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Intestinal Ultrasound to Assess Ulcerative Colitis Disease Activity in Children: External Validation and Comparison of 2 Intestinal Ultrasound Activity Indices

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Background: There is currently no consensus on the definition of an abnormal intestinal ultrasound (IUS) for children with ulcerative colitis (UC). This cross-sectional study aimed to externally validate and compare 2 existing IUS indices in children with UC.

Methods: Children undergoing colonoscopy for UC assessment underwent IUS the day before colonoscopy, assessed with the Mayo endoscopic subscore. The UC-IUS index and the Civitelli index were compared with the Mayo endoscopic score in the ascending, transverse, and descending colon. The area under the receiver-operating characteristic curve for detecting a Mayo endoscopic score ≥2 of both scores was compared and sensitivity and specificity were calculated.

Results: A total of 35 UC patients were included (median age 15 years, 39% female). The area under the receiver-operating characteristic curve was higher for the UC-IUS index in the ascending colon (0.82 [95% confidence interval (CI), 0.67-0.97] vs 0.76 [95% CI, 0.59-0.93]; $P = .046$) and transverse colon (0.88 [95% CI, 0.76-1.00] vs 0.77 [95% CI, 0.60-0.93]; $P = .01$). In the descending colon, there was no difference (0.84 [95% CI, 0.70-0.99] vs 0.84 [95% CI, 0.70-0.98]). The optimal cutoff for the UC-IUS was <1 point to rule out a Mayo endoscopic score ≥2 (sensitivity: 88%, 100%, and 90% in the ascending, transverse, and descending colon, respectively) and a Mayo endoscopic score ≥2 could be detected using a cutoff of >1 (specificity: 84%, 83%, and 87%, respectively). For the Civitelli index, in our cohort, the optimal cutoff was <1 to rule out a Mayo endoscopic score ≥2 (sensitivity 75%, 65%, and 80%, respectively) and a cutoff >1 to detect a Mayo endoscopic score ≥2 (specificity 89%, 89%, and 93%, respectively).

Conclusions: In this cohort, the UC-IUS index performed better than the Civitelli index. The UC-IUS index had both a high sensitivity and specificity in this cohort, when using 1 point as cutoff for a Mayo endoscopic score ≥2.

Lay Summary

In this prospective study, we validated and compared 2 intestinal ultrasound indices to score pediatric ulcerative colitis: the UC-IUS index and the Civitelli index. In our cohort, the UC-IUS index was more accurate.

Key Words: pediatric ulcerative colitis, intestinal ultrasound, disease monitoring, validation

Introduction

Ulcerative colitis (UC) is a chronic relapsing and remitting condition, causing inflammation of the colonic mucosa, which may already start during childhood.[1] Mucosal healing is the most important treatment target, as ongoing inflammation—even in the absence of clinical symptoms—increases risk of clinical disease flares in the short term and risk of colon carcinomas in the longer term.[2,3] Although mucosal healing can accurately be assessed by colonoscopy, disease activity is preferably monitored noninvasively in the pediatric population. Intestinal ultrasound (IUS) is increasingly used as noninvasive monitoring tool. The advantage of IUS over other noninvasive biomarkers of disease activity, such as fecal calprotectin (FC), is the ability to assess disease extension and

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What is already known?
- Intestinal ultrasound (IUS) is increasingly used as point-of-care tool for patients with inflammatory bowel disease.

What is new here?
- This is the first study to externally validate existing IUS indices in children with ulcerative colitis.

How can this study help patient care?
- With the results if this study, caregivers can monitor disease activity of their pediatric ulcerative colitis patients more accurately with the use of IUS.

severity. However, there is currently no consensus on the definition of an abnormal IUS for children with UC.[4] In 2021, an IUS activity index for adults was published by Bots et al (ie, the UC-IUS index),[5] which demonstrated a strong correlation with endoscopic disease activity. In a pediatric UC population, an IUS activity index was developed in 2014 by Civitelli et al (ie, the Civitelli index).[6] Both scores included different IUS features and have not been externally validated in a pediatric population. The aim of this study was to externally validate both scores for usage in children with UC and to compare both scores in terms of diagnostic accuracy.

