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The Simplified MR Index of Activity Score in Pediatric Small-Bowel Crohn Disease: An Interreader Agreement and Responsiveness Study

Jonathan R. Dillman, MD, MSc^{1,2}, Nadeen Abu Ata, MD^{1,2}, Alexander J. Towbin, MD^{1,2,3}, Christopher G. Anton, MD^{1,2}, Ethan A. Smith, MD^{1,2}, Bin Zhang, PhD^{3,4}, Rebecca Imbus, BA, RT¹, Jean A. Tkach, PhD^{1,2}, Lee A. Denson, MD^{3,5}

¹Department of Radiology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, Cincinnati, OH 45244.

²Department of Radiology, University of Cincinnati College of Medicine, Cincinnati, OH.

³Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH.

⁴Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

⁵Division of Gastroenterology, Hepatology, and Nutrition, Cincinnati Children's Hospital, Cincinnati, OH.

Abstract

BACKGROUND.—The simplified MR index of activity (MaRIA) score is used to assess the severity of small-bowel inflammation without use of IV contrast material.

OBJECTIVE.—The purposes of this study were to assess interreader agreement on the use of simplified MaRIA scores for evaluation of the inflammatory activity of terminal ileal Crohn disease in children and young adults and to assess whether simplified MaRIA scores change after biologic medical therapy.

METHODS.—This analysis was ancillary to a previously reported primary prospective research investigation. The study included 20 children and young adults with newly diagnosed ileal Crohn disease and 15 healthy control participants who underwent research small-bowel MRI examinations between December 2018 and October 2021. The participants with Crohn disease underwent baseline MRI and MRI 6 weeks and 6 months after beginning anti-tumor necrosis factor α -treatment as well as weighted pediatric Crohn disease activity index (wPCDAI) and C-reactive protein (CRP) assessment on the day of each examination. Control participants underwent one MRI examination. Four pediatric radiologists independently assigned simplified MaRIA scores using axial and coronal T2-weighted SSFSE images. Median simplified MaRIA score among readers was computed. Interreader agreement was assessed with Fleiss kappa coefficients

Address correspondence to J. R. Dillman (jonathan.dillman@cchmc.org).

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and intraclass correlation coefficient (ICC). Analysis included the Mann-Whitney *U* test, Friedman test, and Spearman rank correlation.

RESULTS.—Simplified MaRIA scores (across time points and study groups) had substantial interreader agreement ($\kappa = 0.65$ [95% CI, 0.56–0.74]; ICC, 0.71 [95% CI, 0.63–0.78]). Median scores were higher in participants with Crohn disease at baseline than in healthy control participants (3.5 [IQR, 2.5–4.9] vs 0.5 [IQR, 0–2.0]; $p < .001$). Scores decreased after medical treatment in participants with Crohn disease ($p = .005$). The median score was 3.5 (IQR, 2.5–4.9) at baseline, 2.3 (IQR, 1.6–3.9) at 6 weeks, and 2.0 (IQR, 0.5–2.5) at 6 months. In participants with Crohn disease, median scores had significant correlations with wPCDAI ($\rho = 0.46$ [95% CI, 0.18–0.64]; $p < .001$) and CRP level ($\rho = 0.48$ [95% CI, 0.27–0.65]; $p < .001$).

CONCLUSION.—Radiologists had substantial agreement in use of simplified MaRIA scores to assess intestinal inflammation in ileal Crohn disease. Scores changed over time after medical therapy.

CLINICAL IMPACT.—The results support the simplified MaRIA score as an objective MRI-based clinical measure of intestinal inflammation in children and young adults with Crohn disease.

Keywords

children; Crohn disease; interobserver agreement; MR enterography; simplified MR index of activity

MRI plays an important role in the evaluation of children and young adults with Crohn disease [1, 2]. Specifically, MR enterography (MRE), an MRI examination tailored to assessing the small bowel, is commonly used to detect intestinal inflammation, assess treatment response, and evaluate known or suspected complications, such as stricturing and penetrating disease [1, 3]. At present, the severity of active inflammation of the bowel wall is typically evaluated in a subjective manner whereby the imaging report provides a qualitative description (e.g., mild, moderate, or severe intestinal inflammation).

MRI-based objective scoring systems have had little clinical use for reporting the degree of intestinal inflammation in patients with Crohn disease. Although several MRI-based scoring systems have been described (e.g., MR index of activity [MaRIA], Clermont score, and London score) [4], they are primarily used as research tools, in part because of their complicated nature. A simplified MaRIA scoring system has recently been described for evaluating the severity of intestinal inflammation in children and adults with Crohn disease. This simplified score has been found to strongly correlate with both the original MaRIA score and with the Crohn disease endoscopic index of severity, particularly for the terminal ileum [5–7]. The simplified MaRIA system, which does not require IV contrast material administration, yields a score that ranges from 0 to 5 for a given bowel segment. A score of 0 indicates no active inflammation; 1 or greater, the presence of active inflammation; and 2 or greater, the presence of severe active inflammation. The system is based on categoric reader assessments of bowel wall thickening, bowel wall intramural edema, perienteric inflammation, and presence of mucosal ulcers. A paucity of studies have evaluated interreader agreement of simplified MaRIA scores or change in score in response

to medical therapy, particularly in children and young adults. Such knowledge is essential if this scoring system is to be routinely used in both clinical practice and research.

The purposes of this study were to assess interreader agreement in the use of the simplified MaRIA scoring system for evaluation of the inflammatory activity of terminal ileal Crohn disease in children and young adults and to assess whether simplified MaRIA scores change in response to biologic medical therapy.

