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Role of Noninvasive Imaging in the Diagnosis and Management of Patients With Suspected and Established Inflammatory Bowel Disease

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In a treat-to-target era, objective disease assessment in inflammatory bowel disease has become increasingly important. For many years, endoscopy has been generally accepted as the gold standard for evaluating the bowel mucosa, additionally facilitating biopsy. However, noninvasive disease assessment is now increasingly demanded, and cross-sectional imaging techniques, as well as video capsule endoscopy, have markedly improved. Emerging evidence demonstrates the added clinical value of transmural assessment both in Crohn's disease and ulcerative colitis, and cross-sectional imaging methods are increasingly used in phenotyping and monitoring patients with inflammatory bowel disease. In the current review, we propose potential algorithms to use noninvasive imaging in various clinical scenarios and for use in daily practice. The readers will come away with an understanding of what imaging they should consider for different clinical situations and the strengths and limitations of each method. Future developments of noninvasive diagnostic strategies and areas in need of further research are highlighted.

Keywords: Diagnostics; IBD; Intestinal Ultrasound; MRE; MRI; Video Capsule Endoscopy.

Although ileocolonoscopy (IC) remains the gold standard for evaluating the mucosa and obtaining biopsy specimens, noninvasive imaging methods have gained prominence in the clinical evaluation and follow-up of patients with inflammatory bowel disease (IBD). Cross-sectional imaging in IBD, including intestinal ultrasound (IUS), magnetic resonance imaging (MRI), and computed tomography (CT), have emerged as appropriate and effective imaging methods in IBD patients. Such procedures are used for diagnosis, assessment of disease activity and severity, and to detect complications without the level of invasiveness associated with endoscopic procedures.[1] Additionally, they facilitate ongoing monitoring of disease activity and treatment response, allowing for timely adjustments in management strategies.

As technology advances, the role of noninvasive imaging techniques continues to evolve, offering clinicians new tools to enhance patient care. Systematic reviews and meta-analyses have described equal accuracy of IUS, CT, and MRI for the evaluation of disease activity and complications in IBD.[2] The use of IUS as a point-of-care test can optimize and speed up the clinical decision-making process in IBD.[2,3] This review will summarize the current applications, benefits, and limitations of noninvasive imaging in the diagnosis and management of IBD, emphasizing their critical role in a multidisciplinary approach to optimizing patient outcomes.

Initial Diagnosis and Phenotyping of Patients With Inflammatory Bowel disease

The diagnosis of IBD, including Crohn's disease (CD) and ulcerative colitis (UC), relies on a combination of clinical symptoms, blood and stool results, and imaging findings (endoscopic, radiologic and histologic).[4] Because symptoms such as chronic diarrhea and abdominal pain are very common, timely differentiation between IBD and irritable bowel syndrome (IBS) is crucial. Early diagnosis of IBD can prevent future complications and disability; however, the economic and psychological burden of invasive investigations, such as ileocolonoscopy (IC), should not be underestimated.

Several biomarkers and noninvasive diagnostic tools can be used during the initial assessment of patients with suggestive gastrointestinal (GI) symptoms. These facilitate risk stratification and prioritization of referral to the gastroenterologist and diagnostic endoscopy. In the appropriate clinical setting, the presence of elevated C-reactive protein (CRP), hypoalbuminemia, thrombocytosis, or iron-deficient anemia should raise the suspicion of inflammatory, structural, or

Abbreviations used in this paper: **AI, artificial intelligence; AUC, area under the curve; BWT, bowel wall thickness; CD, Crohn's disease; CI, confidence interval; CRP, C-reactive protein; CT, computed tomography; CTE, computed tomography enterography; EAUS, endoanal ultrasound; FC, fecal calprotectin; GI, gastrointestinal; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IC, ileocolonoscopy; IUS, intestinal ultrasound; MRE, magnetic resonance enterography; MRI, magnetic resonance imaging; TPUS, transperineal ultrasound; TR, transmural remission; UC, ulcerative colitis; US, ultrasound; VCE, video capsule endoscopy.**

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neoplastic GI disorders. However, these are neither specific nor sensitive for IBD, because many patients may present with laboratory values within normal reference ranges.

Fecal calprotectin (FC) represents a reliable biomarker of intestinal inflammation. Although FC is not specific for IBD, because it can be elevated in many different GI diseases, a negative value has very high negative predictive value for IBD.[5] Typically, a threshold of ≥50 μg/g, has been used to differentiate IBD vs brain-gut disorders. This threshold has been shown to be associated with a good accuracy, with a pooled sensitivity of 85.8% (95% confidence interval [CI], 78.3%–91%), and specificity of 91.7% (95% CI, 84.5%–95.7%). A meta-analysis showed that at a prevalence of IBD of 1%, a 99.8% negative predictive value had been calculated.[6] However, a universal FC threshold for detecting endoscopic activity has yet to be established. Adding biomarkers, such as CRP and FC, to other imaging methods further improves accuracy, although CRP may not be elevated especially in UC, and FC is less sensitive for small bowel diagnosis.[7,8]

Intestinal Ultrasound

IUS is a noninvasive, accessible, patient-friendly, and sustainable technology with high accuracy[4,9,10] and reliability[11,12] for assessing the small and large intestine (Supplementary Table 1). With a high negative predictive value of 95%, IUS serves as a first-line test to differentiate brain-gut from inflammatory bowel disorders.[13] Even though all cross-sectional imaging may miss mild disease, a negative IUS result makes IBD unlikely,[13] whereas a positive result may confirm intestinal inflammation. Systematic reviews and meta-analysis have shown that IUS is as accurate as more expensive magnetic resonance enterography (MRE) and computed tomography enterography (CTE) for assessing IBD activity and most complications[11,14] (Figure 1).

IUS has long been used as a complementary tool to IC for evaluating the small bowel and extraluminal manifestations of CD, and its use in assessing the colon and UC is increasing. A recent meta-analysis reported that IUS has an 86% sensitivity and 88% specificity in detecting colonic inflammation.[15] Thus, IUS can be regarded as a first test for suspected IBD, potentially avoiding unnecessary IC and expediting diagnosis when needed (Figure 2).

Characterizing IBD by location, activity, extent, and behavior is crucial for prognosis and treatment guidance, especially in CD, given its multisegmental and transmural nature. MRE and IUS complement IC for ileal involvement and structuring complications; however, as discussed below, MRE may be more accurate for fully assessing segmental disease location and deeper penetrating disease.[1,16]

The administration of an oral contrast agent may improve the diagnostic accuracy of IUS in determining small bowel disease extent.[14,17] However, use in clinical practice is restricted to limited situations with high suspicion of small bowel CD and negative or equivocal results from IUS or MRE, or both.

Activity of endoscopic inflammation also drives therapeutic decisions in IBD. IUS scores for luminal activity have been developed and validated using IC as the reference standard (Supplementary Table 2). These scores incorporate parameters identified in multivariate analyses as independent predictors of disease activity and have proven to be valid, reliable, and responsive, making them useful in both clinical practice and clinical trials to assess disease activity and response to treatment.[9]

All US scores incorporate bowel wall thickness (BWT) and color Doppler signals, which are the most reproducible and reliable parameters for assessing disease activity.[11,12] The International Bowel Ultrasound Segmental Activity Score,[12] the Bowel Ultrasound Score,[18] and the Simple Ultrasound Activity Score for CD[19] show the strongest correlations with the Simple Endoscopic Score for CD. In UC, the Milan Ultrasound Criteria[20] and International Bowel Ultrasound Segmental Activity Score[12,21] show strong correlation with the Mayo Endoscopic Score.

Rising health care costs make IUS a cost-effective choice, with US machine costs comparable to endoscopy equipment. IUS has minimal cost and health impacts compared with other cross-sectional imaging procedures with intravenous contrast–based methods, which carry risks of adverse reactions, radiation exposure, and procedural discomfort. Frequent IUS evaluations can improve outcomes by guiding timely treatment and preventing costly complications. Use of expensive and more burdensome diagnostic methods, such as endoscopy, CT, and MRI, can be reduced by using IUS.[22] IUS can also be used safely in pregnant women.[23,24] Limitations include lower sensitivity for assessing disease within the proximal small bowel, for loops of bowel deep in the pelvis, or in patients with a high body mass index.[25]

