes,

Table 5. Treatment response monitoring using IUS

	Transmural response	Transmural healing
Definition	Reduction in BWT >25% or >2 mm, or Reduction in BWT >1 mm+reduction in one CDS grade	Not standardized; - BWT ≤3 mm+normal CDS[a)] - Normalized BWT ≤3 mm - Resolution of all inflammatory parameters
Timing of assessment	Baseline, week 14, week 26, or week 52 Early IUS assessment: 4–16 weeks (1–4 months) Late IUS assessment: 48–96 weeks (12–24 months)	
Response rate	–	Early IUS assessment: 13%–27%, average 19% Late IUS assessment: 14%–51%, average 31%
Related studies		
TRUST trial (2017) [64]	Improvement of BWT, CDS, BWS, and mesenteric inflammatory fat in 3 and 12 months correlated with clinical and biochemical improvement	58.5% normalized BWT in terminal ileum in 3 months, concurrent with 52.1% clinical remission (HBI <5)
STARDUST trial (2022) [65]	46% IUS response in week 48 (BWT >25% reduction)	24% TH at week 48 (normalization of all IUS parameters)
Calabrese et al. (2022) [61]	Significant mean BWT and bowel wall flow (Limberg score) improvement at 3, 6, and 12 months	27.5% TH at 12 months (normalization of all IUS parameters)
Allocca et al. (2022) [34]	Change in BUSS[b)] <−1.2: 80% accuracy in detecting endoscopic response	48.7% TH (BUSS <3.52): 78% accuracy in detecting endoscopic remission

IUS, intestinal ultrasonography; BWT, bowel wall thickness; CDS, color Doppler signal; BWS, bowel wall stratification; HBI, Harvey-Bradshaw Index; TH, transmural healing; TRUST, Transabdominal ultrasonography of the bowel in subjects with Crohn disease to monitor disease activity; STARDUST, Study of treat-to-target versus routine care maintenance strategies in Crohn disease patients treated with Ustekinumab.

[a)]Most commonly used definition. [b)]Bowel ultrasound score (BUSS)=0.75×bowel wall thickness+1.65×bowel wall flow (1=presence of Doppler signal, 0=absence).

hospitalization, or surgery [31]. The prognostic significance of achieving transmural response versus healing, or of different TH definitions, requires further study.

Special Techniques: Contrast-Enhanced Ultrasonography and Ultrasound Elastography

Contrast-enhanced ultrasonography (CEUS) is an adjunct for cases indeterminate by B-mode IUS and CDS. It visualizes bowel microvasculature and more sensitively detects mural enhancement patterns, helping determine disease activity. CEUS allows both qualitative assessment of wall enhancement and quantitative analysis using time–intensity curve (TIC) parameters from an ROI in the target bowel segment. This may help distinguish inflammatory from fibrotic stenosis. For example, a disrupted wall echo pattern with transmural or centrifugal enhancement (from mucosa outward to serosa), or submucosal enhancement, suggests active inflammation, while low/absent wall enhancement or centripetal enhancement (from serosa inward to mucosa) suggests predominant fibrosis [66]. TIC analysis can also help quantify disease activity, grade severity, and characterize stenosis type. Studies have found that TIC parameters differ significantly between active inflammation and fibrosis: active inflammation yields higher peak enhancement, faster time to peak, and greater area under the TIC, while fibrosis shows the opposite pattern [67,68]. However, the benefit of these quantitative parameters for diagnostic accuracy remains controversial. Moreover, CEUS requires extra time for contrast injection and TIC analysis, limiting its routine clinical use. Ultrasound elastography assesses tissue stiffness by strain or shear-wave techniques and can serve as a noninvasive marker for fibrosis. Strain elastography measures tissue deformation in response to external compression from the probe, which can be evaluated visually on the color map and via a semiquantitative strain ratio (SR). The SR is calculated as the ratio of mean strain in reference tissue (bowel and adjacent mesenteric fat) to that in the lesion, providing a relative measurement of stiffness. Some studies reported increased SR correlates with increased collagen and fibrosis [69,70], but others found no such correlation with fibrotic stenosis [71,72]. Shear wave elastography (SWE) measures the speed of shear waves induced by mechanical pressure, returning quantitative estimates of tissue elasticity. Increased SWE values are associated with muscular hypertrophy or fibrosis, and SWE may help discriminate the degree of fibrosis [73,74]. However, reported cut-off values and ranges are heterogeneous across studies [71,75], and several studies have found conflicting results, such as poor correlation with fibrosis [75,76]. Overall, elastography techniques have not been fully validated or standardized. Results can also be influenced by the distance between bowel loops and probe, as well as peristaltic motion. Thus, elastography is best used as an adjunct to IUS and CEUS rather than as a primary diagnostic modality.

Limitations

Although IUS offers significant advantages as a simple and widely accessible technique with diverse applications, it also faces important challenges related to universalization and standardization. First, IUS assessment is highly operator-dependent, and study outcomes or the diagnostic accuracy for detecting active inflammation can vary significantly between operators. Second, results may depend on patient characteristics or lesion location. For instance, deep-seated complications or active inflammation in the pelvic ileum can be missed or may be difficult to assess due to a limited sonic window and poor compression. Patients with a larger body habitus may similarly pose challenges for adequate imaging. Third, in contrast to MRE, IUS scoring systems are less validated and lack standardization. Several scoring systems have been proposed for the quantitative and objective evaluation of disease activity, utilizing various combinations of BWT, CDS, BWS, and mesenteric fat stranding. However, none of the current systems have been sufficiently validated for assessing treatment response or remission. Fourth, IUS parameters are susceptible to influences beyond disease activity itself. Measurement of vascularity with CDS, for example, can be affected by the US frequency used, the flow velocity range displayed, B-mode image brightness, the patient's physique, and the lesion's location. As a result, findings are not reliably comparable between similar lesions in different patients or even between lesions in different bowel segments within the same patient. Assessment of bowel wall layering is also influenced by probe frequency, patient condition, and inherent subjectivity, as this parameter cannot be quantitatively measured.

Therefore, these limitations and drawbacks must be carefully considered when utilizing IUS in patient care.

Conclusion

IUS has substantial advantages for the assessment of disease activity during frequent monitoring in patients with CD. Compared to MRE, IUS is a straightforward, radiation-free imaging modality that does not require contrast medium injections or oral contrast administration. In line with the treat-to-target strategy outlined in the STRIDE-II guideline, IUS has emerged as an essential imaging tool for assessing TH, which serves as an adjunct to long-term treatment goals. However, IUS also has several limitations, including operator dependency with limited reproducibility, lack of standardized protocols or validated scoring systems, and imaging parameters that are affected by factors such as patient body habitus,

lesion location, and technical settings. Thus, a balanced approach to IUS assessment is necessary, involving comprehensive interpretation of imaging findings in conjunction with other cross-sectional modalities such as CT or MRE.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Supplementary Material

Video clip 1. A cine image displays flow disturbance with to-and-fro movement in the upstream bowel and decreased peristalsis with rigidity in the stenotic segment (https://doi.org/10.14366/usg.25079.v1).

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