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Intestinal Ultrasound for the Pediatric Gastroenterologist: A Guide for Inflammatory Bowel Disease Monitoring in Children

Expert Consensus on Behalf of the International Bowel Ultrasound Group (IBUS) Pediatric Committee

*Amelia Kellar, MD, MSc, *Michael Dolinger, MD, MBA, †Kerri L. Novak, MD, MSc, ‡Mallory Chavannes, MD, MHSc, *Marla Dubinsky, MD, and §Hien Huynh, MD

ABSTRACT

Crohn disease and ulcerative colitis are chronic inflammatory bowel diseases (IBD) often diagnosed in childhood. A strict monitoring strategy can potentially alter the disease course and facilitate early effective treatment before irreversible bowel damage occurs. Serial colonoscopy in children, the gold standard for monitoring, is impractical. Accurate, real-time, noninvasive markers of disease activity are needed. Intestinal ultrasound is an accurate, noninvasive, real-time, point-of-care, cross-sectional imaging tool used to monitor inflammation in pediatric IBD patients in Europe, Canada, and Australia. It is now emerging in a few expert centers in the United States as a safe, nonradiating, inexpensive, bedside tool used by the treating gastroenterologist for real-time decision-making. Unlike the standard biomarkers of pediatric IBD activity, C-reactive protein, and fecal calprotectin, intestinal ultrasound (IUS) facilitates disease localization, characterizes severity, extent, and accurately detects complications. Perhaps most importantly, IUS may enhance shared understanding and ease the burden of treatment decision-making for both the gastroenterologist and the patient. There is a lack of standardization for bedside IUS among pediatric gastroenterologists. The purpose is to outline a standardized approach to pediatric bedside IUS, including basic equipment requirements and technique, patient selection, preparation and positioning, technical considerations and limitations, documentation of mesenteric and luminal features of IBD, characterization of penetrating disease and strictures, and provide a proposed pediatric IUS monitoring algorithm to guide care.

Key Words: inflammatory bowel disease, intestinal ultrasound, pediatric

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What Is Known

- Intestinal ultrasound (IUS) is an accurate, cross-sectional imaging tool used to monitor inflammation in inflammatory bowel disease.
- With comparable accuracy to computed tomography (CT) and magnetic resonance (MR), IUS is nonradiating, and applied at the bedside to facilitate real-time decision-making.

What Is New

- As IUS use is increasing, we provide a standardized approach and monitoring algorithm for use of pediatric bedside IUS to guide care.
- IUS is best performed at baseline to compliment endoscopy and during, or immediately after therapy induction. Monitoring every 3–6 months until treat-to-target colonoscopy is performed within 1 year is recommended.

Inflammatory bowel disease (IBD) is a chronic condition resulting in transmural inflammation within the gastrointestinal (GI) tract that can cause significant morbidity (1). In children, IBD can

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From the *Department of Pediatric Gastroenterology, Icahn School of Medicine at Mount Sinai, Susan and Leonard Feinstein Inflammatory Bowel Disease Center, New York, NY, the †Inflammatory Bowel Disease Clinic, Division of Gastroenterology and Hepatology, University of Calgary, Calgary, Alberta, Canada, the ‡Division of Gastroenterology, Hepatology, and Nutrition, Children's Hospital Los Angeles, Keck School of Medicine of the University of Southern California, Los Angeles, CA, and the §Department of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition, University of Alberta, Edmonton, Alberta, Canada.

Address correspondence and reprint requests to Amelia Kellar, MD, MSc, Department of Pediatric Gastroenterology, Icahn School of Medicine at Mount Sinai, Susan and Leonard Feinstein Inflammatory Bowel Disease Center, New York, NY (e-mail: Amelia.kellar@gmail.com).

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significantly impact growth, development, and result in a substantial psychosocial burden, particularly when diagnosis is delayed, or disease severity is inaccurately assessed (2). Endoscopic evaluation is the gold standard for diagnosing and monitoring mucosal inflammation in pediatric IBD. However, it presents several challenges in the pediatric population and does not provide transmural assessment of inflammation. Endoscopy is less desirable for children as it is invasive, requires sedation by a pediatric anesthesiologist, requires often poorly-tolerated bowel preparations, and exhibits lower cecal and ileal intubation rates than adults (3,4).