Methods

This analysis was ancillary to a previously reported primary prospective research investigation [8–10]. The study was institutional review board approved and HIPAA compliant. Informed consent was obtained for all participants, and assent was obtained from participants younger than 18 years.

Participants

We recruited children and young adults up to 25 years old with newly diagnosed small-bowel Crohn disease between December 2018 and October 2021 from the Cincinnati Children's Hospital Medical Center inflammatory bowel disease clinics. Eligibility criteria were as follows: newly diagnosed Crohn disease affecting the terminal ileum confirmed by ileocolonoscopy and either CT or MRI, plan for treatment with biologic (anti-tumor necrosis factor [TNF]- α) medical therapy, ability to undergo research MRI before start of biologic therapy and to undergo follow-up research MRI examinations approximately 6 weeks and 6 months into treatment, and age 10–25 years. Patients younger than 10 years were not approached for participation because patients in this age range have increased likelihood of having a genetic or immune defect as the cause of inflammatory bowel disease, which would potentially be associated with unique imaging features, severity of features, and responsiveness to medical therapy. Patients in this age range also have increased need for sedation or general anesthesia to successfully undergo research MRI. A priori exclusion criteria were known or suspected pregnancy and history of intestinal surgery with terminal ileal resection; however, no screened patients were excluded for these reasons. The presence of colonic inflammation and/or treatment with other medical therapies (e.g., immunomodulator or corticosteroid medication) in addition to anti-TNF- α medication were not exclusion criteria.

Healthy control participants between 10 and 25 years old were recruited through an e-mail notification to hospital employees. Potential control participants were considered ineligible if they had a medical condition involving the gastrointestinal tract (e.g., any form of inflammatory bowel disease), history of prior bowel surgery, contraindication to or inability to undergo MRI, or suspected or known pregnancy.

All participants were included in three prior studies that evaluated quantitative mesenteric blood flow measurements calculated from ECG-gated velocity-encoded phase contrast MRI [8], quantitative intestinal motility measurements derived from dynamic cine MRI [9], and quantitative bowel wall T1-relaxation measurements [10] in children and young adults with small-bowel Crohn disease.

MRI Protocol

Patients with Crohn disease and healthy control participants underwent dedicated research MRI examinations of the small bowel in a 1.5-T system (Ingenia, Philips Healthcare). The research MRI examinations were performed with patients awake; no examination was performed with sedation or general anesthesia. The research MRI protocol included standard anatomic sequences and additional quantitative pulse sequences. For this study, only axial and coronal images obtained with T2-weighted SSFSE sequences (without fat saturation) were evaluated. Pulse sequence parameters were as follows: section thickness, 5 mm; TE, 80 ms; FOV, 280 × 280 mm; matrix, 216 × 215; echo-train length, 112; parallel imaging (SENSE) acceleration factor, 2; and number of signals acquired, 1.

Research MRI examinations were performed before initiation of biologic medical therapy, 6 weeks (plus or minus 2 weeks) after treatment initiation (corresponding to the completion of treatment induction), and 6 months (plus or minus 4 weeks) after treatment initiation. Healthy participants underwent a single research MRI examination. Except for contrast material or water immediately before imaging, participants consumed nothing by mouth for a minimum of 4 hours before research examinations. During the 45-minute period before the MRI examination, the participants ingested 1000 mL of oral contrast material (Breeza, Beekley Medical) or, if the oral contrast material could not be tolerated, a similar volume of water. All participants successfully ingested the prescribed volume of oral contrast material or water. No IV contrast material or spasmolytic medication was administered.

Image Review

Four fellowship-trained pediatric radiologists (N.A. with 1, A.J.T. with 14, C.G.A. with 23, and E.A.S with 11 years of postfellowship experience) independently reviewed the axial and coronal T2-weighted SSFSE images from each research MRI examination using a research PACS workstation (Merge PACS, IBM Watson Health Imaging). The reviewers were blinded to one another's interpretations and to diagnosis (patient with Crohn disease vs healthy control participant), endoscopic findings, and other clinical data. The observers reviewed the images and assessed the terminal ileum (defined as the distal 15-cm segment of the ileum, extending to the ileocecal valve) in terms of bowel wall thickening greater than 3 mm, bowel wall intramural edema (i.e., bowel wall signal greater than that of normal loops of bowel), perienteric (i.e., mesenteric) inflammation, and mucosal ulcers. The readers assigned 2 points for mucosal ulcers when present and 1 point for each of the three other findings when present [5] (Fig. 1). They summed the assigned points to derive the overall simplified MaRIA score for the terminal ileum, ranging from 0 to 5 points. Before the assessments, the readers were given examples of the four findings to serve as reference illustrations. They were also given descriptions of the findings from the study by Ordás et al. [5]. There was no formal training session, and no formal training cases were made available.

Clinical Inflammatory Assessments

At each research encounter, a variety of clinical inflammatory assessments were performed in participants with Crohn disease. The weighted pediatric Crohn disease activity index (wPCDAI), a validated instrument used to assess disease activity in participants with

pediatric Crohn disease, was administered [11]. Laboratory inflammatory markers, including C-reactive protein (CRP) and fecal calprotectin, were measured at each research visit.

Statistical Analysis

Continuous data (including ordinal data) were summarized as median and IQR; categorical data were summarized as counts and percentages. The median terminal ileal simplified MaRIA score among the four readers for each MRI examination was calculated, and the Friedman test was used to assess whether these scores longitudinally changed over time in response to medical therapy in participants with Crohn disease. The Dunn multiple comparisons test was used for post hoc pairwise comparison of simplified MaRIA scores between time points (baseline imaging and 6 weeks and 6 months after initiation of treatment). The Mann-Whitney *U* test was used to compare median simplified MaRIA scores between participants with Crohn disease at baseline and healthy control participants.

