

REVIEW

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The intestinal ultrasound role in inflammatory bowel disease in clinical practice and a critical appraisal of the current guidelines (mini-review)

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Abstract

Background Intestinal ultrasound (IUS) is a beneficial tool in the diagnosis and follow-up of patients with inflammatory bowel disease. IUS has long been established in monitoring of Crohn's disease patients. Recent studies and guidelines show similar benefits in ulcerative colitis patients.

Aim To assess the recent guidelines and the effectiveness and practicality of using IUS in the clinical settings.

Methods To assess the role of IUS in different guidelines, a search on the PubMed and Cochrane Library databases was conducted using the following keywords: *inflammatory bowel disease, guidelines, and intestinal ultrasound*—in addition to a search conducted on national and international guideline sites on the use of IUS in IBD. Related references on the topic were examined by a manual separate search.

Results A discussion of the results of different guidelines was conducted regarding the role of IUS in IBD.

Conclusion IUS is a very useful tool in IBD diagnosis and follow-up in the clinical settings. There are some areas that have not been yet validated when compared with other established standard diagnostic tools such as endoscopy, histopathology, or other radiological methods. This makes incorporation into the guidelines in its primary stages, added to the different geographical-dependent experience, and availability of the specialty practitioners. Point-of-care management and learning curve for young practitioners are still areas of debate in clinical practice.

Keywords Inflammatory bowel disease, Intestinal ultrasound, Guidelines, Crohn's disease, Ulcerative colitis

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder that includes both subtypes Crohn's disease (CD) and ulcerative colitis (UC). According to the Selecting Therapeutic Targets in Inflammatory Bowel Disease-II (STRIDE-II) guidelines, symptomatic improvement,

normal fecal calprotectin, and serum activity markers are short-term goals [1, 2].

CD, a transmural disease, is often the most monitored by IUS in the guidelines, while UC, affecting mainly the mucosa and submucosa, is denied the same acknowledgment in clinical practice. This is not the case lately, as the concept "treat to target" (T2T) mandates continuous monitoring of disease activity in response to treatment [3].

IUS is a "point-of-care," real-time tool that can be used in diagnosing and monitoring patients in a clinical setting. Its accuracy is similar to MR enterography (MRE) in the assessment of the terminal ileum and better in the

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assessment of the colon, with the exception of the rectum and anus. Moreover, elastography could have additional benefit detecting bowel wall fibrosis when used with IUS [4].

IUS has the advantage of being a dependable non-invasive tool, offering accurate follow-up for IBD patients, especially the vulnerable populations as pregnant women [5] and children [6, 7]. It considered a “point-of-care” procedure, decreasing the time taken to reach critical decisions in medical treatment of IBD patients [8, 9].

Methods

The author has done a search on PubMed using the following keywords: *inflammatory bowel disease, guidelines, and intestinal ultrasound*. The author searched all the international guideline sites for the most updated versions on the use on intestinal ultrasound in inflammatory bowel disease. The author searched related references on the topic by a manual separate search.

Results

The most recent guidelines were included: European Crohn's and Colitis Organization and the European Society of Gastrointestinal and Abdominal Radiology (ECCO-ESGAR), American Gastroenterological Association (AGA), and Asian guidelines. In addition, we included the individual national practice guidelines (such as the Canadian, Malaysian, Spanish, and German versions). Also, we incorporated separate national guidelines according to their national experience. Moreover, the author extracted data from reviews and individual studies related to the use of IUS in clinical practice and its accuracy and validation in UC and CD (Table 1).

Discussion

How do guidelines incorporate IUS?

The current European Crohn's and Colitis Organization and the European Society of Gastrointestinal and Abdominal Radiology (ECCO-ESGAR) guidelines state that incorporating IUS (including SICUS) in IBD monitoring has variable diagnostic accuracy in different studies depending on the subtype of the disease (CD versus UC), site, and extension of the disease [13].

A recent review on the cross-sectional imaging techniques in IBD showed that IUS clearly presents signs of activity and inflammation such as edema, mucosal ulcerations, and hyperemia (through Doppler signals) in IBD [15].

