REVIEW

OPEN

The use of ultrasound in colonic and perianal diseases

Anna Fábián, Renáta Bor and Zoltán Szepes

Purpose of review
To revise recent literature findings regarding the use of ultrasound in colonic and perianal diseases by focusing particularly on its feasibility in inflammatory bowel diseases (IBD), colorectal neoplastic lesions, and perineal diseases, with further highlight on interventional capabilities.

Recent findings
Treat-to-target approach in IBD raised an interest in intestinal ultrasound (IUS) for monitoring bowel activity considering its noninvasive nature, low costs, and well tolerability. New IUS indices have been developed with ever better methodologies and are at various stage of validation. A standardized over-the-wire technique for colonic US using a flexible overtube enables endoscopic ultrasound (EUS)-guided tissue sampling beyond the rectum, and forward-viewing radial-array echoendoscopes can assist identification of early neoplastic lesions in proximal colon. Intraoperative ultrasound and contrast-enhanced ultrasound carry an additional diagnostic value compared to conventional preoperative imaging modalities in detecting colorectal cancer liver metastases (CRLM).

Summary
The feasibility of IUS in monitoring IBD activity is supported by growing evidence, but uniform IUS indices are still lacking. Recent advancements in EUS are expanding capabilities for determining depth of invasion of colorectal neoplasms, tissue sampling, and EUS-guided interventions to the entire colon. Ultrasonography can be a valuable tool in CRLM diagnostics as well.

Keywords
colorectal neoplasia, endoscopic ultrasound, inflammatory bowel diseases, intestinal ultrasound

INTRODUCTION

Ultrasound (US) has often been overshadowed in the diagnostic process of colonic and perianal diseases by other imaging modalities, such as colonoscopy, computed tomography (CT), and magnetic resonance imaging (MRI) based on their higher diagnostic yield. However, drawbacks and limitations of these modalities are also getting more attention nowadays: invasiveness and poor tolerability of repeated colonoscopies may increase patient burdens, especially in monitoring disease activity of inflammatory bowel diseases (IBD). Risks related to ionizing radiation limits the usage of CT in pediatric and pregnant population, and variabilities in local access to MRI and related costs should also be considered. Ultrasonography on the other hand is a cheap, widely available, noninvasive imaging modality which is well tolerated by patients, and does not require specific preparation and contrast media. Additionally, developments in endoscopic ultrasound (EUS) have broadened its indications, with promising results in distinguishing benign and early malignant lesions, cancer staging, and EUS-guided sampling of subepithelial and extraluminal lesions beyond the rectum, as well as various minimal-invasive interventions. Ultrasonography has also been gaining ground in the diagnosis of colorectal cancer liver metastases (CRLM): intraoperative ultrasound (IOUS) can identify CRLMs undetected by preoperative CT or MRI and alter the therapeutic strategy. IOUS can further serve as a guidance to alternative treatment methods of CRLM.

Department of Internal Medicine, Szent-Györgyi Albert Medical School, University of Szeged, Szeged, Hungary

Correspondence to Anna Fábián, MD, PhD, Department of Internal Medicine, Szent-Györgyi Albert Medical School, University of Szeged, Kálvária sgt. 57, Szeged H-6725, Hungary. Tel: +36 62 545 189; e-mail: fabiananna9@gmail.com

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KEY POINTS

- The treat-to-target approach in inflammatory bowel diseases induced a paradigm shift in the preferred imaging modality for disease monitoring, focusing more on intestinal ultrasound considering its noninvasive nature, low costs, and well tolerability.
- An optimal intestinal ultrasound index to reflect bowel activity is yet to be determined.
- Recently proposed colonic intubation techniques, and newly developed endoscopic ultrasound (EUS) devices and modalities are now expanding capabilities for determining depth of invasion of colorectal neoplasms, tissue sampling, and EUS-guided interventions to the entire colon.
- Intraoperative ultrasound and contrast-enhanced ultrasound carry an additional diagnostic value compared to conventional preoperative imaging modalities in detecting colorectal cancer liver metastases that may alter therapeutic strategy, but their exact place in the diagnostic algorithm is yet to be determined.

This review aims to revise recent literature findings (published between 01/01/2021 and 30/06/2022) regarding the use of US in colonic and perianal diseases by focusing particularly on its feasibility in IBD, colorectal neoplastic lesions, and perineal diseases, with further highlight on interventional capabilities.

