

Positioning Ultrasonography Into Clinical Practice for the Management of Crohn's Disease

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Abstract: Over the past few years, the technical evolution of ultrasound equipment, the use of oral and intravenous contrast agents, and an increase in the expertise of operators have enhanced the role that ultrasonography plays in the assessment of the gastrointestinal tract. For patients with chronic inflammatory conditions, particularly Crohn's disease, it has been suggested that ultrasonography can be used not only for diagnostic purposes but also in disease management. These developments are reviewed in this article.

The investigation of diseases of the gastrointestinal tract, including those involving the liver and the pancreas, represents one of the most important applications of ultrasonography. In recent years, bowel ultrasonography has gained in acceptance owing to technologically advanced equipment that has improved resolution capability, with good cross-sectional imaging of the gut wall and display of the transmural aspects of inflammation. In addition, the possibility of assessing intestinal morphology and motility during real-time ultrasound observation with no discomfort for the patient makes ultrasonography a suitable diagnostic procedure in an acute setting, such as intestinal obstruction, as well as in chronic conditions, such as inflammatory bowel disease.

Ultrasonography in Crohn's Disease

Crohn's disease (CD) is an inflammatory bowel disease typically characterized by variable disease activity, often with repeated periods of relapse and remission. CD may involve various portions of the gastrointestinal tract, although ileal and colonic involvement is most frequent. CD is a transmural, progressive, and destructive disease leading to irreversible bowel damage characterized by stenosis of the intestinal lumen and penetrating lesions such as fistulae and abscesses. The mesentery is often thickened, surrounding the involved walls and containing enlarged lymph nodes.

A noninvasive, low-cost, and repeatable diagnostic test would be of interest to clinicians and patients in order to reduce the num-

Keywords

Ultrasonography, Crohn's disease, cross-sectional imaging techniques, contrast agents



Figure 1. Bowel ultrasonography in a 20-year-old man with Crohn's disease showing bowel wall thickness of the terminal ileum.

ber of invasive and expensive endoscopies and/or cross-sectional imaging studies (computed tomography [CT] or magnetic resonance enterography/enteroclysis) that are undertaken to diagnose suspected CD, determine the extent and severity of mucosal inflammation, evaluate disease activity, follow the course of disease during therapy, and monitor postoperative recurrence.¹ The technical evolution of ultrasound equipment, combined with the use of color or power Doppler imaging and intravenous contrast-enhanced ultrasonography (CEUS), now allows ultrasound to provide detailed information on mural activity. In addition, the use of oral contrast agents such as polyethylene glycol (PEG) solution in small-intestine contrast ultrasonography (SICUS) has been proposed as a way to improve the detection of CD lesions.¹

Several studies have demonstrated that bowel ultrasonography accurately reveals and characterizes inflammation of the bowel walls and assesses peri-gut abnormalities (Figure 1).^{1,2} In CD, not only have these sonographic capabilities been used for purely diagnostic purposes, they also have been proposed for use in the management of the disease.^{3,4} In a systematic review, Panés and colleagues⁵ demonstrated that cross-sectional imaging techniques (ultrasonography, CT, and magnetic resonance imaging [MRI]) have a high degree of accuracy for evaluating suspected and established CD, and reliably measure disease severity and complications. Thus, the authors proposed that bowel ultrasonography and MRI may offer the possibility of monitoring disease progression. Furthermore, the recent European Crohn's and Colitis Organization guidelines note that bowel ultrasonography is an accu-

rate technique for the assessment of CD.⁶ However, it should be kept in mind that bowel ultrasonography is an operator-dependent technique and that local expertise may have a significant influence on its accuracy. Nevertheless, this technique is commonly used in all inflammatory bowel disease treatment centers because it is noninvasive, inexpensive, and radiation-free and because it has shown high accuracy using reference standards.⁷⁻¹⁰