In participants with Crohn disease, Spearman rank correlation was used to evaluate the relationships between median simplified MaRIA scores and wPCDAI and between median simplified MaRIA scores and levels of laboratory inflammatory markers for all three time points in both participant groups combined. Fleiss kappa coefficient was used to assess interreader agreement on simplified MaRIA scores, including the four individual components, between the four radiologists. Intraclass correlation coefficient (ICC) was used to assess absolute agreement in simplified MaRIA scores between readers. Strength of agreement was classified on the basis of kappa coefficients and ICC by use of criteria described by Landis and Koch [12]: < 0.00, no agreement; 0.00–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–1.00, almost perfect agreement.

A value of $p < .05$ was considered significant for all inference testing. In addition, 95% CIs were calculated as appropriate. All statistical analyses were performed with SAS software (version 9.4, SAS Institute).

Results

Participants

The participant flow diagram is shown in Figure 2. During the study period, 42 patients with Crohn disease met eligibility criteria and were recruited for participation; 22 of them declined. The resulting study groups were 20 enrolled patients (eight female and 12 male participants; median age, 14.0 years [IQR, 12.3–16.8 years]) and 15 healthy control participants (eight female and seven male participants; median age, 17.0 years [IQR, 15.0–22.0 years]). The baseline characteristics of the participants with Crohn disease, including baseline clinical measures of inflammatory activity and simplified MaRIA scores, are shown in Table 1.

All 20 participants with Crohn disease underwent baseline research MRI examinations within 8 weeks of diagnosis and before the initiation of anti-TNF medical therapy. Nineteen of the 20 participants underwent research MRI at 6 weeks; one participant was lost to follow-up because of the COVID-19 pandemic. Seventeen of the 20 participants underwent

research MRI at 6 months. The three patients who did not undergo 6-month examinations included the one patient who did not undergo the 6-week examination owing to the COVID-19 pandemic and two participants who underwent ileal surgical resection between the 6-week and 6-month study visits. All three participants with missing data were included in the statistical analyses, and the data from the available time points were used.

Change Over Time

Median simplified MaRIA scores in participants with Crohn disease changed over time in response to medical treatment ($p = .005$) (Fig. 3). The median simplified MaRIA scores were 3.5 (IQR, 2.5–4.9) at baseline, 2.3 (IQR, 1.6–3.9) at 6 weeks, and 2.0 (IQR, 0.5–2.5) at 6 months. The decrease in simplified MaRIA score between baseline and 6 weeks was not significant ($p = .29$), but the decrease between baseline and 6 months was significant ($p = .006$). The simplified MaRIA score did not significantly change between 6 weeks and 6 months ($p = .46$). Figure 4 shows images of a representative patient with Crohn disease with a decrease in simplified MaRIA score at 6 months.

Patients With Crohn Disease Versus Healthy Control Participants

Median terminal ileal simplified MaRIA scores were significantly higher in participants with Crohn disease at baseline than in healthy control participants (3.5 [IQR, 2.5–4.9] vs 0.5 [IQR, 0–2.0]; $p < .001$) (Fig. 3). In the 15 examinations of healthy participants, the four readers recorded the presence of bowel wall thickening greater than 3 mm in four to 10 examinations, intramural edema in two to seven examinations, mucosal ulcers in no to two examinations, and perienteric edema in one to six examinations. Figure 5 shows images from representative healthy participants with abnormal simplified MaRIA scores. In the 56 total examinations across the three time points in the 20 patients with Crohn disease, the four readers recorded the presence of bowel wall thickening greater than 3 mm in 45–49 examinations, intramural edema in 43–47 examinations, mucosal ulcers in 13–47 examinations, and perienteric edema in 11–25 examinations.

The numbers of participants in whom each individual simplified MaRIA feature was recorded as present, stratified by individual reader, are summarized in Table 2.

Correlation With Clinical Inflammatory Markers

Median terminal ileal simplified MaRIA scores exhibited significant correlation with wPCDAI ($\rho = 0.46$ [95% CI, 0.18–0.64]; $p < .001$) and CRP level ($\rho = 0.48$ [95% CI, 0.27–0.65]; $p < .001$) in participants with Crohn disease (Fig. 6). The simplified MaRIA scores also exhibited significant correlation with fecal calprotectin level ($\rho = 0.28$ [95% CI, 0.01–0.56]; $p = .045$).

Interreader Agreement

Interreader agreement among the four radiologists regarding terminal ileal simplified MaRIA scores and the four individual components of the scores for the total of 71 MRI examinations across all time points and participant groups is summarized in Table 3. Agreement on simplified MaRIA scores was substantial ($\kappa = 0.65$ [95% CI, 0.56–0.74], $p < .001$; ICC, 0.71 [95% CI, 0.63–0.78], $p < .001$). Figure 7 depicts the distribution of

simplified MaRIA scores among the four readers. Agreement was moderate for bowel wall thickening greater than 3 mm, intramural edema, and mucosal ulceration ($\kappa = 0.51\text{--}0.57$) and slight for perienteric inflammation ($\kappa = 0.16$).

Discussion

In this prospective study, terminal ileal simplified MaRIA scores had substantial interreader agreement among pediatric radiologists. The simplified MaRIA scores also correlated with multiple clinical markers of disease activity measured the same day MRI was performed, including wPCDAI, CRP, and fecal calprotectin. The scores differed significantly between patients with Crohn disease and healthy control participants with noninflamed bowel. Furthermore, simplified MaRIA scores changed longitudinally over time in response to biologic medical therapy, decreasing significantly 6 months after initiation of treatment.

