Review Article

Intestinal Ultrasound in Inflammatory Bowel Disease: A Novel and Increasingly Important Tool

CME Credits

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Abstract

New and efficacious medical therapies have become available that have greatly enhanced clinicians' ability to manage inflammatory bowel diseases (IBDs). IBD activity should be assessed regularly in scheduled examinations as the part of a treat-to-target strategy for IBD care. The gold-standard approach to investigating IBD is colonoscopy, but this is an invasive procedure. Intestinal ultrasound (IUS) has played a crucial role in recent years regarding the assessment of IBD activity because it is noninvasive, safe, reproducible, and inexpensive. IUS findings could inform changes in therapeutic interventions for IBDs; this would necessitate fewer endoscopies and enable faster decision-making processes. Furthermore, patients are accepting and tolerant of IUS examinations. This review outlines the current evidence and gives indication regarding the use of IUS in the management of IBDs.

Keywords: Crohn's disease, inflammatory bowel disease, intestinal ultrasound, ulcerative colitis

Introduction

Inflammatory bowel diseases (IBDs) can negatively affect people's quality of life and lead to problems in fulfilling social and occupational roles. Including ulcerative colitis (UC) and Crohn's disease (CD), IBDs involve inflammation in the gastrointestinal tract and tend to be destructive and chronic; patients with IBD often experience relapses after short or long reprieves and can need surgery.[1] Monoclonal antibodies against Janus kinase inhibitors, integrins, interleukin-12 and-23, and tumor necrosis factor-alpha, in addition to the growing use of immune modulators, are making it possible to transcend conventional treatments and move toward the more ambitious target of mucosal healing. Symptom relief is a short-term target; by contrast, the long-term targets; restoration of quality of life, endoscopic healing, and normal growth in children; are currently recommended as treat-to-target approaches.[2] The gold standard for the assessment of IBD activity is ileocolonoscopy with biopsy. This procedure is invasive, however, and not tolerated by some patients; additionally, there is a risk of perforation during a severe flare up.[2]

Extraintestinal manifestations, transmural involvement, and mucosal alterations are evaluated in imaging processes for IBDs. The most widely employed imaging tools are magnetic resonance imaging (MRI) and computed tomography (CT), but both approaches have drawbacks, with MRI requiring a long execution time and being expensive and CT having a radiation exposure risk.[3] Intestinal ultrasound (IUS) is as capable as CT and MRI for obtaining cross-sectional images of extraintestinal manifestations and transmural alterations. Scholars have recently reported that for the recognition and monitoring of IBDs, IUS is suitable because it is relatively inexpensive, noninvasive, and well tolerated by patients. Concern about whether the success of its use is dependent on the operator of the equipment has however been a major barrier to its widespread use.[4] In this review, the technologies behind IUS and the existing evidence regarding its practicality for assessing IBD are discussed.

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Technique of Intestinal Ultrasound

Fasting or bowel preparation is not necessarily required for a standard IUS examination.[5] The patient should be in the supine position. The initial systematic scan is recommended to be performed with a low-frequency (3.5–5.0 MHz) curvilinear probe over the whole intestine and extraintestinal area. Then, high-frequency linear probes (5–15 MHz) can be used to obtain the images of the intestinal wall at a higher spatial resolution; this step is crucial if the five-layer wall pattern of the gastrointestinal tract is to be accurately assessed.[6] Intraluminal air can be reduced through the IUS probe gradually compressing the bowel. Fasting for 4–6 h can reduce the luminal content, peristaltic movements, and blood flow of the small bowel.[7] Small-vessel signals at the intestinal wall can be assessed using color Doppler imaging (CDI), as can inflamed bowel segments.[6,7]

