

A simple MR enterography assessment of Crohn disease activity based on the most affected bowel segment

A retrospective cohort study

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Abstract

This retrospective study aimed to propose and validate a simple magnetic resonance enterography (MRE)-based assessment of Crohn disease (CD) activity based on the most inflamed bowel segment. A total of 252 adult patients who underwent MRE for suspected or known CD were included. Three abdominal radiologists assessed the simplified Magnetic Resonance Index of Activity (sMARIA) score using MRE. The Maximal Segmental Score was defined as the largest segmental sMARIA among 6 evaluated bowel segments in a patient. The global sMARIA was obtained from the sum of each segmental sMARIA score. Correlation analysis was performed between global sMARIA and Maximal Segmental Score. For patients with endoscopic results, correlation analysis was performed between the simple endoscopic score for CD (SES-CD) and maximal segmental score. The diagnostic performance of the maximal segmental score to predict endoscopic remission (SES-CD <3) was evaluated using the receiver operating characteristic curve analysis. Global sMARIA and Maximal Segmental Score correlated strongly ($\rho = 0.954$, 95% confidence interval: 0.941–0.964). In 77 patients with endoscopic results, global sMARIA ($\rho = 0.685$) and Maximal Segmental Scores ($\rho = 0.634$) moderately correlated with SES-CD without significant difference between 2 scores ($P = .17$). The area under the receiver operating characteristic curve to predict endoscopic remission was 0.850 for global sMARIA and 0.843 for Maximal Segmental Score without significant difference between them ($P = .73$). The Maximal Segmental Score based on the evaluation of the most inflamed bowel segment can be a simple practical MRE-based index to represent overall disease activity and predict endoscopic remission in CD.

Abbreviations: AUC = area under the curve, CD = Crohn disease, ICC = intraclass correlation coefficient, IQR = interquartile range, MARIA = magnetic resonance index of activity, MEGS = magnetic resonance enterography global score, MRE = magnetic resonance enterography, PCDAI = pediatric clinical disease activity index, PCDMRI = pediatric CD magnetic resonance index, ROC = receiver operating characteristics, SES-CD = simple endoscopic score for Crohn disease, sMARIA = simplified MARIA.

Keywords: Crohn disease, diagnosis, magnetic resonance enterography, magnetic resonance index of activity, maximal segmental score, remission

1. Introduction

Crohn disease (CD) is a chronic progressive inflammatory bowel disease that relapses and remits.^[1] Therefore, an objective and reliable assessment of the disease activity is essential for choosing optimal treatment options and monitoring treatment response in patients with CD. Magnetic resonance enterography (MRE) and ileocolonoscopy are widely accepted techniques for evaluating disease extent and activity in CD.^[2,3] MRE is a

noninvasive, radiation-free cross-sectional imaging that evaluates the entire gastrointestinal tract including the small bowel, and extraluminal structures.

Several MRE-based indices have been developed for objective assessment of disease activity in CD patients, including the magnetic resonance index of activity (MARIA), the CD magnetic resonance imaging index, the MRE global score (MEGS), and the simplified MARIA (sMARIA).^[4–7] However, despite

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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their strengths, the routine use of MRE-based indices is difficult because their calculation methods are time-consuming and complicated.^[8,9] Additionally, even the sMARIA, which is much easier to calculate than the original MARIA, is not routinely used in most clinical practices because repeated measurement for the affected bowel segments using 4 imaging variables is still not very simple. Most MRE-based indices are calculated from many affected or nonaffected bowel segments to match the ileocolonoscopy results.^[4,6,7,10,11]

Assessment of fewer bowel segments could speed up the quantitative assessment of CD activity. A recent study proposed a simplified MRE score using MEGS based on a single bowel segment in 42 pediatric patients with CD, which correlated with the pediatric clinical disease activity index as a global score, suggesting a high impact of the severely inflamed segment on the overall disease activity.^[9] However, MEGS assessment is more complicated than sMARIA, and this concept has not been validated in adult patients with CD.