Methods

This was a prospective cross-sectional study at 2 academic hospitals in Amsterdam between August 2019 and August 2021. Consecutive patients who underwent a colonoscopy for diagnosis or follow-up of UC were requested to participate. Inclusion criteria were age between 6 and 17 years and diagnosis of UC according to the Paris classification.[7] Exclusion criteria were a history of intestinal resection, ongoing gastroenteritis, a histologically proven cytomegalovirus infection, Crohn's disease, and inflammatory bowel disease unclassified. Patients ≤5 years of age were not included, as IUS features such as bowel wall thickness (BWT) are different in this age group.[8]

Study design

Participants underwent IUS on the day before the colonoscopy, before the start of the bowel preparation, with a maximum of 7 days before or after the IUS and colonoscopy. Baseline demographics, including age, sex, body mass index, Paris classification, Pediatric Ulcerative Colitis Activity Index, C-reactive protein, and FC were collected from their medical files by an independent researcher, who was not involved in assessing the IUS or endoscopy (S.L.M.Z.). The maximum window between these data and the IUS was 1 month.

Intestinal ultrasound

The IUS was performed by an ultrasonographer (E.A.v.W.) who followed the International Bowel Ultrasound curriculum prior to the start of the study and who had performed >100 IUS examinations. The ultrasonographer was unaware of the clinical details and was blinded for the results of the colonoscopy, which was the reference standard. Participants did not receive a specific bowel preparation for the IUS but were asked not to take in carbonated fluids or solid food 4 hours prior to the IUS, as is recommended by the European Society of Gastrointestinal and Abdominal Radiology and European Society of Paediatric Radiology guidelines.[9] The IUS examinations were performed with a Philips EPIQ 5 machine (Philips Healthcare, Best, the Netherlands) using a convex probe (2-9 MHz, C9-2; Philips Healthcare) for general screening and a linear probe (4-12 MHz, L12-4; Philips Healthcare) for performing the bowel measurements. Image quality was rated as good, moderate, or bad by the ultrasonographer. Good image quality was defined as a sharp image with the bowel wall clearly visible. Moderate image quality was defined as a less clearly visible bowel wall (eg, because of small air artifacts). Bad image quality was defined as no sharp image with the bowel wall not clearly visible.

IUS measurements

Measurements were performed in the ascending, transverse, and descending and sigmoid colon. For the current study, we left the sigmoid out of the analyses, as we aimed to replicate the findings of the 2 previous studies. The BWT was measured in accordance with the International Bowel Ultrasound group recommendation[10]: from the lumen-mucosa interface to the muscularis-serosa interface in a noncontracted bowel loop, adjacent to a haustration at the most severely inflamed part of every bowel segment. BWT was measured twice in the longitudinal plane and twice in the cross-sectional plane. The mean of these 4 measurements was used. Vascularization of the bowel wall was measured with color Doppler, with a velocity rate of ±10 cm/s (the standard settings of our machine), and was categorized into categories of absent, spots, or stretches. Other parameters included colonic haustrations, wall layer stratification, and presence of mesenteric fat wrapping. The quality of the IUS images was also rated as good, moderate, or bad by the ultrasonographer. All measurements were recorded on a scoring form during the examinations.

IUS indices

The method to calculate the 2 IUS indices are shown in Table 1. The UC-IUS index by Bots et al[5] was designed in adult UC

Table 1. IUS scores

Index	Points
UC-IUS by Bots et al[5]: 0-7 points	
Bowel wall thickness	
≤2 mm	0
>2 mm	1
>3 mm	2
>4 mm	3
Doppler signal	
No signal	0
Spots	1
Stretches	2
Abnormal haustrations	1
Fat wrapping	1
Civitelli et al[6]: 0-4 points	
Bowel wall thickness >3 mm	1
Doppler signal (spots or more)	1
Abnormal haustrations	1
Abnormal wall layer stratification	1

Abbreviations: IUS, intestinal ultrasound; UC, ulcerative colitis.

patients (n = 60, median age 44 years), with endoscopy scored by the Ulcerative Colitis Endoscopic Index of Severity as the reference standard. No cutoff value for the score was proposed in their publication. The score by Civitelli et al[6] was designed in pediatric UC patients (n = 50, median age 13 years), with endoscopy scored by the Mayo endoscopic subscore as reference standard. In the conception cohort, a score >2 points demonstrated a sensitivity of 100% and a specificity of 93% (area under the curve of 0.98) for the detection of severe disease activity (Mayo endoscopic subscore 3) at endoscopy.

