

## **Review Article**

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# Comprehensive Review of Magnetic Resonance Enterography-Based **Activity Scoring Systems** for Crohn's Disease

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Magnetic resonance (MR) enterography (MRE) plays a pivotal role in the management of patients with Crohn's disease (CD) throughout the chronic disease process. With advantages such as its non-invasiveness and the ability to use several MR sequences to reflect findings of active inflammation, several MRE-based indices have been introduced to assess CD inflammatory activity. Although there is no universally accepted gold-standard score for clinical practice, the most studied scores include the Magnetic Resonance Index of Activity, simplified Magnetic Resonance Index of Activity, Nancy score, Clermont score, London score, and CD MRI Index. These MRE-based scoring systems share certain characteristics but also differ in terms of the imaging parameters included, the bowel segments evaluated, and the MR sequences required for assessment. This review article covers the key MR findings of active inflammation incorporated into these scoring systems, along with the detailed characteristics and clinical applications of MRE-based scoring systems in adult patients with CD.

**Keywords:** Crohn's disease; Magnetic resonance imaging; Enterography; Activity

# INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disease that can involve any part of the bowel. CD is characterized by progressive course with remitting and relapsing periods. If not properly managed, CD can eventually lead to various complications, including strictures, and penetrating diseases which often require surgical intervention [1]. Therefore, close monitoring of disease activity is critical for therapeutic decision-making and for assessing treatment responses. Ileocolonoscopy is an essential procedure for assessing CD, as it enables the evaluation of mucosal healing and allows for intestinal biopsies if clinically necessary. However, it has limitations in evaluating the entire small bowel and extraluminal complications. Magnetic resonance (MR) enterography (MRE) is a primary noninvasive method for assessing CD because it can evaluate the entire gastrointestinal tract, including extraluminal findings, without radiation exposure [2]. MRE considers various findings of bowel inflammation in CD, including wall thickening, mural edema, and mural hyperenhancement [3]. Based on these findings, several MRE-based indices have been devel-

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oped to quantitatively assess CD activity, although no standardized score has been established. MRE-based indices serve as tools for response assessment and may aid in outcome measurements in clinical trials for CD [4,5]. This article focuses on the definitions, clinical applications, strengths, and limitations of MRE-based indices for assessing CD activity in adult patients.

## MR FINDINGS OF BOWEL INFLAMMATION IN CD

## **Diagnosis of CD**

The typical finding in CD is the presence of skip lesions, where diseased segments are interspersed with normal bowel segments in a discontinuous distribution. The inflammatory lesions are predominantly located asymmetrically on the mesenteric side, which is a characteristic feature of CD [3,6]. Because inflammatory lesions are distributed along the mesenteric side, scarring can lead to mesenteric contraction, resulting in pseudosacculation on the opposite, antimesenteric sides [7,8]. In cases of severe inflammation with extensive bowel involvement, the discontinuity and asymmetry of the inflammation may be less apparent. Mesenteric lymph node enlargement or fibrofatty proliferation can also be observed in CD, although these findings are somewhat nonspecific and have less correlation with disease activity [3].

# Definitions of MR Features for Active Bowel Inflammation in CD

Bowel wall thickening: Mural thickening is defined as a bowel wall thickness greater than 3 mm in a fully distended segment, and the degree of thickening reflects the inflammatory severity [3,9].

Mural and perimural edema: Mural edema is diagnosed when the bowel wall shows a hyperintense signal on fat-suppressed T2-weighted imaging, compared with normal bowel loops [10]. Perimural edema indicates edema or inflammation in the periintestinal fat tissue, which also presents with hyperintense signal on T2-weighted imaging.

Mural hyperenhancement: Mural hyperenhancement is compared with the enhancement of the surrounding normal bowel segments on contrast-enhanced T1-weighted imaging. This can be assessed during either the enteric or portal phase, with studies reporting no significant differences between these phases [11,12]. Mural hyperenhancement patterns can be asymmetric, layered, or homogeneous. A characteristic finding of bowel involvement in CD is a predominantly asymmetric enhancement on the mesenteric side of the bowel segment [8]. Hyperenhancement of the inner bowel wall or both inner and outer layers may result in a stratified appearance [3,13].

Ulcerations: Ulcers observed during endoscopy can also be

detected using MRE. They are diagnosed on imaging when the luminal fluid extends into the bowel wall due to depression of the inner bowel wall [14,15]. Longitudinal ulcers along the mesenteric side are specific to CD. Ulcers are defects confined to the bowel wall; if the defect extends beyond the serosa into the surrounding fat tissue, it is termed a sinus tract [3].

Restricted diffusion: Active inflammation in CD may show diffusion restriction within the bowel wall [6]. Restricted diffusion is indicated when the signal intensity of the bowel wall exceeds that of the lymph nodes on high b-value images (b = 800–1000 s/mm²) of diffusion-weighted imaging (DWI) and shows decreased apparent diffusion coefficient (ADC) value [16,17]. The advantages of DWI are the lack of contrast enhancement and its ability to increase reader confidence in diagnosing active inflammation and quantifying inflammatory activity using ADC. However, DWI in MRE has limitations, including high false-positive rates owing to susceptibility artifacts from bowel gas and poor luminal distension, which are frequently observed in the jejunum or colon. Therefore, it is important to interpret DWI in conjunction with T2-weighted and contrast-enhanced T1-weighted images [18].

