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**Imaging and endoscopic tools in Pediatric inflammatory bowel disease: What's new?**

Imaging/Endoscopic Tools in Pediatric IBD

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**Abstract**

Pediatric inflammatory bowel disease is a chronic inflammatory disorder, with increasing incidence and prevalence worldwide. There have been recent advances in imaging and endoscopic technology for disease diagnosis, treatment, and monitoring. Intestinal ultrasound, including transabdominal, transperineal, and endoscopic, has been emerging for the assessment of transmural bowel inflammation and disease complications (e.g. fistula, abscess). Aside from surgery, IBD-related intestinal strictures now have endoscopic treatment options including through-the-scope balloon dilatation, injection, and needle knife stricturotomy, and new evaluation tools such as endoscopic functional lumen imaging probe (EndoFLIP). Unsedated transnasal endoscopy may have a role in patients with upper GI Crohn's disease or those with IBD with new upper GI symptoms. Improvements to dysplasia screening in pediatric patients with longstanding colonic disease or primary sclerosing cholangitis hold promise with the addition of virtual chromoendoscopy and ongoing research in the field of artificial intelligence assisted endoscopic detection. Artificial intelligence and machine learning is a rapidly evolving field, with goals of further personalizing IBD diagnosis and treatment selection, as well as prognostication. This review summarizes these advancements, focusing on pediatric patients with IBD.

**Key Words:** Intestinal ultrasound; Endoscopy; Inflammatory bowel disease; Pediatrics

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**Core Tip:** Recent advances to imaging and endoscopic techniques and technology have improved the diagnosis, treatment, and monitoring of pediatric patients with IBD. Options are now less invasive and can help avoid the repeat need for general anesthesia during endoscopy and imaging. Point-of-care ultrasound (transabdominal, transperineal, endoscopic), through-the-scope imaging (EndoFLIP) and treatment tools (balloon dilatation, injection, knife stricturotomy), unsedated transnasal endoscopy, virtual chromoendoscopy, and artificial intelligence are summarized in this current review.

## INTRODUCTION

## INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder consisting of Crohn's disease (CD), ulcerative colitis (UC) and IBD Unclassified (IBDU).[1,2] The incidence of IBD continues to rise, including pediatric-onset disease, with most recent estimates approaching 1.5-2 per 10,000 person years in areas with the highest rates of disease (Europe, North America).[3] The youngest children, being diagnosed with very early onset IBD (<6 years), are the fastest growing diagnosed population in Canada.[4] In the United States, nearly 1% of children and adults are living with IBD.[5] Recently westernized countries around the globe have seen a surge in newly diagnosed cases in places such as Asia and South America, where IBD was rarely diagnosed.[3] The gold standard of confirming a diagnosis of IBD includes macroscopic findings on endoscopy and microscopic findings on histopathology.[6,7] Imaging is a helpful additional tool, particularly in assessing bowel that is unable to be reached by upper and lower endoscopy. In addition to the initial diagnostic phase, endoscopy and imaging are essential tools in the ongoing monitoring and reassessment of disease activity in response to treatment. Disease monitoring has become a critical part of IBD patient care, particularly as mucosal healing has been identified as an important patient outcome to achieve.[8]

The field of IBD has seen ongoing advancement in imaging and endoscopy over recent years. This is particularly of interest for pediatric patients, where better access to more non-invasive diagnostic, therapeutic, and monitoring tools could reduce need for repeat general anesthesia for endoscopy, and help alter the natural history of the disease by identifying when a treatment change is needed. Endoscopic advances may also now allow for the role of therapeutic endoscopy in place of surgery. Given how quickly technology has advanced in this area in the past several years, it is an important topic to review for training and practicing pediatric gastroenterologists. While there have been a few reviews of imaging or endoscopy in pediatric IBD (discussed below), there is a need to combine these topics and review all recent technology advances as a comprehensive approach in pediatric IBD. This review summarizes these recent advances in imaging and endoscopy. This is not a systematic review, but rather a focused review intended to summarize new changes and provide important clinical context.