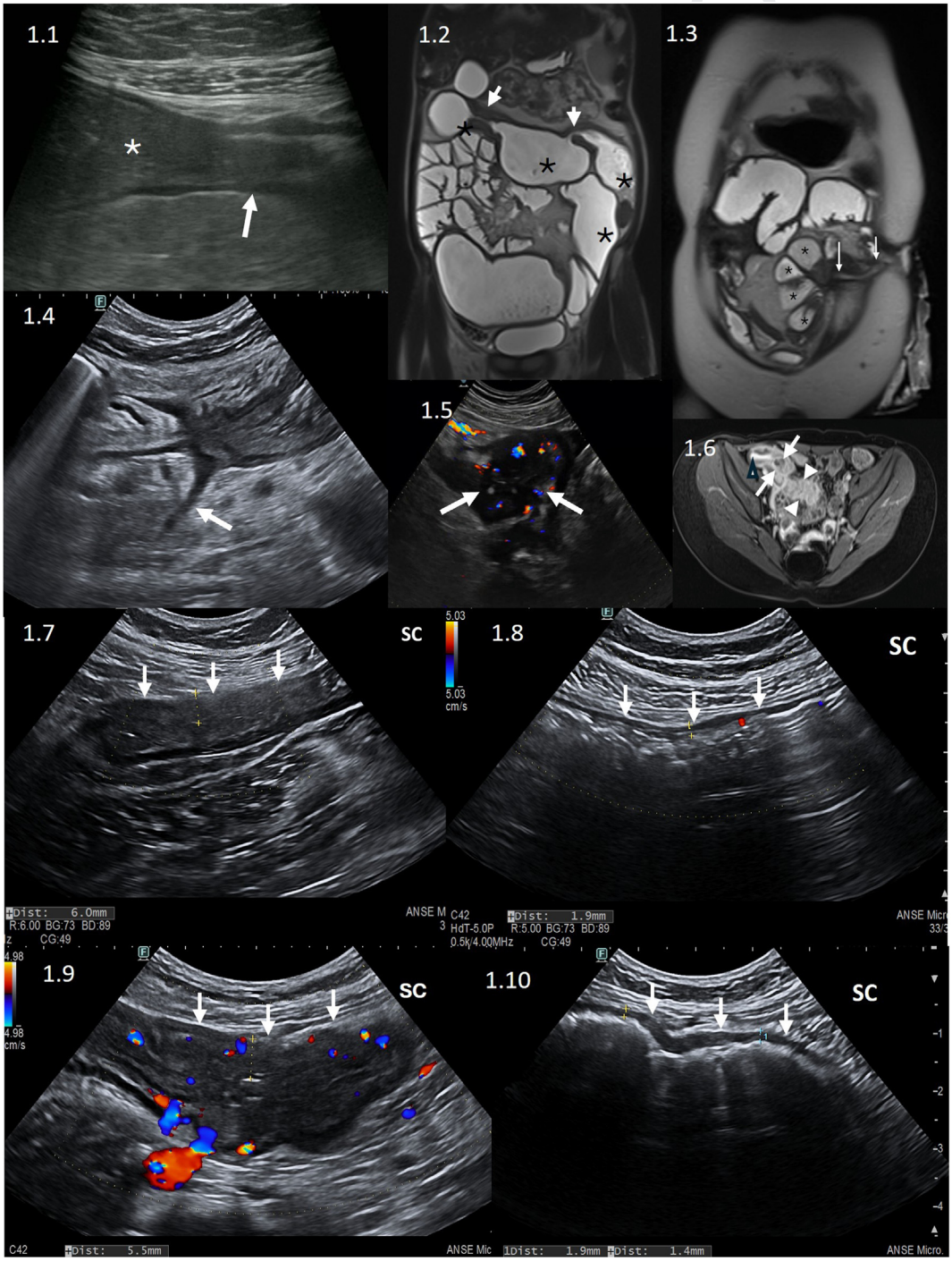
Magnetic Resonance Enterography

MRE is long established in the diagnosis, staging, and phenotyping of patients with inflammatory bowel disease.[26] Patients drink 1 to 1.51 liters of an oral contrast that distends the bowel lumen to facilitate interrogation of the bowel wall and surrounding tissues.[27] MRE is generally well tolerated, but some patients find the cramping and diarrhea associated with the oral contrast agent can be problematic, and claustrophobia in MRI machines may also be an issue for some.[28] In addition, pediatric patients may require general anesthesia, depending on their age.

Meta-analysis data show MRE has high accuracy for diagnosing IBD, particularly in the small bowel.[29] The METRIC (MR Enterography or ulTRasound In Crohn's disease) trial, the largest prospective study to date comparing the diagnostic accuracy of MRE and IUS, reported a 97% (95% CI, 91%–99%) and 92% (95% CI, 84%–96%) sensitivity for MRE and IUS, respectively, for identifying small bowel CD with 80% (95% CI, 72%–86%) and 70% (95% CI, 62%–78%) sensitivity, respectively for full segmental disease location.[30] MRE had slightly higher sensitivity for proximal ileal disease than IUS and may therefore be preferred as the first-line imaging technique for staging small bowel CD at diagnosis. MRE sensitivity was lower in the colon compared with the small bowel (64%; 95% CI, 50%–75%) in the METRIC trial.

Akin to IUS, several MRE observations have been extensively validated as biomarkers of acute inflammation ("active disease"), including wall thickening, increased mural and mesenteric T2 signal, increased postgadolinium contrast enhancement, and deep ulceration,[26,31–33] Ancillary signs of activity also include engorged vasa recta and lymphadenopathy.[34] Recent consensus statements recommend routine documentation of imaging signs supporting disease activity assessment.[35] Various MRE activity scores have been developed and validated, such as the simplified Magnetic Resonance Index of Activity, Clermont, and London scores (Supplementary Table 2), with data supporting responsiveness to treatment effect.[36] Scores are increasingly simple to calculate, which aids clinical translation.

CTE is an accurate alternative to MRE and shares many of the underlying diagnostic attributes. Because of ionizing



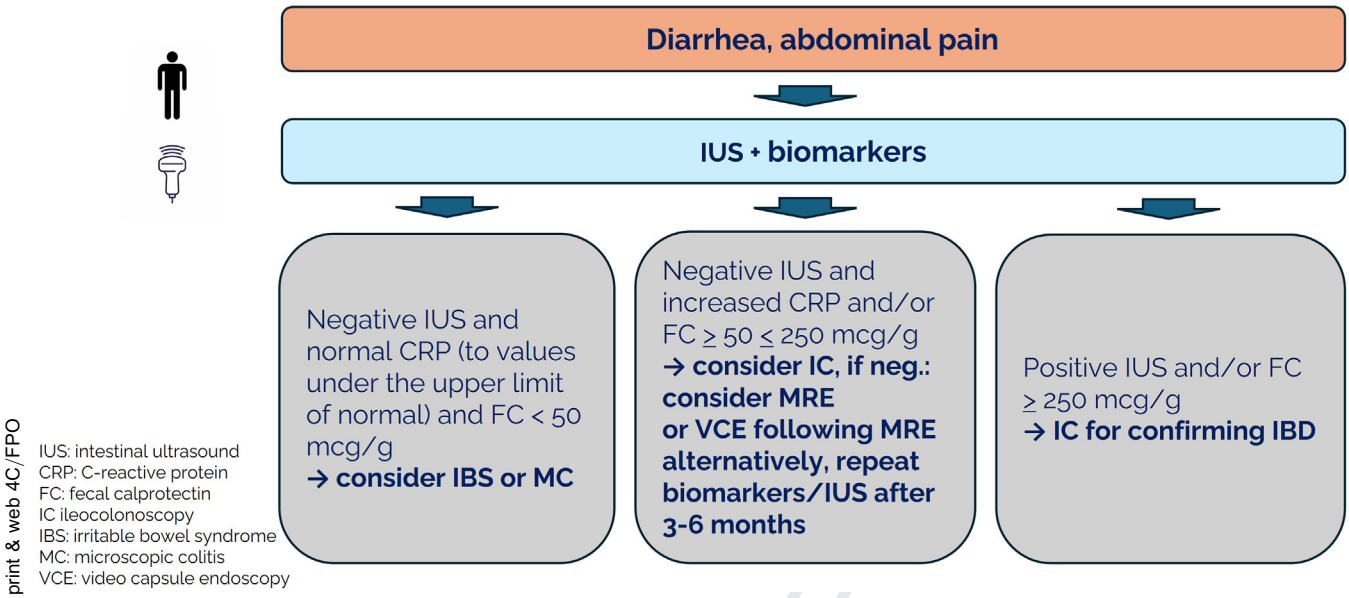


Figure 2. Proposed diagnostic algorithm for suspected IBD.

radiation exposure, CTE use is typical when access to timely IUS or MRE is not possible or contraindicated, in older patients in whom radiation exposure is less problematic, and in the acute setting.[4]

CTE has high diagnostic accuracy for CD and complications. For example, a recent meta-analysis found per-patient sensitivity for small bowel CD was comparable for CT (87%; 95% CI, 050.78%–0.92) and MRE (91%; 95% CI, 0.84–0.95).[37]

CTE activity scores have also been developed, notably, the EMBARK (EMerging BiomARKers in Inflammatory Bowel Disease) score[38] (Supplementary Table 2), which uses features similar to those used in MRE scores, such as BWT and contrast enhancement. The EMBARK score has been successfully used when evaluating treatment response to advanced therapies.[39]

Transperineal Ultrasound

Transperineal US (TPUS) has limited but notable applications in the assessment of IBD. Although it has been primarily recognized for its utility in evaluating perianal complications in CD (TPUS for use in perianal CD will be discussed in a later section), TPUS can still provide valuable information in the context of UC. In particular for assessment of proctitis, TPUS can help visualize changes in the rectal wall and assess for signs of inflammation associated with proctitis. This includes evaluating the BWT and vascularization of the rectal wall, which may indicate active inflammation or may predict endoscopic or even histologic remission.[40] Therefore, reporting of rectal wall thickness and vascularity together where an abnormal distal rectal wall (thickening >4 mm) is detectable on US is recommended. It should be noted that proctitis cannot be excluded

Figure 1. Cross-sectional imaging for detection of complications and for monitoring of IBD. **Detection of complications in IBD**. (*1.1*) IUS: Female patient (23 years old) with CD, stricture of the terminal ileum with BWT of 6.5 mm, abrogation of stratification, narrowing of the lumen, and prestenotic dilatation in a V-shaped form (*). (*1.2*) MRE: Coronal T2-weight fast-spin echo image from an MRE study in a 27-year-old male patient with CD showing multiple chronic strictures (*arrows*) with intervening small bowel dilatation (*). (*1.3*) MRE: Coronal T2-weight fast-spin echo image from an MRE study in a 51-year-old male patient with CD showing an enterocutaneous fistula (*arrows*) arising from a conglomeration of tethered middle ileal small bowel loops (*). (*1.4*) IUS: 45-year-old woman with CD (L1B3) with ileomesenteric fistulae (*arrows*). (*1.5*) IUS: 32-year-old woman with CD (L3B3) with inflammatory mass with peripheral vascularization and central abscess formation (*arrows*). L1, ileal; L3, ileocolonic; B3, penetrating. (*1.6*) MRE: Axial T1 fat-saturated MRE image after intravenous gadolinium administration in a 25-year-old woman with CD. A ring-enhancing abscess (*long arrows*) is present adjacent to an activity-inflamed cecum (*arrowhead*). There is also an associated mesenteric inflammatory mass (*short arrows*) showing homogenous contrast enhancement. **IUS for monitoring IBD**. (*1.7*) IUS in a 64-year-old woman with CD of the sigmoid colon (sc), starting vedolizumab. Longitudinal section; BWT, 6.0 mm; echo pattern lost. (*1.8*) IUS in the same patient with CD, 6 months after starting vedolizumab. Sigmoid colon (sc); BWT, 1.9 mm, echo pattern preserved, color Doppler signals score 0. (*1.9*) IUS in 53-year-old woman with UC (E2; left-sided or distal colitis), starting ustekinumab. Longitudinal section of the sigmoid colon (sc) at baseline; BWT, 5.5 mm; echo pattern lost, color Doppler signal score 3. (*1.10*) IUS in the same patient with UC, 6 months after starting ustekinumab. Sigmoid colon (sc); BWT, 1.65 mm; presence of haustra.

based on cross-sectional imaging findings alone, particularly in patients with mild proctitis. In patients with UC, TPUS can also be used to identify complications such as abscesses or fistulas, although these are more common in CD.