In the original study describing the simplified MaRIA scoring system, Ordás et al. [5] found excellent interreader agreement; the ICC was 0.85 for two readers and 18 MRE examinations. In comparison, in this study, we found an ICC of 0.71 for four readers and 71 MRE examinations. This level of interreader agreement is similar to that observed in earlier studies of a variety of other MRI-based scoring systems for Crohn disease. Rimola et al. [13] assessed interreader agreement on three different scoring systems between two readers for 10 MRE examinations of adult patients. All three scoring systems were found to have substantial interobserver agreement; the ICCs were 0.70 for the original MaRIA score, 0.65 for the Clermont score, and 0.77 for the London score. In a similar study with two readers and 98 adult patients Puylaert et al. [4] found substantial interobserver agreement on the original MaRIA score (ICC, 0.70), Clermont score (ICC, 0.71), and London score (ICC, 0.72). Finally, Roseira et al. [14] found excellent interreader agreement on the simplified MaRIA score in a study with two readers and 84 patients; the ICC was 0.95 across all bowel segments.

Although we found substantial agreement between readers for the terminal ileal overall simplified MaRIA score, interreader agreement was moderate for three of the four individual components (presence of bowel wall thickening greater than 3 mm, bowel wall intramural edema, and mucosal ulcers) and slight for the presence of perienteric (mesenteric) inflammation. The poorer interreader agreement for presence of perienteric (mesenteric) inflammation may be related to difficulty in differentiating mesenteric inflammation from nonspecific free fluid and prominent mesenteric vessels. Although requiring further study, fat suppression techniques might improve the conspicuity of perienteric inflammation and thereby increase interreader agreement.

Simplified MaRIA scores decreased over time at the cohort level in response to biologic medical therapy. A limited number of studies have assessed how simplified MaRIA and other MRI-based scoring systems change in response to medical treatment in patients with small bowel Crohn disease. In a study by Hanžel et al. [15], 41 paired pretreatment and posttreatment MRE examinations were presented to three blinded radiologists. Scores with four different MRI-based systems all changed in response to treatment; both the simplified MaRIA and original MaRIA systems showed moderate-to-large responsiveness. The authors

concluded that the simplified MaRIA score may be preferable to the original MaRIA score because of its relative simplicity, shorter time to derive, and avoidance from IV contrast material administration. Fernández-Clotet et al. [16] found in 46 patients with Crohn disease that the simplified MaRIA score had moderate agreement with ileocolonoscopy for showing treatment response ($\kappa = 0.53$). Finally, in a validation study of the simplified MaRIA scoring system, Capozzi et al. [17] concluded that the simplified MaRIA score was both accurate and reliable in quantifying disease activity and response to treatment without the need for contrast-enhanced sequences. Specifically, simplified MaRIA scores decreased significantly over a 46-week period in bowel segments that exhibited ulcer healing endoscopically but did not change in bowel segments that exhibited persistent ulceration at ileocolonoscopy.

The readers in this study evaluated only axial and coronal T2-weighted SSFSE sequences without fat suppression. Simplified MaRIA scores were not determined with contrast-enhanced sequences, DWI, or other image contrast mechanisms. In their investigation comparing the accuracy of simplified MaRIA scores without and with contrast-enhanced sequences, Fernández-Clotet et al. [16] concluded that classification of treatment response with both methods was similar to that of endoscopy. Although additional studies are needed, the results of our study further support the notion that MRI evaluation of the bowel may be possible with shortened noncontrast protocols, particularly when the goal is to reassess disease activity and treatment response.

This study had limitations. First, all MRI examinations were performed and interpreted by radiologists from the same institution. Second, all MRI examinations were performed with a single 1.5-T unit from a single manufacturer. Third, simplified MaRIA scores were derived only for the terminal ileum; we did not evaluate the jejunum or colon. These bowel segments may not respond to Crohn disease the way the terminal ileum does, potentially impacting interreader agreement, change over time, and correlation with clinical markers of disease activity. In a study by Lepus et al. [6], the simplified MaRIA score was determined to be accurate in reflecting disease activity in the terminal ileum of pediatric patients with Crohn disease while having overall poor sensitivity for colonic disease activity. Fourth, we did not assess associations of simplified MaRIA scores with endoscopic or histologic findings. Finally, although all participants with Crohn disease were treated with an anti-TNF- α medication, some may have also been treated with other medical therapies (e.g., immunomodulator or corticosteroid medication), which could have influenced how simplified MaRIA scores changed over time and correlated with clinical markers of disease activity.

In conclusion, simplified MaRIA scores of the terminal ileum in children and young adults with Crohn disease had substantial interreader agreement. The level of measured interreader agreement was comparable to that previously observed in adults and to that observed for more complex MRI-based scoring systems. Furthermore, simplified MaRIA scores decreased longitudinally over time in response to biologic therapy and had changed significantly at the cohort level 6 months after the start of anti-TNF- α medication. Finally, simplified MaRIA scores correlated significantly with other clinical markers of inflammation, such as w PDAI, CRP level, and fecal calprotectin level. The results support the simplified MaRIA score as an objective MRI-based measure of intestinal inflammation

in children and young adults with Crohn disease that has potential utility in research and clinical settings.

