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PICTORIAL ESSAY

Ultrasound features of pediatric Crohn disease: a guide for case interpretation

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Abstract With the emerging use of ultrasound in the evaluation of children with Crohn disease presenting with acute abdominal symptoms, there is a need to become familiar with the sonographic features of this disease. Our aim is to provide a primer of the characteristic intramural and extramural US findings in children with Crohn disease to serve as a practical and systematic guide to interpretation.

Keywords Children · Crohn disease · Inflammatory bowel disease · Interpretation · Ultrasound

Introduction

Early recognition of the diagnosis of inflammatory bowel disease (IBD) is crucial in a child. Delayed diagnosis may lead to adverse effects on growth, sexual maturation and acute complications. Unfortunately, 25% of children with Crohn disease have symptoms for more than 1 year before diagnosis due to the nonspecific symptomatology [1]. Ninety percent of patients with Crohn disease have involvement of the terminal ileum, but the disease can involve other portions of the small bowel including the colon [2]. Despite the fact that the small intestine is tortuous and extensive in length, we can still evaluate it well with ultrasound (US) [3]. The majority of children with Crohn disease have repeat imaging. This is primarily due to the natural history of Crohn disease, which is manifested by periods of exacerbations and remissions.

The overall trend in imaging these children is to move away from fluoroscopic procedures, conventional CT and CT enteroclysis techniques and move toward enterographic techniques, MR enterography (MRE) and CT enterography (CTE) [4]. However, published literature describes no significant difference in the diagnostic accuracy of the evaluation of IBD with MRE, multidetector CT and US [5]. US is used widely in Europe and Asia to assess the bowel in Crohn disease, but only recently is being used in pediatric radiology practices in the United States [6–8]. US is emerging as a practical alternative to MRE and CTE in the evaluation of known Crohn disease and in its initial diagnosis. Recent publications have focused on the US technique; however, interpretation of these studies is equally important and challenging. Currently, there has been little emphasis placed on this in published literature. The purpose of this article is to provide an atlas of pathology seen on bowel US in pediatric Crohn disease that can serve as a practical guide when interpreting these US cases.

CME activity This article has been selected as the CME activity for the current month. Please visit the SPR Web site at www.pedrad.org/ on the Education page and follow the instructions to complete this CME activity.

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Utilization and standardization of bowel ultrasound

Currently, in our practice, we use bowel US as a screening evaluation in the initial diagnosis for Crohn disease in any child who needs sedation for a MRE, particularly in children younger than 10 years or in any child who has a contraindication to MRE. These young, potential IBD patients undergo a bowel US without prior MRE, CTE or small bowel follow-

through (SBFT). It has been shown that the absence of bowel wall thickening is a strong negative predictive value [9]. In patients who have had prior MRE and have localized disease, bowel US can be used in follow-up to determine improvement or progression of disease. Additionally, it can be used to evaluate abdominal complications of Crohn disease such as intra-abdominal abscesses and strictures [7]. The authors particularly find it helpful in evaluating complex fistulas and strictures that may require real-time imaging to accurately diagnose. Every patient referred for a bowel US receives a standard thorough US examination, as outlined in our technique section. If there is a specific question that needs attention, additional imaging will be performed. Standardized studies will enable easy comparison of diseased segments of bowel, especially if a patient has had a prior bowel US.

Advantages of ultrasound

US evaluation of Crohn disease has several advantages over other imaging techniques. Abdominal US is easily performed, readily available, is less expensive than other modalities such as MRE and CTE, and obviates the use of ionizing radiation [3, 4]. An MRE evaluation can be limited in children younger than age 10 who may require sedation as well as those who have trouble cooperating with oral contrast regimens and motion [8]. US has better patient compliance as sedation, oral contrast or bowel cleansing regimens are not required. Advances in technology have improved the diagnostic accuracy of US in the past decade [10]. High-frequency linear array probes have provided improved spatial and temporal resolution. There has been greater penetration and increased contrast resolution of bowel wall architecture [3, 11]. US has been shown to accurately assess the degree of inflammation of the bowel wall and evaluate extra-intestinal manifestations of IBD [7].

Using imaging modalities without ionizing radiation is essential in pediatric Crohn disease patients who may be at higher risk than the general population of increased diagnostic radiation exposure due to repetitive imaging [12, 13]. For instance, in a study of nearly 1,600 children with IBD, 34% of patients with Crohn disease were exposed to at least one MDCT exam or three fluoroscopy studies during a 2-year period [13]. Using bowel US instead of studies that utilize ionizing radiation can significantly decrease the cumulative radiation burden to these children.

Limitations

There are practical limitations to bowel US. These include operator skills variability, lack of an acoustic window due to bowel gas, large body habitus and distorted anatomy in post-operative patients or postoperative patients with ostomies [6, 13]. Practically, performing a bowel US with adequate compression in an obese patient is challenging. Our pediatric Crohn disease population is not comprised of obese patients and there is no body mass index (BMI) cutoff for performing a bowel US. In fact, these patients are usually underweight and malnourished [2]. Additionally, US has been shown to be less accurate in the evaluation of bowel that is less accessible such as the rectum and upper small bowel in comparison to other locations [14].