Therefore, this study aimed to propose and validate a practical and rapid MRE-based assessment using sMARIA based on the most inflamed bowel segment to evaluate disease activity in adult CD patients.

2. Materials and methods

2.1. Patients

This study was approved by Institutional Review Board of Severance Hospital (No. 4-2022-0815), and the requirement for written informed consent was waived due to its retrospective design. This study was conducted in accordance with Helsinki standards and adhered to STROBE criteria of retrospective studies. We included adult patients (age ≥ 18 years) with clinically suspected or known CD who underwent MRE between October 2014 and December 2018. Among these, we excluded patients for following reasons: final diagnosis other than CD, poor MRE image quality, and prior history of bowel resection (Fig. 1). For the study population, patient demographics, body mass index, C-reactive protein, and CD activity index were retrieved from the electronic medical records. Additionally, MRE scans were retrieved in follow-up cases. Endoscopic images were retrospectively reviewed in patients who underwent ileocolonoscopy within 4 weeks from MRE.

2.2. MR acquisition

Patients started ingesting 1250 mL of polyethylene glycol solution (COOLPREP; Taejoon Pharm, Seoul, South Korea)

40 minutes before scanning for adequate luminal distension. To reduce bowel peristalsis, 10 mg scopolamine-N-butyl bromide (BUSCOPAN; Boehringer-Ingelheim, Ingelheim am Rhein, Germany) was injected intravenously twice before initiating the scan and scanning the coronal T1-weighted sequence.

MRE scans were performed using 3.0-T MR scanners (Ingenia CX or Achieva, Philips Healthcare, Best, the Netherlands; Discovery MR 750, GE Medical Systems, Milwaukee). Routine MRE sequences in our institution include coronal T2-weighted half-Fourier sequence without fat suppression, coronal balanced steady-state gradient-echo sequence with fat suppression, axial T2-weighted half-Fourier sequence with fat suppression, coronal diffusion-weighted imaging (with b factors of 0 and 800 seconds/mm²), and apparent diffusion coefficient map. Coronal T1-weighted spoiled gradient-echo sequences with fat suppression were acquired before and after intravenous injection of gadolinium-based contrast agent (0.2 mL/kg at 2 mL/s) (Prohance; Bracco Diagnostics Inc., Princeton) followed by a saline bolus injection. After acquiring coronal enteric and portal T1-weighted images, axial delayed contrast-enhanced T1 weighted images were sequentially obtained.

2.3. Imaging analysis

Three board-certified abdominal radiologists – with 4, 5, and 10 years of experience in MRE interpretation, respectively – blinded to clinical information and ileocolonoscopy results independently reviewed full-protocol MRE, including contrast-enhanced T1- and T2-weighted images. The radiologists evaluated the presence or absence of the following sMARIA imaging parameters: mural thickening (>3 mm), mural edema, fat stranding, and ulcers for the terminal ileum and 5 colonic segments (ascending, transverse, descending, sigmoid colon, and rectum).^[7] Then, segmental sMARIA was calculated using the formula,^[7]

$$\text{sMARIA} = (1 \times \text{bowel wall thickening}) + (1 \times \text{edema}) \\ + (1 \times \text{fat stranding}) + (2 \times \text{ulcers})$$

In this scoring system, each variable is assigned a binary value (0 = absent, 1 = present), and weighted points are applied based on the presence of findings. Therefore, bowel wall thickening, edema, and fat stranding contribute 1 point each when present, while ulcers contribute 2 points.