Acknowledgments

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References

1. Bruining DH, Zimmermann EM, Loftus EV Jr, Sandborn WJ, Sauer CG, Strong SA; Society of Abdominal Radiology Crohn's Disease–Focused Panel. Consensus recommendations for evaluation, interpretation, and utilization of computed tomography and magnetic resonance enterography in patients with small bowel Crohn's disease. *Gastroenterology* 2018; 154:1172–1194 [PubMed: 29329905]
2. Mollard BJ, Smith EA, Dillman JR. Pediatric MR enterography: technique and approach to interpretation—how we do it. *Radiology* 2015; 274:29–43 [PubMed: 25531478]
3. Bhatnagar G, Von Stempel C, Halligan S, Taylor SA. Utility of MR enterography and ultrasound for the investigation of small bowel Crohn's disease. *J Magn Reson Imaging* 2017; 45:1573–1588 [PubMed: 27943484]
4. Puylaert CAJ, Nolthenius CJT, Tielbeek JAW, et al. Comparison of MRI activity scoring systems and features for the terminal ileum in patients with Crohn disease. *AJR* 2019; 212:[web]W25–W31 [PubMed: 30540212]
5. Ordás I, Rimola J, Alfaro I, et al. Development and validation of a simplified magnetic resonance index of activity for Crohn's disease. *Gastroenterology* 2019; 157:432–439 [PubMed: 30953614]
6. Lepus CA, Moote DJ, Bao S, Mosha MH, Hyams JS. Simplified magnetic resonance index of activity is useful for terminal ileal but not colonic disease in pediatric Crohn disease. *J Pediatr Gastroenterol Nutr* 2022; 74:610–616 [PubMed: 35149649]
7. Ordás I, Rimola J, Rodríguez S, et al. Accuracy of magnetic resonance enterography in assessing response to therapy and mucosal healing in patients with Crohn's disease. *Gastroenterology* 2014; 146:374–382 [PubMed: 24177375]
8. Ata NA, Dillman JR, Gandhi D, et al. Velocity-encoded phase-contrast MRI for measuring mesenteric blood flow in patients with newly diagnosed small-bowel Crohn disease. *AJR* 2022; 219:132–141 [PubMed: 35195433]
9. Dillman JR, Tkach JA, Imbus R, Towbin AJ, Denson LA. MRI-based characterization of intestinal motility in children and young adults with newly diagnosed ileal Crohn disease treated by biologic therapy: a controlled prospective study. *AJR* 2022; 219:655–664 [PubMed: 35544371]
10. Mahalingam N, Tkach JA, Denson LA, Dillman JR. Bowel wall MRI T1 relaxation estimates for assessment of intestinal inflammation in pediatric Crohn's disease. *Abdom Radiol (NY)* 2022; 47:2730–2738 [PubMed: 35657390]
11. Turner D, Levine A, Walters TD, et al. Which PCDAI version best reflects intestinal inflammation in pediatric Crohn disease? *J Pediatr Gastroenterol Nutr* 2017; 64:254–260 [PubMed: 27050050]
12. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; 33:159–174 [PubMed: 843571]
13. Rimola J, Alvarez-Cofiño A, Pérez-Jeldres T, et al. Comparison of three magnetic resonance enterography indices for grading activity in Crohn's disease. *J Gastroenterol* 2017; 52:585–593 [PubMed: 27599973]
14. Roseira J, Ventosa AR, de Sousa HT, Brito J. The new simplified MARIA score applies beyond clinical trials: a suitable clinical practice tool for Crohn's disease that parallels a simple endoscopic index and fecal calprotectin. *United European Gastroenterol J* 2020; 8:1208–1216
15. Hanžel J, Jairath V, Ma C, et al. Responsiveness of magnetic resonance enterography indices for evaluation of luminal disease activity in Crohn's disease. *Clin Gastroenterol Hepatol* 2022 Feb 9 [published online]

16. Fernández-Clotet A, Sapena V, Capozzi N, et al. Avoiding contrast-enhanced sequences does not compromise the precision of the simplified MaRIA for the assessment of non-penetrating Crohn's disease activity. *Eur Radiol* 2022; 32:3334–3345 [PubMed: 35031844]
17. Capozzi N, Ordás I, Fernandez-Clotet A, et al. Validation of the simplified magnetic resonance index of activity (sMARIA) without gadolinium-enhanced sequences for Crohn's disease. *J Crohns Colitis* 2020; 14:1074–1081 [PubMed: 32080712]

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HIGHLIGHTS**Key Finding**

- In patients with Crohn disease, simplified MaRIA scores had substantial interreader agreement ($\kappa = 0.65$; ICC, 0.71; $p < .001$), decreased after biologic therapy (3.5 to 2.3 to 2.0; $p = .005$), and correlated with wPCDAI ($\rho = 0.46$; $p < .001$) and CRP ($\rho = 0.48$; $p < .001$).

Importance

- Simplified MaRIA scores are an objective MRI-based measure of intestinal inflammation in pediatric Crohn disease with potential for use in research and clinical settings.

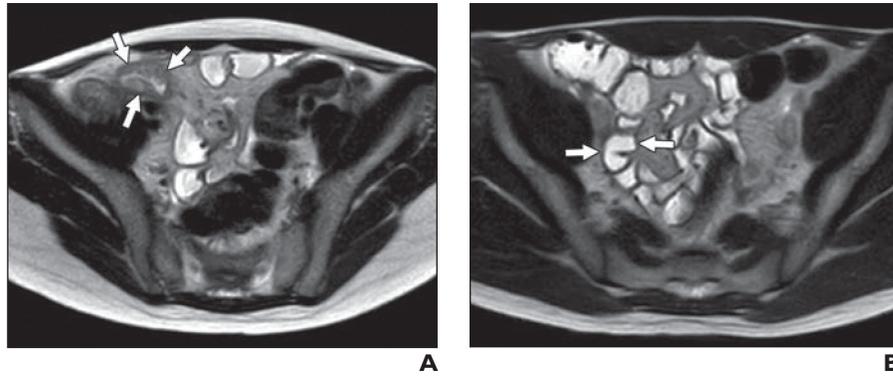


Fig. 1—
Simplified MR index of activity (MaRIA) scoring examples.
A, 17-year-old patient with newly diagnosed ileal Crohn disease. Axial SSFSE MR image shows terminal ileal bowel wall thickening greater than 3 mm, intramural edema, and mucosal ulcers (*arrows*), yielding simplified MaRIA score of 4.
B, 15-year-old healthy control participant. Axial SSFSE MR image shows normal appearance of terminal ileum (*arrows*), without wall thickening, intramural edema, mucosal ulcers, or perienteric inflammation. Simplified MaRIA score is 0.