TPUS offers a noninvasive option for monitoring disease activity and treatment response. This can be particularly beneficial for patients who may require regular assessments but wish to avoid invasive procedures. Recent data suggest that changes in BWT assessed by TPUS already 1 week after treatment induction can predict clinical outcome.[41] It therefore provides an ideal tool for monitoring disease activity in patients with ulcerative proctitis. TPUS can also be used after proctocolectomy to determine pouchitis.[42]

TPUS can be used alongside other imaging methods, such as endoscopy or MRI, to provide a more comprehensive evaluation of the disease. It may serve as an adjunct tool to enhance clinical decision-making.

Video Capsule Endoscopy

Video capsule endoscopy (VCE) provides a high diagnostic yield for small bowel lesions that may indicate CD, particularly for detecting superficial mucosal and proximal bowel abnormalities.[43] Studies have shown that VCE is superior to other cross-sectional imaging techniques for identifying mild small bowel disease. For the more advanced transmural lesions, the diagnostic yield of MRE and IUS is similar to VCE.[44] However, the risk of capsule retention, ranging from 3% to 4% in patients with suspected CD to 10.4% in those with confirmed CD, must be considered.[45]

VCE is typically reserved for cases where IC and the results of other cross-sectional imaging are normal but clinical suspicion of CD remains high or when IBD cannot be classified (Figure 2). In patients with isolated complex perianal disease, VCE has been shown to help establish a CD diagnosis in up to 25% of cases.[46] VCE does not allow biopsy specimens, and therefore usually, after a VCE suggestive of CD, other endoscopic tools (eg, enteroscopy) may be needed to obtain tissue. There are several validated scores to assess disease severity, such as the Lewis Score and Capsule Endoscopy Crohn's Disease Activity Index[47–49] (Supplementary Table 2).

In addition to its role in helping to establish diagnosis, VCE can detect previously unrecognized proximal small bowel lesions and inform therapeutic decisions. Some studies have indicated up to 50% of CD patients may present proximal small bowel lesions unrecognized by other imaging techniques.[50,51] VCE could also be helpful in monitoring endoscopic response to drugs,[52,53] and panenteric capsule endoscopy could serve as a less invasive alternative to IC for assessing mucosal healing in the small and large bowel.[53,54]

Complications in Inflammatory Bowel Disease

Detection and Evaluation of Strictures

Strictures are a common complication of CD, especially of small bowel CD, and are estimated to occur in up to 50% of patients.[55] Stricture formation involves both inflammation-dependent and inflammation-independent mechanisms, with fibrosis and inflammation often coexisting.[56] To standardize stricture definitions in clinical practice and trials, the Stenosis Therapy and Anti-Fibrotic Research (STAR) consortium has introduced the CONSTRICT (CrOhN's disease anti-fibrotic STRICTure therapies) criteria. These criteria emphasize that strictures should not be defined by symptoms alone, requiring endoscopy or cross-sectional imaging, or both. On cross-sectional imaging, naïve ileal strictures are defined by the combination of localized luminal narrowing (reduction ≥50%), BWT (≥25% increase in thickened areas), and prestricture dilation (bowel diameter >3 cm).[57]

For IUS, the same features (BWT, reduction in luminal diameter, and upstream dilation) are appropriate[58]; however, some differences may apply. Increased BWT should be defined as >3 mm for naïve strictures (in the small bowel), and luminal narrowing <1 cm or <50% relative to a normal adjacent bowel loop should be present. IUS typically does not use oral contrast, resulting in less dilation, and a proximal dilation >2.5 cm is used as a cutoff. Fixed narrowing with a rigid segment does not require prestenotic dilation if BWT is >3 mm. A V-shaped appearance seen on IUS is characteristic of a stricture in IUS (Figure 1).

Although CTE, MRE, and IUS (particularly when using oral contrast[59]), all have high diagnostic accuracy for naïve strictures, distinguishing inflammation from fibrosis is more challenging.[60] Fibrosis on MRE and IUS is usually inferred by the absence of the signs of disease activity described above. On MRE, although direct measures of fibrosis, such as delayed mural hyperenhancement and elevated magnetization transfer ratio have been proposed, multicenter validation is lacking.[61,62] Similarly, neither intravenous contrast nor elastography are yet considered reliable to distinguish inflammation from fibrosis in IUS.[62,63]

Detection and Evaluation of Inflammatory Masses

MRE and CTE have high sensitivity for detecting penetrating CD[34] and can detect deep-seated penetrating disease, for example, in the pelvis, which may be more difficult to access with IUS. On MRE, inflammatory masses typically appear as abnormal increased T2 signal in the perimural mesentery, often with ill-defined borders. The differentiation between an inflammatory mass and an abscess is aided by using an intravenous gadolinium contrast agent, with the latter demonstrating "ring" enhancement.[35] Diffusion-weighted imaging is also a useful adjunct, with pus typically manifesting as highly restricted diffusion. CT is the first-line investigation for suspected free perforation.[4]

Abscesses and inflammatory masses both appear as hypoechoic lesions on IUS, but inflammatory masses have irregular walls and may contain air or hyperechoic debris.[16] Contrast-enhanced US helps differentiate these lesions: phlegmons and inflammatory masses show homogeneous enhancement, whereas abscesses have little to no enhancement.[64] Doppler US may be easier to use as point of care; phlegmons show increased vascularization, whereas abscesses

have peripheral signals.[16] CT and IUS can both be used to guide therapeutic abscess drainage. A suggested workup for detecting CD complications is shown in Figure 3*A*.

Perianal Crohn's Disease

MRI is highly efficacious in the diagnosis and staging of perianal CD[65,66] without using endorectal probes, minimizing patient discomfort. Anatomical coverage of MRI is greater than endoanal US (EAUS) and TPUS, meaning that deeper pelvic sepsis commonly encountered in CD may be better visualized. Protocols generally include T2-weighted fluid-sensitive sequences with increasing use of intravenous gadolinium to help assess fistula inflammatory activity. Consensus guidelines recommend reporting according to the Parks classification, documenting fistula classification, number, location, length, and associated complications such as extensions and abscess formation.[67]

MRI is widely used to assess the efficacy of therapeutic and surgical interventions for perianal CD. MRI activity scores have been developed, such as the Van Assche Index, Modified Van Assche Index, and Magnetic Resonance Novel Index for Fistula Imaging in CD (MAGNIFI-CD) (Supplementary Table 3). These scores are relatively time consuming but have the advantage of quantifying treatment response,[68,69] with data supporting construct validity, responsiveness, and reliability.[68,70] They also have prognostic ability. Patients with only residual fibrotic change after therapy tend to have good longer-term outcomes.[71] Response assessment is based on changes in the complexity of fistulae and signal intensity on T2-weighted and postgadolinium enhanced images as surrogates of inflammatory activity.

EAUS and TPUS are other imaging methods potentially used for imaging of perianal fistulae and abscesses in CD, according to local availability and expertise. There are fewer data regarding evaluation of perianal disease activity using EAUS compared with MRI.[72] A meta-analysis showed EAUS and MRI have similar sensitivity for fistula detection, 0.87 (95% CI, 0.63–0.96) for MRI and 0.87 (95% CI, 0.70.0–95) for EAUS, respectively. However, specificity has been higher

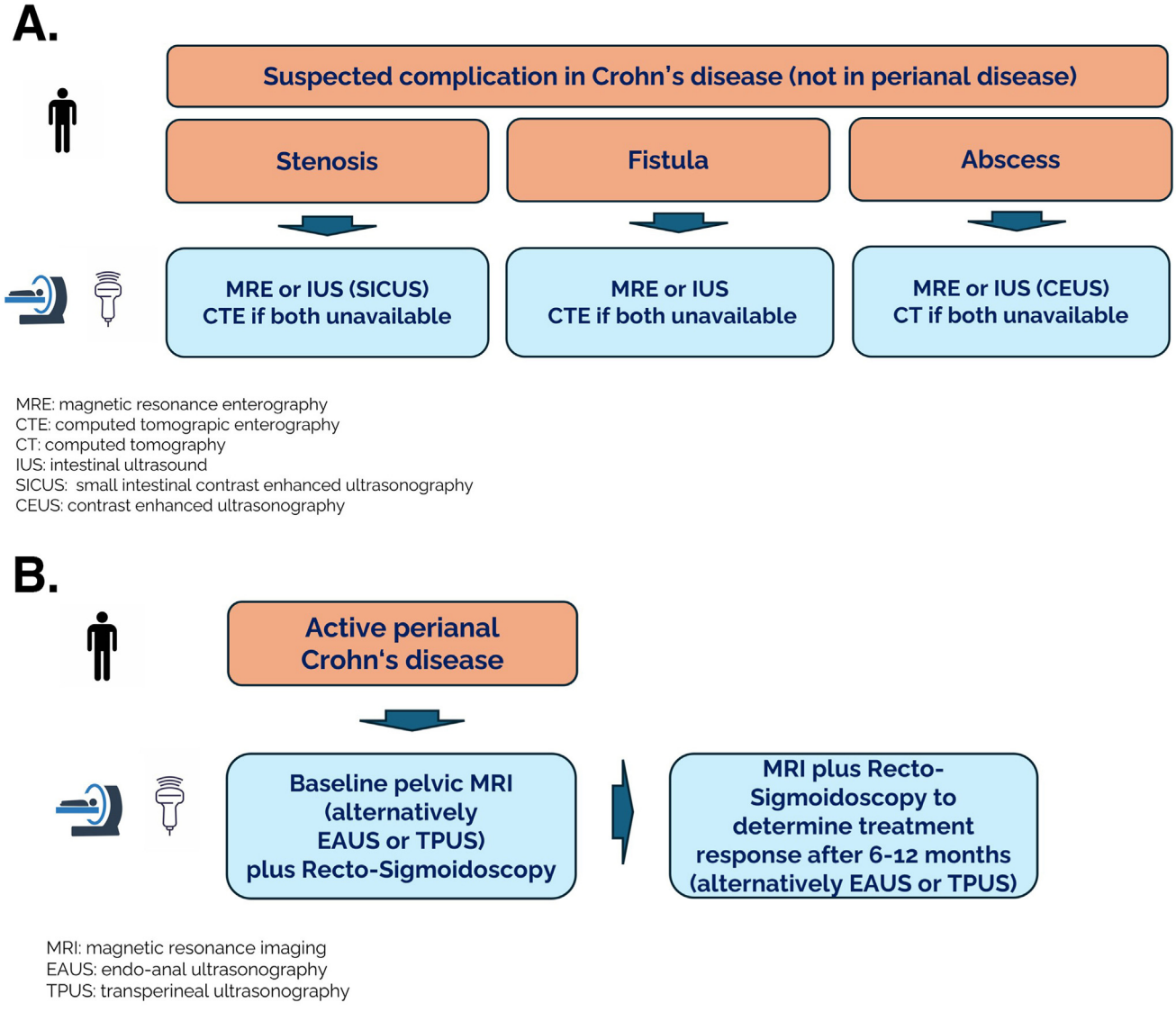


Figure 3. (*A*) Proposed diagnostic algorithm for detection of complications. (*B*) Proposed diagnostic algorithm for perianal CD.

for MRI, with 0.69 (95% CI, 0.51–0.82), compared with EAUS with 0.43 (95% CI, 0.21–0.69). Even though TPUS has been shown to be useful for evaluation of perianal CD,[73,74] EAUS and TPUS may have limitations in imaging high fistulae and abscesses, which are better evaluated using MRI.[74] TPUS may have advantages in detection of very low perianal fistulas.[74] EAUS and TPUS have been less frequently evaluated than MRI for assessing fistula activity and for monitoring perianal CD and may therefore be regarded as a second-line option[75] (Figure 3*B* and Figure 4).