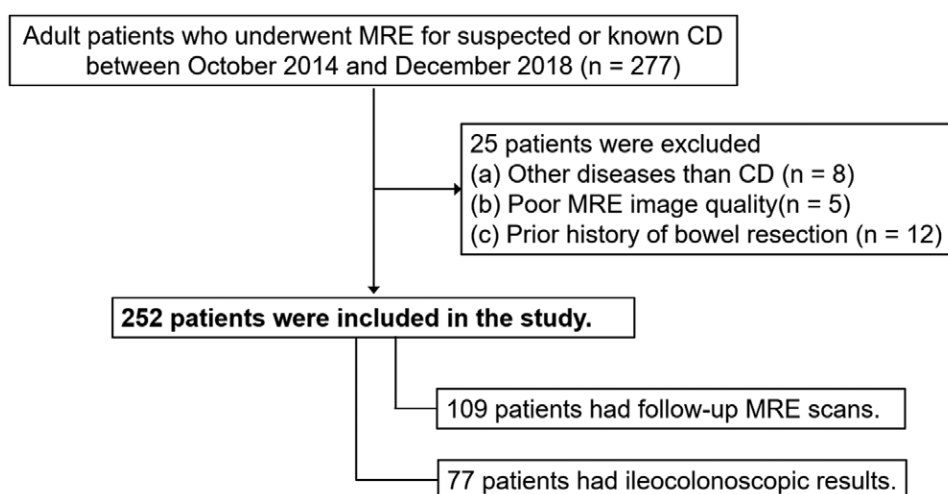


Figure 1. Patient flow diagram. CD = Crohn disease, MRE = magnetic resonance enterography.

The Maximal Segmental Score was defined as the largest segmental sMARIA among 6 evaluated bowel segments, presumably reflecting the most inflamed bowel segment. The global sMARIA was obtained from the sum of the segmental sMARIA of the 6 bowel segments and ranged from 0 to 30. Similarly, for patients with follow-up MRE, segmental and global sMARIA were evaluated. In addition, the presence, type (sinus tract, fistula, or abscess) and location of penetrating disease were evaluated on MRE.^[12] Disagreement in each sMARIA item or penetrating disease among the 3 radiologists was adjusted according to the majority.

2.4. Ileocolonoscopy

For patients who underwent ileocolonoscopy within 4 weeks of MRE, endoscopic images were retrospectively reviewed by 2 board-certified gastroenterologists in consensus who were blinded to the clinical and MRE findings. The simple endoscopic score for CD (SES-CD) was calculated for each bowel segment and used as the reference standard for CD activity in available patients.^[13] Endoscopic remission was considered for patients with SES-CD <3.

2.5. Statistical analysis

First, a correlation between global sMARIA and Maximal Segmental Score was estimated using Spearman correlation. The correlation coefficient (ρ) ranges from -1 to $+1$, with the absolute value indicating the strength of the correlation (0, no correlation; 0.2, weak correlation; 0.5, moderate correlation; 0.8, strong correlation; 1, perfect correlation).^[14] Moreover, changes in CD activity were estimated with Δ sMARIA – the difference in the sMARIA from baseline and follow-up MRE. For patients with follow-up MRE, the correlation between Δ [global sMARIA] and Δ [Maximal Segmental Score] was analyzed. Identical correlation analyses were conducted for the subgroup of patients who had at least 2 bowel segments with active inflammation. In addition, the correlation between SES-CD and sMARIA (global sMARIA and Maximal Segmental Score) was analyzed for the patients with endoscopic results.

Second, the diagnostic ability of sMARIA to predict endoscopic remission (SES-CD <3) was evaluated using the receiver operating characteristic curve analysis. Besides the global sMARIA and maximal segmental score, the area under the curve (AUC) was calculated for the sum of the highest and second highest segmental sMARIA. The optimal cutoff was determined at the point at which Youden J statistic is maximized.^[15] The AUCs were compared between both scoring systems using the DeLong method.

Lastly, the inter-observer agreement of global sMARIA and maximal segmental score between the 3 radiologists was evaluated using intraclass correlation coefficient (ICC): ICC ≤ 0.20 , slight; 0.21 to 0.40, fair; 0.41 to 0.60, moderate; 0.61 to 0.80, substantial; and 0.81 to 1.00, almost perfect reliability.^[16] Statistical analyses were performed using SPSS version 25.0 (IBM Corp., New York). $P < .05$ was considered statistically significant.