Technique

In brief, the US evaluation of the bowel involves graded compression along with additional posterior compression to displace the overlying bowel gas and shorten the distance from the transducer to the loop of bowel of interest. While simultaneously compressing the bowel, anteriorly with the transducer, a hand is placed underneath the patient to apply posterior manual pressure in the same area [6, 15]. At our institution, we begin with the highest frequency linear transducer we have available (12-15 MHz) and then decrease the transducer frequency as needed depending on the body habitus of the patient to evaluate the deeper pelvis to look for fluid collections or abscesses [3, 11, 16]. Beginning with the terminal ileum (TI) and ileocecal junction, each portion of the colon is traced to the sigmoid colon and rectum. Using the lower frequency transducer and with a full bladder as an acoustic window, the rectosigmoid colon can be evaluated. The small bowel, duodenum, jejunum and ileum in all four respective abdominal quadrants are then evaluated. Each bowel segment is scanned in the transverse and longitudinal planes and evaluated with color Doppler to assess hyperemia. Color Doppler should be performed at a low pulse repetition frequency with a low wall filter, low velocity scale and highest Doppler gain [6, 17, 18]. Extra-intestinal structures such as the mesentery are also evaluated with gray-scale and color Doppler simultaneously with each bowel segment [6].

The bowel US is performed non-emergently and patients are restricted from oral intake of solids for 4 h prior to the examination. However, patients are encouraged to drink 12-16 oz of water prior to scanning. This helps to reduce bowel gas and provides a distended bladder, which pushes small bowel loops out of the pelvis and enables adequate imaging of the sigmoid and rectum. Carbonated drinks are discouraged. At our institution, the entire bowel US examination can be completed in about 10-20 min.

Normal bowel and mesentery

When using US frequencies in the range of 7.5 to 14 MHz, normal bowel wall stratification on US consists of five layers:

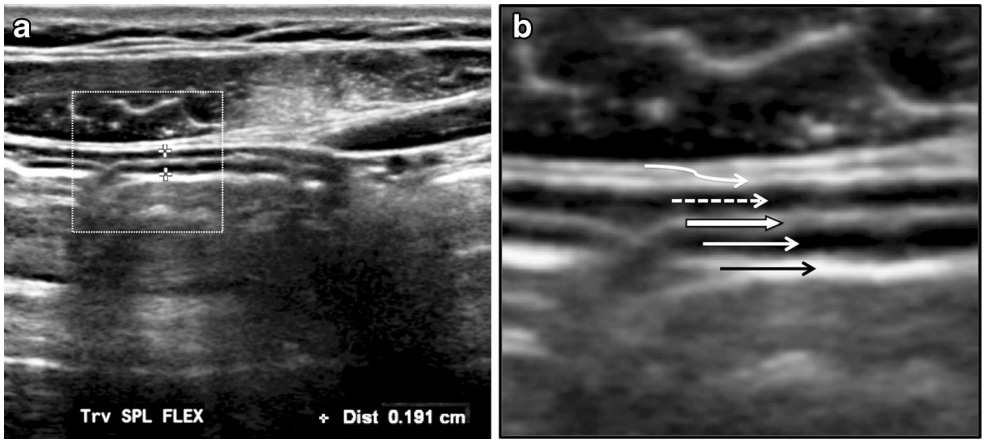

Fig. 1 Normal bowel wall stratification in a non-diseased segment of colon in a 15-year-old boy with Crohn disease. **a** Gray-scale image demonstrates a normal colonic wall thickness of less than 2 mm (*calipers*). **b** Magnification view of inset from the same image shows the hyperechoic mucosal interface (*black arrow*), hypoechoic mucosa (*white arrow*), hyperechoic submucosa (*thick white arrow*), hypoechoic muscularis propria (*dashed arrow*) and hyperechoic serosa (*curved arrow*)

1) echogenic mucosal interface, 2) hypoechoic mucosa, 3) hyperechoic submucosa, 4) hypoechoic muscularis propria and 5) hyperechoic serosa (Fig. 1) [3, 16, 17]. The thickness of each layer of the bowel does not correspond to the actual anatomical thickness since the sonographic image results from echoes secondary to acoustic interfaces rather than the structure itself [16]. Normal small bowel wall thickness is less than 2.5 mm and normal colonic wall thickness is less than 2 mm in children [6, 13]. In our practice, any segment of bowel with a wall thickness of 3 mm or greater is considered abnormal. Normal bowel shows very little or no vascularity on color Doppler with the currently existing US scanners and is compressible and peristaltic [6]. It is challenging to distinguish jejunum from ileum when bowel loops are abnormal. However, the normal jejunum can be differentiated from ileum, as it has more folds that have a distinct pattern on US, similar to their appearance on conventional SBFT (Fig. 2). The normal mesentery is easiest to visualize with increased mesenteric adipose tissue. The mesentery should appear as multiple non-peristaltic parallel echogenic structures [15]. It demonstrates little vascularity. We can deduct this based on data showing that in the setting of IBD there is increased flow in the mesenteric and portal vessels manifesting as increased vascularity in the mesentery due to angiogenesis [19, 20].

Intramural Crohn disease pathology

Mural thickening

Although not the only sonographic finding of Crohn disease, bowel wall thickening is the most commonly used finding (Figs. 3 and 4) [10, 11]. Several studies have evaluated bowel wall thickness showing a strong correlation between wall thickness and Crohn disease [1, 21, 22]. In a meta-analysis, Fraquelli et al. [23] demonstrated a sensitivity of 88% and specificity of 93% for the diagnosis of Crohn disease with a bowel wall thickness of greater than 3 mm and a sensitivity of 75% and specificity of 97% for the diagnosis of Crohn disease with a bowel wall thickness of greater than 4 mm. Maximal