Intestinal ultrasound (IUS) is a cross-sectional imaging tool with comparable accuracy magnetic resonance enterography (MRE) in assessing transmural inflammation in the entire bowel (5), with the advantages of being well tolerated in children, non-radiating, inexpensive, and ideal for repeated examinations. Both IUS and MRE have a high sensitivity for detecting small bowel Crohn disease (CD) activity with substantial practitioner agreement for the presence of active ileal inflammation. This suggests that both modalities are valid tools for disease activity assessment, supporting the use of IUS as an accurate tool for serial monitoring during routine exam visits (6–9). Presently, there is a lack of standardized approach to bedside IUS among gastroenterologists. There is now a formalized training program and curriculum offered through the International Bowel Ultrasound Group (IBUS), and there are several standardized scoring systems for disease activity that are in the process of validation, 2 of which are pediatric-focused (10).

In this article, we provide a general approach to utilizing IUS for disease monitoring in the pediatric IBD clinic, outlining patient preparation and positioning, technical considerations, an anatomical overview, and specific recommendations regarding assessing and documenting transmural features of IBD from mucosa to serosa, the mesentery, and characterization of complications such as penetrating and stricturing disease. We also provide the first proposed pediatric IUS monitoring algorithm. Please refer to Table 1 which outlines key points regarding patient preparation and positioning, technical considerations, limitations, and documentation. More detail is provided in Supplemental Digital Content 1, *http://links.lww.com/MPG/C975* and in video form in Supplemental Digital Content 4, *http://links.lww.com/MPG/C976*.

ANATOMICAL OVERVIEW

Before beginning your bowel assessment, it is important to consider the patient's clinical history and characteristics as this will aid in streamlining and structuring your examination. We recommend performing a complete examination of the colon and small bowel during each examination, however, particular attention should be focused on patients previously known disease location for disease activity monitoring when available. The typical sequence of bowel ultrasound begins distally, by first identifying common anatomical landmarks in the lower pelvis, such as the bladder, iliac artery and vein, and the iliopsoas muscle on each side of the abdomen starting on one side during the beginning of the examination and ending on the other. Visualization of the bowel can begin in either the right lower quadrant of the abdomen for children with a history of ileal disease or the left lower quadrant for patients with a history of colonic involvement. From the left lower abdominal quadrant, the distal sigmoid colon can be identified and mapped from the suprapubic region, crossing over the iliac vessels to the left lower quadrant in most individuals (Fig. 1A). The descending colon can be visualized in longitudinal views with a 90-degree rotation of the transducer in the clockwise direction as you traverse from the left lower quadrant to the left costal margin (Fig. 1B). Difficult visualization of the proximal descending colon can be aided in many cases by moving the transducer towards the left flank with deep inspiration. An intercostal view may be necessary to visualize the splenic flexure adequately. The spleen can often be seen at the left costal margin or through the intercostal space of the inferior ribs and is often best seen on inspiration.

Orienting the ultrasound transducer with the marker (an elevated notch on the external surface of the transducer indicating orientation) superiorly in the epigastric region can facilitate identification of a transverse section of the stomach antrum and the left lobe of the liver to the right and superior to the transducer. The transducer can then be fanned to the right and superiorly to visualize the body and fundus of the stomach. In this instance, the stomach is visualized as an anatomical marker, and not a segment of the GI tract for assessment of disease activity. Moving laterally to the left of the patient, the mid transverse colon can be appreciated. If the transverse colon is not seen in this orientation, the transducer can be moved superiorly and inferiorly as the location of the transverse colon can vary from intercostal to just above the umbilicus. Occasionally, the transverse colon can be quite redundant and found caudally to the umbilicus and almost touching the sigmoid. Transverse views at or above the costal margin are best seen with breath held on inspiration. Once identified, the transverse colon can be followed both distally (to the

TABLE 1. Summary of pertinent technical considerations for IUS outlined in detail in Supplemental Digital Content 1, *http://links.lww.com/MPG/C975*