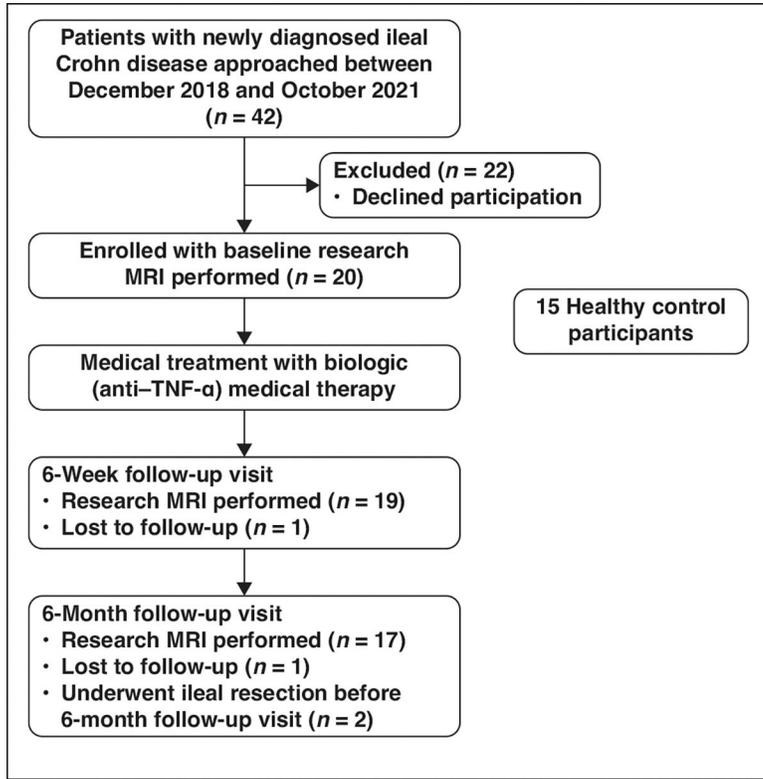


Fig. 2—. Flow diagram shows steps in participant selection. TNF = tumor necrosis factor. (Adapted from [9])

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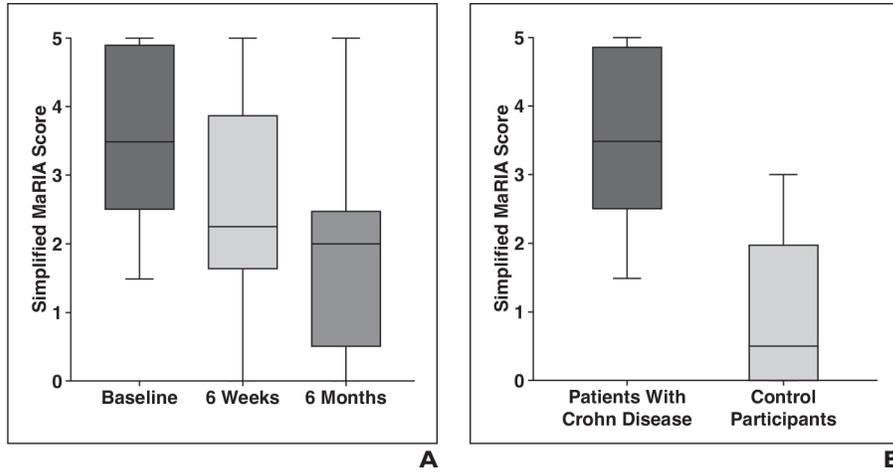


Fig. 3— Median terminal ileal simplified MR index of activity (MaRIA) scores in participants with Crohn disease.

A, Tukey box plot of scores assessed by four readers at baseline, 6 weeks, and 6 months shows significant decrease in score between baseline and 6 months but not between baseline and 6 weeks or between 6 weeks and 6 months. Boxes represent IQR of data; horizontal lines within boxes, median values; whiskers, minimum and maximum values.

B, Tukey box plot of scores in participants with Crohn disease at baseline ($n = 20$) and healthy control participants ($n = 15$) assessed by four readers shows significantly higher scores in participants with Crohn disease than in healthy control participants. Boxes represent IQR of data; horizontal lines within boxes, median values; whiskers, minimum and maximum values.