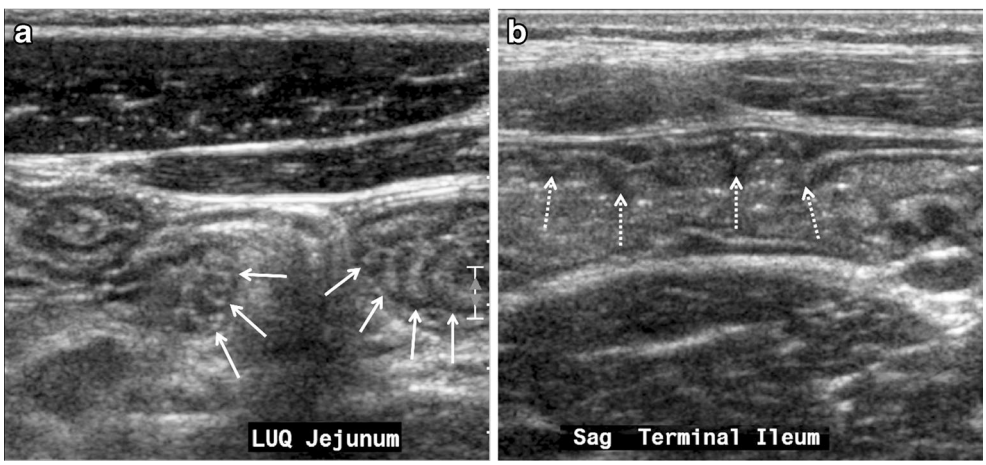

Fig. 2 Normal jejunal and ileal fold patterns in a 20-year-old man with inactive Crohn disease. **a** Normal loops of jejunum in the left upper quadrant are characterized by numerous closely spaced circumferential folds or valvulae conniventes (*arrows*), in contrast to normal loops of ileum in the same patient (**b**), which demonstrate a more sparse distribution of folds (*arrows*)

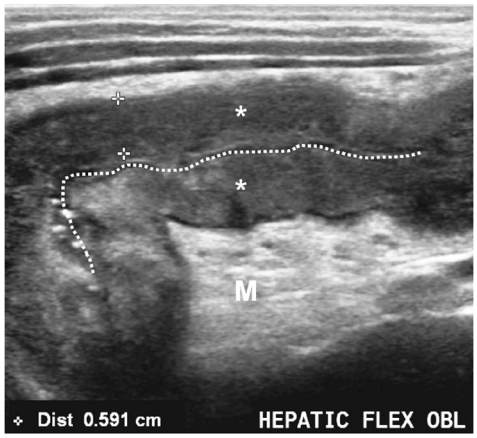

Fig. 3 Bowel wall thickening and loss of mural stratification in a 10-year-old boy with an acute Crohn disease flare. Gray-scale image of the proximal colon demonstrates loss of normal mural stratification, with the colonic wall (*asterisks*) on both sides of the bowel lumen (*dotted line*) appearing homogeneously hypoechoic and thickened (*calipers*). Note the echogenic mesentery, indicative of edema (*M*)

wall thickness and disease activity have also been shown to have a statistically significant correlation [13].

Loss of bowel wall stratification

The loss of bowel wall stratification develops over time with Crohn disease and corresponds pathologically to deep ulcers and fissures (Figs. 3 and 4) [6, 10]. Crohn disease begins with ulcerations at the mucosal level and can extend transmurally into the serosa [7]. Bowel wall stratification is not the only marker of disease. The correlation between active inflammation and loss of stratification in adults was demonstrated on in vitro US examination of the bowel [24]. Additionally, Haber et al. [25] demonstrated that 7 of 8 adults with severe disease activity had loss of stratification, but this was not statistically significant due to a small sample size. Maconi et al. [26] demonstrated that in adults with a stricture, loss of stratification of the bowel wall was associated with