The guidelines stipulated by the European Federation of Societies for Ultrasound (US) in Medicine and Biology recommend the following procedure when the whole intestine is to be evaluated. The probe should first assess the sigmoid colon by beginning from the left iliac fossa, after which it should continue along the colon to the terminal ileum and appendix. The remaining small bowel can then be swept.[7] The process of sigmoid or terminal ileum identification in the left iliac fossa or right iliac fossa can be made easier by utilizing landmarks: the iliopsoas muscle and common iliac vessels, respectively.[5] Visualizing the colonic flexures (especially the left flexure) is difficult due to ligamentous fixation to the diaphragm. In addition, the location of the pelvis means that when using the transabdominal route, accurate visualization of the rectum and anal region is not possible.[6] Transperineal US can be added to assess the rectum, especially in patients with proctitis or perianal lesions.[8] In the small bowel segment, the multiple overlying bowel loops mean that the proximal parts of the ileum or jejunum are difficult to evaluate completely and continuously. However, to search for inflamed small bowel wall segments, a systematic approach can be employed wherein scans can be made in the four positions: the right versus left and upper versus lower abdominal quadrants.[6] In the assessment of extraintestinal abnormalities, the examination could begin in the epigastrium at the duodenojejunal flexure, after which it could progress obliquely toward the right iliac fossa. During the US procedure, the patient should breathe deeply, and the operator of the equipment should apply pressure to the transducer to aid the visualization of the lesion.[5]

Characteristics of Ultrasound Index Parameters

In the clinical practice, numerous IUS features can be identified that indicate the activity of IBD: bowel wall thickening (BWT), bowel wall stratification (BWS), CDI and extraintestinal findings (fat, lymph nodes, and free fluid accumulation). These signs can indicate the complications of CD, such as abscesses, fistulas, and strictures. Inflammatory mucosal changes in IUS images can identify disease extension in patients with UC.

The currently frequently described parameters include BWT, BWS, and CDI.[4] The existing IUS indices use various proportionate contributions and weightings of these three parameters to assess IBD activity.[4] Interest has been growing in the utility of contrast US, contrast-enhanced US, and US elastography as novel tools for evaluating tissue stiffness and increasing the accuracy of disease stricture location and extension. To date, no clinical trials have yet defined validated and reproducible IUS scores for quantifying inflammation and measuring response, but the International Bowel US Group is making progress in this topic.[9] The sonographic parameters that are feasible and reproducible in clinical practice are summarized in Table 1.[4,10-13]

Bowel wall thickening

In UC and CD diagnosis and activity trials, BWT is the most widely used parameter because it is the easiest to reproduce and leads to favorable interrater agreement.[4] There are five layers of the intestinal wall, the echogenicity of which alternates: the interface between the lumen and mucosa, the mucosa, the submucosa, the muscularis propria, and finally, the serosa are hyperechogenic, hypoechogenic, hyperechogenic, hypoechogenic, and hyperechogenic, respectively[14] [Figure 1].

Identifying the small and large bowel is generally easy and is achieved by scanning the colon's haustra and the small intestine's circular folds. The thickness is determined by measuring the wall from the lumen interface to the serosa. For the small bowel and colon, the usual cutoffs are 2–3 and 3–4 mm, respectively.[15]

The bowel wall is usually asymmetric, and BWT can be measured in two orientations, namely transverse and longitudinal sections; this can result in interobserver variability.[15] To prevent this variability, the probe should be placed perpendicular to the wall, and haustrations and mucosal folds should be avoided. BWT measurements are performed on the anterior wall in a longitudinal section, and two representative measurements are averaged.[8] In affected

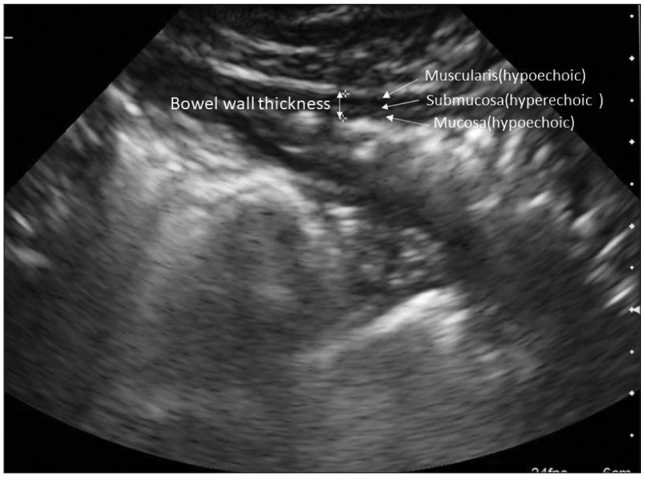

Figure 1: Five layers of the intestinal wall

Table 1: Feasibility of intestinal ultrasound features and tools in clinical practice of inflammatory bowel disease care