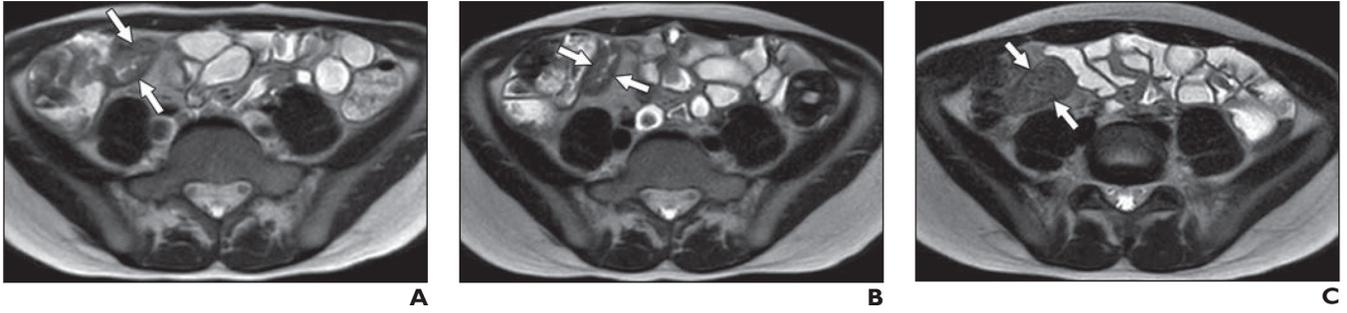


Fig. 4—
14-year-old patient with Crohn disease.
A, Axial SSFSE MR image from examination performed before medical therapy shows bowel wall thickening, intramural edema, and areas of mucosal ulcerations involving terminal ileum (*arrows*). All four readers assigned simplified MR index of activity (MaRIA) score of 5.
B, Axial SSFSE MR image from examination performed approximately 6 weeks after initiation of treatment shows findings involving terminal ileum (*arrows*) are similar to those in **A**. Simplified MaRIA scores ranged from 3 to 5 among four readers.
C, Axial SSFSE MR image from examination performed approximately 6 months after initiation of treatment shows decreased inflammation of terminal ileum (*arrows*) and stoollike material within lumen of terminal ileum. Simplified MaRIA scores ranged from 0 to 2 among four readers.

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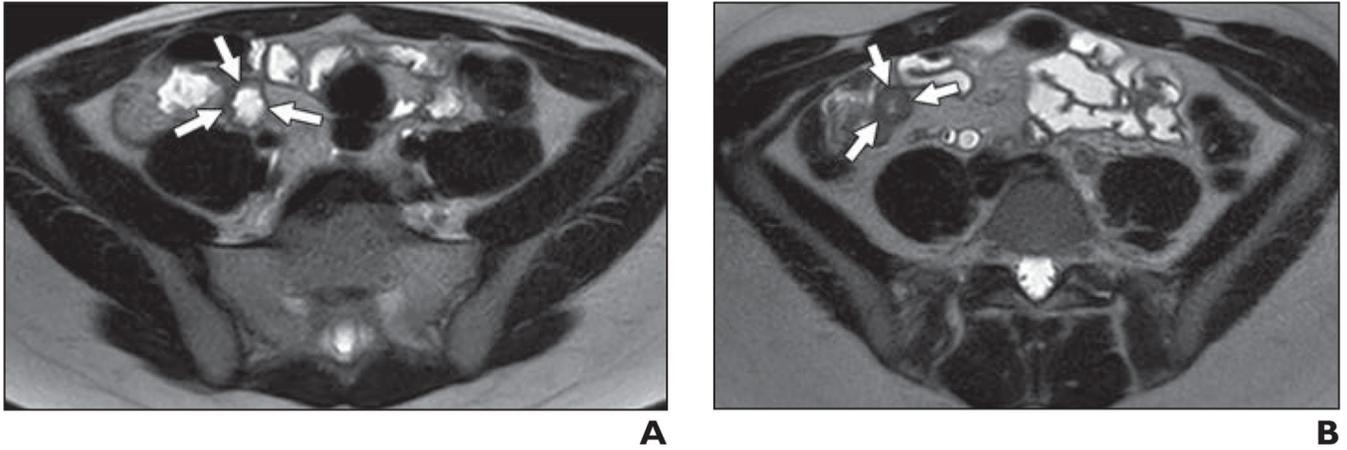


Fig. 5—

Two healthy control participants with abnormal (> 0) median simplified MR index of activity (MaRIA) scores among four readers.

A, 21-year-old participant. Axial SSFSE MR image shows mural thickening, intramural increased signal intensity, and potential mucosal ulcers of terminal ileum (*arrows*).

Simplified MaRIA scores ranged from 1 to 4 among four readers.

B, 25-year-old participant. Axial SSFSE MR image shows mural thickening, intramural increased signal intensity, and potential mucosal ulcerations of terminal ileum (*arrows*).

Simplified MaRIA scores ranged from 0 to 3 among four readers.

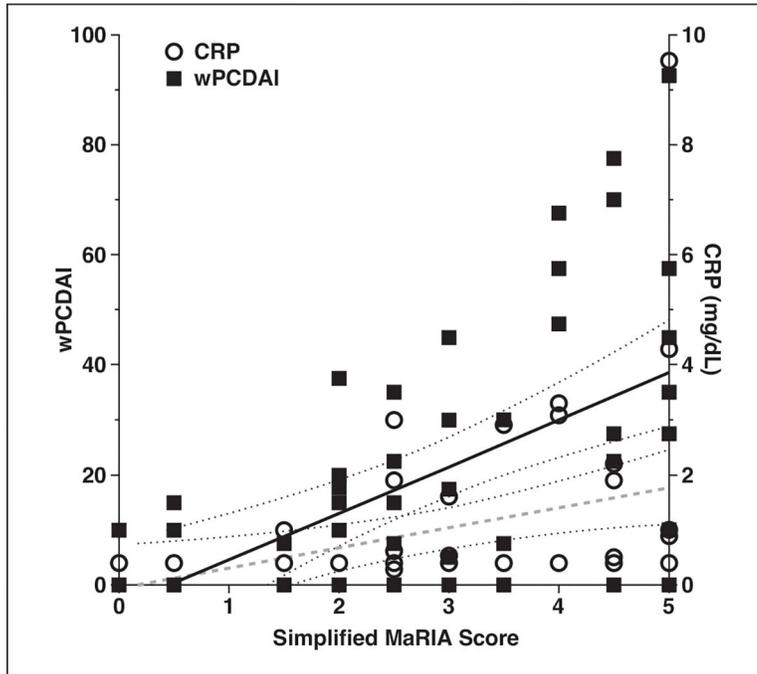


Fig. 6— Scatterplot shows relationships between median terminal ileal simplified MR index of activity (MaRIA) scores and both weighted pediatric Crohn disease activity index (wPCDAI) ($\rho = 0.46$, $p < .001$) and C-reactive protein (CRP) level ($\rho = 0.48$; $p < .001$) for all three time points combined in participants with Crohn disease. Solid (wPCDAI) and dashed (CRP) lines represent least-squares fit lines; dotted lines, 95% CIs for fit lines.