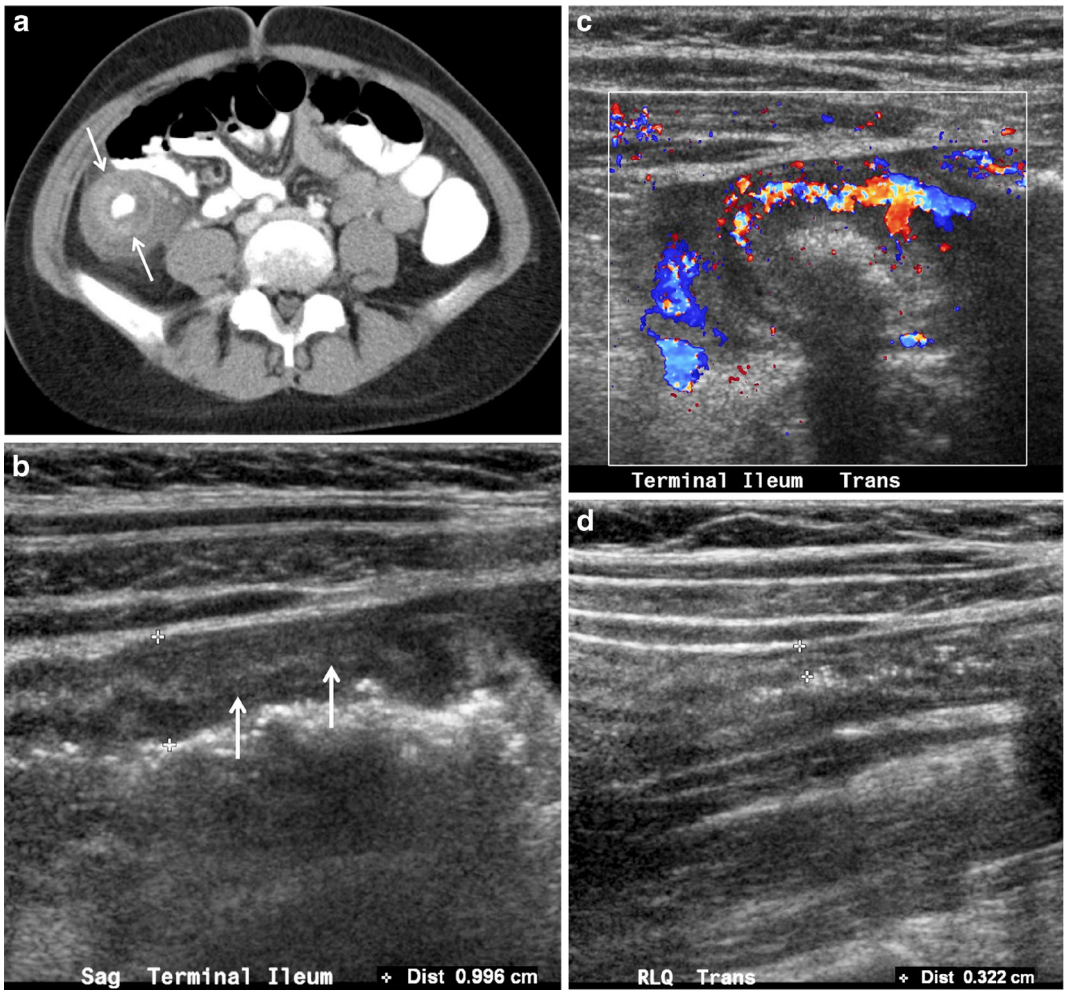

Fig. 4 A 9-year-old girl with Crohn disease. **a** Contrast-enhanced axial CT performed at an outside institution demonstrates marked thickening of the terminal ileum (*arrows*). **b** Gray-scale image from US performed upon patient transfer demonstrates the thickened terminal ileum (*calipers*) with loss of mural stratification (*arrows*). **c** Color Doppler image reveals hyperemia of the thickened terminal ileal wall. **d** Gray-scale image from US performed 1 week following initiation of treatment demonstrates marked improvement of bowel wall thickening (*calipers*)

inflammation. However, it is important to keep in mind that making the distinction between active disease and fibrosis is very challenging as both can exist in the same segment of diseased bowel. In our practice, given that the supporting evidence in the literature is limited, we do not routinely use the presence or loss of bowel wall stratification to differentiate inflammation from fibrosis. The reported literature is limited and larger cohort studies are needed to validate these findings before applying them to daily practice.

Bowel wall hyperemia

Hyperemia on color Doppler imaging is characteristic of active disease (Figs. 4 and 5) [6, 10, 16]. Although there is currently no objective scale for the determination of bowel wall hyperemia using color Doppler, we most commonly utilize subjective grading in our practice [11]. Others have used a quantitative approach to determining hyperemia based on vessel density (Doppler signals per square cm) in a segment of bowel. By estimating the vessel density in the intestinal wall using Doppler color signals per square centimeter, Spalinger et al. [19] demonstrated a sensitivity of 81% and specificity of 69% for active Crohn disease with high vessel density (greater than 5 signals per square centimeter) and a sensitivity of 98% and specificity of 89% for active Crohn disease with moderate to high vessel density (3 to 5 signals per square centimeter). Additionally, residual hyperemia following treatment had an unfavorable clinical course [18].

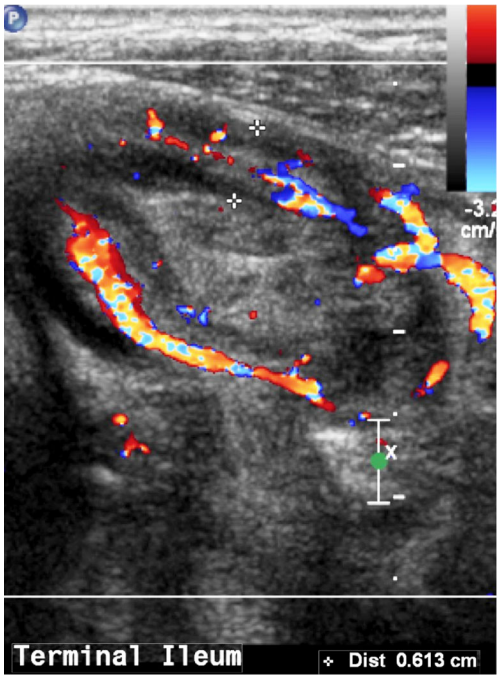

Fig. 5 Bowel wall hyperemia in a 17-year-old girl with newly diagnosed Crohn disease. Color Doppler image of the terminal ileum demonstrates marked hyperemia circumferentially involving the bowel wall. Note the mural thickening (*calipers*) and the partial loss of stratification within the bowel wall between the calipers

Strictures

Strictures develop in 21% of patients with ileal Crohn disease and are the most common cause of surgical intervention [7]. US definition and features of a stricture are a narrowed lumen with upstream proximal bowel dilatation. There is usually pseudo-fecalization of the more proximal loops and there may be hyperperistalsis under real-time imaging, an added advantage of US (Figs. 6 and 7) [6, 7]. US has been reported to be 100% sensitive and 91% specific for identifying strictures in adults [27], but other numbers report that US accurately diagnosed strictures in only 70-79% [6, 7].