	Simple	Objective	Interobserver agreement
Bowel wall thickness	○	○	○
CDI	△	○	△
BWS	○	△	△
Extraintestinal findings (abscess, fluid)	○	○	○
Extraintestinal findings (lymph node, fistula)	○	△	△
Extraintestinal findings (fibro-fatty wrapping, stenosis)	○	△	X
Contrast US	X	○	△
Contrast-enhanced US	X	○	△
Elastography	△	○	○

*Based on data from[4,10-13]. ○: Appropriate, △: May be appropriate, X: Inappropriate, US: Ultrasound, CDI: Color doppler imaging, BWS: Bowel wall stratification

bowel segments (BWT >3 mm), BWT should be calculated as the mean of four measurements in the thickest section: two individual measurements performed in each orientation, with these two measurements separated by at least 1 cm for the longitudinal sections and at least 90° for the transverse sections.[9] Colorectal segments with a BWT of <3 mm were reported by one meta-analysis to be highly likely in mucosal healing; the negative predictive value was 92.7%.[16] In active UC and CD, the mucosal layer and submucosal layer, respectively, are generally found to be considerably thickened.[17]

Color doppler imaging

IBD activity is typically assessed through CDI of the bowel wall.[18] Increased vascularization in the penetrating vessels of the muscularis propria and in the submucosal layer is a sign of active inflammation.[4] The use of CDI is feasible when the BWT of segments exceeds 3 mm, and this technique is implemented using standard scanning presets. The IUS gain can be increased until flash artefacts occur and then decreased to make these artefacts disappear.[19] CDI measurement is not suitable for the rectum because the deeper segments of the bowel are relatively insensitive.[19]

The quantitative measurement of CDI parameters is complex and not yet widely performed due to the variety of the parameters.[5] Currently, the simple Limberg score can be employed for a semiquantitative characterization of vascularization;[20] in this approach, vascularization that is visible during CDI is divided into four categories [1 = no vascularization (>3 mm); 2 = spotty vascular signals; 3 = longer vascular signals; 4 = considerable signals within the bowel wall and extending beyond the mesentery; Figure 2].

Bowel wall stratification

Inflammation can disrupt the usually clear definition of the five layers of the bowel wall. BWS is the third most frequently used parameter in assessing disease activity. Extension of an inflamed segment is defined as focal or extensive disruption, and the commonly used cutoff is 3 cm. A lack of standardization has resulted in studies' interobserver agreement being low.[10,21] The use of BWS is more common for UC than for CD.[4] Loss of BWS at the stenosis level is suggestive of inflammation,

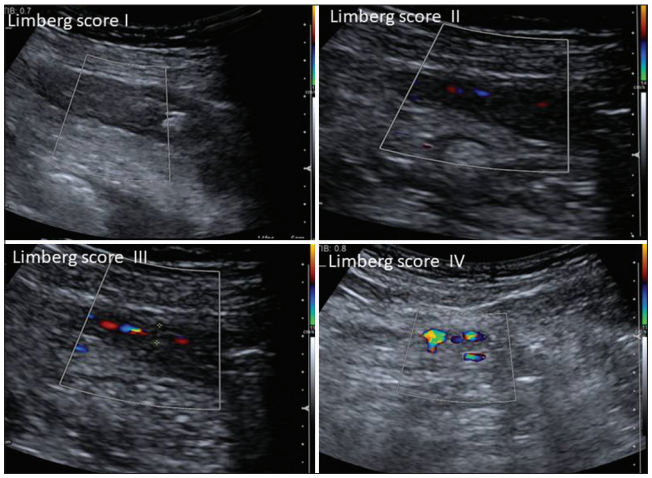

Figure 2: Examples of Limberg scores. Grade I: No vascularization; Grade II: Spotty vascular signals; Grade III: Longer vascular signals; and Grade IV: Significant signals within the bowel wall and extending beyond the mesentery