## IMAGING

### *Transabdominal intestinal ultrasound*

Until recent years, magnetic resonance (MR) and computed tomography enterography have been the mainstay of IBD imaging.[9] Gastroenterologist-performed point of care intestinal ultrasound (IUS) is now becoming more accessible in pediatric gastroenterology clinics worldwide, particularly since the implementation of the standardized International Bowel Ultrasound Group (IBUS) curriculum and available IUS scoring systems.[10] Bowel wall thickness, hyperemia, echogenicity, bowel wall stratification and surrounding fat proliferation, are some of the items that can be measured to assess bowel inflammation, with bowel wall thickness being one of the most relevant **(Figure 1).** Wall thickness has been shown to correlate well with MR and endoscopy.[10] It also allows for transmural assessment of the bowel, which endoscopy is unable to do. Importantly, IUS is well-received by pediatric patients and their caregivers, preferring it over other investigation modalities.[11] The optimal use of IUS in the decision-making tree during a patient's treatment course is under investigation. Whether or not IUS can replace repeat endoscopy is an important ongoing research question.

***Transperineal ultrasound***

Over a quarter of pediatric patients with IBD will have perianal disease in the form of fistulas and abscesses, most often associated with Crohn's disease.[12] MRI pelvis and exams under anesthesia (EUA) by a general surgeon are currently the only options for diagnosis and follow-up of both simple and complex perianal abscesses and fistula. Transperineal ultrasound, using micro-convex and micro–linear probes against the perineum, is a tool that is being explored in clinical practice for this use. Its use in clinic or at the same time as endoscopy may be a valuable means of perianal disease monitoring. Just like IUS, transperineal US is more accessible than MR, and avoids the general anesthetic associated with endoscopy and EUA, making it very favorable and accessible for repeated use as well as pediatric patients.

Another evolving utility is to use the transperineal probe to assess for rectum mucosal disease activity in ulcerative colitis, an area that is very difficult to see on transabdominal IUS.[13] A recent study in pediatric pateints with UC found transperineal US accuracy to be comparable to endoscopy.[13] It has also been shown to be able to distinguish between active IBD proctitis compared to non-IBD proctitis in children, by detecting thicker bowel wall in those with inflammation.[14] Therefore, combining transperineal and transabdominal US would allow for a more complete assessment in ulcerative colitis, colonic Crohn's disease, and IBD-associated perianal disease.

### *Endoscopic Ultrasound*

Mainly used in adult gastroenterology, endoscopic ultrasound (EUS) has thus far been focused on pancreatic and biliary tree disease. The use of EUS in IBD has been limited mainly to assess bowel wall thickness[15], as well as perianal fistula tracts[9,16,17]. Similarly to perineal US, its use to assess perianal fistulas and transmural inflammation, with the advantage of timing during colonoscopy, is an important area for further exploration. It may also be a helpful adjunct in guiding a surgical exam under anesthesia (EUA), and avoiding delay of the EUA by skipping the need for a pre-operative MRI pelvis.[17,18] Future research is also needed to learn more about the EUS measurement of bowel wall thickness, similarly to IUS, and if this could help us risk stratify or prognosticate patients at the time of their endoscopy.

## ENDOSCOPY

Upper and lower endoscopy is an essential diagnostic and assessment tool in pediatric inflammatory bowel disease.[6] It is the only IBD tool we have to assess mucosal disease both macroscopically and microscopically. Over recent years, there have been improvements in the quality of endoscopes (e.g. more high definition images), as well as available endoscopic tools such as balloon dilators and endoscopic needles.[16,18]