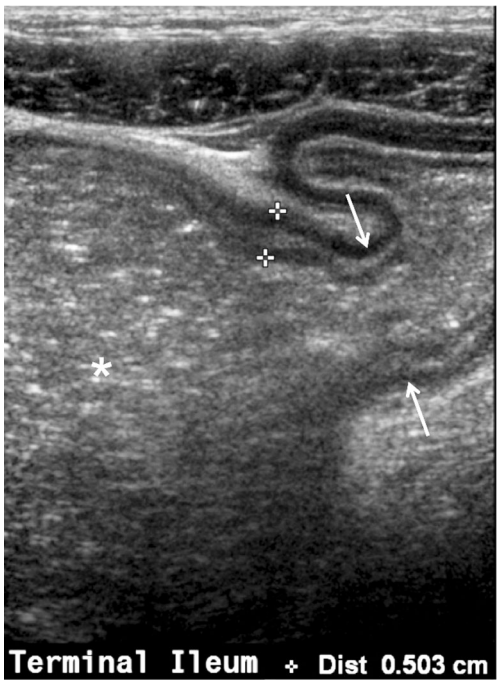

Fig. 6 Stricture in a 13-year-old boy with treatment-refractory Crohn disease. Gray-scale image demonstrates a fixed luminal narrowing (*arrows*) of the terminal ileum with marked pre-stenotic dilatation of the upstream bowel segment (*asterisk*). The wall of the terminal ileum is thickened *(calipers)*

Peristalsis

Peristalsis can be assessed by US during real-time imaging to provide functional information of abnormal bowel segments. We can pinpoint the abnormality with the transducer and simulate the patient's symptoms in real time. Abnormal small bowel loops lose their distensibility, are spastic and are hypoperistaltic [10]. When there is a transition from a dilated to a narrowed loop of bowel, the prestenotic loop of bowel is hyperperistaltic [6].

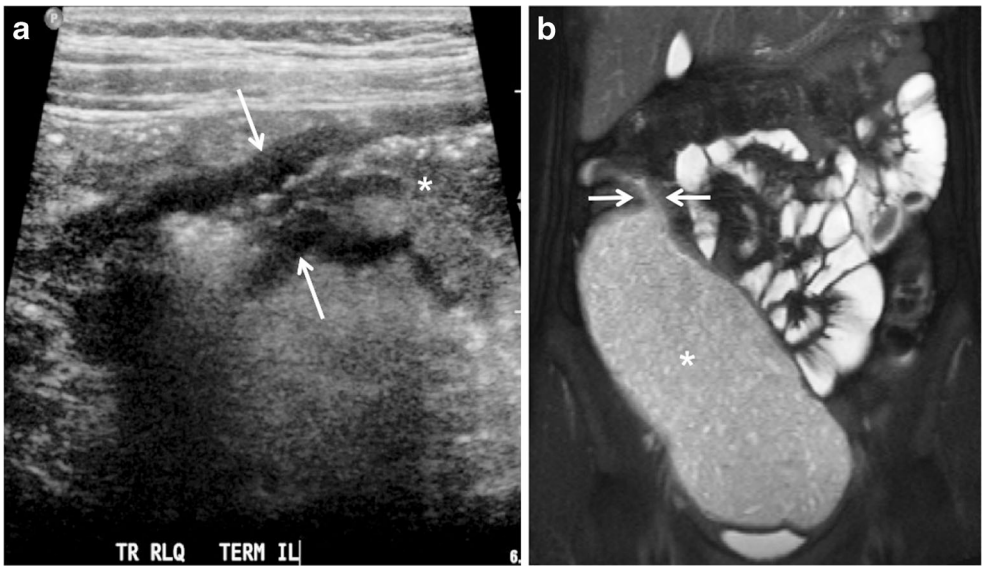

Fig. 7 A 17-year-old girl with a history of long-standing Crohn disease. **a** Gray-scale image demonstrates a focal stricture in the terminal ileum (*arrows*), with pre-stenotic dilatation of the upstream bowel segment (*asterisk).* **b** Coronal T2-weighted image from an MR enterography performed 1 day later redemonstrates the terminal ileal stricture (*arrows*) with marked associated pre-stenotic dilatation (*asterisk*)

Extramural Crohn disease pathology

Mesenteric inflammation

Perienteric inflammation produces US findings of inflammation and thickening of the mesentery (Figs. 8 and 9). This also manifests as increased echogenicity of the mesenteric fat and hyperemia when evaluated by color Doppler [6, 11]. The hypertrophy of the mesentery can be manifested as "creeping fat," which appears as fingerlike projections over the serosal surface of the bowel (Fig. 6) [28].

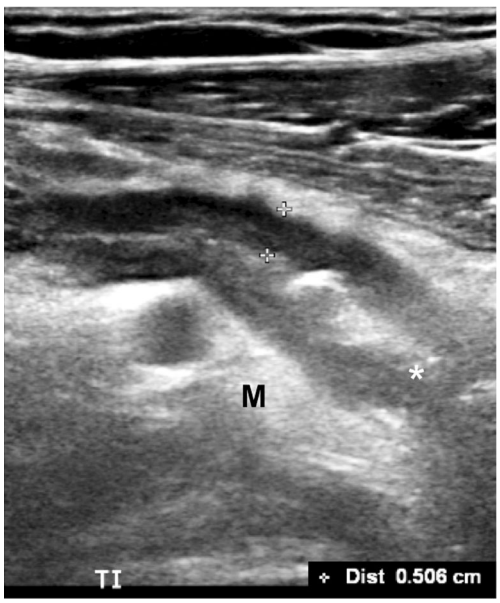

Fig. 8 Mesenteric edema in a 17-year-old boy with a Crohn disease flare and obstructive symptoms. Gray-scale image demonstrates increased echogenicity and hypertrophy of the mesentery surrounding the terminal ileum (*M*). There is thickening of the terminal ileal wall with loss of normal mural stratification (*calipers*), as well as mild dilatation of the upstream bowel segment (*asterisk*)

Free fluid and abscess

US is extremely sensitive for the detection of free fluid [11]. Additionally, US has proven to be a successful modality for the identification of an abscess (Figs. 10 and 11). US sensitivity for the identification of abscesses ranges from 81% to 100% with a specificity ranging from 92% to 94% [14]. US has been reported to be superior to CT for the evaluation of small abscesses [16]. In a study by Gasche et al. [27], US successfully identified 9 of 9 abscesses and excluded 22 of 25 abscesses in patients with Crohn disease. A limitation of US is that there is a higher rate of false-positive results in comparison to CT. Abscesses within the deep pelvis and adjacent to the stomach are more difficult to evaluate [14].