Colonoscopy

Colonoscopy was performed by experienced pediatric gastroenterologists (>10 years of experience), and was recorded. Videos were centrally read and scored per segment using the Mayo endoscopic subscore by a single experienced pediatric gastroenterologist (B.G.P.K.) who was blinded for the results of the IUS. Participants were prepared for the colonoscopy with Kleanprep or Moviprep (Norgine, Amsterdam, the Netherlands) according to local protocol.

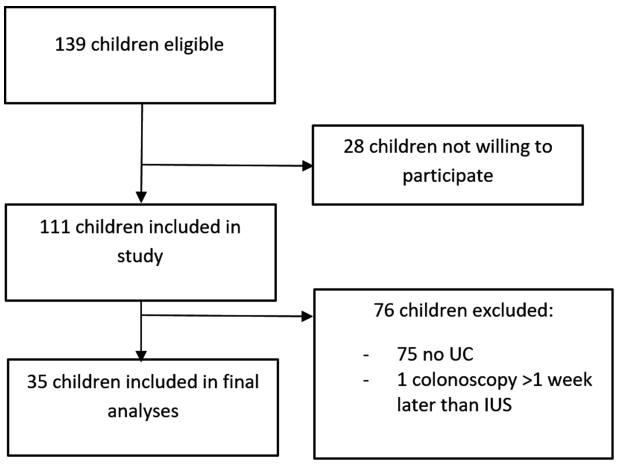

Figure 1. Flowchart of patient recruitment and inclusion. IUS, intestinal ultrasound; UC, ulcerative colitis.

Statistical analyses

Descriptive statistics were used to describe the population and the IUS measurements. The area under the receiver-operating characteristics curve (AUROC) was calculated, and the optimal cutoff value for the UC-IUS index was chosen based on the receiver-operating characteristic curve. Sensitivity and specificity including 95% confidence intervals (CIs) of both scores for detecting moderate severe disease activity (ie, Mayo endoscopic subscore ≥2) were calculated. The difference in AUROC was tested using MedCalc v 20.014 (MedCalc, Ostend, Belgium), using Hanley and McNeill's method. All other analyses were performed with SPSS version 25.0 (IBM, Armonk, NY, USA). *P* values of <.05 were considered significant. Hypothesizing the sensitivity of the IUS to be 90%, based on previous literature,[6] including 35 to 40 patients would result in a 95% CI of ±10%.

Ethical considerations

Informed consent was obtained from all patients aged between 12 and 18 years of age and all caregivers of patients <16 years of age. This study was approved by the institutional review board of the Amsterdam UMC, location AMC.

Results

A total of 36 patients with UC entered the study (Figure 1). One patient was excluded because the IUS was done >7 days

Table 2. Patient demographics (N = 35)

Age, y	15 (13-16)
Female	14 (39)
BMI, kg/m^2	19 (16-22)
Disease duration, y	0 (0-5)
Paris classification	
E1—ulcerative proctitis	3 (8)
E2—left-sided colitis	7 (19)
E3—extensive colitis (hepatic flexure distally)	6 (17)
E4—pancolitis (proximal to hepatic flexure)	19 (53)
S—ever severe	8 (22)
PUCAI	40 ± 23
CRP, mg/L	2 (1-8)
FC, mg/kg	2015 (1168-2691)

	Mayo Endoscopic Subscore 0	Mayo Endoscopic Subscore 1	Mayo Endoscopic Subscore 2	Mayo Endoscopic Subscore 3
Ascending colon	17 (47)	2 (6)	8 (22)	8 (22)
Transverse colon	14 (39)	4 (11)	8 (22)	9 (25)
Descending colon	11 (31)	4 (11)	8 (22)	12 (33)

Values are median (interquartile range), n (%), or mean (SD).
Abbreviations: BMI, body mass index; CRP, C-reactive protein; FC, fecal calprotectin; PUCAI, Pediatric Ulcerative Colitis Activity Index.

after the endoscopy, leaving 35 patients for the final analyses. The baseline characteristics are displayed in Table 2. Most patients (n = 27 [77%]) underwent the colonoscopy because of suspected IBD.

Ultrasound examinations

The colon was assessed by the IUS and the endoscopy in all 35 patients in all segments. The IUS measurements per segment are displayed in Table 3. The image quality of the IUS examinations was rated good in 28 (80%) patients and moderate in 7 (20%) patients.

Ultrasound indices

The total scores per segment for the UC-IUS index and the Civitelli index are displayed in Table 4. Most patients with a Mayo endoscopic score of 3 scored 4 points on the UC-IUS index and 2 points on the Civitelli index.