3. Results

3.1. Patient characteristics

Among 277 consecutive adult patients underwent MRE for suspected or known CD, 25 patients were excluded due to the following reasons: final diagnosis other than CD ($n = 8$), poor MRE image quality ($n = 5$), and prior history of bowel resection ($n = 12$). Finally, 252 patients were included in this study (178 men; median age: 31 years; interquartile range [IQR]: 24–39 years; Fig. 1). The clinical characteristics of the 252 patients

are summarized in Table 1. Among the 252 patients, 109 had follow-up MRE (time interval between baseline and follow-up MRE: median: 372 days, IQR: 285–575 days). A total of 77 patients had ileocolonoscopy results, and the median time interval between MRE and ileocolonoscopy was 1 day (IQR: 0–17 days). The median global SES-CD was 5 (IQR, 1–13), and the median global sMARIA and Maximal Segmental Score for the inflamed segments were 4 (IQR, 2–7) and 3 (IQR, 2–5), respectively. Penetrating complications were diagnosed in 43 patients (17%) on baseline MRE. Among 181 patients with active bowel inflammation, more than 1 segment was involved in 66 patients (36%).

3.2. Correlation between global sMARIA, maximal segmental score, and SES-CD

Spearman correlation results between global sMARIA and maximal segmental score are summarized in Table 2. Global sMARIA and maximal segmental score correlated strongly for both baseline and follow-up MRE scans ($\rho = 0.954$ and $\rho = 0.971$, respectively). Similarly, Δ [global sMARIA] and Δ [maximal segmental score] were correlated strongly ($\rho = 0.902$, Figs. 2 and 3) for 109 patients with follow-up MRE scans.

A subgroup analysis was additionally performed in 66 patients with 2 or more bowel segments demonstrating active inflammation to evaluate the discriminatory performance of the maximal

Table 1

Characteristics of included patients (n = 252).

Parameter	Value
Age (year)	31 (24–39)
Male (%)	178 (71)
Body mass index (kg/m ²)	20.9 (19.3–23.2)
CRP (mg/L)	3.0 (0.9–10.5)
CD activity index	94.5 (47.5–159.0)
Number of patients with endoscopic results (%)	77 (31)
SES-CD, global*	5 (1–13)
Global sMARIA [†]	4 (2–7)
Maximal segmental score [‡]	3 (2–5)
Duration between MRE and colonoscopy (days)	1 (0–17)
Disease location by MRE (%)	
Terminal ileal	99 (39)
Colonic	22 (9)
Ileocolonic	60 (24)
No active inflammation in the terminal ileum or colon	71 (28)
Number of involved bowel segments by MRE (%)	
0	71 (28)
1	115 (46)
2	39 (15)
3	17 (7)
4	3 (1)
5	4 (2)
6	3 (1)
Penetrating disease on MRE (%)	43 (17)
Sinus tract/fistula	34 (13)
Abscess	9 (4)
Treatment (%)	
5-ASA	216 (86)
Immunomodulator	152 (60)
Steroid	8 (3)
Anti-TNF	50 (20)

Continuous values are expressed as median (interquartile range).

5-ASA = 5-aminosalicylates, CD = Crohn disease, CRP = C-reactive protein, MRE = magnetic resonance enterography, SES = simple endoscopic score, sMARIA = simplified magnetic resonance index of activity, TNF = tumor necrosis factor.

*Values of SES-CD are summarized for 77 patients with endoscopic results.

[†]Values of Global sMARIA, and maximal segmental score are summarized for 181 bowel segments with active inflammation.

[‡]Maximal segmental score was defined as the largest segmental sMARIA among 6 bowel segments in a patient.

Table 2
Correlation between global sMARIA and maximal segmental score.