### *Endoscopic balloon dilatation*

Approximately 10% of pediatric IBD patients will present with an intestinal stricture at IBD diagnosis, with even more experiencing a stricture later on in the disease course (inflammatory or fibrotic) or as a post-surgical anastomotic stricture.[19] In addition to surgery, through-the-scope balloon dilatation has become a therapeutic option for short (<4cm) single intestinal strictures in the setting of treated IBD **(Figure 2).** In the first year post-dilatation, surgery-free rates have been reported in over 80%, although up to one-third may need repeat dilatation.[6,20,21] The European Society of Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) recently published a position paper on the use of endoscopic balloon dilatation for pediatric stricturing Crohn's disease, and highlighted the importance an experienced endoscopist performing the dilation on short strictures (up to 5cm) in the duodenum, terminal ileum, or colon, with no associated fistula, phlegmon, or abscess.[22] Fluoroscopy at the same time could be considered but is not necessary for all patients. Both primary and post-surgical anastomotic strictures, as well as inflammatory *vs* fibrotic strictures, have had similar success rates with endoscopic dilatation.[22]

***Endoscopic injection***

After dilatation disruption of strictured intestinal tissue, there is resulting inflammation that can lead to fibrosis and potentially reformation of the stricture. In an effort to reduce this inflammation and risk of re-stricturing, endoscopic intra-lesional anti-inflammatory medication injections (e.g. steroids, infliximab) have been studied, with mixed results.[6] One small pediatric randomized controlled trial found that compared to placebo injection, intra-stricture injection of corticosteroid after endoscopic balloon dilatation had increased time free of re-dilatation and surgery.[23] Topical mitomycin application post-dilatation, an anti-proliferative agent, has been reported for refractory esophageal strictures with mixed results[24] but is not yet widely explored in intestinal IBD strictures. Due to lack of sufficient evidence, intra-lesional injections and topical medication application during endoscopic balloon dilatation in pediatric IBD is not currently recommended.[6]

***Endoscopic stricturotomy***

Endoscopic needle knife stricturotomy performed by an experienced endoscopist is an alternative for the treatment of persistent IBD strictures despite attempts at endoscopic balloon dilatation.[25] Circumferential or radial incisions are carefully made at the stricture site with the through-the-scope needle knife. One recent study of IBD patients with anastomotic strictures reported an improvement rate of 20% with this technique, with over 80% not needing surgical resection of the stricture.[25] Endoscopic stricturotomy has been reported in CD strictures, post-IBD surgery anastomotic strictures, as well as ileal-pouch strictures.[26] Comparison between stricturotomy and balloon dilatation in CD anastomotic strictures in adult patients found that stricturotomy appeared to be more effective, although both carry perforation and bleeding risks.[27] This has not yet been widely studied in pediatric IBD patients.

***EndoFLIP***

Endoscopic functional lumen imaging probe (EndoFLIP) is a newer tool that is used at the time of endoscopy to assess lumen distensibility and stiffness, most commonly in the esophagus. It uses impedance planimetry to measure cross-sectional area, lumen diameter, distension pressure, and overall motility.[28] Its reported uses have been in patients with achalasia, eosinophilic esophagitis, as well as pre- and post- esophageal dilatation. The role of EndoFLIP in IBD-related intestinal strictures, as well as pre- and post-intestinal dilatation, has not been widely described. A recent case report described its use in a 31-year-old IBD patient with a Crohn's disease ileocolonic anastomotic stricture, demonstrating low lumen distensibility that improved after balloon dilatation.[29] This was able to demonstrate its use in objectively quantifying the degree of fibrosis and the amount of improvement following a dilatation, similar to studies on EndoFLIP in esophageal strictures. Other potential uses include quantification of the length of the intestinal stricture and the lumen size, particularly in cases where the stricture is unable to be traversed by the scope. If this tool is able to confirm that a stricture is relatively short (<4cm), it may be amenable to treatment by endoscopic balloon dilatation rather than surgery, as discussed above.