The accuracy of ultrasonography in detecting and localizing CD lesions within the bowel has been assessed in several studies.^{7,11-13} Most of these studies have agreed that ultrasonography is highly sensitive (approximately 90%) in detecting ileal lesions, but less accurate in detecting lesions located in the upper small bowel and rectum. The accuracy of the detection of CD lesions in the proximal small bowel can be significantly improved with the use of oral contrast agents, whereas the sensitivity in detecting ileal and colonic lesions is comparable to that of conventional oral contrast ultrasonography.¹⁴ With regard to the accuracy of assessing the length of small bowel involvement, different researchers have shown that the extent of pathologic bowel wall thickening detected by bowel ultrasonography is significantly correlated with the extent of ileal CD, as measured by radiology and surgery.^{15,16} The use of oral contrast agents has been shown to be of value in accurately defining the extent of diseased ileal walls, which has significantly increased the correlation between the ultrasound-detected and radiographically detected extent of ileal disease and reduced interobserver variability in interpreting such evaluations.¹⁴ A recent study demonstrated that SICUS and CT enteroclysis correlated in the determination of bowel wall thickness ($r=0.79$) and disease extent ($r=0.89$; $P<.0001$ for both).¹⁰ These findings suggest that SICUS may be used as an alternative to invasive procedures to assess ileal lesions and monitor their progression in CD patients.

The use of bowel ultrasonography for direct evaluation of inflammatory activity in CD has been suggested, but its role remains controversial. Attempts have been made to correlate bowel wall thickness with disease activity, particularly with the Crohn's Disease Activity Index. According to Maconi and colleagues,⁷ the degree of bowel wall thickening and the extent of the thickened bowel wall on ultrasonography showed a significant but weak direct correlation between these features and clinical and biochemical parameters.

In addition, the use of power Doppler ultrasonography to assess the vascularity of the bowel walls has been evaluated as a quantitative method for determining CD activity. Vascularity within the bowel wall has been evaluated using a subjective scoring system according to the semiquantitative intensity of color signals and/or by the analysis of Doppler curves (measurement of