	Correlation coefficient (95% CI)	P-value
All segments		
Baseline MRE (n = 252)	0.954 (0.941–0.964)	<.001
Follow-up MRE (n = 109)	0.971 (0.958–0.980)	<.001
Differences between baseline and follow-up MRE (n = 109)	0.902 (0.860–0.932)	<.001
Involved bowel segments ≥ 2		
Baseline MRE (n = 66)	0.681 (0.526–0.792)	<.001
Follow-up MRE (n = 31)	0.900 (0.801–0.951)	<.001
Differences between baseline and follow-up MRE (n = 31)	0.884 (0.771–0.943)	<.001

CI = confidence interval, MRE = magnetic resonance enterography, sMARIA = simplified magnetic resonance index of activity.

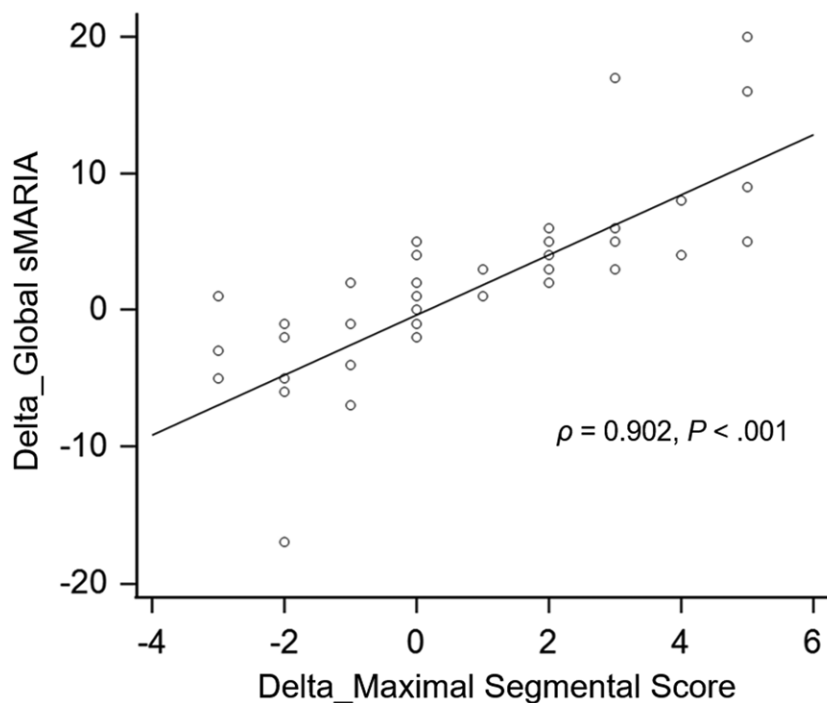


Figure 2. Correlation between changes in global sMARIA and maximal segmental score for baseline and follow-up MRE scans. The correlation coefficient was 0.902 (95% confidence interval, 0.860–0.932). MRE = magnetic resonance enterography, sMARIA = simplified magnetic resonance index of activity.

segmental score. The correlation between global sMARIA and maximal segmental score was moderate ($\rho = 0.681$) on baseline MRE. For 31 patients with follow-up MRE scans, Δ [global sMARIA] and Δ [maximal segmental score] correlated strongly ($\rho = 0.884$, Table 2).

For patients with endoscopic results, the correlation between SES-CD and sMARIA was analyzed (Table 3). Global sMARIA and maximal segmental score correlated moderately with SES-CD ($\rho = 0.685$ and $\rho = 0.634$, respectively) on baseline MRE, and correlated strongly on follow-up MRE ($\rho = 0.829$ and $\rho = 0.812$, respectively). No significant difference was observed between global sMARIA and maximal segmental score correlation coefficients relative to SES-CD ($P = .17$ for baseline MRE and $P = .78$ for follow-up MRE).