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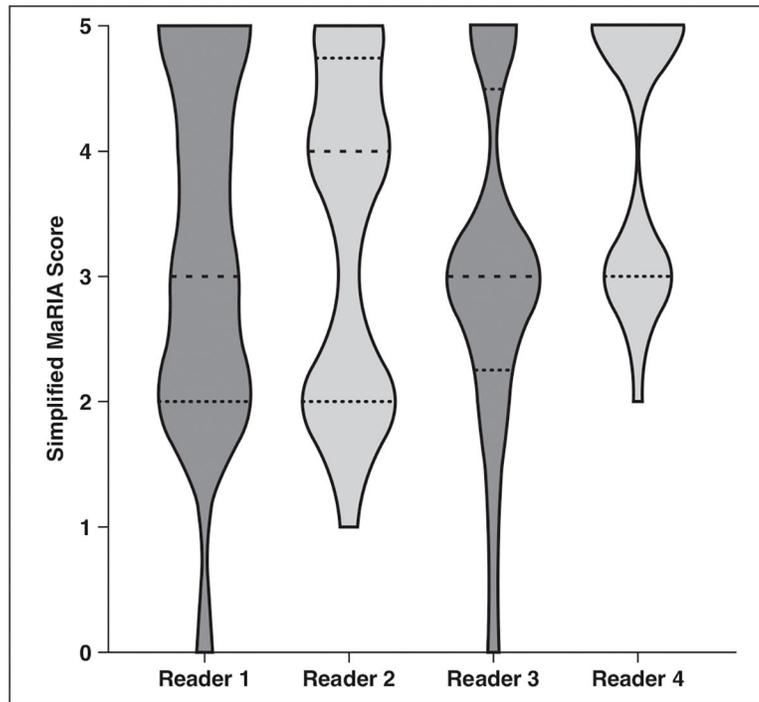


Fig. 7—. Truncated violin plot shows distribution of terminal ileal simplified MR index of activity (MaRIA) scores assigned by four pediatric radiologists in participants with Crohn disease at baseline before biologic medical therapy ($n = 20$ MR enterography examinations in 20 patients). Dashed lines represent medians, and dotted lines denote quartiles.

TABLE 1:

Baseline Characteristics of Participants With Crohn Disease ($n = 20$)

Characteristic	Median	IQR	Minimum	Maximum
Age (y)	14.0	12.3–16.8	12.0	18.0
wPCDAI (range, 0–125)	30.0	18.1–54.4	0	92.5
CRP level (mg/dL) ^a	0.8	0.4–2.7	0.4	9.5
Fecal calprotectin level ($\mu\text{g/g}$ of feces) ^b	290.2	120.1–851.5	64.2	1406.0
Simplified MaRIA score (range, 0–5)				
Median of four readers	3.5	2.5–4.9	1.5	5.0
Reader 1	3.0	2.0–5.0	0	5
Reader 2	4.0	2.0–4.8	1	5
Reader 3	3.0	2.3–4.5	0	5
Reader 4	5.0	3.0–5.0	2	5

Note—wPCDAI = weighted pediatric Crohn disease activity index, CRP = C-reactive protein, MaRIA = MR index of activity.

^aNormal, 0.4 mg/dL.^bNormal, < 50 $\mu\text{g/g}$ of feces.

Number of Examinations Showing the Individual Features Contributing to the Simplified MR Index of Activity Score, Summarized for Independent Readers

TABLE 2:

Characteristic	Reader 1	Reader 2	Reader 3	Reader 4
Healthy control participants (n = 15)				
Bowel wall thickness > 3 mm	4	5	10	6
Intramural edema	3	2	7	4
Perienteric inflammation	1	1	5	6
Mucosal ulcers	0	2	0	1
Participants with Crohn disease (n = 56) ^a				
Bowel wall thickness > 3 mm	47	45	49	48
Intramural edema	43	45	46	47
Perienteric inflammation	14	13	37	47
Mucosal ulcers	15	25	11	23

^a: All three time points combined.

TABLE 3: Interreader Agreement Between Four Radiologists on Simplified MR Index of Activity (MaRIA) Scores and Individual Findings Contributing to Scores (*n* = 71)

Characteristic	Fleiss K			ICC		
	Value	95% CI	<i>p</i>	Value	95% CI	<i>p</i>
Simplified MaRIA score	0.65	0.56–0.74	< .001	0.71	0.63–0.78	< .001
Bowel wall thickening > 3 mm	0.51	0.41–0.61	< .001	—	—	—
Intramural edema	0.54	0.44–0.63	< .001	—	—	—
Perienteric inflammation	0.16	0.06–0.26	.02	—	—	—
Mucosal ulcerations	0.57	0.48–0.67	< .001	—	—	—

Note—Results across all examinations performed at all time points in participants with Crohn disease and healthy control participants. Dash [—] indicates not applicable. ICC = intraclass correlation coefficient.