whereas the existence of stratification is suggestive of a greater degree of fibrosis in the intestinal stricture.[22] In human organs other than the bowel, hyperechogenicity indicates the fibrosis typical of a stratified echo pattern. In IBD, the bowel wall's third layer exhibits elevated echogenicity, indicating fibrosis segments, due to more collagen being deposited in the submucosa than in the normal intestinal wall.[23]

Extraintestinal findings

A peri-intestinal inflammatory reaction comprises surrounding structures of fibro-fatty wrapping, free fluid accumulation, and enlarged mesenteric lymph nodes. Because both extraintestinal and intraluminal features can be identified using IUS, this type of US is particularly useful for the assessment of common complications in CD, including strictures, fistulas, and abscess formation[7] [Figure 3]. Real-time observation of motility and the possibility of evaluating fibrosis are why IUS is particularly advantageous in contrast to other cross-sectional imaging approaches.[9]

Fibro-fatty wrapping is a hyperechoic zone surrounding an IBD-affected bowel loop. Enlarged mesenteric lymph nodes

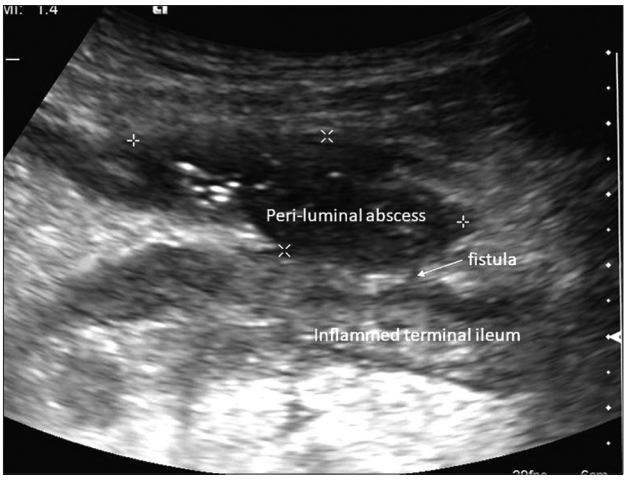

Figure 3: Inflamed terminal ileum with fistula and abscess formation in a patient with CD in its active stage. CD: Crohn's disease

are lymph nodes adjacent to an affected segment and >4 mm in diameter.[9] However, the discovery that lymph nodes are mesenteric is too vague and, in CD, is not strongly correlated with biochemical and clinical disease activity.[24] IUS has high sensitivity for detecting free fluid accumulation. A stricture is an intestinal section with increased BWT (>3 mm), a lumen with no or small diameter, and no peristaltic movement being present with or without increased lumen diameter of a proximal loop (3 cm).[11,12] Fistulas are hypoechoic narrow tracts between the bowel loop and other tissues. In IUS, an abscess looks like an approximately circular anechoic lesion with an irregular wall, internal echoes, and posterior echo enhancement.[12] Gas overlying the bowel means that the task of diagnosing deep pelvic or retroperitoneal abscesses is challenging; it can be difficult to differentiate an abscess from bowel loop fluid.[12] Interobserver agreement is perfect for the detection of abscesses and favorable for that of fistulas or lymph nodes, whereas it is poor for detecting fibro-fatty wrapping and stenosis.[10]