***Transnasal endoscopy***

Unsedated transnasal endoscopy (TNE) has been gaining popularity in the last few years, particularly for follow-up of eosinophilic esophagitis (EoE).[30] Being able to perform awake TNE in the GI clinic allows for faster patient access and the avoidance of a general anesthetic. It also can help ease wait times for endoscopy, and improve patient access. Its images and pathology specimens have been found to be comparable to standard peroral esophagogastroduodenoscopy.[30] Its use in IBD has not yet been explored. Approximately one-quarter of new pediatric IBD patients will have upper GI tract involvement.[19] Esophageal disease and stricturing due to Crohn's disease is rare but a possible disease complication, reported in up to 10% of adult patients with IBD.[31] In addition, patients with IBD have an increased risk of developing EoE.[32] Therefore, unsedated TNE may be a helpful clinic-based assessment tool in pediatric IBD patients presenting with dysphagia or upper GI symptoms, or in the reassessment of known complex upper GI tract CD.

***Virtual chromoendoscopy***

The development of virtual chromoendoscopy (using a filter rather than a spray dye during endoscopy) has allowed for improved visual enhancement of mucosal architecture during endoscopy. The majority of the literature has focused on its use in dysplasia detection, including colorectal adenocarcinoma.[33] Although rare in pediatric patients, colonoscopy for dysplasia surveillance is recommended annually starting at the time of diagnosis in patients with concurrent primary sclerosing cholangitis, as well as 8-10 years post-diagnosis of IBD affecting the colon (UC or colonic CD/IBDU).[34] Given the increasing rates of very early onset IBD (<6 years old at diagnosis), these patients will start undergo dysplasia screening while still under the care of pediatric gastroenterology specialists. Increasing accessibility and training of this technology in pediatric IBD would be highly valuable.

## ARTIFICIAL INTELLIGENCE (AI)

There has been a recent emerging role of AI in gastroenterology, to be able to improve endoscopic disease detection, diagnosis, and severity grading, due to high endoscopic inter-rater variability that currently exists.[35] It has also been proposed as a potential IBD research tool to replace the need for a central endoscopy reader, which could help with the speed of trial completion.[36] In addition to diagnostic endoscopy, the use of AI to help detect small bowel ulceration and non-obstructive bowel stenosis in video capsule endoscopy is a developing field.[37] Furthermore, similarly to virtual chromoendoscopy, there is much interest in the use of AI to detect pre-malignant and malignant lesions in long-term IBD patients.[38]

AI and its machine learning capabilities also holds promise in helping predict treatment response.[38] With the rapidly increasing number of available IBD biologics and small molecule medications, there is a important need for the development of personalized IBD care with the use of predictive markers. A recent systematic review of AI and machine learning in IBD identified 78 studies that have used clinical and microbiome data sets to aid in IBD diagnosis, disease course, and disease severity.[39] The number of recent publications on this subject has nearly doubled in the past 3 years, highlighting its growing interest.[37] Integrating AI at the time of patient diagnosis to help inform a treatment path with the highest likelihood of success, would be of particular interest.

## DISCUSSION

In conclusion, there have been exciting advances in imaging and endoscopic technology in pediatric IBD in recent years. Further development of less invasive diagnostic and therapeutic tools is always important for the pediatric population. There is new technology emerging from eosinophilic esophagitis and motility disorders that have not yet been explored in IBD (e.g. EndoFLIP, unsedated transnasal endoscopy). Limitations of this current review include it being a non-systematic review (possibility of missed studies), as well as paucity of available pediatric literature given that the majority of research has focused on adult IBD patients.

## CONCLUSION

The future of IBD will certainly benefit from diagnostic, assessment, and therapeutic tools that can aid in more personalized treatment to help establish early and sustained clinical, biochemical, and endoscopic remission. Future research should include prospective studies assessing efficacy, safety, and patient/caregiver satisfaction with these new imaging and endoscopic tools. It would also be of interest to identify if any of these tools are able to aid in the development of a treatment decision-tree and eliminate need for repeat sedated endoscopy or MRI in the pediatric IBD patient. Given the chronicity of IBD, and with young pediatric patients being the fastest growing population with newly diagnosed IBD, there is a need to continue to develop these tools for use in patients that will live with this disease and potential disease-related complications for multiple decades.

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