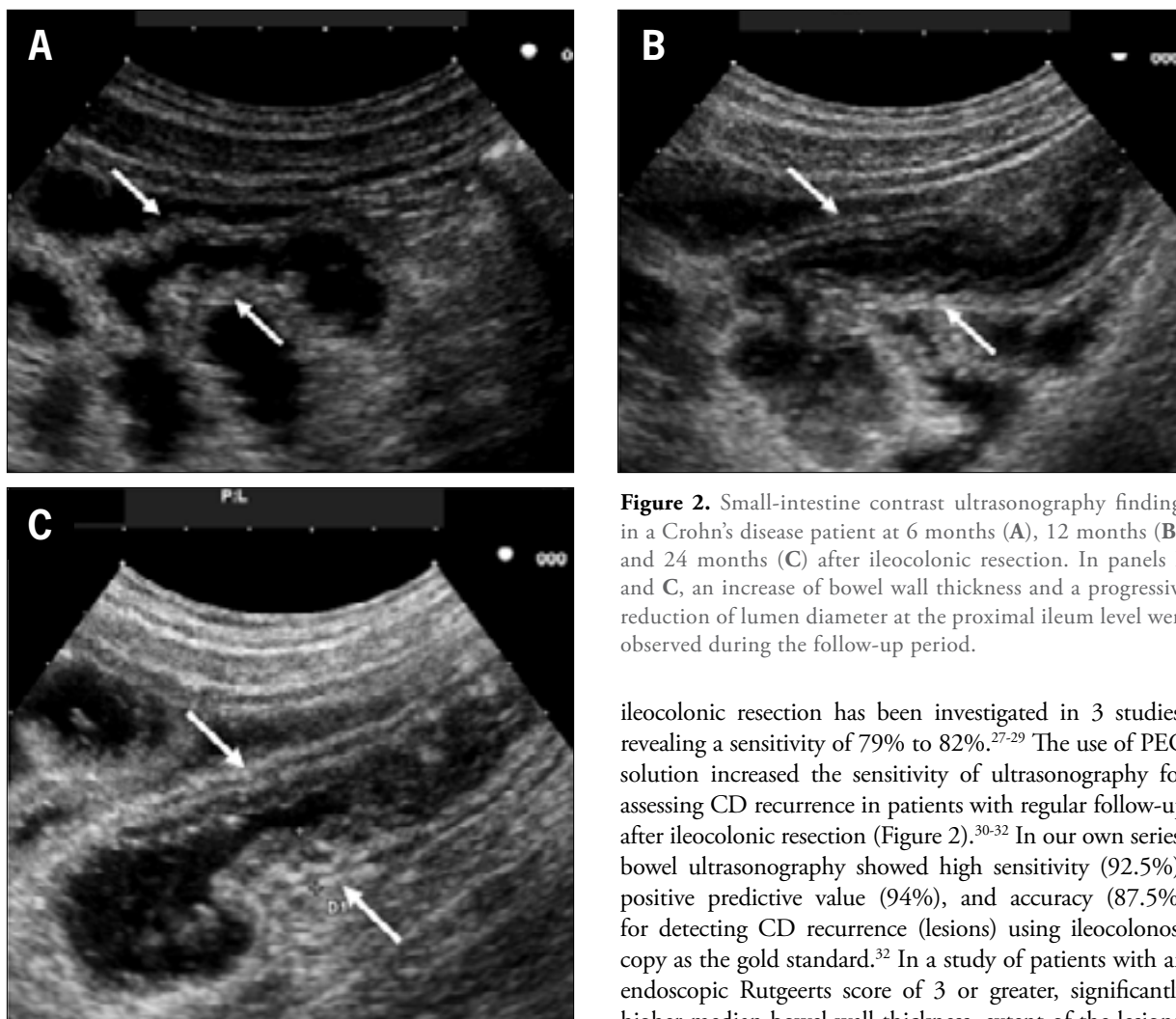


Figure 2. Small-intestine contrast ultrasonography findings in a Crohn's disease patient at 6 months (A), 12 months (B), and 24 months (C) after ileocolonic resection. In panels B and C, an increase of bowel wall thickness and a progressive reduction of lumen diameter at the proximal ileum level were observed during the follow-up period.

resistance—ie, the resistive index) obtained from vessels detected within the bowel wall. In most studies, no correlation between ultrasound parameters and clinical or biochemical activity was observed, whereas vascularity evaluations and endoscopic/radiologic activity often correlated.¹⁷⁻²³ To increase the sensitivity of Doppler ultrasonography in detecting vascularity of the diseased bowel wall, ultrasound intravenous contrast agents have been introduced. However, the effectiveness of intravenous contrast agents with bowel ultrasonography in detecting and assessing CD activity also remains controversial, despite some positive findings.²⁴⁻²⁶ In a prospective study, Migaletto and colleagues²⁵ reported that CEUS showed 93.5% sensitivity, 93.7% specificity, and 93.6% overall accuracy in detecting inflammatory activity, calculated using endoscopy/biopsy as the gold standard. The linear correlation coefficient for CEUS vs the Crohn's Disease Activity Index was 0.74 ($P < .0001$).

The sensitivity of bowel ultrasonography (without oral contrast agents) in identifying endoscopic recurrence after

ileocolonic resection has been investigated in 3 studies, revealing a sensitivity of 79% to 82%.²⁷⁻²⁹ The use of PEG solution increased the sensitivity of ultrasonography for assessing CD recurrence in patients with regular follow-up after ileocolonic resection (Figure 2).³⁰⁻³² In our own series, bowel ultrasonography showed high sensitivity (92.5%), positive predictive value (94%), and accuracy (87.5%) for detecting CD recurrence (lesions) using ileocolonoscopy as the gold standard.³² In a study of patients with an endoscopic Rutgeerts score of 3 or greater, significantly higher median bowel wall thickness, extent of the lesions, and prestenotic dilation were observed in comparison to patients with an endoscopic Rutgeerts score of 2 or less. Accordingly, the lumen diameter was significantly lower in patients with a Rutgeerts score of 3 or greater.³²

Bowel ultrasonography may have a role for predicting disease course and prognosis in CD.^{33,34} In a study, bowel wall thickness was shown to be higher in patients whose bowels were resected within a year after the ultrasonography than in those who did not have the operation, suggesting that bowel thickness (≥ 7 mm) may be independently associated with the risk for surgery.³³ In another study, bowel-wall pattern and thickness were independently and significantly associated with the need for surgery regardless of the presence of intestinal complications or disease activity; Rigazio and colleagues³⁴ developed a semiquantitative ultrasound score that served as a predictor of short-term surgery risk within 1 month.