Fat stranding: Fat stranding is defined as the loss of a normal clear interface between the bowel wall and mesentery [10].

Creeping fat: Creeping fat refers to the wrapping of mesenteric fat around the inflamed bowel, and it is known to be associated with intestinal stricture [19]. However, evaluating creeping fat on MRE is challenging; it can be diagnosed during surgery or through pathological examination [19,20].

Engorged vasa recta: Engorged vasa recta refer to the dilation of vessels surrounding the inflamed bowel, also known as the comb sign [21]. This can be attributed to both current and previous inflammation.

The MR findings of active bowel inflammation and examples of activity scoring with several MRE-based indices are shown in Figures 1 and 2.

# MRE-BASED INDICES FOR ASSESSING CD ACTIVITY

There are several MRE-based scoring systems to quantify the inflammatory activity in CD. The following representative MRE scoring systems will be reviewed in this section; MR Index of Activity (MaRIA), simplified MaRIA, Clermont score, Nancy score, CD MRI Index (CDMI), London score, and MR enterography global score (MEGS). The study design and MR features of these MRE-based scoring systems are summarized in Tables 1 and 2. The suggested cutoff values for active and severe inflammation for the scoring systems are presented in Table 3.



## MR Index of Activity

The segmental MaRIA is calculated as follows:  $1.5 \times \text{wall}$  thickness (mm) +  $0.02 \times \text{relative}$  contrast enhancement (RCE) +  $5 \times \text{edema} + 10 \times \text{ulceration}$ .

Rimola et al. [14] first developed MaRIA, an MRE-based index, for the quantitative assessment of CD activity. The reference standard for the MaRIA score was the CD Endoscopic Index of Severity (CDEIS), derived from ileocolonoscopy. The

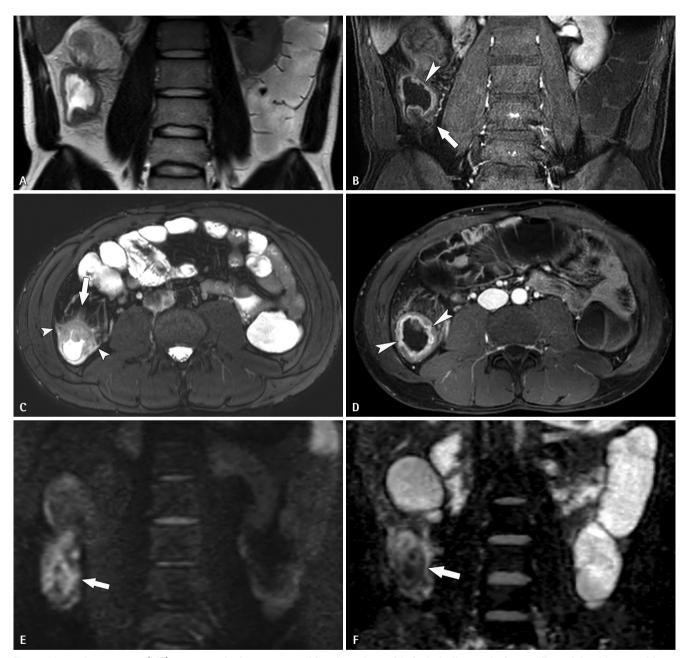


Fig. 1. Magnetic resonance (MR) enterography in a 28-year-old male patient with Crohn's disease. A: Coronal T2-weighted image without fat saturation. B: Coronal enteric phase T1-weighted image (T1WI). C: Axial T2-weighted image with fat saturation. D: Axial delayed phase T1WI. E: Coronal diffusion-weighted image (DWI, b = 800 s/mm²). F: Coronal apparent diffusion coefficient (ADC) map. A−D: Mural thickening and ulceration (long arrowheads) in the ascending colon. The maximum mural thickness was 10 mm. The axial T2-weighted image with fat saturation (C) shows markedly increased mural T2 signal (mural edema) and increased perimural T2 signal with a small fluid rim (≤2 mm, short arrowheads). The interface between the colonic wall and the pericolic fat is obscured (arrows) in (B) and (C), suggesting fat stranding. Contrast-enhanced T1WI (B and D) shows rapid and moderate contrast enhancement of the ascending colonic wall. DWI and ADC (E and F) show high DWI signal intensity in the ascending colon, with a corresponding low ADC value (1 × 10<sup>-3</sup> mm²/s, arrows). The segmental scores in the ascending colon were as follows: MaRIA = 30.23, simplified MaRIA = 5, Clermont score = 39.71, Nancy score = 6, CDMI = 10, and London score = 8.63. MaRIA, MR Index of Activity; CDMI, CD MRI Index.