The AUROC for the UC-IUS index for detecting Mayo endoscopic score ≥2 was 0.82 (SE: 0.08; 95% CI, 0.67-0.97), 0.88 (SE: 0.06; 95% CI, 0.76-1.00), and 0.84 (SE: 0.07; 95% CI, 0.70-0.99) for ascending, transverse, and descending colon, respectively (Figure 2). As no cutoff value for the score was proposed in their publication, we determined the optimal cutoff based on the receiver-operating characteristic curve. The optimal cutoff was <1 point was to rule out a Mayo endoscopic score ≥2 (sensitivity: 88%, 100%, and 90%, respectively) and with a cutoff of >1 a Mayo endoscopic score ≥2 could be detected (specificity: 84%, 83%, and 87%, respectively) for the ascending, transverse, and descending colon, respectively (ie, a BWT of 2-3 mm [1 point] combined with another feature of inflammation [1 point] is predictive for a Mayo endoscopic score of 2).

The AUROC for the Civitelli index was 0.76 (SE: 0.09; 95% CI, 0.59-0.93), 0.77 (SE: 0.08; 95% CI, 0.60-0.93), and 0.84 (SE: 0.07; 95% CI, 0.70-0.98) for the ascending, transverse, and descending colon, respectively (Figure 2). When using the proposed cutoff by the authors (score >2) for detecting Mayo endoscopic score ≥2, the sensitivity of the Civitelli index was 6%, 24%, and 25% and the specificity was 95%, 100% and 93%, respectively, for the same segments. However, in our cohort, a cutoff of <1 was most optimal to rule out a Mayo endoscopic score ≥2 (sensitivity 75%, 65%, and 80%, respectively) and a cutoff >1 to detect a Mayo endoscopic score ≥2 (specificity 89%, 89%, and 93%, respectively).

The AUROC for the UC-IUS index was significantly higher in the ascending and transverse colon (P = .046 and .01, respectively).

Discussion

In this validation cohort of children with UC, the UC-IUS index performed better than the Civitelli index. The UC-IUS index had both a high sensitivity and specificity in this cohort, when using 1 point as cutoff for detecting moderate-to-severe disease activity (Mayo endoscopic subscore ≥2).

Table 3. IUS measurements per segment

	Mayo Endoscopic Subscore 0	Mayo Endoscopic Subscore 1	Mayo Endoscopic Subscore 2	Mayo Endoscopic Subscore 3
BWT, mm				
Ascending colon	1.46 (1.23-1.65)	3.09(1.67-3.09)	2.18 (1.44-3.59)	3.33 (2.49-4.09)
Transverse colon	1.71 (1.46-2.06)	1.58 (1.09-3.14)	2.82 (2.48-3.73)	3.69 (2.81-4.60)
Descending colon	1.79 (1.43-2.19)	1.54 (1.46-2.36)	2.62 (1.91-3.39)	3.73 (2.73-4.37)
Doppler signal				
Ascending spots	2 (12)	0	3 (38)	4 (50)
Ascending stretches	1 (6)	1 (50)	0	4 (50)
Transverse spots	2 (14)	0	4 (50)	3 (33)
Transverse stretches	1 (7)	1 (25)	0	4 (44)
Descending spots	2 (18)	0	3 (38)	4 (33)
Descending stretches	0	1 (25)	0	5 (42)
Abnormal haustrations				
Ascending colon	0	0	0	1 (13)
Transverse colon	0	0	2 (25)	4 (44)
Descending colon	0	0	2 (25)	7 (58)
Abnormal wall layer stratification				
Ascending colon	1 (6)	0	0	1 (13)
Transverse colon	1 (7)	0	1 (13)	2 (22)
Descending colon	1 (9)	0	0	2 (17)
Fat wrapping				
Ascending colon	1 (6)	1 (50)	1 (13)	3 (38)
Transverse colon	1 (7)	1 (25)	2 (25)	2 (22)
Descending colon	0	1 (25)	1 (13)	6 (50)

Values are median (interquartile range) or n (%).
Abbreviations: BWT, bowel wall thickness; IUS, intestinal ultrasound.