FEASIBILITY OF INTESTINAL ULTRASOUND IN MONITORING INFLAMMATORY BOWEL DISEASES' ACTIVITY

The treat-to-target approach in IBD requires tight monitoring of disease activity. For this purpose, a simple, noninvasive tool is required that is well tolerable and acceptable for patients, even if repeated examinations are necessary. The costs and significant patient burden related to repeated colonoscopies and limited access to magnetic resonance enterography in Crohn's disease (CD), have been putting the spotlight to intestinal ultrasound (IUS) recently [1▪,2▪▪,3▪▪,4▪,5▪▪,6▪,7▪▪,8▪].

TECHNICAL ASPECTS OF INTESTINAL ULTRASOUND

IUS allows systematic scanning of the entire abdomen: after gaining panoramic view with a lower frequency (1–5 MHz) convex probe to localize pathologic conditions, detailed examination of the bowel wall is performed with higher frequency (4–8 MHz) linear probes providing a five-layer pattern (Table 1) [2▪▪,9]. A recent ECCO-ESGAR topical review [10▪▪] providing guidance on reporting of IUS parameters [2▪▪,11] (Table 2) recommends reporting of thickness of the most involved small bowel and/or colonic segment (bowel wall thickness, BWT) with a 3 mm cut-off value indicating mural inflammation, as well as disruptions of bowel wall. Intestinal vascularization should be reported by a semi-quantitative grading based on color Doppler. To overcome visual vascular scoring's dependency on operator experience, device quality, and patients' characteristics (body weight, thickness of subcutaneous tissue), a newly developed software Color Quantification can quantify the tissue vascularization by calculating the ratio of the number of pixels in the whole region of interest and that of pixels colored by color Doppler. Utilities of this technique were observed at the ascending and descending colon, and terminal ileum [8▪]. Alternatively, additional structure-based IUS parameters, such as the submucosa index (defined as the percentage of submucosal thickness in the total BWT) can be used instead of bowel wall flow (BWF) to estimate endoscopic remission [6▪].

Table 1. Layers of the bowel wall as seen with intestinal ultrasound

Layer	Ultrasound appearance
Mucosal interface to the bowel lumen	Hyperechoic
Deep mucosa with muscularis propria	Hypoechoic
Submucosa	Hyperechoic
Muscularis propria	Hypoechoic
Adventitia or serosa	Hyperechoic

Visibility of intestinal wall depends on anatomical localization: IUS has a higher diagnostic accuracy for detecting colonic than rectal inflammation based on meta-analytic calculations evaluating data from 84 patients with Crohn disease (CD) and 420 patients with ulcerative colitis (UC) [7▪▪]. Combination of transabdominal and transperineal US can further improve accuracy and might even have good utility for assessing prepouch ileitis and pouchitis [12▪].

NEW ULTRASOUND INDICES ASSESSING ULCERATIVE COLITIS DISEASE ACTIVITY

Limitations of BWT as a sole parameter in the assessment of UC activity (due to co-existence and similar IUS appearance of acute and chronic changes in the

Table 2. Intestinal ultrasound parameters

Parameter	Definition or features [2▪▪,11]
Bowel wall thickness (BWT)	Distance between the mucosal interface and the serosa–muscularis propria interface (mm); normal values up to 3 mm (both in colon and ileum)
Bowel wall pattern (BWP)	Multilayered (normal)/disrupted (focally [≤3 cm] or extensively [>3 cm])/lost
Bowel wall flow (BWF)	Presence of vascular signals detected with color or power Doppler (no blood flow/small, circular intramural vascular signal/longer linear intramural vascular signal/longer stretches of vascular signal with extension into mesentery)
Ulceration	Depression in the mucosal layer
Stricture	Wall thickening with narrowed lumen with or without proximal loop dilation
Fistula	Hypoechoic tract with or without hypoechoic content
Abscess	Anechoic lesion with irregular wall without vascular signs
Inflammatory mass	Irregular hypoechoic lesion with vascular signs
Colonic haustration	Absent/present
Intestinal motility	Absent/reduced/present/increased
Free abdominal fluid	Anechoic lesion at certain locations (between bowel loops, Douglas pouch etc.)
Enlarged mesenteric lymph nodes	Lymph nodes greater than 4 mm in short axis diameter, located in the mesentery adjacent to an affected segment
Mesenteric hypertrophy	Hyperechoic area around the pathological intestinal tract

bowel wall) [4▪,10▪▪] have resulted in development of new IUS indices [1▪,5▪▪,6▪], such as the Milan Ultrasound Criteria (MUC, Table 3) [1▪]. External validation of this score has recently been reported, with 43 patients undergoing IUS and colonoscopy in a tertiary referral center. Authors found an MUC score >6.2 discriminated patients with active vs. nonactive UC with a sensitivity of 0.85 (95% confidence interval [CI] 0.66–0.96) and specificity of 0.94 (95% CI 0.70–0.99) [1▪].