The usefulness of IUS in IBD was discussed in a review article. They proposed an algorithm for CD follow-up of the mural and transmural healing using only IUS and biomarkers and the modification of therapy accordingly. In case of UC, they pointed that the follow-up of the colonic

mural thickness, hyperemia, and loss of haustrations are the most important features in disease monitoring [21].

The histological T2T is still debatable, as it means repeated endoscopy and biopsy, which is an invasive procedure, without proper scoring algorithms, making IUS the perfect non-invasive T2T tool [22].

Lee et al. performed a survey on the current practice of IBD monitoring in Asian countries. In China, Korea, and Japan, the use of IUS in monitoring of IBD is still limited in the number of performed cases, while CT and MRE are the more preferred modalities by the clinicians. However, half the practitioners surveyed from China preferred IUS in monitoring their cases. This could be related to the different availability of the equipment in different regions [23].

The German and Radiological Society (DRG) and the German Competence Network for Inflammatory Bowel Diseases in association with the IBUS group agreed that enough level of standardization in the parameters of MRE, CT, and IUS is present, but not elastography or CEUS, where both are more helpful in detecting the level of bowel stenosis or fibrosis [12].

All studies included in the IUS evaluation of a European consensus were assessing the biological and immunomodulatory drug-dependent improvement. However, there was no data on the effect of 5-amino-salicylic acid on IUS parameters, but there was abundant data on treatment with steroids. Besides, they found that the bowel wall thickness (BWT) response to medical treatment took shorter time periods in UC than in CD [24].

However, some limitations of IUS include the following: the increased abdominal fat and high BMI limiting the bowel visualization and the complex anatomy of the bowel, which could be difficult to assess. Moreover, detection of colon cancer is limited, especially in high-risk patients (> 8 years of UC), when compared with colonoscopy [8]. In addition, most of the observational studies conducted did not elaborate on the method of BWT measuring, the number of measurements, or the values measured. This limited the usable information from those studies or their validation [25].

Moreover, limitations of IUS include lower accuracy in assessing certain parts of the gut including the duodenum, jejunum, and rectum than the MRE. It also has lower inter-observer reliability than MRE, due to the operator-dependent visualization, in the assessment of the following parameters: Doppler sign, inflammatory fat, and stratification of bowel layers [26].

The training for the IUS must include about 200 supervised cases for a practitioner to have enough experience [10]. The AGA and Crohn's and Colitis Foundation have started in 2022 to endorse the IBUS group training modules to practitioners in the USA to achieve a reliable

Table 1 Different guidelines and organizational sites (accessed in April 2024)

No.	Name of the organization	Latest update	Site	Recommendations for IUS
1	The International Bowel Ultrasound Group (IBUS)	Monthly updated courses	https://ibus-group.org/	Yes, with monthly meetings to discuss cases and guidelines Research teams
2	European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)	2018 [2]	https://efsumb.org/	Yes, on the details of applying IUS in IBD
3	Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU)	2021 [10]	https://geteccu.org/	Yes, POCUS with an algorithm on how to use in clinical practice in diagnosis and monitoring
4	Argentinian group of Chron's disease and ulcerative colitis (GADECCU)	2022 [11]	https://www.gadeccu.org.ar/	No
5	The German and Radiological Society (DRG)	2023 [12]	https://www.drg.de/	Yes, consensus on IUS in comparison to MRE
6	The German Competence Network for Inflammatory Bowel Diseases (KNCED)	2023 [12]	https://kompetenznetz-darmerkrankungen.de/	Yes, consensus on IUS in comparison to MRE
7	Inflammatory Bowel Disease Competence Network	NA	NA	NA
8	ECCO-ESGAR: European Crohn's and Colitis Organization and the European Society of Gastrointestinal and Abdominal Radiology	2019 [13, 14] 2022 (a review) [15]	https://esgar.org/research/guidelines	Yes, guidelines on the diagnosis, monitoring, and detection of complications of IBD using IUS
9	European Crohn's and Colitis Organisation [ECCO]	See ECCO-ESGAR	https://www.ecco-ibd.eu/	See ECCO-ESGAR
10	American Gastroenterological Association (AGA)	2020 [16]	https://gastro.org/	No
11	The Canadian Association of Gastroenterology (CAG)	2019 [17]	https://www.cag-acg.org/	Yes, mentioned as one of the tools for detecting of remission
12	The German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS)	2019 [18]	https://www.dgvs.de/	Yes, IUS is recommended as a part of the diagnoses and monitoring procedures (evidence grade 2, recommendation grade B, strong consensus)
13	Asian Organization for Crohn's and Colitis	2021 [19]	https://aocc-ibd.org/index2.html	Perianal IUS to exclude perianal disease
14	Asia Pacific Association of Gastroenterology (APAGE)	2020 [20] 2021 [19]	https://www.apage.org/practiceguidelines.html	No
15	Egyptian Society of Crohn's and Colitis (ESCCO)	NA	https://escoco-ibd.org/	NA