Patient preparation and positioning	• Perform in quiet, dimly-lit room with parent involvement • No fasting or bowel preparation required
Technical considerations	• Utilize at least 1 high and low frequency transducer with colour Doppler capability, linear transducer is often best in children for more detail • Left to right standardized anatomy-based approach from the large to small bowel is recommended
Limitations	• In larger body habitus, lower frequency transducers provide deeper penetration • Small bowel can be more challenging to visualize, but can be differentiated from large bowel by increased motility • Visualization of penetrating and stricturing disease is aided by a standardized anatomical approach • More widespread use of IUS requires standardized training programs and the development of compensation and billing codes
Documentation	• Four general components to the pediatric IUS report: clinical data, disease activity, presence of and characterization of complications, and overall impression including clinical plan • Description of disease activity should include: BWT, blood flow, echostratification, and inflammatory fat for each anatomic segment • Overall impression is essential to guide clinical decision-making

BWT = bowel wall thickness; IUS = intestinal ultrasound.

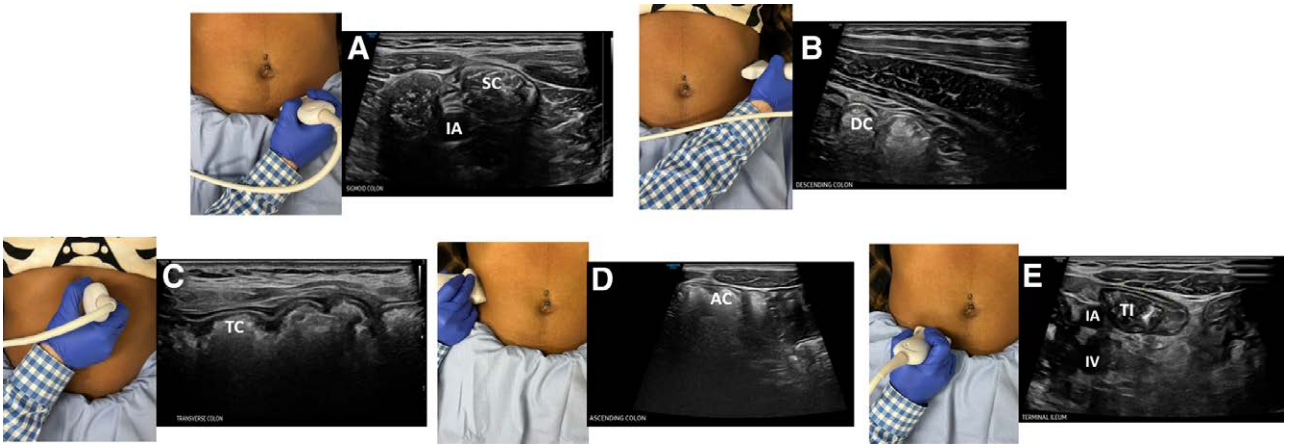

FIGURE 1. (A) The sigmoid colon (SC) is identified by the iliac artery (IA) and vein as it lies directly over the iliac vessels as identified with the transducer in the patients left lower quadrant. (B) The descending colon (DC) can be visualized, often on the patients left flank, by moving the transducer towards the spleen and rib cage from the left lower quadrant and then moving the transducer onto the patients left flank and further towards the back if necessary. (C) The transverse colon (TC) can be identified by locating the aorta through the application of color Doppler, and then moving the transducer upward towards the patient's xyphoid process. Note the haustral folds of the colon that may differentiate the transverse colon from under or overlying proximal small bowel. (D) The ascending colon (AC) can be found on the child's right abdomen, by identification of the liver and then moving the transducer downward. (E) The terminal ileum (TI) identified in the child's right lower quadrant, identified as lying just above the iliac artery and vein.

left of the patient) and proximally (to the right of the patient) for complete assessment (Fig. 1C). As the transducer is progressed from the epigastrium to the right upper quadrant, the ascending colon will become visible. This can be traced inferiorly by slowly transitioning the transducer to keep the ascending colon in longitudinal view as the transducer is moved to the right lower quadrant (Fig. 1D). In the majority of the subjects, the cecum is identified lateral and cranial to the right iliac vessels. However, with a redundant left colon, the cecum may be lower in the right pelvis and medial to the iliac vessels and can be confused with terminal ileum. In a shortened ascending colon, the cecum can be high and closer to the hepatic flexure.