Nevertheless, some concerns were raised about methodologies used in development of most IUS indices, i.e., predefining index parameters and cut-offs before comparison to reference standard. Recently, a new IUS index for UC have been developed by comparing IUS parameters and endoscopic results for each colonic segment (except the rectum) evaluating 207 colonic segments and selecting parameters to be best correlated with endoscopic disease activity (Table 3). The reason behind the use of multiple BWT cut-offs is to enable disease activity stratification according to different Mayo scores. The index is currently being validated in prospective studies [5▪▪].

Table 3. Newly developed ultrasound indices for ulcerative colitis

Milan ultrasound criteria [1▪]		UC-IUS index [5▪▪]	
Parameter	**Values**	**Parameter**	**Values**
BWT	Average of 3 measurements, normal values ≤3 mm	BWT	1 = BWT >2 mm, 2 = BWT >3 mm, 3 = BWT >4 mm
BWP	0 = normal, multilayered, 1 = prevalently hypoechogenic, 2 = prevalently hyperechogenic, 3 = lost	Doppler signal	1 = spots, 2 = stretches
BWF	0 = absence, or 1 = presence of blood signals at color Doppler	Abnormal haustrations	
Enlarged mesenteric lymph nodes (short axis >5 mm)		Fat wrapping	
Mesenteric hypertrophy (hyperechoic area surrounding pathologic intestinal tract)			

BWF, bowel wall flow; BWP, bowel wall pattern; BWT, bowel wall thickness.

FEASIBILITY OF INTESTINAL ULTRASOUND IN DETERMINING ACTIVITY AND MONITORING CROHN'S DISEASE

Recently, a noninvasive quantitative ultrasound score (bowel ultrasound score, BUSS) has been developed based on comparison of baseline IUS parameters (incl. BWT, bowel wall pattern [BWP], BWF, stricture, fistula, abscess, mesenteric lymph node enlargement, and mesenteric hypertrophy) and endoscopic activity in a large prospective cohort of 225 patients with CD. A BUSS cut-off of 3.52 (odds ratio [OR] 6.97; 95% CI 2.87–16.93) and the presence of at least 1 complication (stricture, fistula, abscess) at baseline IUS was associated with worse outcome throughout a 12-month period. Nevertheless, lack of external validation of BUSS was a study limitation [3▪▪].

Contrast media (intravenous or oral) use can improve IUS's accuracy in CD, but increased exam duration, and invasiveness and complexity of the process can limit its use in everyday practice [2▪▪,13▪].

IUS might also be able to monitor biologics-induced bowel activity improvement in CD based on results from a multicenter study including 188 patients. In this study, BWT improved significantly from baseline at 3 and 12 months, with normalization of all IUS parameters (transmural healing, TH) in 27.5% at 12 months. A greater BWT at baseline was associated with lower risk of TH at 3 and 12 months [14▪▪]. Recently, an expert consensus statement has also provided definitions for key parameters for IUS response in IBD [15▪].

ULTRASONOGRAPHY IN PERIANAL DISEASES

Accurate preoperative imaging of perianal fistulas is essential for their optimal management. A recent systematic review comparing the two primary imaging modalities (pelvic MRI and endoanal ultrasound [EAUS]) found the superiority of pelvic MRI over EAUS in most articles [16▪]. Nevertheless, EAUS can identify intersphincteric and transsphincteric fistulas, and internal fistula opening with high sensitivity and specificity, and results can be further improved with implementation of 3D-technique and hydrogen peroxide enhancement [17,18]. The latter may not be without risks as a case of hydrogen peroxide-induced proctitis after EAUS has recently been reported [19▪].

Although EAUS is the gold-standard modality of sphincter muscles assessment in fecal incontinence, considering its invasiveness, perianal ultrasound might be a good, noninvasive alternative suiting patient preference [20].