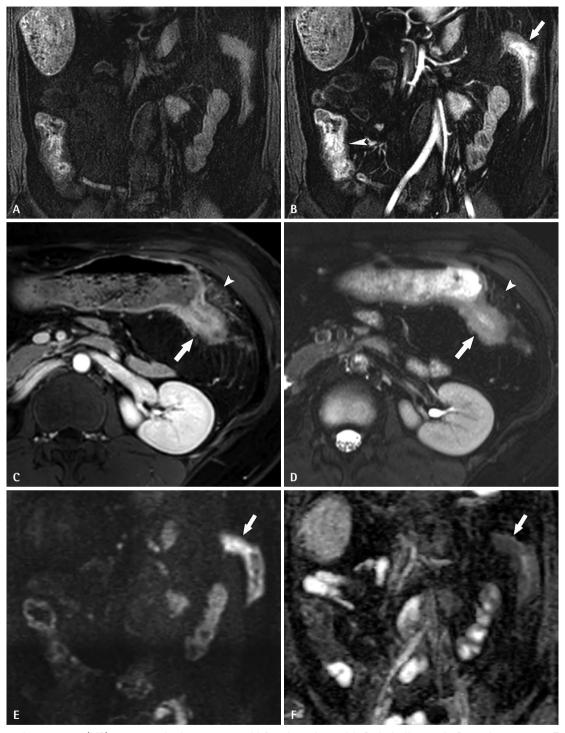


Fig. 2. Magnetic resonance (MR) enterography in a 27-year-old female patient with Crohn's disease. A: Coronal precontrast T1-weighted image (T1WI). B: Coronal enteric phase T1WI. C: Axial delayed phase T1WI. D: Axial T2-weighted image with fat saturation. E: Coronal diffusion-weighted image (DWI, b = 800 s/mm²). F: Coronal apparent diffusion coefficient (ADC) map. A–C: Mural thickening and hyperenhancement in the distal transverse colon. The maximum mural thickness was 9 mm. Contrast-enhanced T1WI (B and C) shows rapid and marked contrast enhancement of the transverse colon (arrows). Ascending colon also shows mural thickening and hyperenhancement (B, long arrowhead), suggesting active inflammation. The axial T2-weighted image with fat saturation (D) shows moderately increased mural and perimural T2 signal of the transverse colon, suggesting edema (arrow). There is also fat stranding around the transverse colon (short arrowheads) in (C) and (D). DWI and ADC (E and F) show high DWI signal intensity in the transverse colon, with a corresponding low ADC value (0.96 × 10<sup>-3</sup> mm²/s, arrows). The segmental scores in the transverse colon were as follows: MaRIA = 19.67, simplified MaRIA = 3, Clermont score = 24.23, Nancy score = 5, CDMI = 9, and London score = 5.41. MaRIA, MR Index of Activity; CDMI, CD MRI Index.



bowel segments to be evaluated are the terminal ileum; ascending, transverse, descending, and sigmoid colon; and the rectum. The global MaRIA score is the sum of the segmental scores for these six bowel segments. RCE is based on the wall signal intensity (WSI) measured before (WSI pre) and after intravenous contrast injection (WSI post). RCE is calculated using the following formula: RCE = ([WSI post - WSI pre] / [WSI

pre])  $\times$  100  $\times$  (standard deviation [SD] noise pre / SD noise post). The WSI is measured in areas with a predominantly thickened wall and calculated as the average of three WSI measurements. The SD noise is measured outside the body and calculated as the average of three SD measurements before and after contrast injection. Therefore, at least 12 region of interests measurements are required for RCE calculation per segment.

Table 1. Summary of MR enterography-based scoring systems for the assessment of Crohn's disease activity

Score	Year	Reference standard	Calculation formula	No. of variables	Quantitative measurement
MaRIA [14]	2009	Endoscopy	$1.5 \times \text{wall thickness (mm)} + 0.02 \times \text{relative contrast}$ enhancement + $5 \times \text{edema} + 10 \times \text{ulceration}$	4	Yes (wall thickness, relative contrast enhancement)
Simplified MaRIA [10]	2019	Endoscopy	1 × wall thickness (>3 mm) + 1 × edema + 1 × fat stranding + 2 × ulcers	4	No
Clermont score [41]	2013	MaRIA	$-1.321 \times ADC \text{ (mm}^2\text{/s)} + 1.646 \times \text{ wall thickness (mm)} + 8.306 \times \text{ulcers} + 5.613 \times \text{edema} + 5.039$	4	Yes (ADC, wall thickness)
Nancy score [43]	2010	Endoscopy	Ulceration + parietal edema + bowel wall thickening + differentiation between (sub)mucosa and muscularis propria + rapid contrast enhancement + DWI hyperintensity	6	No
CDMI [9]	2012	Histopathology	Mural thickness + mural T2 signal + perimural T2 signal + mural hyperenhancement	4	Semiquantitative assessment
London score [9]	2012	Histopathology	$1.79 + 1.34 \times \text{mural thickness} + 0.94 \times \text{mural T2 score}$	2	Semiquantitative assessment
MEGS [46]	2014	Fecal calprotectin, CRP, HBI	Score per segment × multiplication score per segment + additional score per patient (lymph node + comb sign + abscess + fistula)	11	Yes (disease length), semiquantitative assessment for score per segment

MaRIA, MR Index of Activity; CDMI, Crohn's disease MRI index; MEGS, MR enterography global score; CRP, C-reactive protein; HBI, Harvey–Bradshaw index; ADC, apparent diffusion coefficient.