Similarly, the location of the terminal ileum can be highly variable as well. Slowly advance the transducer in the right lower quadrant and fan the transducer superiorly and inferiorly as well as clockwise and counter-clockwise to identify the location of the cecum and subsequent transition through the ileocecal valve to the terminal ileum (Fig. 1E). If seen, the appendix can be a useful marker in identifying this transition. Once visualized, follow the terminal ileum in the longitudinal plane medially and often inferiorly into the right side of the pelvis.

An important distinction of small bowel versus large bowel is motility. The small bowel can be differentiated based on increased peristalsis and movement of intestinal contents. This can be particularly useful to take into consideration when loops of small and large bowel overlap and visualization is challenging. The haustrae of the large intestine may be easily delineated in the absence of inflammation and within the small bowel, the circular folds of Kerckring can be seen proximal to the ileum which can be helpful in differentiating transverse colon from underlying or overlying small bowel loops.

The final component of the assessment is identification of the distal rectum, which lies deep in the pelvis. Utilization of the lower frequency transducer is necessary to allow for deeper penetration in the pelvis. Advance the transducer inferiorly from the umbilicus and the distal rectum should become visible caudal to the bladder. In male patients the prostate should be visible superiorly and in female patients, the uterus and ovaries may be appreciated. Visualization of the distal rectum can be affected by the fullness of the bladder secondary to attenuation of sound waves, while an under-distended bladder fails to allow acoustic transmission of sound waves hindering visualization, and the rectum is best seen in in transverse orientation. Generally, the rectum may not be as well seen as other segments of bowel.

In summary, we recommend beginning with identification of the bladder in the suprapubic region, followed by the iliac artery, vein, and psoas muscle in either the right lower quadrant or left lower quadrant, depending on the clinical scenario, and then progressing distal to proximal to assess the large intestine or proximal to distal from small intestine to large intestine.

TRANSMURAL FEATURES

Bowel Wall Thickness (BWT)

When performing bowel ultrasound for assessment of pediatric IBD, there are several essential transmural features to assess, the most important of which is BWT. There is insufficient evidence to date in children for IUS detection of mucosal surface abnormalities alone compared to transmural inflammation. BWT is the best-described parameter for assessment of IBD both in adult and pediatric populations (14). On an adequate image without severe inflammation, 5 layers can be differentiated. However, the presence of inflammation may cause loss of layer stratification and blurring of the layers with only the hyperechoic lumen and serosa clearly distinguishable. In the longitudinal view, the bowel lumen appears hyperechoic. Moving outwards, the mucosa will appear hypoechoic or black in stark contrast to the lumen beneath it. The submucosa is then hyperechoic, and lying overtop is the muscularis propria which is again hypoechoic. The serosal lining is typically the most superior layer and appears hyperechoic. For the most accurate and reproducible measurement of the BWT, we recommend measurement beginning from the interface between the hypoechoic and hyperechoic lumen to the hypo-hyperechoic interface between the muscularis propriate and the serosa (Fig. 2). Maintaining caliper positioning perpendicular to the lumen when scanning longitudinally to avoid