Relapse of Inflammatory Bowel Disease

In patients with IBD experiencing symptoms of relapse, objective disease activity assessment should be performed after excluding infectious etiologies. IC is invasive and poorly accepted by patients. FC is highly sensitive but less specific, whereas CRP is more specific but less sensitive.[76,77] Thus, a CRP level within normal reference ranges does not rule out intestinal inflammation.[8] Elevated FC can indicate an active UC in the absence of infection, although values between 50 and 250 μg/g are considered a "gray zone."[5] FC may poorly correlate with active ileal inflammation.

IUS and MRE have proven to be accurate and reliable for detecting intestinal inflammation. Both are valid alternatives when histologic samples or colonic surveillance are not required. A large systematic review reported 85% and 80% sensitivity and 91% and 82% specificity for IUS and MRE, respectively, in detecting intestinal activity in CD.[1] A later meta-analysis confirmed a sensitivity and specificity >80% in detecting small bowel activity for MRE.[78] A meta-analysis recently demonstrated high diagnostic accuracy of IUS in detecting colonic inflammation of 86% sensitivity, 88% specificity, 81% positive predictive value, and 93% negative predictive value.[15] Finally, a study comparing IUS with MRE and IC showed strong concordance in management decisions for CD patients based on IUS alone vs full clinical assessment ($\kappa = 0.768$, $P < .001$), highlighting the value of IUS in guiding treatment decisions.[79]

Imaging can detect signs of mild disease activity also before symptoms appear, enabling earlier interventions. Its ease of use for ongoing monitoring supports tracking disease progression and treatment response. Combined with biomarkers, IUS may help predict relapse and complications, allowing timely treatment adjustments.

Monitoring Inflammatory Bowel Disease

Role of Intestinal Ultrasound in Short- and Long-term Response and Transmural Remission. Although transmural disease activity has been mainly described in patients with CD, most patients with moderate to severe UC demonstrate increased mucosal and submucosal thickening, and the term is increasingly also applied to UC.[80] Because

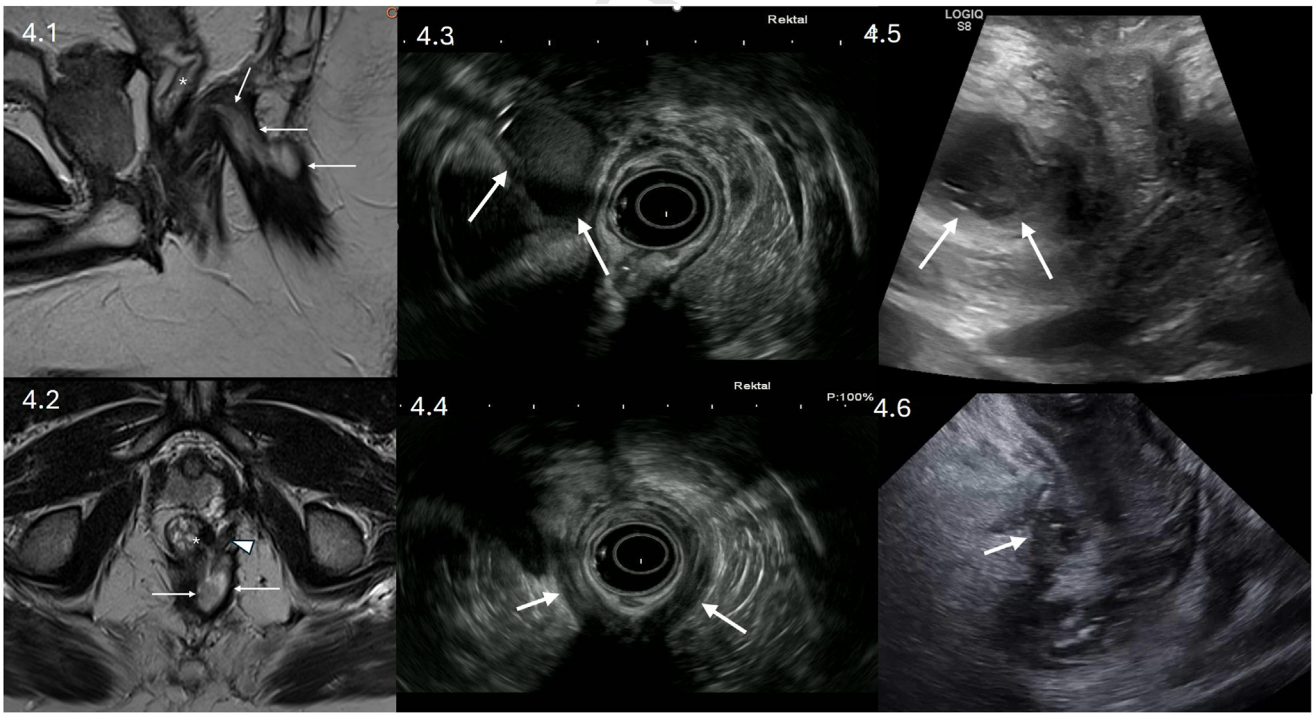


Figure 4. (*4.1*) MRI: Sagittal T2-weight fast-spin echo image from a pelvic MRI study from a 36-year-old male patient with CD showing an extra-sphincteric fistula (*arrows*) arising from an inflamed distal rectum (*) demonstrating high T2 signal in the bowel wall. (*4.2*) MRI: Axial T2-weight fast-spin echo image from a pelvic MRI study from the same patient as *4.1* showing 1.4-cm abscess (*arrows*) lateral to the puborectalis muscle (*arrowhead*) in the roof of the left ischioanal fossa complicating an extrasphincteric fistula arising from the distal rectum at 5 o'clock (*). (*4.3*) TRUS: Abscess (*arrows*) in the ischioanal fossa in a 29-year-old man with perianal CD (L3B3p) with complex fistulae. L3, ileocolonic; B3, penetrating; p, perianal disease modifier. (*4.4*) TRUS: Horseshoe fistula (*arrows*) in the same patient. (*4.5*) TPUS: Perianal abscess (*arrows*) in a 27-year-old man with CD L3B3p. (*4.6*) TPUS: Transsphincteric fistula (*arrows*) in a 52-year-old man with perianal CD.

BWT is the most responsive disease activity marker in patients with UC and CD, it can be used for monitoring treatment response. Even though the terms *transmural response* and *transmural remission* (TR) are the predominantly used terms in CD,[81] they are now increasingly used in patients with moderate to severe UC as well.[82–84]

TR independent of mucosal healing may better predict long-term outcomes than response assessed by endoscopy.[85,86] Improved 1-year clinical outcomes with biologics in CD have been demonstrated in prospective studies.[86] IUS response can predict endoscopic outcomes in CD.[87] Treatment adjustment and reevaluation to achieve this goal should therefore be considered, although some caution should be applied given the nuances of IUS changes in longstanding disease and the need for holistic treatment decisions adapted to the individual patients. In addition, even though the terms TR and transmural response have been characterized in a recent consensus,[88] precise definitions of overall therapeutic response, therapeutic targets, or end points in imaging studies on IBD are still lacking.[85,89]

Different imaging features, including BWT, vascularization, stratification, and mesenteric fat, are responsive after medical therapeutic intervention and are used to categorize treatment efficacy. Compared with previous examinations, change in bowel wall activity can be classified as TR, response, stable inflammation, or progression of inflammation.[35] In clinical practice, transmural remission is influenced by different factors, such as treatment duration and by the therapeutic agent used, which needs to be considered.[90] Janus kinase inhibitors, for example, may achieve more rapid transmural response compared with anti-tumor necrosis factor and to anti-interleukin 12/23.

Even within the group of different biologicals, heterogeneous response rates are observed, and in some patients, longer treatment duration may increase the likelihood of TR.[81,90,91] In CD, response and TR is more pronounced in biologically naïve patients.[81] In addition, transmural response may differ between small bowel and large bowel.[81] More data on the timelines for achieving TR across individual drugs are needed (Supplementary Table 3).

Point-of-Care Intestinal Ultrasound. Using IUS as a point-of-care test has optimized clinical decision-making, changing treatment strategies in 60% of patients with IBD.[2,92] IUS has showed strong correlation with IC and MRE in >80% of cases ($\rho > 0.70$; $P < .0001$),[13] and enhanced patient understanding and engagement, improving treatment adherence ($P < .05$).[93] In this context, point-of-care IUS should be considered as an extension of the physical examination.

IUS can be performed during outpatient visits together with a review of the patient's history, physical examination, and biomarkers, facilitating informed medical decisions. In real time, IUS can reduce or delay the need for invasive and costly examinations such as CT, MRE, and IC, reducing health care costs and improving patient convenience by avoiding extra appointments and reducing time away from work or school. Recently, the use of IUS for disease monitoring in routine clinical practice has grown substantially in many countries.[94]

Role of MRE. MRE has a well-established role in assessing treatment response in CD. Although activity scores can quantify therapeutic response, in clinical practice, changes in the various signs of activity, such as BWT, T2 signal intensity, and mesenteric signal changes, are subjectively assessed, and the therapeutic response is graded as for IUS.[35] A consensus definition of TR on MRE is lacking, although a normalization of all MRE parameters has been proposed.[95,96] MRE is reliably able to detect treatment response at ~1 year,[97] but data suggest responsiveness as early as 12 weeks after commencing therapy.[36,98] MRI can also detect therapeutic response in acute colitis, [99] although its role in this context is much more limited to that of IUS.