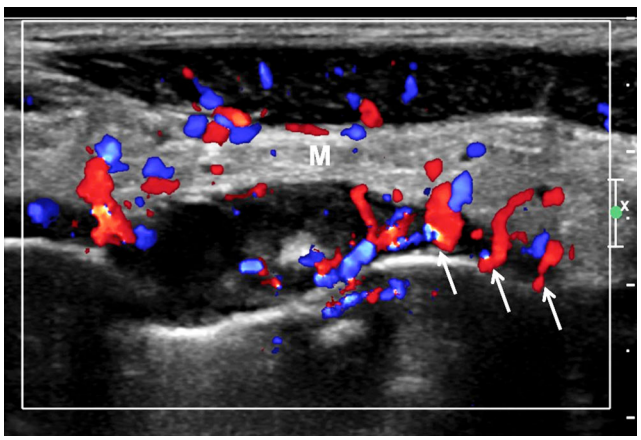

Fig. 9 Mesenteric hyperemia in an 8-year-old boy with active Crohn disease. Color Doppler image shows pronounced hyperemia of the thickened and echogenic mesentery (*M*). Note the radial orientation of blood vessels (*arrows*) corresponding to the engorged vasa recta

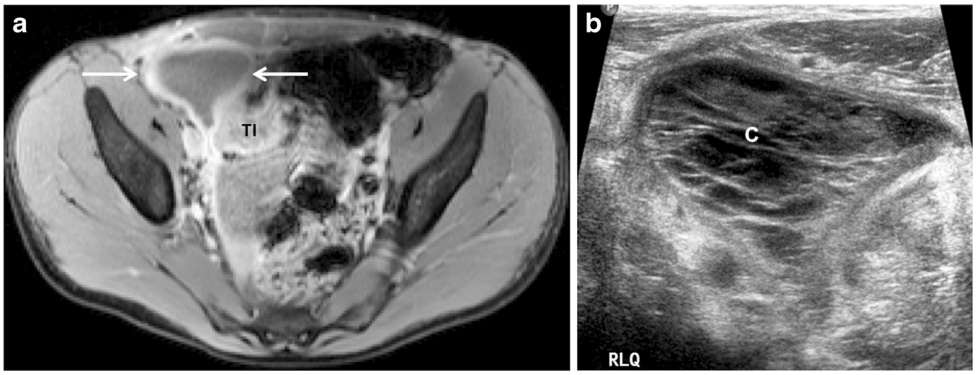

Fig. 10 Intra-abdominal abscess in a 16-year-old boy with penetrating Crohn disease. **a** Contrast-enhanced fat-saturated T1-weighted image from an MR enterography demonstrates a rim-enhancing fluid collection (*arrows*) adjacent to the inflamed terminal ileum (*TI*). **b** Gray-scale image from bowel US performed 1 day later to establish a sonographic baseline clearly demonstrates the complex collection (*C*)

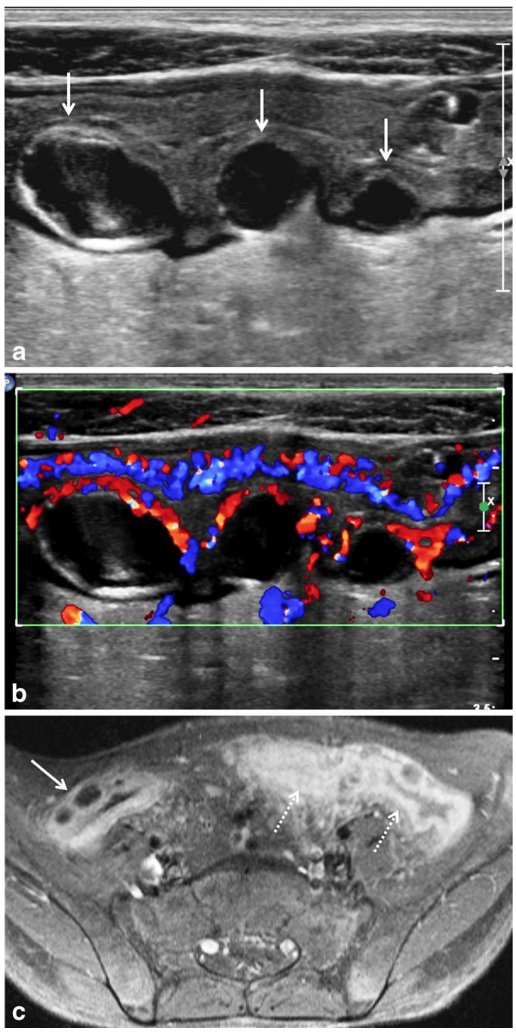

Fig. 11 Intramural abscesses in an 8-year-old boy with uncontrolled Crohn disease. **a** Gray-scale image demonstrates multiple fluid collections within the wall of the sigmoid colon (*arrows*), representing intramural abscesses. **b** Color Doppler image of the same bowel segment shows marked surrounding hyperemia. **c** Axial contrast-enhanced T1-weighted image from an MR examination of the pelvis performed 1 day later demonstrates the intramural collections within the wall of the sigmoid colon (*solid arrow*), as well as thickening and enhancement of the descending colon (*dotted arrows*)

Lymphadenopathy

Although the presence of regional lymphadenopathy is weakly correlated with active Crohn disease, US is a useful tool to identify enlarged lymph nodes, which may be associated with Crohn disease [11, 29]. Regional lymphadenopathy is common in Crohn disease [7]. Mesenteric lymph nodes adjacent to and draining abnormal segments of bowel, commonly in the right lower quadrant, are often increased in number and size. They are usually oval hypoechoic structures within the mesentery, most commonly within the right lower quadrant. There may be a conglomeration of nodes forming a lobulated mass [28].