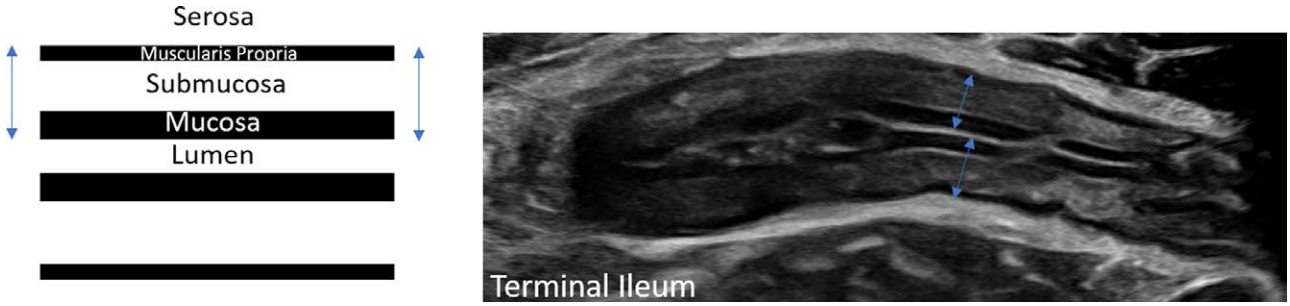

FIGURE 2. Schematic on the left identifying the bowel wall layers and optimal points to measure bowel wall thickness beginning at the lumen-mucosa interface to the muscularis propria-serosa interface. On the right, a still ultrasound frame with an inflamed terminal ileum is shown with measurement of bowel wall thickness with blue arrows.

tangential measurements is recommended. We recommend obtaining measurements from the most affected segment of bowel. It has been suggested that the most affected segment is defined by the most pathological BWT; however, if two segments have the same BWT, it is important to consider secondary parameters for defining severity of inflammation in the following order: grading of color Doppler signals, bowel wall stratification, and then inflammatory mesenteric fat, respectively (15).

Compression, stool contents, and bowel distension can alter visualization and it is important to be mindful of this with regard to caliper placement. A mild degree of compression may be applied when performing BWT measurements to compress any air that may interfere with measurement as well as to improve visibility, accuracy, and reproducibility of measurements.

BWT can vary by bowel region and the degree of bowel distension, but a cut-off of <3 mm is generally used to differentiate normal bowel from pathologic bowel, with measurements <2 mm being normal (16–18). Emerging data suggests that for patients with ulcerative colitis (UC) (<2 mm) and children with CD may have a lower cut off (2.5 mm). In our experience, the ratio of the prominence of submucosa in relation to total BWT is important to note, as milder disease may present with technically normal BWT values (<2 mm), but increased ratio of submucosa to total BWT (19,20).

A systematic approach to BWT measurements should be employed. Each segment of the bowel should be evaluated with 2 separate measurements in both the transverse and longitudinal views for a total of 4 separate BWT measurements per segment assessed. It is imperative that the most affected segment be measured in this manner and measurements should be 1–2 cm apart in longitudinal and more than 90 degrees apart in cross-section (21). If there is a concern for dilation or short segment disease then additional measurements in both views are recommended. If there is presence of increased BWT, then it is important to note whether the patient has long segment, continuous disease, or skip lesions. The length of each segment should be estimated utilizing the caliper measurement tool available on standard US machines.in the longitudinal plane to assess the length of the bowel involved. The frame can then be adjusted to the next longitudinal bowel segment and each length added together to estimate the full length of the segment involved. The total length of disease should be documented as well as the presence and length of skip lesions, where applicable. This should be documented and described in the small and large bowel, but is of particular importance in the small bowel, in which skip lesions are most often identified.

Echostratification

Echostratification or bowel wall layers seen sonographically can be disrupted in more severe disease, reflecting both severe acute inflammation and bowel damage. Here, mural layers are disrupted, making differentiation challenging, secondary to inflammation and edema (Fig. 3A). In more chronic disease, increased accentuation has been documented with smooth muscle hypertrophy due to fibrosis (22). Milder disease is more difficult to appreciate, often appearing normal, but prominence of submucosa to mucosa may be a promising area for future studies in terms of identifying chronicity. A description of the pattern of BWT, echostratification, length of disease as well as reference to anatomical location in the abdomen are helpful for identification of diseased areas and can be utilized for comparison with future ultrasound examinations as well as other forms of cross-sectional imaging.

Hyperemia (Color Doppler Signal)

BWT and hyperemia have been established as the 2 most significant parameters in predicting disease severity with IUS and are important components of validated ultrasound scoring systems (14,15). Hyperemia can be appreciated with color Doppler assessment which is a standard component of bowel ultrasound assessment (Fig. 3B). Increased vascular signal in the submucosa that penetrates into the muscularis propria has been identified as a significant marker of inflammation in patients with IBD and increased signal is predictive of more severe disease in both pediatric and adult populations (14,15). The Limberg score (23) can be used as a measure of vascularity, however, given its semi-quantitative nature, there is potential for inter-rater variability and more reliable quantitative measurements have been proposed. Color Doppler pulse repetition frequency should be set to 5–7 cm/s to optimize sensitivity for capturing flow in small caliber vessels/capillaries with gain set to remove artifact. To date, there is no standardized protocol for measurement of color Doppler in children, but given its value in predicting disease severity, this is the focus of ongoing studies.