Table 2. MR features included in the scoring systems

MR finding	MaRIA	Simplified MaRIA	Clermont score	Nancy score	CDMI	London score	MEGS
Mural thickening	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mural edema	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Perimural edema					Yes		Yes
Ulcers	Yes	Yes	Yes	Yes			
Fat stranding		Yes					
Contrast enhancement	Yes			Yes	Yes		Yes
Enhancement pattern							Yes
DWI			Yes	Yes			
Differentiation between M-SM and MP				Yes			
Lymph node							Yes
Comb sign							Yes
Abscess							Yes
Fistula							Yes
Haustral loss							Yes
Length of disease							Yes

MaRIA, MR Index of Activity; CDMI, Crohn's disease MRI index; MEGS, MR enterography global score; DWI, diffusion-weighted imaging; M-SM, mucosal-sub-mucosa; MP, muscularis propria.



Table 3. Cutoff values for active and severe inflammation in patients with Crohn's disease

Score	Active disease	Severe disease
MaRIA	≥7	≥11
Simplified MaRIA	≥1	≥2
Clermont score	>8.4	≥12.5
Nancy score	≥6 (G), ≥2	
CDMI	≥3	
London score	≥4.1	
MEGS	>10 (G)	

Unless otherwise specified, the cutoff values were for the segmental score. (G) Cutoff value of the global score.

MaRIA, MR Index of Activity; CDMI, Crohn's disease MRI index; MEGS, MR enterography global score.

The segmental MaRIA showed a strong correlation with segmental CDEIS (r = 0.81, p < 0.001) [14]. The global MaRIA also showed a significant correlation with CDEIS (r = 0.78, p < 0.001) [14]. MaRIA demonstrated high accuracy for detecting active inflammation (area under the receiver operating characteristic [AUROC], 0.891; sensitivity/specificity, 81%/89%) and ulcerative lesions (AUROC, 0.978; sensitivity/specificity, 95%/91%).

In their validation study, the same group established the cutoff points of MaRIA for active CD (≥7) and severe CD (≥11) [22]. The reference standard for active and severe CD was endoscopy, and severe disease was defined as the presence of endoscopic ulcerations. MaRIA has also been externally validated in other studies, showing a good correlation with the endoscopic scores, CDEIS or Simplified Endoscopic Score for CD (SES-CD) [12,23-28]. Evaluating treatment response is essential during monitoring CD activity. Several studies demonstrated the responsiveness of MaRIA to treatment and its correlation with endoscopic appearance, including mucosal healing [15,29,30].

Several studies have evaluated MaRIA scores to predict treatment response or adverse outcomes, including bowel surgery [31-34]. A study by Naganuma et al. [31] demonstrated the potential prognostic impact of MaRIA in patients treated with anti-tumor necrosis factor (TNF). The MaRIA score was significantly higher in the group with clinical recurrence than in the group that maintained remission. Time to recurrence was significantly longer in patients with global MaRIA score <36.3, compared with those with global MaRIA score ≥36.3. Several studies have reported discordant results regarding the role of MaRIA in predicting adverse outcomes. In these studies, Ma-RIA was not a predictive factor for bowel surgery or CD-related hospitalization [32,33]. However, a recent study demonstrated that the persistence of severe lesions (MaRIA ≥ 11) at 46 weeks after starting biological therapy predicted long-term adverse outcomes, including the risk of surgery, endoscopic balloon dilation, and clinical relapse in CD [35].

#### Simplified MaRIA Score

The segmental simplified MaRIA score is calculated as: 1  $\times$  wall thickness (>3 mm) + 1  $\times$  edema + 1  $\times$  fat stranding + 2  $\times$  ulcers.

In 2019, the simplified MaRIA was introduced, evaluating the presence or absence of four key features: wall thickening, mural edema, ulcer, and fat stranding [10]. The evaluation is performed across the same six bowel segments, as those used in the assessment of the original MaRIA score.

The cutoff point of the simplified MaRIA for active lesions was  $\geq 1$ , and for severe lesions (with ulcers), it was  $\geq 2$  [10]. The sensitivity and specificity of the simplified MaRIA for detecting active CD were 90% and 81%, respectively [10]. For diagnosing severe inflammation, the sensitivity and specificity were 85% and 92%, respectively [10]. The simplified MaRIA showed a strong correlation with the CDEIS (r = 0.83) and the original MaRIA (r = 0.93) (p < 0.001). Inter-reader agreement between two readers was excellent (intraclass correlation coefficient [ICC] = 0.85; 95% confidence interval [CI]: 0.78–0.90; p < 0.001) [10]. The time required to calculate the global simplified MaRIA was significantly shorter than that for the MaRIA (4.77 min vs. 17.14 min; p < 0.001) [10].