Fistula

Fistulas in IBD are more common in adults than in children. Fistulas can be a communication of the bowel with other loops of bowel, the vagina, the urethra, bladder or prostate [6]. The sensitivity of US for the diagnosis of fistulas is 74% with a specificity of 95% [14]. Fistulas are manifested by hypoechoic communicating tracts extending from the bowel (Fig. 12) [6]. The use of power Doppler may help to identify the fistula given its rich microvascularization [16].

Future imaging

Utilization of techniques such as intravenous contrast-enhanced ultrasound (CEUS) and US elastography have demonstrated great promise in the differentiation of acute from chronic fibrostenotic disease. CEUS involves the interrogation of the wall of the intestine following intravenous injection of US contrast agents [30]. In the United States, there are two FDA-approved contrast agents for off-label use in children and both have a high safety profile: Optison® (GE Healthcare, Princeton, NJ) and Lumason® (Bracco Diagnostics Inc.,

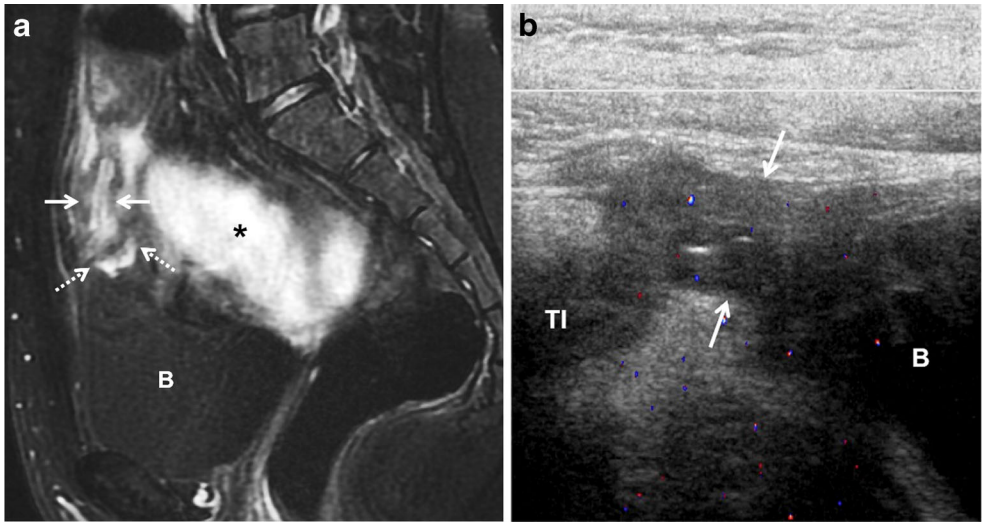

Fig. 12 Enterovesical fistula in a 13-year-old girl with treatment-refractory Crohn disease. **a** Sagittal fat-saturated T2-weighted from an MR enterography demonstrates a thickened terminal ileum (*solid arrows*) with mural irregularity and edema of the adjacent bladder dome (*dotted arrows*). The upstream bowel is dilated (*asterisk).* The bladder lumen (*B*) is hypointense due to the presence of intravenous contrast on this delayed phase image. **b** Color Doppler image 1 day later much more clearly demonstrates a hypoechoic tract (*arrows*) extending from terminal ileum (*TI*) to the urinary bladder (*B*), confirming an enterovesical fistula

Monroe Township, NJ). Following the injection of an US contrast agent, the enhancement pattern can be visually assessed. Submucosal enhancement with sparing of the muscularis propria and complete transmural enhancement beginning at the mucosa and extending outward to involve the entire bowel wall are two patterns that are related to active inflammatory Crohn disease [31]. Given that the assessment of enhancement by visual analysis is limited by interobserver variability, quantitative analysis using a region of interest can be performed. On quantitative analysis, active Crohn disease has shown reduced time to peak enhancement, increased percentage of maximal enhancement and increased area under the time-intensity curve in comparison to nonactive disease in adults [31]. Additionally, in adults with Crohn disease, the degree of bowel wall enhancement has correlated well with the severity of disease on endoscopy and with contrast-enhanced MRE evaluation of bowel wall vascularity (Fig. 13) [32, 33].

US elastography measures tissue stiffness based on Young's E modulus. There are two main techniques to perform US elastography: strain or shear wave. In strain elastography, an external force is applied to the tissue, usually by manual compression (stress) with an US probe [3, 34]. This elastogram image is created based on the tissue displacement and strain is displayed as a color map adjacent to or superimposed on the B mode images of the bowel. Color images provide a visual map of degree of bowel wall stiffness (Fig. 14) [34]. Materials that demonstrate low strain in