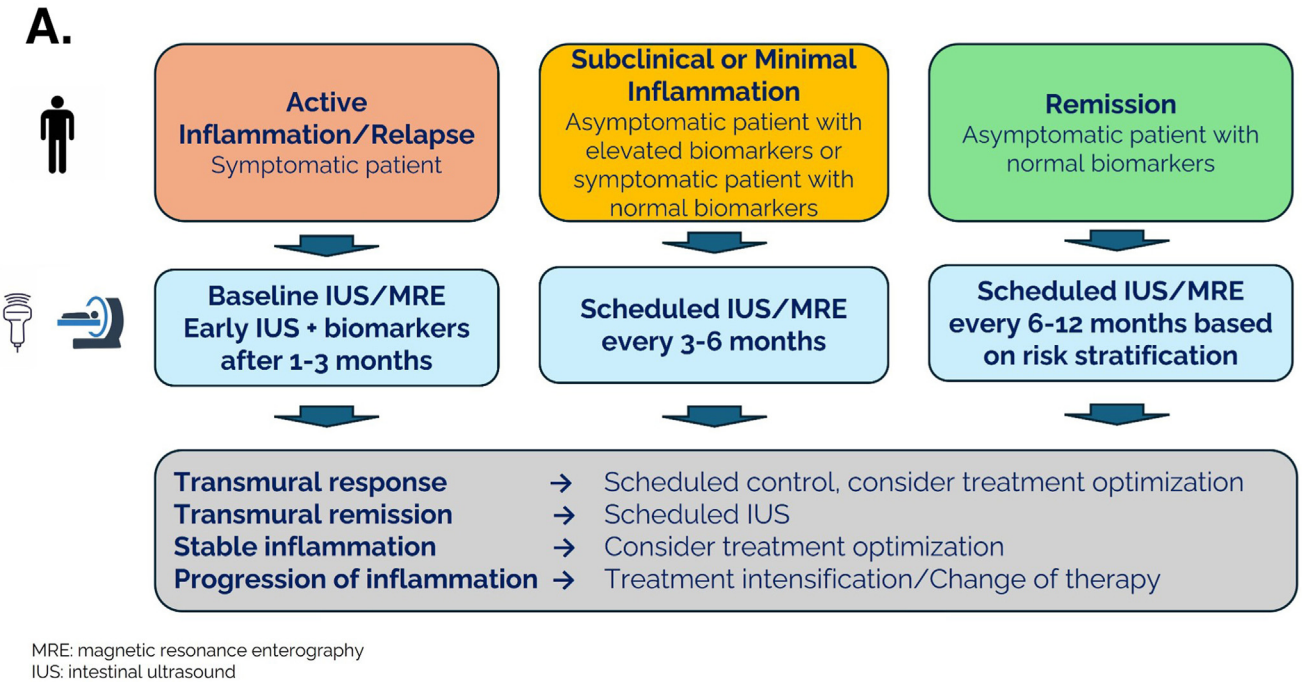
Time Points for Scheduled Monitoring After Relapse

Many data have shown that treatment response can be detected as early as 3 months after treatment initiation, and in a subgroup of patients, even after 4 weeks with IUS.[81,87,90,91,100] In patients with CD after treatment optimization or initiation, early clinical, biochemical (CRP or FC, or both), and cross-sectional imaging (IUS or MRE) within 12 weeks is useful to modify treatment, if required.[88] Results should always be interpreted based on prior baseline assessment. Early IUS improvement in CD has been shown to be predictive of long-term outcome.[101] Point-of-care IUS assessment may therefore be beneficial in certain situations between weeks 4 and 8. For patients who still exhibit symptoms, mild sonographic activity, or abnormal levels of biomarkers, 3- to 6-month intervals should be considered. For patients who are asymptomatic, with normalized IUS parameters and normal FC, longer intervals every 6 to 12 months based on risk stratification might be sufficient (Figure 5*A*).

In patients with UC who require treatment optimization, US response in combination with FC can be determined at early time points, usually in <12 weeks.[102] To assess treatment response and to modify treatment if required, IUS may therefore be suggested within the first 12 weeks.[88] The results should always be interpreted based on a prior baseline assessment. In acute severe UC, very early assessment with IUS may be useful because treatment response on IUS can be detected as early as 24 to 48 hours after treatment initiation, and early changes on IUS can provide prognostic information for long-term outcomes.[84] In patients in remission, scheduled point-of-care IUS combined with FC every 6 to 12 months based on risk stratification might be sufficient (Figure 5*B*).

Imaging in Remission

Symptoms alone do not adequately reflect mucosal inflammation, so objective measurements are essential to accurately guide treatment adjustments in patients with IBD.[103,104] However, in a cohort of >27,000 patients with IBD, nearly 50% had no mucosal disease assessment (via endoscopy, enterography, or FC) within 12 months of starting biologics. Lack of early (≤6 months) proactive



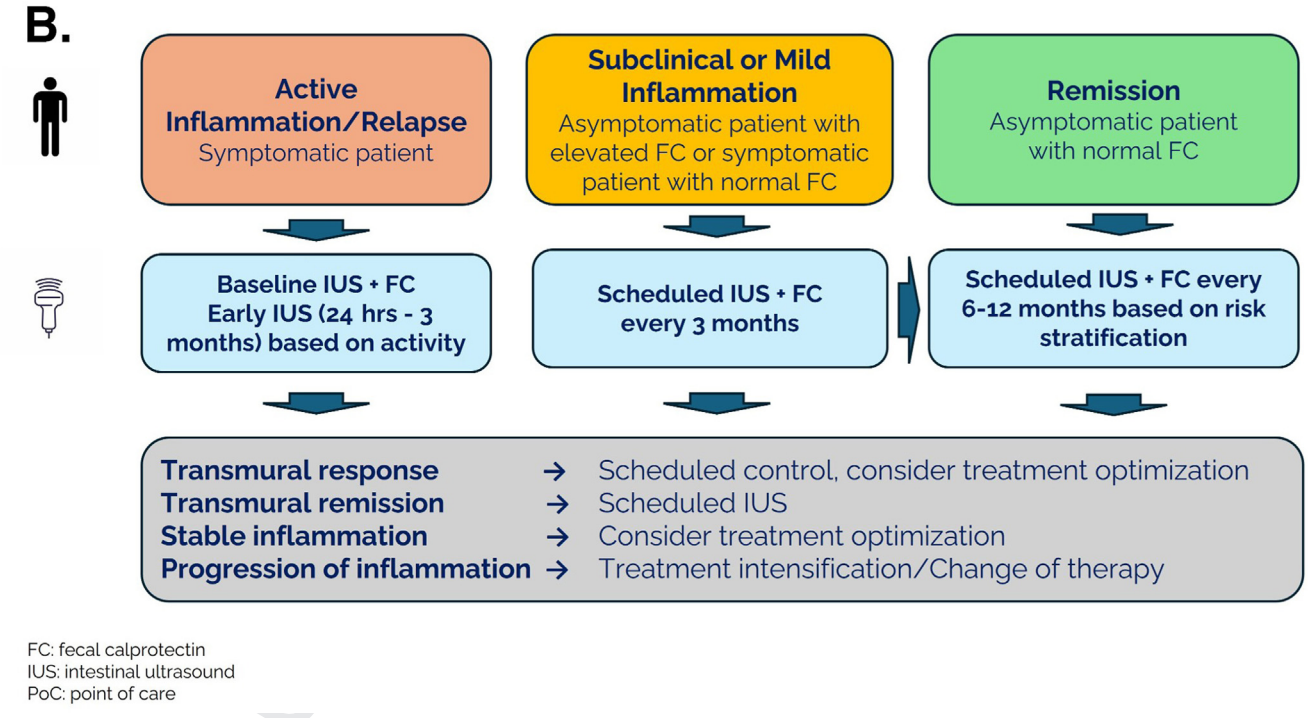


Figure 5. (*A*) Proposed diagnostic algorithm for non-invasive monitoring of active CD. (*B*) Proposed diagnostic algorithm for non-invasive monitoring of active UC.

monitoring of inflammation was associated with an increase in disease-related complications over 24 months.[101,105]

The lack of objective monitoring may result from practitioner or patient preferences, burden of endoscopy or fecal collection, reimbursement issues (especially for FC), limitations of the health care infrastructure, or doubts about the effectiveness of these strategies. Using IUS as a point-of-care test in IBD outpatient consultation can help address some of these challenges, detecting inflammation or complications in 54.3% of asymptomatic patients (60.5% of

asymptomatic CD patients and in 10.0% of asymptomatic UC patients).[13]

Optimal monitoring intervals for asymptomatic IBD patients remain unknown. Measuring FC levels every 3 months and repeating the test if elevated has been suggested, because 2 consecutive increases predict relapse.[4] Considering costs and insurance coverage, it may be reasonable to check FC only in high-risk patients at 3-month intervals and schedule longer intervals between 6 and 12 months for low-risk asymptomatic patients. For asymptomatic patients with biomarkers within normal reference ranges, cross-sectional imaging could be performed every 6 to 12 months, with shorter intervals if biomarkers rise (Figure 5). IUS is particularly suited to shorter-interval follow-up.

How to Determine Postoperative Complications in Inflammatory Bowel Disease

Although detecting extraluminal free gas on MRI and IUS is possible, CT Is the most sensitive test for intestinal perforation and is the first-line investigation when this complication is suspected, for example, as postoperatively or secondary to toxic megacolon.[35,106] Plain abdominal x-ray imaging has a very limited role. CT is also recommended to detect complications in the immediate postoperative period, including anastomotic leaks or bleeding[107,108] when diagnostic accuracy is increased by the administration of oral or rectal contrast, dependent on surgical anatomy. Fluoroscopic examinations with water-soluble contrast agents also have a role, particularly for evaluating the integrity and caliber of low colonic anastomosis. Postoperative venous thrombotic complications can be assessed using CT or Doppler US, depending on the location.