Additional Tools in Bowel Ultrasonography

Contrast ultrasound

Polyethylene glycol solution, an oral contrast medium, has been proposed to distend CD-related lesions in the small bowel wall, thus rendering it appropriate for characterizing them.[12] The related procedure is time-consuming; however, it takes from 25 to 60 min after the intake of 400–800 mL of the contrast fluid.[25] Oral contrast agents are highly accurate for determining how many stenoses there are in the proximal small bowel or ileum lesion as well as how big they are. The detection of CD stricturing and penetrating complications has been reported to be increased when oral contrast agents are used.[12] For postoperative patients, this technique has been found to be valuable in the evaluation of anastomosis and detection of postoperative CD recurrence.[26]

Contrast-enhanced ultrasound

The ability of Doppler US to detect mural blood flow can be increased by using an intravenous contrast agent. This approach provides both subjective and objective quantification and is highly sensitive to the classic complications of CD.[27] SonoVue (1.2–4.5 mL), which enhances echo signals, is generally injected as a bolus into an antecubital vein. Subsequently, 10 mL of normal saline solution is injected. Imaging is performed continuously for 40 s, with this period beginning a few seconds prior to the agent's injection.[28] It is time-consuming to perform this examination, and it is currently unclear how effective contrast-enhanced US is in regards to the evaluation of CD activity.[12]

Elastography

US elastography is a novel radiation- and contrast-free type of imaging used in the assessment of IBD. There are three commonly used US elastography techniques: acoustic radiation force impulse (ARFI), shear-wave elastography (SWE), and strain elastography (SE). The elastography techniques can be divided into qualitative and quantitative methods. SE is a qualitative elastography technique, whereas ARFI and SWE are quantitative methods.[29] Currently, the majority of studies on US elastography in IBD have focused on patients with CD because fewer patients with UC present with stricture and fibrosis.[29]

A comparative analysis of SE, ARFI, and SWE using histopathology from an endoscopy biopsy was performed on 25 patients with CD. The researchers concluded that SWE is superior to SE and ARFI for evaluating fibrotic and inflammatory stenosis.[13] In a study involving 35 patients with CD in which SWE was performed within 1 week of surgical resection, significantly higher mean SWE value of stenotic bowel wall was found in regions where there was severe fibrosis; no significant difference was discovered among different grades of inflammation.[30] Therefore, the type of intestinal stricture can feasibly be determined by combining SWE with CDI.

Clinical Practice of Use of Intestinal Ultrasound in Crohn's Disease

IUS is widely accepted, particularly in Europe, as being suitable for use in CD, a transmural disease. The hallmark of active CD on IUS is increased BWT and hypervascularity that mostly affects the submucosa. A specific feature of CD is asymmetric mural thickening along the bowel's mesenteric side.[31]

Recently, two IUS scores for evaluating CD activity have been proposed: the Simple US Activity Score for CD (SUS-CD) and International Bowel US Segmental Activity Score (IBUS-SAS). The SUS-CD combines the BWT and CDI, whereas the IBUS-SAS uses four parameters: BWT, BWS, CDI, and inflammatory fat.[4,32] In patients with CD, BWT is the most crucial parameter for the assessment of postoperative recurrence at 6 months and correlates well with the CD activity index.[33] The IUS parameters BWT, BWS, presence of fistula, abscess, and stenosis are the reliable prognostic markers

regarding the short-term (30 days) risk of surgery for CD and are correlated with the Harvey Bradshaw index.[34]

In an observational longitudinal study conducted to evaluate transmural healing through IUS in 66 patients with CD receiving biologic treatment, MRI could define CD extension and enteroenteric fistulas more accurately than could IUS. These techniques have high agreement in terms of disease location and abscesses.[35] Therefore, follow-up IUS is feasible and beneficial for patients with CD and complications after an MRI or CT imaging study. IUS was compared with MRI combined with colonoscopy in a single-center study involving 60 patients with CD; disease activity and complications were assessed. The study reported the potential usefulness of IUS for detecting ulcers in this population. Regarding localization of the disease, the diagnostic accuracy was found to be 91%, whereas regarding complications, it was 81%, 98%, and 96% for strictures, fistulas, and abscesses, respectively.[36]

A multicenter prospective study of 234 patients with CD revealed that a reduction in BWT or BWS, decreased volume of fibro-fatty lesions, and increased signals in CDI were correlated with a decrease in disease activity (Harvey–Bradshaw index score).[37] Early evaluation of the response to a medical treatment appears to be an excellent use of IUS.