3.3. Diagnostic performance of sMARIA to predict endoscopic remission

Using receiver operating characteristic curve analysis, the diagnostic performance of global sMARIA and maximal segmental score to predict endoscopic remission (SES-CD <3) was compared (Table 4). The AUCs of global sMARIA and Maximal Segmental Score to predict endoscopic remission were 0.850

and 0.843, respectively, without significant difference ($P = .73$, Fig. 4). Moreover, the AUC of the sum of the highest and second highest segmental sMARIA was identical with that of the global sMARIA (0.850, $P > .99$). The cutoff value for endoscopic remission was 3 for global sMARIA, Maximal Segmental Score, and the sum of the highest and second highest segmental sMARIA.

3.4. Inter-observer agreement

Inter-observer agreement between the 3 reviewers was almost perfect for global sMARIA on baseline MRE (ICC, 0.919 [95% confidence interval: 0.900–0.935]) and follow-up MRE (0.896 [0.858–0.925]). Similarly, the maximal segmental score showed almost perfect inter-observer agreement on baseline (ICC, 0.856 [0.823–0.885]) and follow-up MRE (0.850 [0.795–0.891]).

4. Discussion

We proposed and validated the maximal segmental score using MRE based on the most affected bowel segment in adult patients with CD. The maximal segmental score strongly correlates with global sMARIA, which has already been validated to reflect disease severity and treatment response in CD. Notably, in patients

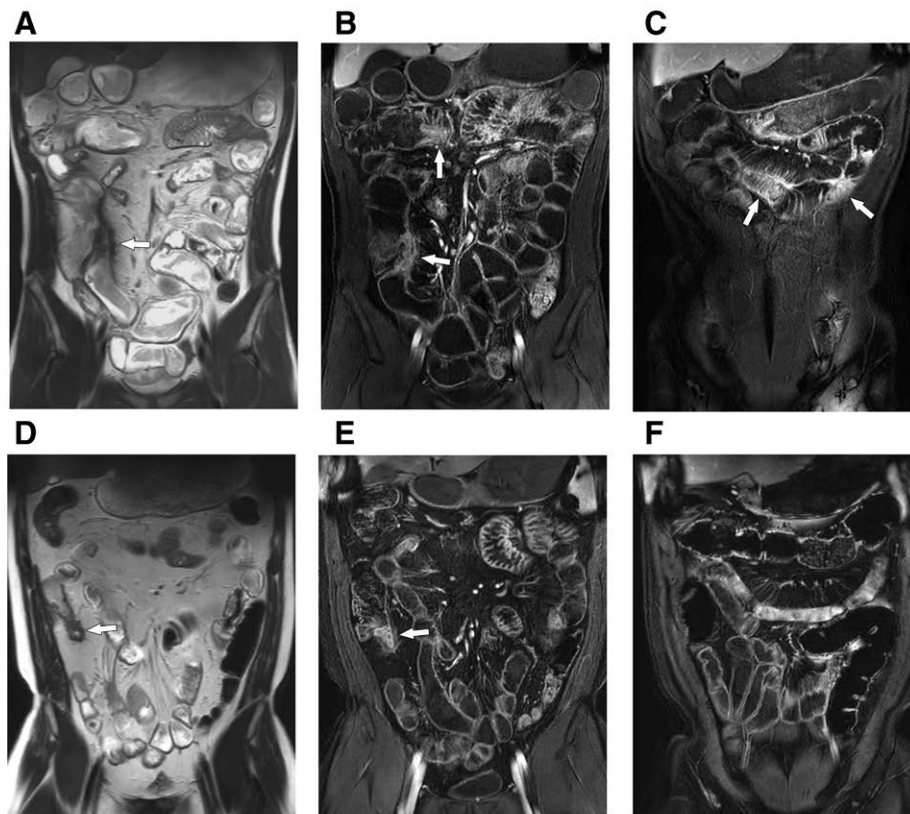


Figure 3. A 26-yr-old man with Crohn disease. Baseline coronal T2-weighted image and contrast-enhanced T1-weighted images (A–C) show active inflammation (arrows) in the terminal ileum, jejunum, ascending colon (not seen), and transverse colon. The global sMARIA was 12, and maximal segmental score was 5. Follow-up MRE images (D–F) show decreased and remaining wall thickening and edema in the terminal ileum (arrow) and much improved active inflammation in the other colonic segments. The global sMARIA was 3, and maximal segmental score was 2. MRE = magnetic resonance enterography, sMARIA = simplified magnetic resonance index of activity.