Postoperative Recurrence

Although IC is recommended 6 to 12 months after IC resection to detect postoperative recurrence, noninvasive imaging techniques, such as IUS, MRE, and VCE, could be considered valid alternatives.[37] These procedures have shown comparable accuracy in detecting postoperative recurrence, using IC and the Rutgeerts score as reference standard, with pooled sensitivity and specificity of 100% and 69% for CE (area under the curve [AUC], 0.94), 97% and 84% for MRE (AUC, 0.98), and 89% and 86% for IUS (AUC, 0.93).[109]

CE can visualize the full length of the small bowel and detect proximal lesion missed by IC, but the risk of capsule retention makes prior cross-sectional imaging or patency capsule advisable. IUS and MRE assess transmural and extramural lesions, although they may be less sensitive for mild mucosal lesions.

A meta-analysis confirmed the accuracy of IUS in detecting postoperative recurrence. A BWT >3 mm showed 82% sensitivity, 88% specificity, and 87% accuracy for diagnosing postoperative recurrence (Rutgeerts score ≥1). A BWT ≥5.5 mm was identified as the best cutoff for detecting severe postoperative recurrence (Rutgeerts score ≥3), with 84% sensitivity and 98% specificity (negative likelihood ratio, 0.165; positive likelihood ratio, 36.4).[110]

Based on the available evidence, the European Crohn's and Colitis Organisation recently suggested that IUS should be performed at 3 to 6 months, and if BWT is ≥5.5 mm, IC can be avoided, allowing for treatment adjustments. Additionally, combining IUS with FC may increase the sensitivity and be useful in early postoperative recurrence detection.[111,112]

Implementation of Cross-sectional Imaging in Daily Clinical Practice

Training Requirements to Obtain Proficiency

Interpretation of cross-sectional imaging and VCE is complex, and adequate initial and on-going training is fundamental. Ideally, this should be embedded in resident training programs so newly qualified personnel in all relevant specialties are able to perform high-quality image interpretation. There is, however, also a need to train practicing practitioners because cross-sectional imaging becomes integral to the care of IBD patients.

Training in IUS is particularly variable among gastroenterologists, radiologists, and sonographers, with the fundamental need for hands-on training an additional barrier. Training standards have been defined,[113] and there are good examples of established programs, such as the International Bowel Ultrasound Group (IBUS), that include e-learning modules to overcome current training limitations. The 3 pillar program includes a 3 days' workshop, 4 weeks of hands-on tuition at a training center, and an advanced workshop that finishes with a postcourse test and a certificate. Such training programs can be used by those without a local high-quality training opportunities (IBUS training program).

The formal learning curve and competency assessment criteria for IUS, MRE, and VCE are not fully established. In the case of IUS, an international Delphi consensus has defined essential knowledge and skills for newly certified practitioners.[113] A recent study identified the minimum number of scans required to achieve competency: 84 examinations to detect increased BWT and 97 for identifying intra-abdominal complications.[74] Although basic competency may be acquired with a moderate number of examinations, proficiency requires more extensive training and experience.[114] In the case of MRE, interobserver agreement among trained radiologists is reasonable,[115] but training is required before accurate MRE interpretation.[116]

Documentation and Reporting of Cross-sectional Imaging

The optimization and standardization of imaging reporting is currently an unmet need and would facilitate the comparison between different techniques and communication between the different specialties. A recent European Crohn's and Colitis Organisation and European Society of Gastrointestinal and Abdominal Radiology topical review identified various core elements required for reporting

cross-sectional imaging in IBD.[35] Similarities and differences in reporting between MRI/CT and IUS were identified and have been addressed.

Reporting of findings should be structured to improve communication to clinicians, ensure inclusion of all important disease features, and improve report structure and reproducibility. Parameters assessing inflammation, such as BWT, vascularization, mural changes, as well as mesenteric fat, should be described in a standardized fashion for both MRE and IUS. Whenever possible, activity scores should be used. For follow-up examinations, reporting should focus on changes from the previous examination and should be categorized as TR, significant transmural response, stable disease, or progression of inflammation. Key quality indicator reporting of IUS and MRE should also include an indication, scan quality, and any uncertainties in interpretation. All segments examined should be reported in detail and stored. Picture archiving in a communication system for digital storage is suggested. For perianal manifestations, an imaging reporting template for patients with perianal manifestations of IBD should be used.[35]

Future Perspectives

Novel Treatment Targets and Unmet Needs

The most recent Updated Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) II criteria did not define TR as a formal treatment target but as a relevant parameter indicating a good prognosis.[8] Many new data have been derived since then, and the prognostic relevance of TR for CD and for UC has been demonstrated. TR may become a formal target in the near future, representing a shift toward a more thorough approach to treatment, focusing on complete healing of the intestinal tissue. Major future steps include the development of clear definitions of TR in CD and UC and appropriate time points when specific parameters of cross-sectional imaging need to be reached. The clinical consequences, if TR as a formal target could not be achieved, need to be discussed as well. Prospective studies aiming to assess whether the use of IUS in the clinical decision-making process is associated with better outcomes in increasing treatment response and avoiding disease progression are lacking and required. Many ongoing trials now include IUS as secondary end point and are assessing the best ways to measure and achieve TR and determine its prognostic value.

Intestinal Ultrasound

Clear indications have been defined for the use of IUS of in clinical practice. However, there are many evidence gaps and unmet needs, with some listed in Supplementary Table 3. Many unmet needs relate to the validation of IUS activity scores for response and for prediction of disease outcome. Treat-to-target studies with induction or treatment based on IUS findings are currently lacking. Many educational aspects on global enrolment of IUS still need to be solved, including optimal ways for assessing competency. Data are required how IUS can improve global patient care, and these data assessments need to be accompanied by cost-effectiveness studies.

Technical issues still need to be solved as well as challenges accessing machines or issues with remuneration in many countries. Hand-held US devices have demonstrated promising diagnostic accuracy comparable to conventional IUS in single expert centers.[117] However, before making them a valuable tool for routine monitoring of IBD in both inpatient and outpatient settings, technically improved devices and more studies are required. These portable devices could potentially evolve into home health tools in the future, allowing trained patients to perform self-scans and transmit images to their medical team, improving outpatient care and patient autonomy.[118]

Inflammatory and fibrotic infiltration and systemic effects of inflammation contribute to reduced motility in bowel affected by CD. Although IUS is promising for real-time detection of motility biomarkers, clear, quantifiable parameters remain underdeveloped.

US elastography is a promising method for evaluating intestinal fibrosis, with bowel wall stiffness as a key biomarker. Even though results are still heterogeneous, most studies report moderate to good accuracy in detecting histologic fibrosis, with point-shear wave elastography showing the greatest potential,[119] but its clinical value, potentially in combination with other imaging methods or biomarkers, still needs to be proven.

Contrast-enhanced IU has been used to detect inflammation and fibrosis and to differentiate inflammatory masses in IBD. However, its adoption into clinical practice for other indications is limited by a lack of standardized technique, reliable quantification tools, and strong supporting evidence, which still needs to be provided.

Artificial intelligence (AI) is increasingly used in IBD imaging, offering reduced operator variability, improved accuracy, and faster analysis. Carter et al[120] applied deep learning models using a convolutional neural network to detect US signs of CD activity, achieving an AUC of 0.97. More recently Gu et al[121] confirmed that US radiomic features could detect inflammatory activity in IBD patients with 94% accuracy (AUC, 0.98), outperforming a convolutional neural network model.[121] These advances show promise for enhancing diagnostic precision and supporting less-experienced operators.

Magnetic Resonance Imaging/Computed Tomography

There is considerable interest in using functional MRI techniques, particularly the quantification of inflammatory activity and the differentiation between inflammation and fibrosis/smooth muscle hypertrophy.[122] Software-quantified MRI motility has been extensively validated as a biomarker of inflammatory activity against endoscopic and histologic standards of reference[123,124] and has potential to act as a quantitative biomarker of treatment response.[125] Diffusion-weighted imaging provides information on tissue composition by capturing differential Brownian motion of water molecules, which can be quantified using an apparent diffusion coefficient map.[122]

Apparent diffusion coefficient values are reduced in active CD inflammation,[126] although they are also reduced in fibrotic tissue, and utility in assessing stricture composition is therefore somewhat limited.[127] Interactions between protons in free water and those trapped in larger macromolecules, such as collagen, underpin magnetization transfer imaging, which has shown promise as a biomarker of fibrosis in CD.[128] However, when tested in a prospective multicenter study, the ability of magnetization transfer imaging to quantify fibrosis was weak.[129] Additional functional MRI techniques under investigation included tissue elastography[130] and MRI relaxometry,[131] although research is nascent.

AI provides considerable promise as a way of speeding image interpretation and reducing variability and more robustly quantitating both existing and new biologically relevant imaging biomarkers. Some methodologies have entered routine clinical care, such as reconstruction techniques to lower the CT dose,[132] but most AI techniques are in the early stages of development. Promising data have been published using machine learning methods to aid with disease identification[133] and segmentation,[134,135] differential diagnosis,[136] quantitating disease activity and fibrosis,[137] and identifying treatment resistance.[138] AI models are also being developed to predict adverse disease outcomes, such as need for surgery.[139]

Video Capsule Endoscopy

Future VCE systems may feature panenteric capsules, longer battery life, and self-navigating or dissolvable capsules to reduce retention risks and lower costs. Research is focusing on integrating AI and machine learning into VCE for real-time image analysis and automated disease scoring, improving diagnostic accuracy and reducing workload.[140,141] Innovations such as microsensors in wireless capsules could allow real-time biochemical analysis and targeted drug delivery. Magnetically guided and robotic capsules could enhance localization and enhance imaging precision, whereas US capsule endoscopy could differentiate the bowel wall.[142] A US capsule endoscopy tested in the intestines of anesthetized pigs was able to achieve differentiating images of the lumen wall up to a depth of 10 mm.[143]