In a recent study, Castiglione and colleagues³ showed that transmural healing (normalization of bowel wall thickening) could be achieved in approximately 25%

of CD patients after 2 years of maintenance treatment with biologic agents and in a much smaller proportion of patients (4%) treated with traditional immunosuppressants. Our group developed an instrument for assessing small-bowel CD and created a quantitative lesion index using SICUS.³⁵ Our sonographic lesion index for CD (SLIC) takes into account both the extent and severity of small-bowel damage, including stricturing and penetrating lesions as assessed by SICUS. SLIC and consequent severity scale class allocation were based on discrete and continuous variables reflecting transmural intestinal damage. SLIC also offers the potential for evaluating the progression of small-bowel disease over time through serial assessment, including possible changes in disease progression after treatment. SLIC incorporates items considered important by experienced gastroenterologists and can be calculated using a dedicated software program. We conducted a study that showed a significant improvement of SLIC and SLIC subscores after induction therapy with anti-tumor necrosis factor agents. SLIC and SLIC subscores significantly decreased after induction therapy in clinical responders but not in nonresponders.⁴

Acute Conditions in Crohn's Disease

Bowel ultrasonography can be used in severe acute cases of CD with clinical suspicion of obstructive symptoms (such as abdominal pain and vomiting) and septic complications (such as an abdominal mass or fever). In these settings, the use of ultrasonography could be crucial in quickly resolving diagnostic questions and directing physicians to the most appropriate management. The role of point-of-care ultrasonography in CD management is also important because the clinician can manage the patient's symptoms and therapies and can address all of the questions derived from the clinical assessment without other health care providers (eg, a radiologist). The concept of a focused examination implies that the physician is addressing binary questions (eg, does the patient have an abdominal abscess or not?); hence, the concept of an "ultrasound stethoscope" has been derived and is rapidly moving from theory to reality.³⁶

CD flares are often characterized by obstructive symptoms that are usually caused by 2 main events: transmural inflammation and intestinal stricture. Identification of the underlying mechanism is essential for selecting the medical or surgical approach. Kohn and colleagues³⁷ showed that in patients with acute obstructive symptoms, bowel ultrasonography was more highly specific in the detection of obstruction (100%) than enteroclysis (69%), with good overall diagnostic accuracy (89%). Bowel stenosis can be detected by ultrasonography because thickened bowel walls are associated with a narrowed lumen, with the lumen diameter of the proximal loop increased

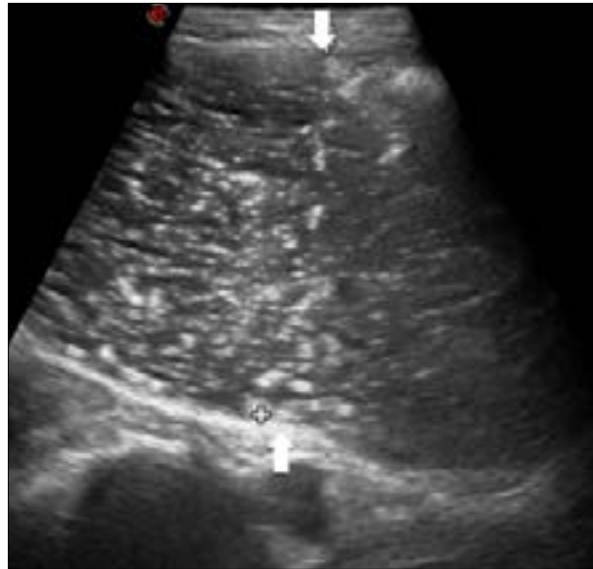


Figure 3. Ileal dilation in a Crohn's disease patient with obstructive symptoms and stenosis of the terminal ileum.