with endoscopic results, the correlation between SES-CD and maximal segmental score was not significantly different from that between SES-CD and global sMARIA. Moreover, maximal segmental score could reflect changes in overall disease activity between sequential MRE exams. This result suggests that the overall disease activity improvement in CD is mainly accompanied by the decreased inflammatory activity of the most affected segment. When patients with more than 1 affected segment were included, the maximal segmental score still correlated well with changes in overall disease activity between baseline and follow-up MRE.

Currently, most MRE-based scoring systems, including sMARIA, are based on the sum of segmental scores from each bowel segment. These systems assess the terminal ileum and colorectum except MEGS, which evaluates the jejunum and ileum.^[4–7] Although clinical trials and academic research might require a comprehensive evaluation of all bowel segments, quantification tools for clinical practice should be practical and simple. A previous study, including pediatric patients with CD, introduced a simplified MRE score based on the MEGS of the most affected bowel, named the pediatric CD magnetic resonance index (PCDMRI).^[9] The PCDMRI was positively correlated with SES-CD, and PCDMRI and the global MEGS equally correlated with the pediatric clinical disease activity index.^[9] However, because MEGS requires evaluation of numerous parameters, including mural enhancement pattern, haustral loss, or length of disease involvement, it is considered the most complex scoring system to assess CD activity, which may limit its feasibility for routine clinical application.^[6] Furthermore, the PCDMRI was validated in only pediatric

patients.^[9] In contrast, our study evaluated CD activity using sMARIA, one of the widely used scoring systems that is simpler and more practical to apply. Another strength of our study is that it included a larger population of adult patients with CD ($n = 252$), compared with the previous study that involved 42 pediatric patients.^[9] Notably, the maximal segmental score based on sMARIA demonstrated a strong correlation with the global sMARIA score, suggesting that this simplified approach may serve as a feasible alternative for assessing inflammatory burden in clinical practice.

Quantitative imaging biomarkers should be reproducible to be used as an objective monitoring tool. In this study, the inter-observer agreement between 3 abdominal radiologists was almost perfect for Maximal Segmental Score and global sMARIA ($ICC > 0.8$). This is consistent with the original study that developed sMARIA, which reported excellent ICC (0.85) between 2 readers,^[7] and another validation study which reported an almost perfect inter-reader agreement ($ICC = 0.95$) for segmental sMARIA.^[17] Although we assessed complete MRE sequences, including contrast-enhanced T1-weighted images, sMARIA can be evaluated on non-contrast sequences only.^[18,19] Further studies to evaluate the reproducibility of the maximal segmental score using non-contrast MRE would be valuable for a more rapid and noninvasive scoring method.

This study has some limitations. First, a selection bias is possible due to the retrospective study design. Since consecutive CD patients were enrolled during the study period, a relatively large proportion of patients with no or single bowel segment with active inflammation were included. Moreover, this may be attributed to the tendency for less colonic involvement in Asian

Table 3**Correlation between SES-CD and sMARIA in patients with endoscopic results.**

	Correlation coefficient (95% CI)	P-value	P-value*
Baseline MRE (n = 77)			
Global sMARIA	0.685 (0.545–0.788)	<.001	–
Maximal segmental score	0.634 (0.477–0.751)	<.001	.17
Follow-up MRE (n = 17)			
Global sMARIA	0.829 (0.579–0.936)	<.001	–
Maximal segmental score	0.812 (0.542–0.930)	<.001	.78

CI = confidence interval, MRE = magnetic resonance enterography, SES-CD = simple endoscopic score for Crohn disease, sMARIA = simplified magnetic resonance index of activity.

*P-values are obtained from comparison of correlation coefficients between global sMARIA and maximal segmental score.