Ultrasonography might also play a role in the treatment of perianal abscesses: although surgery and percutaneous drainage are the usual approaches, cases of EUS-guided transrectal drainage have also been reported with good results [21,22].

ENDOSCOPIC ULTRASOUND-GUIDED INTERVENTIONS

Curvilinear array ultrasound transducers enable tissue sampling and therapeutic interventions with EUS. These capabilities had long been limited to the rectum as colonic intubation and maneuvering with these transducers is technically challenging. Recently, a standardized over-the-wire technique for colonic US using a flexible overtube has been reported with promising results: EUS-guided fine-needle aspiration (EUS-FNA) of lesions located proximal to the rectum was performed successfully in 13 patients with a diagnostic yield of 60% [23▪▪]. Another successful EUS-FNA sampling of a descending colon schwannoma was reported with a similar colonic intubation method [24].

Other recently reported EUS-guided therapeutic interventions are pushing more the boundaries. Perregaard *et al.* [25▪▪] demonstrated their technique of lateral internal sphincterotomy using EAUS with results from 148 patients, and cases of EUS-guided colonic anastomosis formation were also reported for inoperable patients with more complex/distal small bowel obstruction where standard techniques are not possible. Technical notes are also added, like filling the colon with fluid, choosing the access point based on the shortest distance to the colon, and potential necessity of a forward viewing echoendoscope [26▪].

COLORECTAL CANCER

The main directions in the spotlight of recent colorectal cancer (CRC)-related US research are determining depth of invasion of early colorectal neoplasms (also beyond the rectum) and setting up the most accurate diagnosis of CRLM to optimize management strategy and prevent recurrence, as well as developing alternative US-guided modalities for improving CRLM's treatment.

DETERMINING DEPTH OF INVASION OF COLORECTAL NEOPLASMS BY NEW ENDOSCOPIC ULTRASOUND MODALITIES

Although advancements in endoscopic treatments of early colorectal cancers allow more patients to be treated endoscopically, precise preprocedural assessment of depth of invasion and careful patient selection is necessary. Magnifying endoscopy with optical enhancement, dye-spraying, and EUS might

assist determining depth of invasion. However, technical difficulties regarding deep colonic insertion of oblique-viewing echoendoscopes and attenuation arising due to high-frequency ultrasound probe use limited their use in proximal colonic lesions. The newly developed forward-viewing radial-array echoendoscopes (FRE) might solve this problem. Their ability to predict depth of invasion of early carcinomas was investigated in 110 patients: FRE insertion was technically successful in all cases with no difference in correct prediction rate, accuracy, specificity, positive and negative predictive value, and frequency of unevaluable cases compared to the pit pattern method. FRE also offered higher sensitivity in predicting deep pT1b or deeper invasion (97.0% vs. 81.3%, $P = 0.048$), without accuracy being affected by lesion size [27▪▪]. However, in protruded-type lesions, addition of another imaging modality might be necessary, such as EUS elastography (EUS-EG) which quantifies the relative hardness of different tissues.

The diagnostic yield of EUS-EG, magnifying chromoendoscopy, and EUS was found to be similar in superficial colorectal neoplasms, with substantial inter- and intra-observer agreements of elastic scores of colorectal neoplasms, even for nonexpert endoscopists [28▪▪]. Determination of sound speed correction, a noninvasive, nonoperator dependent modality providing absolute quantification of tissue hardness is an additional promising option. Its cutoffs for the diagnosis of a colorectal neoplasm, and that of depth of invasion deeper than that of muscularis propria were determined based on results from 40 patients [29▪].

A newly developed deep neural network-based computer-aided diagnosis system might also aid distinction of benign and early malignant colorectal neoplasms. The system was validated by a multiview endorectal ultrasound image dataset of CRC, and surpassed expert diagnosis in accuracy, sensitivity, and specificity [30▪▪].