“point-of-care monitoring” for IBD. The training started in two American states and is expected to cover most of the states in the next decade [27].

The International Bowel Ultrasound Group (<https://ibus-group.org/>) provides an international layered training program on site and online, with associated webinars for discussion of the latest data globally for the international members. In the United States, this introduction of the IUS to the gastroenterology field is progressing. This happened after overcoming essential learning barriers, offering grants for the three-tier course learning by the IBUS group locally in the USA [28].

There is a controversy on the learning curve of IUS in IBD. A recent study on four trainees (two inexperienced and two experienced) by Bezzio et al. showed that

the basic competence for a gastroenterologist in clinical practice is acquired in few training sessions, but extensive competence is only acquired with a longer training experience. The advanced IUS competence is reached with a minimum of 97 examinations to detect intra-abdominal complications [29].

Besides, recently, an artificial intelligence-based operator model was created using 1008 CD images, half normal and half with lesions. The accuracy in detecting the lesion was 90.1%, with a sensitivity of 86.4% and a specificity of 94% [30]. This could decrease the time of the learning curve in some centers and improve the diagnostic accuracy.

The Canadian guidelines state that acquiring special probes and high-resolution machines, along with keeping

them under continuous maintenance, is expensive. They concluded that the need for specialized practitioners is difficult to achieve in the Canadian clinical practice [31].

Figure 1 shows the expected learning curve hierarchy of IUS. Although it is expected that the radiologist have the highest degree of learning and experience in IUS, the clinician has the advantage of deciding during or immediately after the procedure. Thus, the health-care provider has the advantage of helping the patients who cannot tolerate to go to far tertiary centers or make delayed appointments (that is the concept of point-of-care). Moreover, the patient self-monitoring is reserved for high-risk patients who cannot afford the delay in the follow-up appointments or need continuous monitoring of treatment.

In the answer to the important question: “are we ready to use IUS in clinical practice now?” The answer is: Yes, it is already being used as the standard of care in Germany and Italy. The practicing gastroenterologist needs 300 cases in Germany and 400 cases in Italy to acquire the skill under supervision. No other countries have similar formal or standardized training programs incorporated in their clinical practice [32].

Regarding the *proposed algorithms* for the use of IUS in clinical practice, the normal BWT in the small bowel is 2 mm, yet the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) consensus recommends a cutoff of > 3 mm BWT in CD to increase the activity detection sensitivity of IUS [10].

A study by Dolinger and Kayal proposed a treatment response-timed IUS monitoring algorithm. In case of complete remission achieving normal BWT < 2.5, then there would longer follow-up periods (every 12–24 weeks), whereas in case of a partial clinical response with BWT denoted by a decrease by 25% or 1–2 mm, then there would be monitoring every 12 weeks. Lastly, in case of non-response without any improvement of BWT, then there would be monitoring every 8 weeks, with mandatory change of treatment [33].

Moreover, the IBUS group recommends in their IUS follow-up algorithm the monitoring of the treatment response of IBD after 14 weeks (± 2) of starting treatment and later between weeks 26 and 52 or monitor “on-demand” when disease activity increases as indicated by elevated fecal calprotectin or worsening of clinical symptoms [26].

In the Spanish recommendation by Spanish Working Group on Crohn’s Disease and Ulcerative Colitis (GETECCU), there is a proposed algorithm for the use of IUS along with other imaging modalities and biomarkers. They recommend the continuous monitoring in CD mucosal and transmural healing every 6–12 months with biomarkers every 3–6 months and removed MRE, CT, or endoscopy. They consider the IUS as complimentary to colonoscopy in UC especially in cases of stricter or incomplete colonoscopy [10].