Summary and Future Perspectives

The use of noninvasive imaging techniques has revolutionized phenotyping and monitoring of patients with IBD in recent years. IUS, in particular, has evolved as an accurate and patient-centered tool to monitor IBD. Focusing on transmural disease activity and monitoring novel treatment targets with biologics and small molecules that specifically target inflammatory pathways, the use of imaging can help to define the decision-making process. Given the importance of transmural assessment, personalized management of the disease with treatment plans based on inflammation depths determined by IUS and MRE, as well as with VCE, is likely to yield better long-term outcomes and may reduce the risk of complications associated with disease. IUS will likely be the preferred tool for regular monitoring of IBD in the future. Recent advances in the standardized use of cross-sectional imaging, together with advances in biomarkers and novel therapeutic options, allows for better guidance of our patients with IBD. Novel development, in particular, the increased use of AI technology will further help to improve and facilitate the use of non-invasive imaging in the future.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://dx.doi.org/10.1053/j.gastro.2025.06.002

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Supplementary Table 1. Strengths and Limitations of Imaging Methods in Different Clinical Scenarios

Variable	MRE		IUS		VCE	
	Strengths	Limitations	Strengths	Limitations	Strengths	Limitations
CD initial diagnosis	Highly accurate for assessing extent of disease, and defining proximal small bowel involvement No ionizing radiation exposure	Access Motion artifacts may impact quality of examination Oral contrast preparations can give rise to cramping, bloating and diarrhea Claustrophobia in MRI machines No tissue sampling	Availability Highly sensitive and specific to assess extent of disease, and complications Suitable for pediatric patients No radiation POC examination Patient centered	Lower sensitivity for detecting lesions in the duodenum, proximal jejunum, rectum, and deep pelvic structures No tissue sampling	High sensitivity for detecting small bowel lesions in suspected CD Superior detection of proximal and superficial lesions Incremental diagnostic yield inpatients with high clinical suspicion but negative initial evaluations	Low specificity (healthy individuals may present erosions) Risk of capsule retention Needs bowel preparation Localization of lesions may be difficult No tissue sampling
CD complications	High accuracy in detecting mural, perienteric, and extraenteric complications Superior soft tissue contrast allows better characterization of penetrating lesions	Accuracy in detecting fibrosis decreases when there is concomitant active inflammation Inadequate bowel distension may compromise assessment of strictures or incipient fistulizing disease	High sensitivity for complications Allows for quick evaluation and is suitable for frequent follow-ups Can guide therapeutic abscess drainage Lower cost	May be difficult to assess deep pelvic loops Detection of bowel strictures potentially compromised without oral contrast	No role in CD complications	Risk of capsule retention in strictures Cannot assess extraluminal complications Limited ability to locate lesions precisely
CD monitoring	No radiation exposure Activity scores have high accuracy for predicting endoscopic remission	Access Costs Less preferred by patients than IUS Some variability in reporting across radiologists Consensus definition of transmural remission on MRE is lacking	Can be performed as POC No preparation needed Fast results Early transmural response predicts endoscopic response Reduces the need for more costly imaging or endoscopy Can be used in pregnant patients	Lack of universal definition of transmural healing Challenging in multifocal small bowel disease	Can assess mucosal healing	Risk of retention in strictures Time consuming to read Costs

Supplementary Table 1. Continued

Variable	MRE		IUS		VCE	
CD flare	Highly sensitive and specific for assessing extent and severity of inflammation	Difficult to have access in timely fashion Less preferred by patients than IUS	Can expedite clinical decisions Preferred by patients		Can assess mucosal lesions	Requires bowel preparation
CD perianal	Excellent for perianal fistula mapping Can detect abscesses Several scores exist for quantifying response to Rx	Accessibility Cost	TPUS has high sensitivity for perianal fistulae	Limited expertise among sonographers in assessing perianal and perineum Lower sensitivity for deep fistulae and abscesses May cause discomfort to patient if abscess is present Limited data on assessing fistula activity	Can help to establish diagnosis of CD in those with isolated perianal disease and normal cross-sectional imaging and colonoscopy	-
UC initial diagnosis	Can assess disease extent, exclude small bowel involvement, and assess extraintestinal complications May have a diagnostic role in excluding undiagnosed CD in UC patients with refractory disease or those with complications after proctocolectomy	Not routinely performed in the setting of UC Lower sensitivity for colonic disease than colonoscopy or IUS No tissue sampling	Can assess disease extent, assess disease activity, exclude small bowel involvement	Difficulty to assess the rectum No tissue sampling	Can exclude small bowel lesions in patients with unclassified colitis and improve disease classification	Not typically used for UC initial diagnosis No tissue sampling
UC flare	No role in UC flare	…	Changes in BWT occur very early in the context of ASUC and can predict outcomes	Difficulty to assess the rectum No tissue sampling	No value in UC flare	…

Supplementary Table 1. Continued

Variable	MRE		IUS		VCE	
UC monitoring	May detect chronic changes in the wall that result from longstanding inflammation	Limited evaluation of superficial mucosal changes Costs Accessibility Reduced patient tolerance	Rapid transmural response Good correlation with endoscopic findings and biomarkers, useful for longitudinal monitoring Can detect chronic changes	Mild endoscopic disease may not be detected by IUS Moderate only correlation with FC No tissue sampling	Colonic capsule could be used to assess mucosal healing; endoscopic scores with colonic capsule show a strong correlation with scores obtained by conventional colonoscopy	Costs Need for good bowel preparation Time consuming to read

POC, point-of-care.

Supplementary Table 2. Activity Scores for Cross-Sectional Imaging and Video Capsule Endoscopy—Pros and Cons for Use in Clinical Practice

Disease	Imaging method	Scoring index	Variables	Formula	Pros	Cons	Comments
CD	MRE	MaRIA[e1]	BWT (continuous in mm) Relative contrast enhancement Mural edema (present vs absent) Ulceration (present vs absent)	1.5 × BWT + 0.02 × RCE + 5 × edema + 10 × ulcer	Very well validated against colonoscopy. Grading by disease severity Responsive Cutoffs for disease severity Good interreader and intrareader reproducibility	Requires IV gadolinium Time consuming to calculate	Used mainly in clinical trials
	MRE	sMaRIA[e2]	BWT >3 mm Mural edema (present vs absent) Fat stranding (present vs absent) Ulcers (present vs absent)	(1 × BWT >3 mm) + (1 × wall edema) + (1 × fat stranding) + (2 × ulcers)	Good validation Does not require IV gadolinium Cutoffs for disease severity Responsive Good interreader and intrareader reproducibility Quick to calculate	Currently less well validated than full MaRIA	Use in clinical trials increasing Simple for use in routine clinical care
	MRE	London score[e3]	BWT measured in mm: (0 = absent, 1 = mild, 2 = moderate, 3 = marked) Mural T2 signal: (0 = absent, 1 = mild, 2 = moderate, 3 = marked)	1.79 + 1.34 × mural thickness + 0.94 × mural T2 score	Validated against histology and endoscopy Does not require IV gadolinium Quick to calculate Good interreader and intrareader reproducibility	No cutoffs for disease severity	Simple for use in routine clinical care
	MRE	London extended score[e3]	BWT measured in mm: (0 = absent, 1 = mild, 2 = moderate, 3 = marked) Mural T2 signal: (0 = absent, 1 = mild, 2 = moderate, 3 = marked) Perimural T2 signal (0 = absent,	Mural thickness + mural T2 score + perimural T2 signal + contrast enhancement	Validated against histology and endoscopy Quick to calculate Good interreader and intrareader reproducibility	Requires IV gadolinium No cutoffs for disease severity	Simple for use in routine clinical care

Supplementary Table 2. Continued

Disease	Imaging method	Scoring index	Variables	Formula	Pros	Cons	Comments
			1 = mild, 2 = moderate, 3 = marked) Mural contrast enhancement: (0 = absent, 1 = mild, 2 = moderate, 3 = marked)				
	MRE	Clermont score[e4]	BWT (continuous in mm) Apparent diffusion coefficient (ADC) value Mural edema (present vs absent) Ulceration (present vs absent)	1.646 × mural thickness − 1.321 × ADC (mm^2/s) + 8.306 × ulcers + 5.613 × edema + 5.039	Does not require IV gadolinium Good validation Proposed thresholds for active and ulcerating disease	Time consuming to calculate Potential suboptimal reproducibly of ADC across different MRI platforms	
	CTE	EMBARK[e5]	Mural postcontrast enhancement: (normal vs hyperenhancement) BWT measured in mm: (0 = normal, 1 = 3.0 to 4.9 mm, 2 = 5 to 9.9 mm, 3 = ≥10 mm) Additional findings: perienteric stranding, ulceration (present or absent)	0 = no imaging findings of inflammation 1 = mural hyperenhancement with absent or equivocal wall thickening of 3.0–4.9 mm 2 = mural hyperenhancement with wall thickening between 5 and 9.9 mm 3 = findings of severity score 2 with perienteric stranding, luminal ulcerations, or mural thickness of ≥10 mm in thickness	Validated against colonoscopy Quick to calculate	Exposure to ionizing radiation Requires IV iodinated contrast medium Requires further multicenter validation	Has been used to assess response to advanced therapies
Perianal CD	MRI	Van Assche Index (VAI)[e6]	Fistula number: 0 = none, 1 = unbranched, 2 = branched, 3 = multiple (score, 0–3)	Fistula number score + Hyperintensity of fat suppressed T2-weighted sequence score + Location score + Extension	Does not require IV gadolinium Some responsiveness data	Time consuming to calculate Limited interobserver variability data Precise responsiveness	Requires further clinical validation

Supplementary Table 2. Continued

Disease	Imaging method	Scoring index	Variables	Formula	Pros	Cons	Comments
			Hyperintensity of fat-suppressed T2-weighted sequence: 0 = none, 4 = mild, 8 = pronounced Location: 1= extra or intersphincteric, 2 = transsphincteric, 3 = suprasphincteric extension: 1 = infralevator, 2 = supralevator Collections >3 mm: 0 = none,4 = present Rectal wall involvement: 0 = none, 2 = thickened	score + collections score + Rectal wall involvement score		cutoffs need further validation	
	MRI	Modified Van Assche Index[e7]	Hyperintensity of fat-suppressed T2-weighted sequence: 0 = none, 1 = mild, 2 = pronounced Dominant feature of primary track and extensions: 0 = fibrous, 1 = granulation tissue, 2 = fluid or pus Extension: 0 = none, 1 = infralevator, 2 = horseshoe, 3 = supralevator Inflammatory mass: 0 = none, 1 = diffuse, 2 = focal, 3 = small collection, 4 = medium collection, 5 = large collection Proctitis : 0 = none, 2 = present	(1.5 × extension score) + (2.3 × T2 hyperintensity score) + (1 × proctitis score) + (1.2 × inflammatory mass score) + (1.2 × dominant features of the tract score)	Some responsiveness and interobserver variability data	Requires IV gadolinium Time consuming to calculate Precise responsiveness cutoffs need further validation	