Use in Clinical Practice of Intestinal Ultrasound in Ulcerative Colitis

IUS has a more well-defined clinical role in CD than in UC. With clinicians being more familiar with using IUS in UC, the use of this technique will increase in the future. IUS can make colonoscopy less necessary and is considered reliable, objective and well accepted. A solitary rectal location of UC is difficult to assess because of the rectum's pelvic location.[16] In UC, a superficial pattern of inflammation is thickening of the mucosa and submucosa. When active inflammation is present in a patient with US, edema is reflected by hyperechoic thickening of the submucosa.[15] In UC, the bowel wall usually thickens around its full diameter and without any gaps, which is different from the case in CD. During periods of high UC activity, IUS can reveal extraintestinal signs of fibro-fatty proliferation, ascites, or even mesenteric streaks.[15]

The diagnostic accuracy of IUS in the rectum was found in one meta-analysis study to be lower than that in the right, transverse, and left colon.[16] A prospective observational study reported IUS to be feasible for monitoring the short-term treatment response in 224 patients with UC. Rapid BWT improvement was observed as early as 2 weeks after the intensification of the treatment, and this was followed by clinical improvement as determined using the Short Clinical Colitis Activity Index. BWT normalization and clinical response were strongly correlated after 12 weeks of treatment.[38]

A systematic review indicated that disease activity is most commonly assessed by applying the two criteria: increased BWT and blood flow, as revealed through CDI.[39] A recent expert panel discovered the most reliable IUS parameters to be BWT and CDI features; the panel recommended that these be combined to create an index of UC disease activity.[40]

Conclusion

Evidence is increasing regarding the usefulness of IUS, and this method has become well defined. This technique is suitable for use in IBDs for evaluating and monitoring disease activities, complications, and treatment responses.

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Conflicts of interest

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References

1. Lo B, Prosberg MV, Gluud LL, Chan W, Leong RW, van der List E, *et al.* Systematic review and meta-analysis: Assessment of factors affecting disability in inflammatory bowel disease and the reliability of the inflammatory bowel disease disability index. Aliment Pharmacol Ther 2018;47:6-15.
2. Turner D, Ricciuto A, Lewis A, D'Amico F, Dhaliwal J, Griffiths AM, *et al.* STRIDE-II: An update on the selecting therapeutic targets in inflammatory bowel disease (STRIDE) initiative of the international organization for the study of IBD (IOIBD): Determining therapeutic goals for treat-to-target strategies in IBD. Gastroenterology 2021;160:1570-83.
3. Walsh AJ, Bryant RV, Travis SP. Current best practice for disease activity assessment in IBD. Nat Rev Gastroenterol Hepatol 2016;13:567-79.
4. Goodsall TM, Nguyen TM, Parker CE, Ma C, Andrews JM, Jairath V, *et al.* Systematic review: Gastrointestinal ultrasound scoring indices for inflammatory bowel disease. J Crohns Colitis 2021;15:125-42.
5. Atkinson NS, Bryant RV, Dong Y, Maaser C, Kucharzik T, Maconi G, *et al.* How to perform gastrointestinal ultrasound: Anatomy and normal findings. World J Gastroenterol 2017;23:6931-41.
6. Strobel D, Goertz RS, Bernatik T. Diagnostics in inflammatory bowel disease: Ultrasound. World J Gastroenterol 2011;17:3192-7.
7. Maconi G, Nylund K, Ripolles T, Calabrese E, Dirks K, Dietrich CF, *et al.* EFSUMB recommendations and clinical guidelines for intestinal ultrasound (GIUS) in inflammatory bowel diseases. Ultraschall Med 2018;39:304-17.
8. Nylund K, Hausken T, Ødegaard S, Eide GE, Gilja OH. Gastrointestinal wall thickness measured with transabdominal ultrasonography and its relationship to demographic factors in healthy subjects. Ultraschall Med 2012;33:E225-32.
9. Christian M, Giovanni M, Torsten K, Mariangela A. Ultrasonography in inflammatory bowel disease – So far we are? United European Gastroenterol J 2022;10:225-32.
10. Calabrese E, Kucharzik T, Maaser C, Maconi G, Strobel D, Wilson SR, *et al.* Real-time interobserver agreement in bowel ultrasonography for diagnostic assessment in patients with Crohn's disease: An international multicenter study. Inflamm Bowel Dis 2018;24:2001-6.
11. Sævik F, Eriksen R, Eide GE, Gilja OH, Nylund K. Development and validation of a simple ultrasound activity score for Crohn's disease. J Crohns Colitis 2021;15:115-24.
12. Calabrese E, Maaser C, Zorzi F, Kannengiesser K, Hanauer SB, Bruining DH, *et al.* Bowel ultrasonography in the management of Crohn's disease. A review with recommendations of an international panel of experts. Inflamm Bowel Dis 2016;22:1168-83.