The simplified MaRIA score has been externally validated in several studies. In a study with 84 patients with CD, the sensitivity and specificity of simplified MaRIA ≥1 for active bowel inflammation were 90% and 98%, and the simplified MaRIA highly correlated with SES-CD (r = 0.94 for the ileal segment, and r = 0.82 for the colonic segment) [36]. Another study, which included 121 patients with CD, demonstrated a linear correlation between the MaRIA and simplified MaRIA (r = 0.93) [37]. Assessment of the simplified MaRIA showed higher inter-reader agreement compared with that of the MaRIA (96.1% vs. 79.3%, p < 0.001), and it required less calculation time than that taken in the original MaRIA (4.50 min vs. 12.35 min). In a recent study by Tao et al. [38], the simplified MaRIA demonstrated high accuracy in detecting active and severe inflammation against SES-CD, and the global simplified MaRIA was highly correlated with SES-CD.

A few recent studies have evaluated the diagnostic accuracy and treatment response using the simplified MaRIA without contrast-enhanced sequences, as the simplified MaRIA can be assessed with non-contrast sequences [39,40]. According to a study by Bae et al. [39], simplified MaRIA evaluated on T2WI images showed a moderate correlation with SES-CD (r = 0.722), comparable to simplified MaRIA evaluated on conventional contrast-enhanced sequences (r = 0.795). Notably, with the addition of DWI to T2WI-based sequences, the simplified MaRIA showed significantly higher performance in detecting ac-



tive inflammation than the T2WI-based sequence alone (AU-ROC, 0.863 vs. 0.827; p = 0.017). Another prospective study involving 46 patients who started biological treatment demonstrated that simplified MaRIA, with and without contrastenhanced sequences, comparably determined endoscopic ulcer healing, treatment response, and remission [40].

### **Clermont Score**

The segmental Clermont score is calculated as:  $-1.321 \times ADC \text{ (mm}^2\text{/s)} + 1.646 \times \text{ wall thickening (mm)} + 8.306 \times \text{ ulcers} + 5.613 \times \text{ edema} + 5.039.$ 

Among several MRE-based indices, two incorporate DWI: the Clermont score and the Nancy score. The Clermont score includes ADC measurements from DWI acquisition [41]. The reference standard for the Clermont score was the MaRIA score. Except for the replacement of RCE with ADC, the other parameters (wall thickness, ulceration, and edema) are the same as those derived from the MaRIA score. The cutoff value for ADC was determined to be  $1.6 \times 10^{-3}$  mm²/s to detect active inflammation, with high sensitivity (82.4%) and specificity (100%) [41].

The Clermont score was validated in a prospective observational study by the same study group [42]. It was strongly correlated with the MaRIA score in ileal CD (rho = 0.99) but not in colonic CD (rho < 0.8). A cutoff value of >8.4 for the Clermont score predicted active ileal disease (MaRIA ≥ 7) (AUROC 0.99, p = 0.0001), and a cutoff value of  $\geq$ 12.5 predicted severe ileal disease (MaRIA ≥ 11). In another study, which included 55 patients with ileal CD, the Clermont score was significantly correlated with MaRIA (r = 0.91, p < 0.0001) and SES-CD (r =0.76, p < 0.0001) [27]. In addition, ADC correlated with SES-CD (r = -0.63; p < 0.0001), especially in non-operated patients. A recent post hoc analysis of 63 patients with CD from two prospective studies demonstrated that complete bowel wall healing on MRI (defined as no segmental MaRIA score >7 or no segmental Clermont score >8.4) predicted a lower risk of bowel surgery and prolonged corticosteroid-free remission [34].

## **Nancy Score**

The segmental Nancy score is calculated as: ulceration + parietal edema + bowel wall thickening + differentiation between the (sub)mucosa and muscularis propria + rapid contrast enhancement + DWI hyperintensity.

The Nancy score is another scoring system that uses a DWI sequence. Unlike the Clermont score, which uses quantitative ADC values obtained from DWI, the Nancy score requires a visual DWI assessment, the presence or absence of DWI hyperintensity [43]. Notably, in the development study of Nanc score, MR colonography for evaluating colonic CD does not necessitate fasting or any oral contrast agent [43]. The Nancy score

consists of six MR features: ulceration, edema, bowel wall thickening, differentiation between the mucosa-submucosal complex and muscularis propria, rapid contrast enhancement, and DWI hyperintensity. The presence or absence of these MR findings in a segment was rated as one or zero, respectively. The segmental score is assessed in six bowel segments (the terminal ileum; ascending, transverse, descending, and sigmoid colon; and rectum), and the global Nancy score is the sum of the six segmental scores, ranging from 0 to 36. DWI hyperintensity was defined as hyperintensity in the bowel wall on the DWI sequence [43]. Rapid contrast enhancement was defined as contrast enhancement in the arterial phase. Differentiation between the mucosa-submucosa complex and muscularis propria was defined as the distinction between two layers in the colonic wall (hyperintense mucosa-submucosa complex and hypointense muscularis propria), evaluated on T2WI [43]. In patients with CD, a segmental Nancy score >2 detected endoscopic colonic inflammation with a sensitivity and specificity of 58.33% and 84.48%, respectively (AUROC = 0.779, p = 0.0001), and the total Nancy score correlated with SES-CD (r = 0.539, p = 0.001) [43].