Table 4. IUS index scores per segment

	Mayo Endoscopic Subscore 0	Mayo Endoscopic Subscore 1	Mayo Endoscopic Subscore 2	Mayo Endoscopic Subscore 3
UC-IUS index				
Ascending colon	0 (0-0)	2 (0-2)	1 (0-2)	3 (2-4)
Transverse colon	0 (0-1)	0 (0-4)	3 (1-3)	4 (1-5)
Descending colon	0 (0-1)	0 (0-2)	2 (0-3)	4 (2-5)
Civitelli index				
Ascending colon	0 (0-0)	1 (0--)	1 (0-1)	2 (1-2)
Transverse colon	0 (0-0)	0 (0-2)	2 (0-2)	2 (0-4)
Descending colon	0 (0-0)	0 (0-1)	1 (0-2)	2 (1-3)

Values are median (interquartile range).
Abbreviations: IUS, intestinal ultrasound; UC, ulcerative colitis.

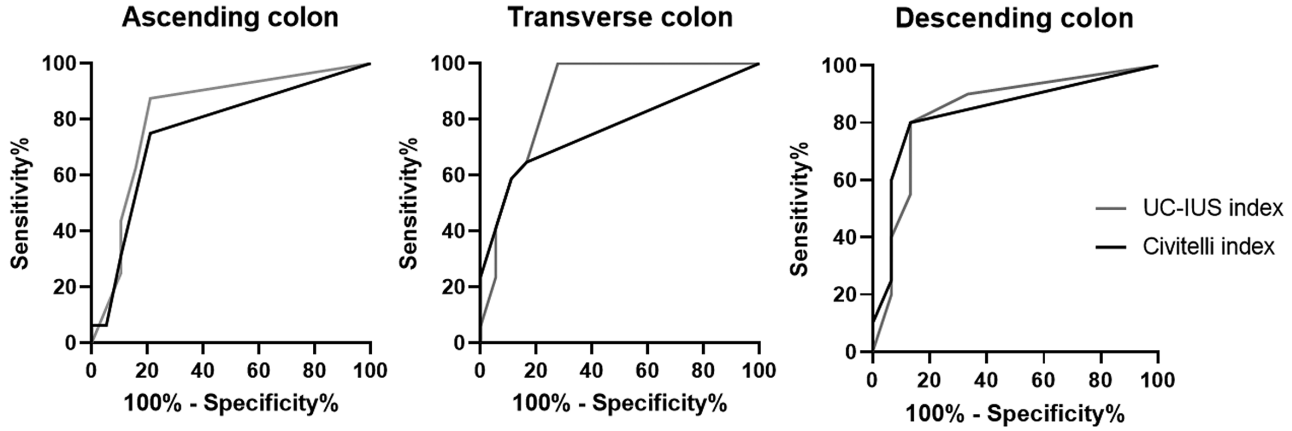

Figure 2. Receiver-operating characteristic curves of the ulcerative colitis intestinal ultrasound (UC-IUS) index (gray line) and the Civitelli index (black line) for detecting a Mayo endoscopic subscore of ≥2 in the ascending colon, transverse colon, and descending colon. The area under the receiver-operating characteristic curve was significantly higher for the UC-IUS index in the ascending colon (0.82 [SE = 0.08; 95% confidence interval (CI), 0.67-0.97] vs 0.76 [SE = 0.09; 95% CI, 0.59-0.93]; $P = .046$) and transverse colon (0.88 [SE = 0.06; 95% CI, 0.76-1.00] vs 0.77 [SE = 0.08; 95% CI, 0.60-0.93]; $P = .01$). There was no difference in the area under the receiver-operating characteristic curve in the descending colon between the UC-IUS index and Civitelli index (0.84 [SE = 0.07; 95% CI, 0.70-0.99] vs 0.84 [SE = 0.07; 95% CI, 0.70-0.98]; $P > .05$).

As IUS is an operator dependent technique, assessing UC disease activity with a reliable and accurate IUS index is important to ensure consistency in scoring among ultrasonographers. Many IUS indices have been designed and published, such as the Milan Ultrasound Criteria,[11] but most were found to have suboptimal methodology in a recent systematic review.[12] To our knowledge, the only 2 IUS indices for UC patients with good methodology that did not predefine cutoff values, but that determined these based on endoscopic disease activity, are the 2 indices validated in the current study.[5,6]