13. Ding SS, Fang Y, Wan J, Zhao CK, Xiang LH, Liu H, *et al.* Usefulness of strain elastography, ARFI imaging, and point shear wave elastography for the assessment of Crohn disease strictures. J Ultrasound Med 2019;38:2861-70.
14. Sporea I, Popescu A. Ultrasound examination of the normal gastrointestinal tract. Med Ultrason 2010;12:349-52.
15. Kucharzik T, Kannengiesser K, Petersen F. The use of ultrasound in inflammatory bowel disease. Ann Gastroenterol 2017;30:135-44.
16. Sagami S, Kobayashi T, Miyatani Y, Okabayashi S, Yamazaki H, Takada T, *et al.* Accuracy of ultrasound for evaluation of colorectal segments in patients with inflammatory bowel diseases: A systematic review and meta-analysis. Clin Gastroenterol Hepatol 2021;19:908-21.e6.
17. Ellrichmann M, Wietzke-Braun P, Dhar S, Nikolaus S, Arlt A, Bethge J, *et al.* Endoscopic ultrasound of the colon for the differentiation of Crohn's disease and ulcerative colitis in comparison with healthy controls. Aliment Pharmacol Ther 2014;39:823-33.
18. Nuernberg D, Ignee A, Dietrich CF. Current status of ultrasound in gastroenterology – Bowel and upper gastrointestinal tract – Part 2. Z Gastroenterol 2008;46:355-66.
19. Spalinger J, Patriquin H, Miron MC, Marx G, Herzog D, Dubois J, *et al.* Doppler US in patients with Crohn disease: Vessel density in the diseased bowel reflects disease activity. Radiology 2000;217:787-91.
20. Limberg B. Diagnosis of chronic inflammatory bowel disease by ultrasonography. Z Gastroenterol 1999;37:495-508.
21. Goodsall TM, Jairath V, Feagan BG, Parker CE, Nguyen TM, Guizzetti L, *et al.* Standardisation of intestinal ultrasound scoring in clinical trials for luminal Crohn's disease. Aliment Pharmacol Ther 2021;53:873-86.
22. Maconi G, Carsana L, Fociani P, Sampietro GM, Ardizzone S, Cristaldi M, *et al.* Small bowel stenosis in Crohn's disease: Clinical, biochemical and ultrasonographic evaluation of histological features. Aliment Pharmacol Ther 2003;18:749-56.
23. Geboes KP, Cabooter L, Geboes K. Contribution of morphology for the comprehension of mechanisms of fibrosis in inflammatory enterocolitis. Acta Gastroenterol Belg 2000;63:371-6.
24. Maconi G, Di Sabatino A, Ardizzone S, Greco S, Colombo E, Russo A, *et al.* Prevalence and clinical significance of sonographic detection of enlarged regional lymph nodes in Crohn's disease. Scand J Gastroenterol 2005;40:1328-33.
25. Calabrese E, Zorzi F, Pallone F. Ultrasound in Crohn's disease. Curr Drug Targets 2012;13:1224-33.
26. Castiglione F, Bucci L, Pesce G, De Palma GD, Camera L, Cipolletta F, *et al.* Oral contrast-enhanced sonography for the diagnosis and grading of postsurgical recurrence of Crohn's disease. Inflamm Bowel Dis 2008;14:1240-5.
27. Medellin A, Merrill C, Wilson SR. Role of contrast-enhanced ultrasound in evaluation of the bowel. Abdom Radiol (NY) 2018;43:918-33.