Table 4**Diagnostic performance of global sMARIA and maximal segmental score for endoscopic remission (SES-CD <3).**

	Cutoff	AUC	95% CI	Sensitivity (%)	Specificity (%)	P-value
Global sMARIA	≤3	0.850	0.750–0.921	86.4	72.7	–
Maximal segmental score	≤3	0.843	0.742–0.916	95.5	65.5	.73
Sum of segmental sMARIA*	≤3	0.850	0.750–0.921	86.4	72.7	>.99

P-values are obtained from comparison of AUCs between global sMARIA and each of segmental scores.

AUC = area under the curve, CI = confidence interval, SES-CD = simple endoscopic score for Crohn disease, sMARIA = simplified magnetic resonance index of activity.

*Sum of segmental sMARIA indicates the sum of the highest and second highest segmental sMARIA.

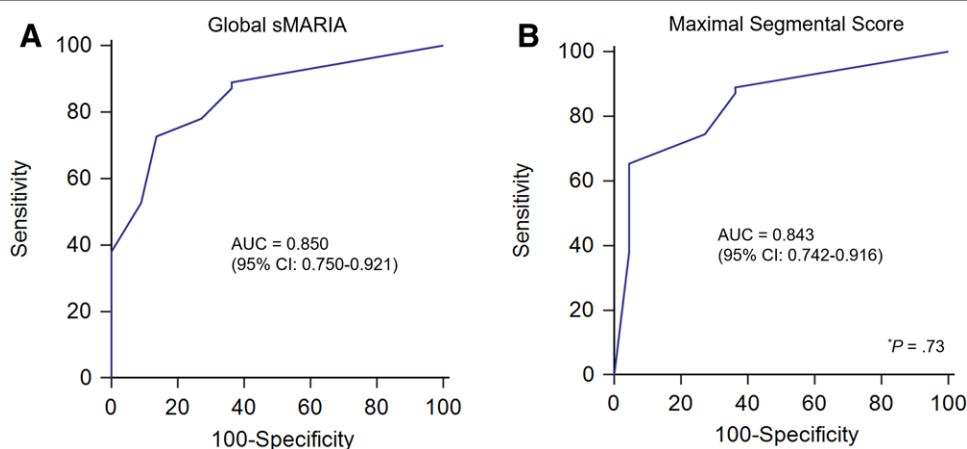


Figure 4. Receiver operating characteristic curves of global sMARIA (A) and maximal segmental score (B) for the prediction of endoscopic remission (SES-CD <3). The area under the curve was not significantly different between global sMARIA and maximal segmental score (0.850 vs 0.843, $P = .73$). *P-value was obtained by comparing AUCs between global sMARIA and maximal segmental score. AUC = area under the curve, sMARIA = simplified magnetic resonance index of activity, SES-CD = simple endoscopic score for Crohn disease.

patients with CD.^[20–22] Second, our routine MRE protocols do not include colonic preparation or adequate colonic filling by the enteral contrast. This could limit the evaluation of disease activity in some colonic segments. Third, the endoscopic reference standard was available for only 31% of patients, and the retrospective interpretation of endoscopic results has limitations. Fourth, the maximal segmental score was determined retrospectively in this study. In real clinical practice, the score could be calculated for only apparently the most affected segment to speed up the quantification process. Further studies with prospective selection of the most inflamed bowel segment based on the visual assessment are warranted. Finally, the Maximal Segmental Score was evaluated for the terminal ileum and colorectum but not for the proximal small bowel. We confined the assessment to these bowel segments, to match the results from Maximal Segmental Score to global sMARIA and SES-CD. However, to apply this scoring system to clinical practice, all bowel segments should be evaluated using an appropriate reference standard, which can comprehensively assess CD activity.

In conclusion, the maximal segmental score based on the most inflamed bowel segment can be a rapid and reproducible MRE-based method representing overall disease activity in adult patients with CD. However, further prospective studies, including whole bowel segments and endoscopic reference standards, are warranted to generalize the study results.

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