In the derivation cohort of Civitelli et al,[6] the sensitivity of the score was much higher (sensitivity 75%-96% vs 6%-25%) when using the cutoff value they proposed (score >2). Apart from risk for overfitting in the derivation cohort, this might be explained by a higher proportion of patients with severe endoscopic disease activity (56% with Mayo endoscopic subscore 3 vs 33% in our cohort). Interestingly, in our cohort, the mean BWT was lower compared with the cohorts of Civitelli et al and Bots et al (3.3-3.7 mm vs 5-5.5 mm in segments with Mayo endoscopic subscore 3),[5,6] partly explaining the low sensitivity values that we observed. Although the measurement method for BWT was comparable in both studies, it is well established that BWT can vary due to haustrations and mucosal folds. Therefore, the European Federation of Societies for Ultrasound in Medicine and Biology recommends to avoid these when measuring BWT.[13] We cannot establish whether difference in methodology of IUS explains the observed difference.

The cutoff for BWT in children with inflammatory bowel disease has been a subject of debate. The most frequently used cutoff in published studies has been 3 mm[4]; however there is no publication to substantiate this cutoff. In concordance with the study by Bots et al,[5] our results suggest that a mildly increased BWT (2-3 mm), combined with 1 or more other features of inflammation, or a BWT >3 mm alone is already indicative of moderate-to-severe endoscopic disease activity. This cutoff for BWT is in line with a systematic review on bowel ultrasound measurements in healthy children, which reported a pooled mean colonic BWT of ± 1.2 ± 0.2 mm, with a maximally reported BWT of 1.9 mm.[8]

IUS is currently still underutilized in many pediatric IBD centres[14]; however our findings support the uptake of IUS scored with the UC-IUS score as point-of-care tool in the management of pediatric UC. Our results confirm that IUS is accurate as a noninvasive tool to detect disease activity and thus could prevent need to repeat endoscopies and could

guide clinical decision making in the pediatric population. The advantage of IUS over other noninvasive tools such as FC is the information on disease extent, which is of value when deciding between systemic and local therapies (ie, enemas). In addition, most children in puberty prefer to undergo an IUS over collecting stool,[15] which is experienced as embarrassing by teenagers.[16] The responsiveness of IUS over time has already been demonstrated in a cohort of 224 adult UC patients,[17] making it a suitable monitoring tool. IUS has also been suggested as prediction tool for corticosteroids failure in children with acute severe colitis in a small retrospective study, although these findings are still to be replicated in a larger prospective cohort.[18] Data on the predictive value of IUS for UC flares are also needed.

The strengths of our study are the prospective design, short interval between IUS and colonoscopy, blinding of the ultrasonographer for clinical details, and central reading procedure for the colonoscopies. The limitation of this study is the relatively high velocity rate for Doppler. We used the standard settings of our ultrasound machine as used by our pediatric radiology department, but we might have missed some subtle Doppler signals. Another limitation is the relatively small sample size. Including more participants would have decreased the 95% CI of the AUROC.

Conclusions

With this study, we externally validated the UC-IUS index for usage in the pediatric UC population. In our cohort, the UC-IUS index performed better than the Civitelli index. Increased BWT (>2 mm) in combination with 1 or more other signs of inflammation or BWT >3 mm accurately predicted endoscopic disease activity in this cohort.

Author Contribution

Conception and design of the study: E.A.v.W., R.R.v.R., J.v.S., G.R.D., MA, B.G.P.K. Data acquisition: E.A.v.W., R.R.v.R., S.L.M.Z., F.A.E.d.V., J.v.S. Analyses and data interpretation: all authors. Preparing first draft: E.A.v.W. Revising the work critically for important intellectual content: all authors. All authors approved the final version of the manuscript

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Conflicts of Interest

All authors report no conflicts of interest in relation to the submitted work.