Using IUS in CD

IUS in CD has a high diagnostic accuracy when compared with endoscopic activity, with sensitivity ranging 75–94% and specificity ranging 67–100% [8]. However, we find that the intestinal ultrasound findings in CD are weakly correlated with fecal calprotectin and C-reactive protein and do not correlate with IUS detection of complications. The fecal calprotectin at the cutoff value of 100 $\mu\text{g/g}$ has a moderate sensitivity and specificity of approximately 70% for detecting IUS inflammatory signs [34]. In pregnant women, it is found that FC complements IUS in monitoring activity of structuring CD [5].

MRE is considered the gold standard for cross-sectional monitoring of luminal thickness in CD. However, studies show that MRE has a comparable diagnostic accuracy to IUS in detecting terminal ileal disease, with a sensitivity of 97% for MRE and 92% for IUS. Moreover, the MRE needs a tertiary or large hospital setting, which could be unavailable for a large number of IBD patients [28].

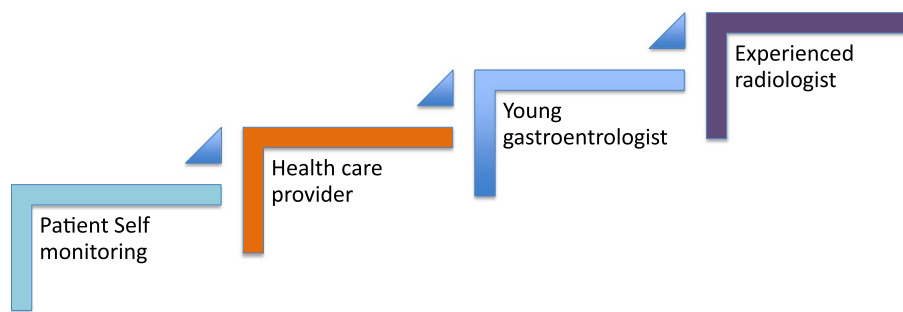


Fig. 1 The expected learning curve hierarchy of IUS

In CD IUS has similar accuracy in detecting strictures, abscesses, and abdominal complications as MRE and higher accuracy in detecting disease extension and fistula formation. Monitoring of the transmural inflammation is an important parameter in monitoring therapy and could be totally missed in the endoscopic assessment of the patients [4].

Two randomized controlled clinical trials (CALM and STARDUST) were conducted to assess the T2T in a real-world clinical setting [35]. The STARDUST trial assessed the T2T versus the standard-of-care groups of CD patients treated by ustekinumab. There was no difference between the two groups after 48 weeks in endoscopic remission or response, mucosal healing, or clinical remission. However, the clinical response was lower in the clinical response as compared with the standard of care [36]. Incorporating the IUS parameters as a goal for the T2T is a hope for medical practice.

In a large German multicenter study, CD patients receiving anti-inflammatory drugs had improvement in all IUS parameters after 3 and 6 months. Both BWT < 3 mm and absent hyperemia are important parameters of decreased activity which can be achieved in quarter to one third of the patients after 2 years [33].

An algorithm of IBD patients' monitoring with IUS was proposed in patients receiving biological or small molecular therapy by Dolinger et al. (2023). An oral contrast agent could be added for better visualization of the small bowel in CD. Monitoring of the biological therapy effect starts as early as 2 weeks post initiation of treatment and continue with the duration adjusted according to the patient's response [4].

Small intestine contrast ultrasound (SICUS) is performed through using a contrast agent polyethylene glycol (PEG) to improve the intestinal loop visualization in CD. The diagnostic accuracy of SICUS in CD-associated small bowel lesions had an AUC of 92.7%, with a specificity of 86.1% and a sensitivity of 88.3% [37]. Both contrast enhanced ultrasound (CEUS) and SICUS could enhance the visualization of anastomotic areas [38].

The post-surgical recurrence of CD detected by IUS, when compared with endoscopy, showed a diagnostic accuracy with AUC of 75%, whereas inflammatory and clinical parameters showed a lower diagnostic accuracy (AUCs were 66% and 64%, respectively) [39].

Regarding the validation and standardization of IUS in CD, the International Bowel Ultrasound Segmental Activity Score (IBUS-SAS) expert consensus showed an intra-class correlation coefficient of 0.96 for BWT [25].