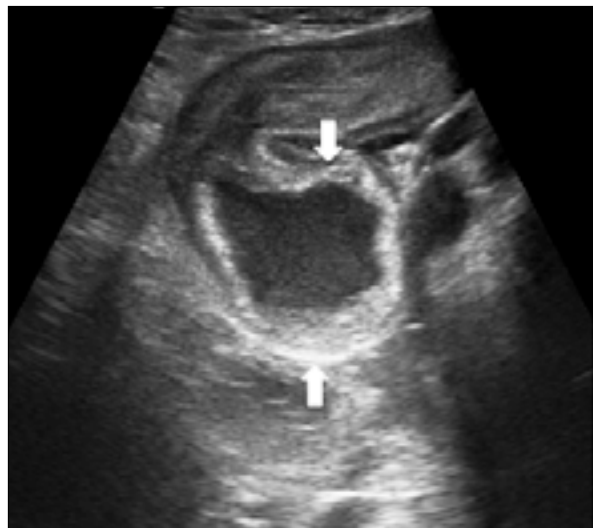


Figure 4. Small-intestine contrast ultrasonography showing stenosis of the terminal ileum with prestenotic dilation in a 50-year-old patient with Crohn's disease.

to greater than 25 mm (Figure 3).¹⁴ Stenoses are often associated with liquid and gas entering the lumen, and increased peristalsis. Bowel ultrasonography currently diagnoses stenosis in 70% to 79% of unselected CD patients and in more than 90% of those with severe bowel stenoses needing surgery, with false-positive diagnoses limited to 7%.^{16,38} The use of PEG during the ultrasound procedure significantly increases accuracy in detecting the presence and number of stenoses (Figure 4).^{14,16} Bowel ultrasonography with an oral contrast agent detected at least 1 stenosis in at least 10% more patients than bowel

ultrasonography without an oral contrast agent, and detected 2 or more stenoses in at least 20% more patients, resulting in a sensitivity of approximately 90% for detection of a single stenosis and greater than 75% for detection of multiple stenoses.¹⁶ Ultrasound assessment of the echo pattern of the bowel wall in strictures may also offer the possibility of discriminating between fibrotic and inflammatory strictures more accurately than clinical and biochemical markers of activity.³⁹ Loss of stratification of the bowel wall, for example, at the level of the stricture suggests an inflammatory nature with a low degree of fibrosis, whereas the presence of stratification suggests a higher degree of fibrosis of the stenosis.³⁹

Intra-abdominal abscesses occur in 12% to 30% of patients with CD, usually as a complication of fistulating disease or as a consequence of surgery (Figure 5). CT and MRI are considered to be nonsurgical gold standards for the diagnosis of CD-related abscesses.⁴⁰ However, bowel ultrasonography is also considered to be a first-level procedure, mainly because it is simple to use. Different studies have prospectively assessed the accuracy of bowel ultrasonography in the detection of intra-abdominal abscesses, showing a mean sensitivity and specificity of 91% and 92%, respectively.^{8,38,41,42} In these studies, bowel ultrasonography showed a higher sensitivity in the detection of superficial intraperitoneal abscesses, whereas the diagnosis of deep pelvic or retroperitoneal abscesses was more difficult owing to the presence of overlying bowel gas.

Findings emerging from preliminary studies showed that the assessment of vascularity within intra-abdominal masses may distinguish inflammatory masses from abscesses, although this must be confirmed by further studies. CEUS is performed after the injection of sulfur hexafluoride-filled microbubbles (SonoVue, Bracco Imaging), and the total duration of the sonographic scan is 2 to 5 minutes longer than that of normal bowel ultrasonography. These observations were confirmed by a recently published retrospective study conducted by Ripollés and colleagues.⁴³ They demonstrated that the specificity of CEUS for abscess diagnosis was 100%. The kappa coefficient between CEUS and other techniques in the diagnosis of phlegmon or abscess was excellent ($\kappa=0.972$). Only in 1 patient did surgery detect a small abscess (<2 cm) within a phlegmon that was not detected by CEUS.