The Nancy score was validated in a study of 96 patients with CD [44]. A segmental score <2 and a global score <6 showed AUROCs of 0.80 (95% CI, 0.73–0.87) and 0.82 (0.69–0.94) for mucosal healing. The Nancy score was also highly sensitive to changes in the CDEIS, and radiologic remission on DW-MRI after treatment indicated a low cumulative probability of surgery (p = 0.0251) [44].

### **CDMI** and London Score

The segmental CDMI is calculated as: mural thickness + mural T2 signal + perimural T2 signal + mural hyperenhancement. The segmental London score is calculated as:  $1.79 + 1.34 \times \text{mural thickness score} + 0.94 \times \text{mural T2 score}$ .

The CDMI and London score were introduced in 2012, using histopathologic grading of the terminal ileum as the reference standard [9]. The MRE features were scored from zero to three, according to Table 4. In univariate analysis, four parameters evaluated on MRE were statistically significant for active CD inflammation: mural thickness, mural T2 signal, perimural T2 signal, and the degree of mural enhancement. Among these, mural thickness and mural T2 signal showed a significant correlation with active inflammation in multivariate analysis; thus, these two factors were included in the London score. This score demonstrated a sensitivity of 81%, specificity of 70%, and an AUC of 0.77, with a cutoff value of 4.1 for predicting acute inflammation. The London score has been validated in several studies in comparison with other indices, which are discussed later in this article.

On the other head, the simple sum of the four parameters



Table 4. Definitions for the calculation of the CDMI, London score, and MEGS

MR features	Per-segment score					
win reacures	0		2	3		
Mural thickness*†	<3 mm	>3-5 mm	>5-7 mm	>7 mm		
Mural T2 signal* <sup>†</sup>	Equivalent to normal bowel wall	Minor increase in signal: bowel wall appears dark grey on fat-saturated images	Moderate increase in signal: bowel wall appears light grey on fat-saturated images	Marked increase in signal: bowel wall contains areas of white high signal approaching that of luminal content		
Perimural T2 signal*	Equivalent to normal mesentery	Increased in mesenteric signal but no fluid	Small fluid rim (≤2 mm)	Large fluid rim (>2 mm)		
T1 enhancement*	Equivalent to normal bowel wall	Minor enhancement: bowel wall signal greater than normal bowel but significantly less than nearby vascular structure	Moderate enhancement: bowel wall signal increased but somewhat less than nearby vascular structures	Marked enhancement: bowel wall signal approaches that of nearby vascular structures		
Mural enhancement pattern	N/A or homogeneous	Mucosal	Layered	-		
Haustral loss (colon only)	None	<1/3 segment	1/3 to 2/3 segment	>2/3 segment		
	Multiplication factor for segmental score					
	×1		2	×3		
Length of disease	0–5 cm	5-15	5 cm	>15 cm		
MR features	Per-patient score					
Will redeales	0		5			
Lymph nodes	Absent		Present			
Comb sign	Absent		Present			
Abscess	Absent		Present			
Fistula	Absent		Present			

CDMI = mural thickness + mural T2 signal + perimural T2 signal + mural hyperenhancement. London score = 1.79 + 1.34 × mural thickness score + 0.94 × mural T2 score. MEGS total score = score per segment (jejunum, ileum, terminal ileum, cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum) × multiplication score per segment (involved length) + additional score per patient (lymph node + comb sign + abscess + fistula). Same criteria are used for variables included in CDMI (\*) and London score (†) calculations. CDMI, Crohn's disease MRI index; MEGS, MR enterography global score.

that were significant in univariate analysis showed a slightly improved correlation with the histopathological score compared to the London score, achieving a sensitivity of 87%, specificity of 70%, and an AUROC of 0.83 [9]. This overall sum of the four variables has been referred to by various terms, such as the extended London score, CDMI, or overall CDMI score, in previous studies. For clarity, we refer to this index as the CDMI. The CDMI showed a moderate correlation with the CDEIS (r=0.59) and good reproducibility (ICC = 0.78) [28]. In a previous retrospective study, CDMI showed responsiveness to anti-TNF treatment [45]. In this study, the CDMI significantly decreased in the anti-TNF responder group for all lesions (5.19 to 3.12, p < 0.0001) and for stenotic lesions (6.33 to 4.58, p = 0.01). However, the score did not change significantly in non-responders before and after treatment.