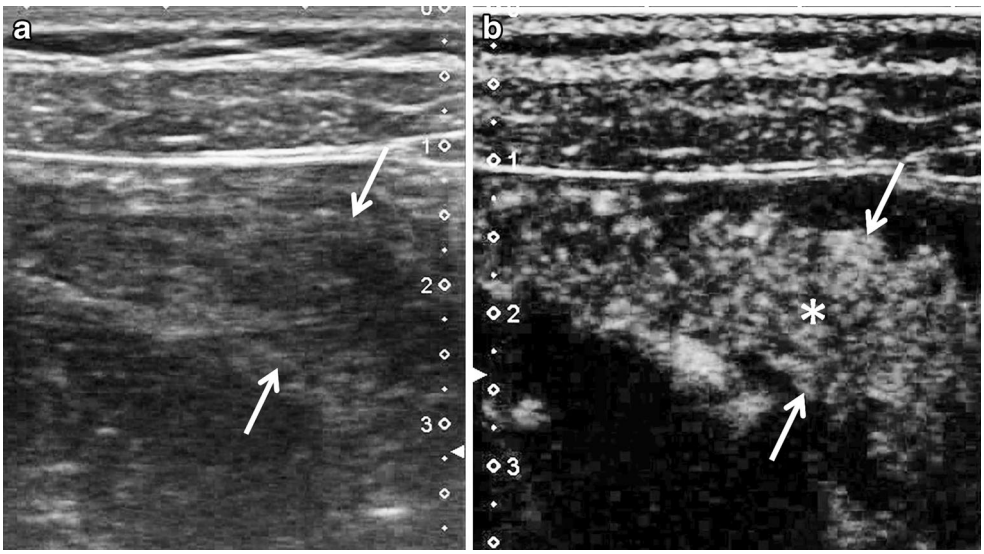

Fig. 13 Contrast-enhanced US in a 13-year-old girl with Crohn disease. **a** Gray-scale image demonstrates a thick-walled segment of small bowel in the mid abdomen (*arrows*). **b** Image following the administration of intravenous SonoVue (Bracco, Italy) demonstrates the thick-walled segment of small bowel (*arrows*). There is transmural enhancement of the thickened bowel wall (*) suggesting active inflammation

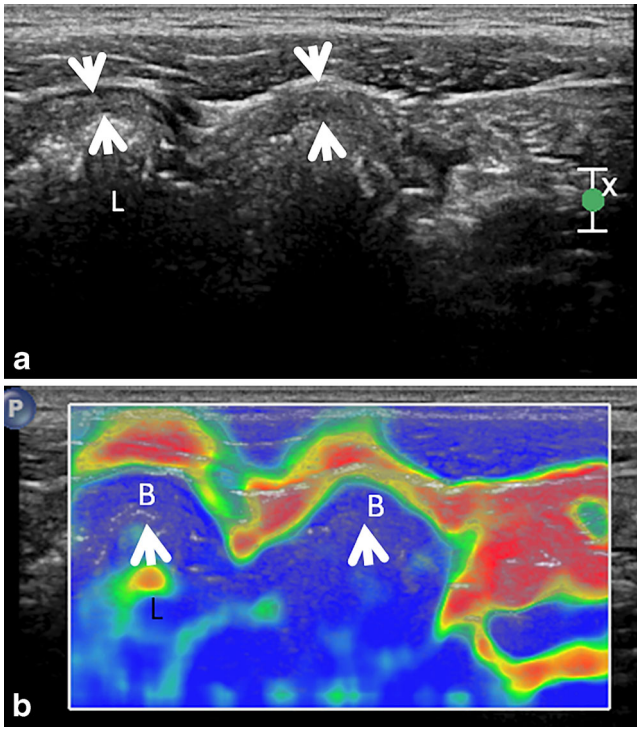

Fig. 14 Ultrasound elastography in a 10-year-old boy with suspected new diagnosis of IBD. Gray-scale US image (**a**) demonstrates a focal area of bowel wall thickening (between the *arrows*) involving the distal descending/ proximal sigmoid colon. Strain elastography was performed on a Philips iU22 US scanner. The generated elastogram with color map depicts different colors based on tissue stiffness. Specific to our vendor here, red and yellow correspond to soft tissues and blue represents harder tissue. In this elastogram with color map (**b**), the bowel wall (*B, arrows*) is depicted in blue as it is thickened as seen in the gray-scale image and is stiffer compared to the more superficial soft tissues, muscles and the bowel lumen (*L*). Without quantitative measures, the strain elastography merely confirms that this segment of colon is abnormal

response to a degree of compression have decreased compliance and are stiffer than materials that demonstrate high strain [35]. This technique is easy to perform; however, it is limited to superficial anatomy and is operator dependent and therefore can be difficult to reproduce. If the applied stress is unknown, tissue elasticity cannot be quantified.

In shear wave elastography, a wave perpendicular to the tissues is created by one of several methods. Tissue stiffness is then quantified based on the speed of propagation of this shear wave through the tissue. The advantages of shear wave over strain elastography are user independence, strain quantification and the ability to image relatively deeper tissues. Qualitative color maps can also be created. Similar to strain techniques, soft and hard tissues are assigned a color; however, these color maps are elastography technique and vendor specific.

Acoustic Radiation Force Impulse technology (ARFI) is a type of shear wave elastography. In this method, the US sends out low velocity shear waves that displace the tissues and the velocities of these waves are detected by the US probe. Waves propagate faster in stiffer tissues [34]. Both qualitative and quantitative analysis can be performed. Preliminary data in both animal and human models have been described which suggest elastography can help to differentiate inflammation from fibrosis in stricturing Crohn disease [35, 36].

Conclusion

By evaluating both mural and extramural findings, US has the potential to be efficacious in the evaluation of children with Crohn disease. It is noninvasive, can be performed without sedation and lacks ionizing radiation. Expanding the use of US can significantly decrease the radiation dose to patients with IBD. We have provided a bowel US primer of the spectrum of Crohn disease pathology seen in children and a practical approach to interpretation in the hopes to expand the use of US as stand-alone or complementary to other enterographic techniques.

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Conflicts of interest None

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