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

References

1. Domènech E, Mañosa M, Cabré E. An overview of the natural history of inflammatory bowel diseases. *Dig Dis*. 2014;32(4):320-327. doi:10.1159/000358131
2. Sarbagili-Shabat C, Weiner D, Wardi J, Abramas L, Yaakov M, Levine A. Moderate-to-severe endoscopic inflammation is frequent after clinical remission in pediatric ulcerative colitis. *J Pediatr Gastroenterol Nutr*. 2021;72(4):569-573. doi:10.1097/MPG.0000000000003018
3. Duricova D, Burisch J, Jess T, Gower-Rousseau C, Lakatos PL. Age-related differences in presentation and course of inflammatory bowel disease: an update on the population-based literature. *J Crohns Colitis*. 2014;8(11):1351-1361. doi:10.1016/j.crohns.2014.05.006
4. van Wassenaer EA, de Voogd FAE, van Rijn RR, et al. Diagnostic accuracy of transabdominal ultrasound in detecting intestinal inflammation in paediatric IBD patients—a systematic review. *J Crohns Colitis*. 2019;13(12):1501-1509. doi:10.1093/ecco-jcc/jjz085
5. Bots S, Nylund K, Löwenberg M, Gecse K, D'Haens G. Intestinal ultrasound to assess disease activity in ulcerative colitis: development of a novel UC-ultrasound index. *J Crohns Colitis*. 2021;15(8):1264-1271. doi:10.1093/ecco-jcc/jjab002
6. Civitelli F, Di Nardo G, Oliva S, et al. Ultrasonography of the colon in pediatric ulcerative colitis: a prospective, blind, comparative study with colonoscopy. *J Pediatr*. 2014;165(1):78-84.e2. doi:10.1016/j.jpeds.2014.02.055
7. Levine A, Koletzko S, Turner D, et al. ESPGHAN revised porto criteria for the diagnosis of inflammatory bowel disease in children and adolescents. *J Pediatr Gastroenterol Nutr*. 2014;58(6):795-806. doi:10.1097/MPG.0000000000000239
8. van Wassenaer EA, de Voogd FAE, van Rijn RR, et al. Bowel ultrasound measurements in healthy children — systematic review and meta-analysis. *Pediatr Radiol*. 2020;50(4):501-508. doi:10.1007/s00247-019-04567-2
9. Taylor SA, Avni F, Cronin CG, et al. The first joint ESGAR/ ESPR consensus statement on the technical performance of cross-sectional small bowel and colonic imaging. *Eur Radiol*. 2017;27(6):2570-2582. doi:10.1007/s00330-016-4615-9
10. Novak KL, Nylund K, Maaser C, et al. Expert consensus on optimal acquisition and development of the International Bowel Ultrasound Segmental Activity Score (IBUS-SAS): a reliability and inter-rater variability study on intestinal ultrasonography in Crohn's Disease. *J Crohns Colitis*. 2021;15(4):609-616. doi:10.1093/ecco-jcc/jjaa216
11. Allocca M, Filippi E, Costantino A, et al. Milan Ultrasound Criteria are accurate in assessing disease activity in ulcerative colitis: external validation. *United European Gastroenterol J*. 2021;9(4):438-442. doi:10.1177/2050640620980203
12. Bots S, Nylund K, Löwenberg M, Gecse K, Gilja OH, D'Haens G. Ultrasound for assessing disease activity in IBD patients: a systematic review of activity scores. *J Crohns Colitis*. 2018;12(8):920-929. doi:10.1093/ecco-jcc/jjy048
13. Maconi G, Nylund K, Ripolles T, et al. EFSUMB Recommendations and Clinical Guidelines for Intestinal Ultrasound (GIUS) in inflammatory bowel diseases. *Ultraschall Med*. 2018;39(3):304-317. doi:10.1055/s-0043-125329
14. Gamboa HE, Molle-Rios Z, Anupindi SA. Underutilization of bowel ultrasound in North America in children with inflammatory bowel disease. *Dig Dis*. 2020;38(5):390-397. doi:10.1159/000503920
15. van Wassenaer EA, van der Klift RR, Staphorst MS, van der Lee JH, Benninga MA, Koot BGP. The child's perception on monitoring inflammatory bowel disease activity. *Eur J Pediatr*. 2022;181(3):1143-1149. doi:10.1007/s00431-021-04315-5
16. Heida A, Dijkstra A, Dantuma SK, van Rheenen PF. A cross-sectional study on the perceptions and practices of teenagers with inflammatory bowel disease about repeated stool sampling. *J Adolesc Health*. 2016;59(4):479-481. doi:10.1016/j.jadohealth.2016.06.009
17. Maaser C, Petersen F, Helwig U, et al. Intestinal ultrasound for monitoring therapeutic response in patients with ulcerative colitis: results from the TRUST&UC study. *Gut*. 2020;69(9):1629-1636. doi:10.1136/gutjnl-2019-319451
18. Scarallo L, Maniscalco V, Paci M, et al. Bowel ultrasound scan predicts corticosteroid failure in children with acute severe colitis. *J Pediatr Gastroenterol Nutr*. 2020;71(1):46-51. doi:10.1097/mpg.0000000000002677