Motility

Real-time motility assessment is an important aspect of disease activity; however, standardization is lacking. Differentiation of large versus small bowel is facilitated, as the small bowel exhibits liquid contents with active peristalsis (fed state) in comparison to the more static appearance of colonic stool. Peristalsis can be helpful in examining areas that are suspicious for stenosis and/or stricture formation with proximal dilation, while small bowel stool is also commonly seen in stricturing CD and not used to differentiate large intestine from small intestine. The proximal segment may appear hyperperistaltic in comparison to the area of luminal narrowing with hypoperistaltic features. Luminal diameter is highly variable and dependent on recent intake and activity levels, but generally a diameter >3 cm in the small bowel is considered abnormal

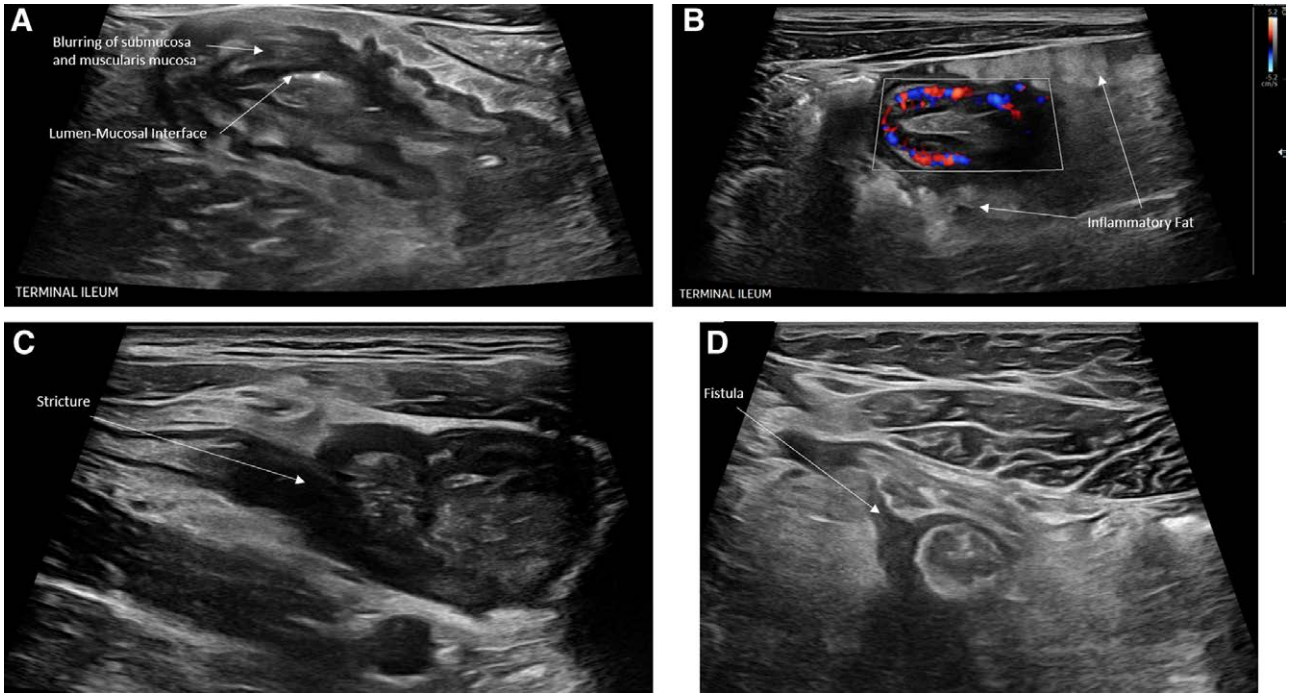

FIGURE 3. (A) Ultrasound still frame showing loss of bowel wall stratification shown in the terminal ileum with disruption between the bowel layers in a thickened terminal ileum. (B) Ultrasound still frame displaying increased color Doppler signal representing increased bowel wall hyperemia in the terminal ileum encased in surrounding hyperechoic inflammatory fat. (C) Ultrasound still frame highlighting inflamed terminal ileum with a stricture characterized by luminal narrowing and proximal bowel dilation. (D) Ultrasound still frame highlighting a fistula tract from an inflamed terminal ileum leading to an intraabdominal wall abscess.