Using IUS in UC

In UC, IUS measurement of BWT with a cut-off 2.8 mm has a good diagnostic accuracy in detecting endoscopic

remission with AUC of 87% [33]. Moreover, IUS in UC is highly correlated with endoscopic activity and Mayo score but not clinical activity nor FC [8]. UC response-to-treatment is detected using IUS by change in the BWT as early as 14 days [40]. The TRUST&UC study is the largest cohort till the time being which included 42 medical centers, with 224 UC patients. The BWT decreased as early as 2 weeks post-treatment of UC patients, and the main improved regions were the sigmoid and descending colons; this was correlated with improved clinical activity scores. After 12 weeks of follow-up, 90.5% had a normalized BWT [41].

In Malaysia, the first Southeast Asian study on IUS in IBD, a tertiary center found that IUS has a low sensitivity (67%) and a high specificity (97%) in detecting UC activity, when compared with endoscopy. BWT > 3 mm has the highest accuracy in detecting endoscopic activity [22].

Few scores have been validated for the IUS in UC; however, the simplest is Milan Ultrasound Criteria (MUC). The BWT is the parameter with highest inter-rater agreement [26]. Bots et al. developed an updated UC IUS index. The BWT was accurate (AUC 91%) in differentiating between Mayo scores 0 and 1–3 (cut-off > 2.1 mm) with a sensitivity of 82.6% and specificity of 93%. The BWT was accurate (AUC 95%) in differentiating between Mayo scores 0–1 and 2–3 (cut-off 3.2 mm) with a sensitivity of 89% and specificity of 92%. The BWT was accurate (AUC 91%) in detecting a Mayo score of 3 (cut-off > 3.9 mm) with a sensitivity of 80.6% and specificity of 92% [42].

Transperineal ultrasound (TPU) has been proposed as a complementary tool to IUS in viewing the rectum of UC patients, as this is usually a blind spot in IUS. When compared with histologic remission, the TPU showed a diagnostic accuracy with an AUC of 89%. Moreover, when compared with endoscopic remission, the diagnostic accuracy of TPU had an AUC of 90% [43].

A new concept of "at home monitoring" for severe UC patients was introduced recently. One patient "single case" was introduced to IUS without any previous medical learning. The patient spent only 1 day at the clinic to learn the procedure of measuring the parameters by a handheld portable device. This helped to change the course the treatment of the patient, and later a definitive surgery was performed based on the worsening of his BWT [44].

Conclusions

IUS offers a useful tool for IBD monitoring, but the data on the frequency of follow-up visits is still unknown. A lot of consensus proceedings had tried the

standardization of IUS in both CD and UC with promising clinical practice outcomes. However, the cost of acquiring and maintenance of ultrasound machines with high-resolution qualities, Doppler, and specified probes is still a burden on primary and small clinical centers. The financial burden of teaching IUS to young practitioners and their unexamined learning curve in clinically validated studies are still an area of debate across different regions of the world; while European countries endorse it, US and Asian and African countries have not completely.

Abbreviations

AGA	American Gastroenterological Association
AUC	Area under the curve
BWT	Bowel wall thickness
CAG	The Canadian Association of Gastroenterology
CD	Crohn's disease
DGVS	The German Society for Gastroenterology, Digestive and Metabolic Diseases
DRG	The German and Radiological Society
ECCO-ESGAR	European Crohn's and Colitis Organization and the European Society of Gastrointestinal and Abdominal Radiology
EFSUMB	European Federation of Societies for Ultrasound in Medicine and Biology
FC	Fecal calprotectin
GETECCU	Spanish Working Group on Crohn's Disease and Ulcerative Colitis
IBD	Inflammatory bowel disease
IUS	Intestinal ultrasound
KNCED	The German Competence Network for Inflammatory Bowel Diseases
MUC	Milan Ultrasound Criteria
MRE	MR enterography
SICUS	Small intestine contrast ultrasound
STRIDE-II	Selecting Therapeutic Targets in Inflammatory Bowel Disease-II
T2T	Treat to target
TPU	Transperineal ultrasound
UC	Ulcerative colitis

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Declarations

Ethics approval and consent to participate

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Consent for publication

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Competing interests

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