Supplementary Table 2. Continued

Disease	Imaging method	Scoring index	Variables	Formula	Pros	Cons	Comments
	MRI	MAGNIFI-CD[e8]	Fistula: 0 = none, 1 = unbranched, 2 = complex Enhancement: 0 = none or mild, 1 = pronounced Dominant feature: 0 = fibrous, 1 = granulation tissue, 2 = fluid or pus Fistula length (mm): 0 <25, 1 = 25–50, 2 >50 Extension: 0 = none, 1 = horseshoe, 2 = infralevator or supralevator Inflammatory mass: 0 = none, 1 = focal, 2 = diffuse, 3 = small collection, 4 = medium collection, 5 = large collection	(3 × no. of fistula tracts score) + (2 × Postcontrast hyperintensity score) + (2 × dominant feature score) + (2 × fistula length score) + (2 × extension score)	Increasingly responsiveness data available Suggested disease severity cutoffs proposed	Requires IV gadolinium Time consuming to calculate Precise responsiveness cutoffs need further validation	Currently often favored in clinical trials
	MRI	PEMPAC[e9]	Fistula number: 0 = none, 4 = single 8 = multiple 1 T2 hyperintensity: 0 = none, 2 = mild, 4 = pronounced Total length of all fistulas expressed as mm: 0 = none , 2 = short (<25) , 4 = medium (26–50), 6 = long (>51) Location: 0 = none, 3 = intershpincteric, 6 = transsphincteric 9 = extrasphincteric 12 = transsphincteric and intersphincteric Collections 0 = absent, 11 = present	Fistula number score + T2 hyperintensity score + : Total length of all fistulas score + Location score + Collection score	Does not require IV gadolinium Cutoffs for remission, active and severe activity and response criteria proposed	Time consuming to calculate Limited interobserver variability data Precise responsiveness cutoffs need further validation	Used in pediatric populations Requires further clinical validation

Supplementary Table 2. Continued

Disease	Imaging method	Scoring index	Variables	Formula	Pros	Cons	Comments
CD	IUS	SUS-CD[e10] (0–5). Cutoff point <1 for SES-CD ≤2	BWT (0 = <3 mm; 1= 3–4.9 mm; 2 = 5–7.9 mm; 3 = ≥8 mm); CDS (0 = absent or single vessels; 1 = 2–5 vessels/cm^2; 2 = >5 vessels/cm^2)	BWT + CDS	Validated. Simple to calculate. BWT and CDS are the most reliable and reproducible US parameters. Strong correlation with endoscopic activity. Correlated with sMaRIA and histologic activity index	Less detailed than IBUS-SAS	Accurate and simple scoring, especially in clinical practice
	IUS	BUSS[e11] Cutoff point 3.52 for SES-CD ≤2	BWT (normal ≤3 mm; active >3 mm); CDS (0 = absent; 1 = present)	0.75 × BWT + 1.65 × CDS	Simple to calculate. BWT and CDS are the most reliable and reproducible US parameters. Strong correlation with endoscopic activity. Correlated with sMaRIA and histologic activity index	Less detailed than IBUS-SAS	Accurate and simple scoring, especially in clinical practice
	IUS	IBUS-SAS[e12] (0–100)	BWT (normal ≤3 mm; active >3 mm); iFAT (0 = absent; 1 = uncertain; 2 = present); CDS (0 = absent; 1 = short signals; 2 = long signals inside bowel; 3 = long signals inside and outside bowel wall); BWS (0 = normal; 1 = uncertain; 2 = focal ≤3 cm; 3 = extensive >3 cm)	4 × BWT + 15 × i-fat + 7 × CDS + 4 × BWS	Validated. More granular. Strong correlation with severe endoscopic activity. Correlated with sMaRIA	Laborious to calculate	Accurate and detailed scoring, especially for clinical trials
	IUS	Simple-US[e13] Cutoff point 5.5 for SES-CD ≤ 3	BWT (normal ≤3 mm; active >3 mm); CDS (0 = absent;	BWT + CDS	Validated. Simple to calculate. BWT and CDS are the	Less detailed than IBUS-SAS. Less investigated	Accurate and simple scoring,

Supplementary Table 2. Continued

Disease	Imaging method	Scoring index	Variables	Formula	Pros	Cons	Comments
			1 = 1–2 points/cm^2; 2 = 3–5 points/cm^2; 3 = >5 points and vessels outside bowel wall)		most reliable and reproducible US parameters. Strong correlation with endoscopic activity		especially in clinical practice
Small bowel CD	VCE	Lewis Score[e14,e15]	Villous edema, ulceration, stenosis	Maximum tertile score {[(Villous parameter × extent × descriptor) + (Ulcer parameter × extent × size)] for tertile 1 or [(Villous parameter × extent × descriptor) + (Ulcer parameter × extent × size)] for tertile 2 or [(Villous parameter × extent × descriptor) + (Ulcer parameter × extent × size)] for tertile 3}[15] + (Stenosis number × ulcerated × traversed).	Validated Prognostic cutoff values for risk of clinical relapse and disease outcome have been defined	Laborious to calculate	Difficult to use in clinical practice
	VCE	Capsule Endoscopy Crohn's Disease Activity Index (CECDAI)[e16]	Inflammation (A, 0–5), extent of disease (B, 0–3), and stricture (C, 0–3), in both the proximal and distal segments of the small bowel	Final score CECDAI = ([A1 × B1] + C1) + ([A2 × B2] + C2)	Validated	Laborious to calculate	Difficult to use in clinical practice
UC	IUS	MUC[e17] Cutoff point 6.2 for MES ≤1; 4.3 for MES = 0	BWT (normal ≤3 mm; active >3 mm); CDS (0 = absent; 1 = present)	1.4 × BWT + 2 × CDS	Simple to calculate. BWT and CDS are the most reliable and reproducible US parameters. Strong correlation with endoscopic activity. Correlated with histological activity	Less granular than IBUS-SAS. More investigated than IBUS-SAS	Accurate and simple scoring, especially in clinical practice

Supplementary Table 2. Continued

Disease	Imaging method	Scoring index	Variables	Formula	Pros	Cons	Comments
	IUS	UC-IUS index[e18]	BWT (1 = >2 mm; 2 = >3 mm; 3 = >4 mm); CDS (1 = spots; 2 = stretches); Abnormal haustrations = 1; presence of iFAT = 1	BWT + CDS + Haustra + iFAT	Validated. Strong correlation with endoscopic activity	Less investigated	Accurate and simple scoring, especially in clinical practice
	IUS	IBUS-SAS[e12,e19] (0–100)	BWT (normal ≤3 mm; active >3 mm); iFAT (0 = absent; 1 = uncertain; 2 = present); CDS (0 = absent; 1 = short signals; 2 = long signals inside bowel; 3 = long signals inside and outside bowel wall); BWS (0 = normal; 1 = uncertain; 2 = focal ≤3 cm; 3 = extensive >3 cm)	4 × BWT + 15 × i-fat + 7 × CDS + 4 × BWS	Validated. More granular. Strong correlation with endoscopic activity	Laborious to calculate. No differences in accuracy compared with MUC and UC-IUS index	Accurate and detailed scoring, especially for clinical trials

BUSS, Bowel Ultrasound Score; BWS, bowel wall stratification; CDS, color Doppler signals; IBUS-SAS, International Bowel Ultrasound Segmental Activity Score; iFAT, inflammatory fat; IV, intravenous; MaRIA, Magnetic Resonance Index of Activity; MES, Mayo Endoscopic Score EMBARK-EMerging biomARKers in Inflammatory bowel disease; MUC, Milan Ultrasound Criteria; PEMPAC, pediatric MRI-based perianal Crohn disease; RCE, relative contrast enhancement; SES-CD, Simple Endoscopic Score for Crohn's disease; Simple-US, Simple Ultrasound Score; sMaRIA; Simplified Magnetic Resonance Index of Activity; SUS-CD, Simple Ultrasound Score for Crohn's disease; UC-IUS index, Ulcerative Colitis-Intestinal Ultrasound index.

Supplementary Table 3. Unmet needs and Evidence Gaps for the Use of Cross-sectional Imaging in Inflammatory Bowel Disease

What is known?	Unmet needs/evidence gaps
Many cross-sectional imaging activity scores for CD and UC already exist	Scores for responsiveness and prediction of outcomes need to be validated/developed
We know how to assess disease activity and complications of disease with cross-sectional Imaging	Treat-to-target studies with induction and optimizing treatment according to imaging findings are needed How can IUS be used to assess disease severity in CD and UC?
IUS and MRE can be used to predict disease outcome	Parameters for response and non-response need to be defined
Transmural response and remission can be induced by various drugs	What is the timing for transmural healing for individual drugs? Is achieving transmural healing better than endoscopic healing for longer-term patient outcomes?
There is poor correlation between clinical symptoms and endoscopy in CD	Do clinical symptoms better correlate with transmural healing/ response in CD?
Faster transmural healing in the colon compared with the ileum has been described in CD	What is the mechanism behind differences in transmural healing?
We know how to assess postoperative recurrence using IUS and MRE	What are the best time points to assess for recurrence with or without additional biomarkers? How does IUS compare with MRE and endoscopy?
IUS and MRE can determine small bowel motility and dysmotility	Techniques to quantify small bowel motility using IUS are required
IUS machine and examination costs can be defined	Data on cost-effectiveness of IUS compared with other cross-sectional imaging modalities and to endoscopy are required
Central reading (CR) for cross-sectional studies has been established	How can we improve the technical process of uploading and reading data, particularly for IUS? Data on intra- and interreader variability of CR are needed
Intravenous contrast for IUS can be used to differentiate abscesses from phlegmons in inflammatory masses in CD	Standardization of intravenous contrast techniques for different indications is required. Reliable quantification tools are missing
Technical equipment specifications for performing IUS are well defined	Technical improvement of handheld machines is required. Studies demonstrating their effectiveness in daily clinical practice are needed before implementation
IUS has already been established in daily clinical practice in many countries	How can global implementation of IUS be achieved to improve IBD care in particular in low income countries?
IUS teaching programs for physicians and radiologists have already been developed	IUS teaching programs for nurses and physician assistants need to be developed

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