## MR Enterography Global Score

The total MEGS is calculated as: score per segment × multiplication score per segment + additional score per patient (lymph node, comb sign, abscess, and fistula).

Makanyanga et al. [46] developed the MEGS by modifying the CDMI to reflect the overall disease extent, colonic findings such as haustral loss, and extraluminal complications. Most MRE-based indices, except MEGS, assess the terminal ileum and colorectum because they have been validated based on ileocolonoscopic results. MEGS, however, evaluates the entire small and large bowel, including the proximal small bowel. A total of nine bowel segments are evaluated for the MEGS score: the jejunum, ileum, terminal ileum, cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. The following MR features, evaluated per segment, were scored between zero and three: mural thickness, mural T2 signal, perimural T2 signal, degree of enhancement, mural



enhancement pattern, and colonic haustral loss (Table 4). The total disease length within each bowel segment was measured to yield a per-segmental multiplication factor. Additionally, several per-patient MR features are assessed, with five points added if the feature is present: enlarged lymph node (shortest diameter ≥1 cm), comb sign, fistula, and abscess. The total MEGS is calculated by summing the segmental scores from the nine segments and the per-patient scores.

MEGS significantly correlated with fecal calprotectin (r = 0.46, p < 0.001) and C-reactive protein (r = 0.388, p = 0.002) [46]. The AUROC of MEGS for predicting active disease (fecal calprotectin >100  $\mu$ g/g) was 0.75 (95% Cl, 0.62–0.88) [46]. A previous study demonstrated the responsiveness of MEGS to anti-TNF $\alpha$  drugs, although combined clinical reference standards were used rather than an endoscopic standard [47]. MEGS showed a moderate correlation with clinical activity (r = 0.53; p < 0.001), and it significantly decreased in clinical responders but not in non-responders.

### COMPARISON OF THESE SCORING SYSTEMS

Several studies have compared different MRE-based indices intra-individually. The MaRIA, Clermont score, CDMI, and London score were developed relatively early; thus, these scores were included in many comparative studies rather than the recently developed simplified MaRIA.

## MaRIA vs. CDMI

Tielbeek et al. [28] compared MaRIA and CDMI for interobserver agreement and correlation with the CDEIS. Both MaRIA and CDMI showed similarly good interobserver agreement (ICC = 0.74 and 0.78, respectively) among four radiologists, and both scores showed a moderate correlation with the CDEIS (r = 0.51 and r = 0.59, respectively).

#### MaRIA vs. Clermont Score

Studies have compared the diagnostic performance and treatment responsiveness of MaRIA and Clermont scores. Both MaRIA and Clermont score showed similar performance in detecting active CD, with a significant correlation with the SES-CD (r=0.83, p<0.0001 for MaRIA; and r=0.76, p<0.0001 for the Clermont score) [27]. Buisson et al. [48] compared the accuracy of the both scores in determining mucosal healing in 44 patients with CD. Radiologic remission predicted mucosal healing well, with a specificity/negative predictive value of 85.3%/85.3% for MaRIA (no segmental MaRIA >7) and 88.2%/85.7% for the Clermont score (no segmental Clermont score >8.4).

#### MaRIA vs. Clermont Score vs. London Score

A retrospective study compared the diagnostic accuracy of the MaRIA, Clermont, and London scores for detecting and grading CD activity, using the SES-CD as the reference standard [49]. The AUROC for detecting active disease was significantly higher for MaRIA (0.930) than for the Clermont score (0.840, p < 0.0001) and London score (0.853, p = 0.0086). The accuracy of MaRIA for detecting severe lesions with ulceration was significantly higher than that of the Clermont score (91.1% vs. 88.4%, p = 0.03). The London score was not included in the analysis for detecting ulcers because there was no predetermined cutoff value for predicting ulcers for the London score. To validate the preexisting cutoff values for each index, the authors suggested optimal cutoff values from their cohort, including a new cutoff value for the London score for active (3.4) and severe lesions (3.8) [49]. Notably, the optimal cutoff value for the MaRIA score was almost the same as that previously established.

#### MaRIA vs. Clermont Score vs. London Score vs. CDMI

A study by Puylaert et al. [50] compared four MRE-based scoring systems for the terminal ileum: MaRIA, Clermont score, London score, and CDMI, using CDEIS and histopathological scores as reference standards. All MRE-based indices demonstrated comparable interobserver agreement, correlation with endoscopic and histopathologic standards, and diagnostic performance.

## Simplified MaRIA vs. London Score vs. CDMI

A prospective multicenter study compared the simplified MaRIA, London score, and CDMI in 111 patients using the terminal ileal histologic activity index as a reference standard [51]. The three scoring systems showed high sensitivity to active inflammation: 83% for simplified MaRIA, 76% for the London score, and 81% for CDMI. However, the specificity was quite low: 41%, 64%, and 41% for the simplified MaRIA, London score, and CDMI, respectively. This low specificity might be related to the limitations of endoscopic biopsy, which can only confirm inflammation of the luminal surface, unlike the transmural MRE evaluation.