FEASIBILITY OF INTRAOPERATIVE ULTRASOUND IN THE DIAGNOSIS OF LIVER METASTASES OF COLORECTAL CANCER

Despite accurate preoperative staging with contrast-enhanced CT scan and liver-specific contrast enhanced MRI, intraoperative open liver ultrasound can identify additional CRLM during surgery that may alter surgical strategy and negatively affect long-term outcomes. Contrast enhancement can further improve sensitivity and positive predictive value: two recent meta-analysis (with a slightly different study selection) evaluating outcomes of contrast enhanced IOUS (CE-IOUS) for patients with CRLM undergoing surgery concluded superiority of CE-IOUS over multidetector CT, MRI, and IOUS [31▪,32▪]. The potential reasons include CE-IOUS's higher spatial resolution enabling the identification of smaller lesions, reduction of artifacts from overlying structures due to direct probe placement on the liver surface, and contrast agent use that assists the differentiation of metastatic lesions [31▪]. Prospective analysis of 264 CRLM from 47 high tumor load patients revealed that a combination of palpation, IOUS, and CE-IOUS was accurate in 98%, compared to 63%, 71%, and 92% accuracy of preoperative CEUS, CT, and MRI performed within 2 weeks, respectively [33▪▪].

The dramatic increase of laparoscopically performed liver resections might also require application of laparoscopic ultrasound; its sensitivity in CRLM detection is superior to that of MRI (93.1% vs. 85.6%, respectively), with similar specificities (96.5% vs. 98.6%, respectively). New nodules might be found in 10.9% of patients, resulting in intraoperative surgical strategy modification in 13% [34▪].

To improve reliability of preoperative CRLM diagnostics, CEUS might also be recommended when CT or MRI findings are inconclusive, based on results from a prospective study comparing diagnostic accuracy of preoperative CEUS, CT, and MRI. An additional 2.7% of CRLMs were reported with CEUS compared to CT that altered the therapeutic strategy [35▪▪].

ALTERNATIVE ULTRASONOGRAPHY-GUIDED TREATMENT OPTIONS FOR CRLM

Unresectable lesions in 85–90% of patients with CRLM may require application of chemotherapy and thermal ablation techniques (e.g. radiofrequency or microwave ablation [MWA] – performed percutaneously, or with IOUS-guidance during open surgery) alone or besides hepatectomy. IOUS-guided open MWA combined with hepatectomy has similar oncological outcomes as hepatectomy alone [36▪], and US-guided percutaneous MWA has similar overall long-term survival rates, fewer complications and shorter hospital stay, yet worse local tumor progression free survival rates than CRLM resection[37▪]. A risk classification system has also been developed to facilitate personalized assessment of intrahepatic progression free survival for patients receiving US-guided percutaneous MWA for CRLM [38▪▪].

High-intensity focused ultrasound treatment focusing US waves on the lesions and inducing targeted hyperthermia can be a treatment alternative. To date, a phase I clinical trial found it safe and

effective providing good tumor response, but being applied as combined treatment, the risk of overestimation of efficacy must be acknowledged [39▪]; another multicenter retrospective study revealed an objective response rate of 97.7% with a median overall survival of 31 months, without any adverse events [40].

DIVERTICULAR DISEASE

Ultrasonography may serve as an initial diagnostic tool in diseases potentially requiring emergency surgery. It can differentiate complicated and noncomplicated acute colonic diverticulitis (as compared to CT) with a sensitivity and specificity of 84% and 95.8%, respectively; most cases falsely classified as uncomplicated by US prove to be stage 1A on CT scan [41].

CONCLUSION

The treat-to-target approach in IBD has induced a paradigm shift in disease monitoring with more focus on IUS considering its noninvasive nature, low costs, and well tolerability. Although guidance on reporting of IUS parameters is now available [10▪▪], and several promising indices have been developed with ever better methodologies, an optimal IUS index to reflect bowel activity is yet to be defined. Rising interest in IUS also creates a demand for a training curriculum [11]. Knowledge and skills expected from newly certified IUS practitioners has recently been established based on an international, expert consensus [42▪▪].

Recently proposed colonic intubation techniques, newly developed EUS devices and modalities are now expanding capabilities for determining depth of colorectal neoplasia invasion, tissue sampling, and EUS-guided interventions to the entire colon. However, further evidence from larger cohort studies would still be necessary to confirm promising results. Recent data also supports the benefits of IOUS, and CEUS in detecting additional CRLM after preoperative imaging, but their exact place in the diagnostic algorithm is yet to be defined.

Future research will hopefully clarify these issues and might also focus on the development of new devices with multiple capabilities [43], techniques allowing precise assessment of lymphatic involvement of CRC [44▪], and molecular imaging that might enable predication of response to anti-TNF therapy in IBD [45▪].

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
- ▪▪ of outstanding interest

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