and indicates proximal dilation with distal stricture formation (Fig. 3C). In accordance, small bowel luminal diameter <10 mm may be suggestive of stenosis/stricture formation (24).

MESENTERIC FEATURES

Mesenteric features of importance in pediatric IBD assessment include hyperemia (as assessed with color Doppler blood flow to the bowel wall), lymphadenopathy, and inflammatory fat.

Mesenteric Inflammatory Fat

Mesenteric inflammatory fat, or "creeping" fat is a well-recognized feature of inflammation associated with CD (15). Increased inflammatory fat can be visualized as hyperechoic areas extending from the serosa into the mesentery, essentially wrapping the outer bowel wall (Fig. 3B). Significant thickening of the mesenteric fat can have a mass-effect, displacing adjacent bowel loops. There is no standardized measure to quantify mesenteric inflammatory fat visualized on ultrasound and thus, many sonographers will comment on the presence or absence of inflammatory fat.

Lymphadenopathy

Lymphadenopathy, and more specifically, enlargement of mesenteric lymph nodes >10 mm in short axis, has been associated with active CD inflammation, although are nonspecific (15). The interpretation of enlarged mesenteric lymph nodes is challenging in the pediatric population as children commonly have mesenteric adenitis related to intercurrent infection or other etiologies. There is limited data on interpretation and reporting lymphadenopathy in children and more research is needed before standardized reporting can be recommended.

FEATURES OF PENETRATING DISEASE

Fistulae and abscesses can also be identified with bowel ultrasound with studies performed primarily in adult patients demonstrating a sensitivity and specificity of 72%–87% and 90%–96% for fistulae and a sensitivity and specificity of 71%–100% and 77%–94%, for abscesses, respectively (25,26). Fistulae may appear as hypoechoic tracts from the bowel wall with inner hypoechoic areas (air) in the center (Fig. 3D). Areas that appear to have rounded anechoic centers within the mesenteric inflammatory fat are suspicious for abscess or fistula tract into an inflammatory mass (phlegmon). Detection can be challenging as they are often accompanied by abnormal bowel wall appearance, with gas-filled abscesses mimicking air-filled bowel, and thus, penetrating disease identification is an advanced skill. Also of note, but of unclear clinical significance, is the presence of free fluid in the abdomen, which appears anechoic (27).

MONITORING DISEASE WITH IUS IN CHILDREN

Strict disease monitoring with a goal of treat-to-target mucosal and transmural healing in children requires accurate noninvasive tools to serially monitor disease activity. IUS has been shown to be accurate for the detection of IBD activity (15). In addition, changes in BWT and hyperemia can be seen as early as 2 weeks after initiation of antitumor necrosis factor-alpha therapy, and changes in these parameters are persistent over time (26). Early changes on IUS, including normalization of hyperemia, may be able to predict responsiveness to biologic therapy treatment in children (30).

When monitoring response to IBD therapy in children, IUS is best performed first at baseline (ideally at or near the time of