### MaRIA vs. Simplified MaRIA vs. London Score vs. CDMI

A recent study evaluated the responsiveness of four MRE indices to treatment: MaRIA, simplified MaRIA, London score, and CDMI [52]. The simplified MaRIA showed the greatest responsiveness and correlation with the endoscopic score. The responsiveness of the simplified MaRIA was statistically larger than that of the London score but comparable to that of MaRIA or CDMI.



# STRENGTHS AND LIMITATIONS OF MRE-BASED SCORING SYSTEMS

MRI-based scoring systems have the advantages of being noninvasive, free from radiation exposure, and suitable for repeated applications. Despite these advantages and their potential to reflect inflammatory activity, most of them are not widely used in clinical practice and are primarily limited to specific research settings. Some of these scores have been validated in only a few institutions with a limited number of experienced radiologists, often including the same institutions involved in score development. Understanding the strengths and weaknesses of the current scoring systems is crucial for their effective clinical use and for the new score development. Table 5 summarizes the strengths and limitations of these indices.

MaRIA is the most validated index in various aspects, including diagnostic accuracy, interobserver agreement, treatment response, and as a prognostic tool. In addition, its diagnostic performance has been proven against different reference standards, such as endoscopy, clinical scores, inflammatory biomarkers, and histopathology. However, the evaluation of the MaRIA score is time-consuming, particularly for RCE measurements, and requires contrast enhancement. The simplified MaRIA is the most recently developed score; thus, it needs to be validated in future studies. Compared to the original MaRIA,

the simplified MaRIA consists of simple dichotomous variables, requires a shorter calculation time, and does not require gadolinium enhancement. The Clermont score includes ADC from the DWI technique, and its calculation does not require contrast enhancement. This score has also been investigated in validation studies and has shown a strong correlation with the MaRIA. However, the Clermont score was initially developed using the MaRIA score as a reference standard rather than an endoscopic or histopathological standard. Assessment of the Clermont score is time-consuming, and the measurement of the ADC within the bowel wall is often not reproducible. The Nancy score incorporates a visual assessment of DWI rather than ADC measurement, and omitting the standard preparation for MR colonography scans may enhance patient tolerability. However, the Nancy score has only been validated in a few studies and requires both DWI and contrast-enhanced sequences. The London score and CDMI are simple and rapid to calculate. However, these scores have limited severity grading because their cutoff values for ulcerative lesions have not been established. MEGS is the only score that evaluates the entire small bowel and reflects the length of bowel involvement. However, the reference standards for MEGS are limited and include the largest number of parameters to be evaluated.

Table 5. Strengths and limitations of the MR enterography-based scoring systems

Score	Strength	Limitation
MaRIA	- Most validated score against various reference standards	<ul><li>Complex to use and time-consuming</li><li>Does not evaluate entire small bowel</li><li>Contrast enhancement is required</li></ul>
Simplified MaRIA	<ul><li>Simple to use without quantitative measurement</li><li>Can be obtained without contrast enhancement</li></ul>	<ul><li>Less validated compared to MaRIA score</li><li>Does not evaluate entire small bowel</li></ul>
Clermont score	<ul> <li>Incorporation of DWI</li> <li>Can be obtained without contrast enhancement</li> </ul>	<ul> <li>Used MaRIA as reference standard in their original study</li> <li>Time-consuming and limited reliability of ADC measurement</li> <li>Does not evaluate entire small bowel</li> <li>Limited performance for colon evaluation in validation study</li> </ul>
Nancy score	<ul><li>Does not require fasting or oral preparation for patients with only colonic disease</li><li>Qualitative assessment of DWI</li></ul>	<ul><li>Both DWI and contrast-enhanced sequence are required</li><li>Small number of validation studies</li></ul>
CDMI, London score	<ul><li>- Validated against histopathology</li><li>- Simple to use</li></ul>	<ul><li>Does not evaluate entire small bowel</li><li>No established cutoff values for severe inflammation</li></ul>
MEGS	<ul><li>Evaluation of the entire small bowel and colorectum</li><li>Reflection of length of disease</li><li>Incorporation of extra-intestinal findings</li></ul>	<ul> <li>Not validated against endoscopy or histopathology (limited reference standard)</li> <li>Largest number of included features, time consuming</li> <li>Small number of validation studies</li> </ul>

MaRIA, MR Index of Activity; CDMI, Crohn's disease MRI index; MEGS, MR enterography global score; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient.



### CONCLUSION

Currently, MRE is a major imaging modality for CD diagnosis and monitoring. Although several MR scores have been introduced to assess CD activity, radiologists and clinicians are not generally familiar with these scoring systems. This article comprehensively reviews the key MRE-based indices developed over the past decades, focusing on their calculation methods, clinical applications, and advantages and disadvantages. Knowledge of these indices will help radiologists and clinicians use them in clinical practice and incorporate them into clinical research or trials.

### **Conflicts of Interest**

The author has no potential conflicts of interest to disclose.

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