Abdominal pain due to biliary or kidney disease may be associated with CD. If biliary colic or acute cholecystitis is suspected, these conditions are easy to diagnose with ultrasonography as a dilation of the intrahepatic bile ducts, gallbladder hydrops, and large gallbladder stones (Figure 6). In these clinical conditions, ultrasonography can also document the morphologic signs of acute cholecystitis (the presence of thickened walls or fluid peripheral collections), the presence of biliary sludge or pus, infun-

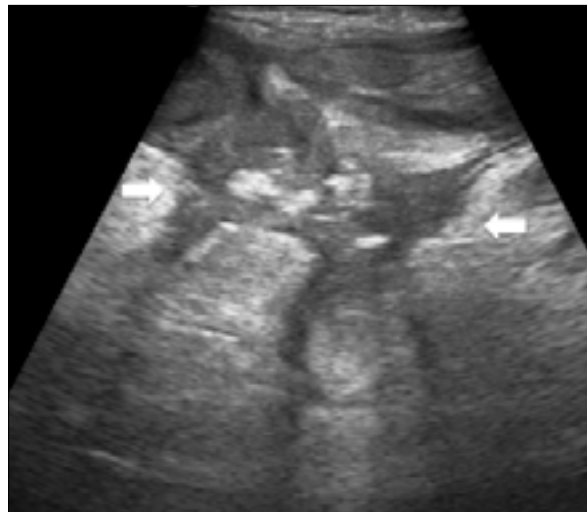


Figure 5. Bowel ultrasonography showing an abscess at the terminal ileum level in a 20-year-old Crohn's disease patient.

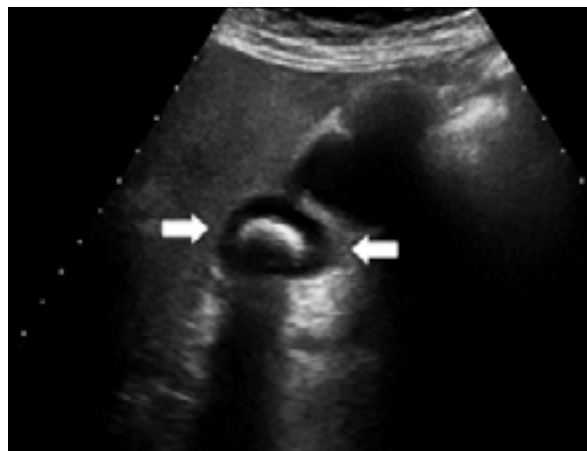


Figure 6. A gallbladder stone in a 30-year-old woman with stricturing Crohn's disease.

dular microlithiasis, and causes of distal common bile duct obstruction.

Similarly, in acute renal failure, a simple ultrasound scan allows for the differential diagnosis of obstructive vs nonobstructive diseases (eg, bladder globe and hydronephrosis), and in cases of renal colic, ultrasonography can better document small stones (Figure 7).³⁶

Conclusion

Bowel ultrasonography with or without intravenous/oral contrast agents has become an alternative first-line imaging procedure in patients with CD. Because the clinical diagnosis is often challenging, imaging in CD plays an important role in ensuring accurate and prompt diagnosis and therapy. The radiation exposure associated with

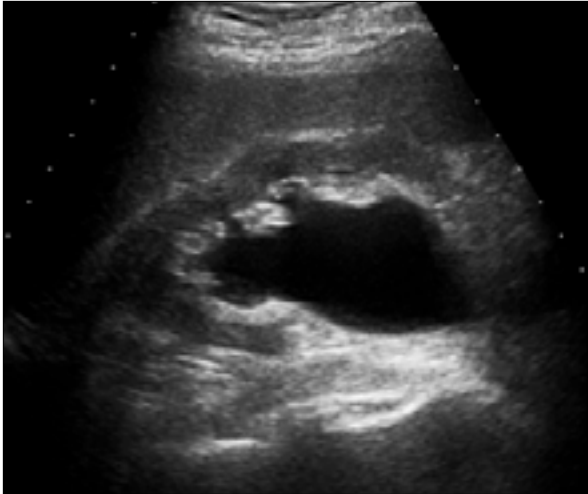


Figure 7. Dilation of the pelvis and right ureter in a 40-year-old Crohn's disease patient with kidney stones.

imaging must be balanced with its benefits to establish a rational approach for appropriate point-of-care ultrasonography utilization. Drawbacks to using point-of-care ultrasonography are false-negative results due to the inexperience of the operator, limitations with obese patients, lack of patient preparation (fasting condition), and duration of the examination. However, bowel ultrasonography is easy to use and offers good repeatability and accuracy, making it an important tool to use in following patients known to have CD, especially for the monitoring of the progression of lesions over time.

The authors have no relevant conflicts of interest to disclose.

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