28. Wilson SR, Burns PN. Microbubble-enhanced US in body imaging: What role? Radiology 2010;257:24-39.
29. Ślósarz D, Poniewierka E, Neubauer K, Kempiński R. Ultrasound elastography in the assessment of the intestinal changes in inflammatory bowel disease-systematic review. J Clin Med 2021;10:4044.
30. Chen YJ, Mao R, Li XH, Cao QH, Chen ZH, Liu BX, *et al.* Real-Time shear wave ultrasound elastography differentiates fibrotic from inflammatory strictures in patients with Crohn's disease. Inflamm Bowel Dis 2018;24:2183-90.
31. Limantoro I, Lee AF, Rosenbaum DG. Spectrum of bowel wall thickening on ultrasound with pathological correlation in children. Pediatr Radiol 2022;52:1786-98.
32. Kerri L Novak, Kim Nylund, Christian Maaser, Frauke Petersen, Torsten Kucharzik, Cathy Lu, *et al.* Expert consensus on optimal acquisition and development of the international bowel ultrasound segmental activity score [IBUS-SAS]: A reliability and inter-rater variability study on intestinal ultrasonography in Crohn's disease. J Crohns Colitis 2021;15:609-16.
33. Calabrese E, Petruzziello C, Onali S, Condino G, Zorzi F, Pallone F, *et al.* Severity of postoperative recurrence in Crohn's disease: Correlation between endoscopic and sonographic findings. Inflamm Bowel Dis 2009;15:1635-42.
34. Rigazio C, Ercole E, Laudi C, Daperno M, Lavagna A, Crocella L, *et al.* Abdominal bowel ultrasound can predict the risk of surgery in Crohn's disease: Proposal of an ultrasonographic score. Scand J Gastroenterol 2009;44:585-93.
35. Castiglione F, Testa A, Rea M, De Palma GD, Diaferia M, Musto D, *et al.* Transmural healing evaluated by bowel sonography in patients with Crohn's disease on maintenance treatment with biologics. Inflamm Bowel Dis 2013;19:1928-34.
36. Allocca M, Fiorino G, Bonifacio C, Furfaro F, Gilardi D, Argollo M, *et al.* Comparative accuracy of bowel ultrasound versus magnetic resonance enterography in combination with colonoscopy in assessing Crohn's disease and guiding clinical decision-making. J Crohns Colitis 2018;12:1280-7.
37. Kucharzik T, Wittig BM, Helwig U, Börner N, Rössler A, Rath S, *et al.* Use of intestinal ultrasound to monitor Crohn's disease activity. Clin Gastroenterol Hepatol 2017;15:535-42.e2.
38. Maaser C, Petersen F, Helwig U, Fischer I, Roessler A, Rath S, *et al.* Intestinal ultrasound for monitoring therapeutic response in patients with ulcerative colitis: Results from the TRUST & UC study. Gut 2020;69:1629-36.
39. Allocca M, Filippi E, Costantino A, Bonovas S, Fiorino G, Furfaro F, *et al.* Milan ultrasound criteria are accurate in assessing disease activity in ulcerative colitis: External validation. United European Gastroenterol J 2021;9:438-42.
40. De Voogd F, Wilkens R, Gecse K, Allocca M, Novak K, Lu C, *et al.* A reliability study: Strong inter-observer agreement of an expert panel for intestinal ultrasound in ulcerative colitis. J Crohns Colitis 2021;15:1284-90.