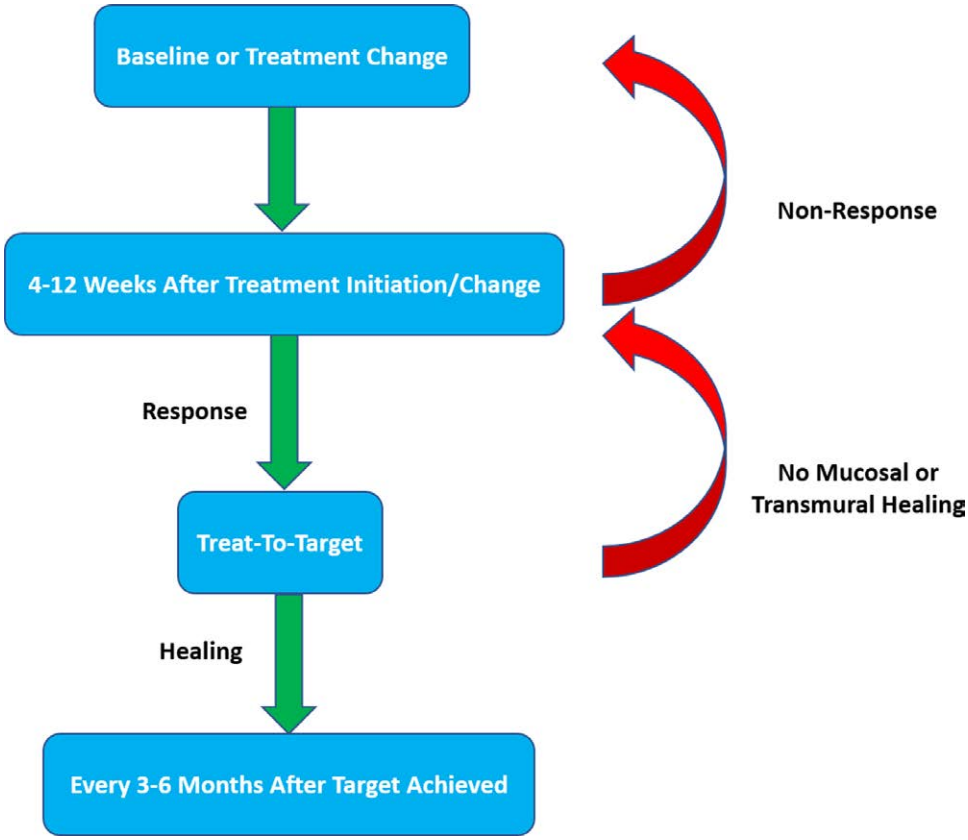

FIGURE 4. Proposed ultrasound monitoring algorithm. Ultrasound performed at baseline (time of colonoscopy or diagnosis) and/or when making a treatment change. Repeat ultrasound performed post-induction or 4–12 weeks after a treatment change and if no significant improvement on ultrasound in bowel wall thickness and hyperemia, treatment should be escalated/optimized or therapy change should be considered if there is evidence of worsening on ultrasound. The ultrasound should ultimately be repeated at treat-to-target colonoscopy and can then be utilized for serial monitoring moving forward every 3–6 months if targets achieved.

diagnostic ileocolonoscopy to confirm accuracy) and then repeated during induction or immediately after (4–8 weeks) therapy initiation to assess for improvement in IUS parameters. Follow-up can be planned every 3–6 months thereafter until treat-to-target colonoscopy is performed within the first year (Fig. 4). If there is no improvement or worsening of inflammation on IUS at 8 weeks, correlation with other biomarkers and potentially serum trough drug concentrations may guide treatment optimization with the goal of achieving improvement on IUS. IUS may then be used during each subsequent follow-up clinic visit to confirm transmural remission or healing after mucosal healing is confirmed on treat-to-target ileocolonoscopy. Ultimately, this IUS monitoring algorithm aims to detect persistent subclinical inflammation facilitating timely therapeutic adjustments aimed to alter the natural history of disease for children with the goal of preventing future complications including the need for surgery and hospitalizations.

CONCLUSIONS

An understanding of GI anatomy is fundamental to performing accurate examinations with IUS. A standardized approach to assessment of children with IBD with regard to identification of anatomical landmarks, technical considerations, and sequential evaluation and documentation of mesenteric and luminal features as well as penetrating disease are vital to the reliability of gastroenterologist-performed bedside IUS. Further studies are needed to establish normalized values for the pediatric population with regard to BWT, and prospective validation of IBD scoring systems is ongoing. Ultrasound provides a unique opportunity for both children and parents to engage in their care with safe, real-time, noninvasive bedside assessment. As an imaging modality, IUS has the potential to revolutionize clinical care with regard to monitoring of IBD disease activity, provision of care and resources, as well as clinical decision-making for the next generation of gastroenterologists and their patients.

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