

Role of MR Enterography in Evaluation of Disease Activity in Pediatric Crohn's Disease: Correlation between MR Enterography and Pediatric Crohn's Disease Activity Index Scores

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J Gastrointestinal Abdominal Radiol ISGAR:2020;3:118–125

Abstract

Objectives The aim of the study was to assess the role of MR Enterography (MRE) in the diagnosis and follow-up of children with Crohn's disease (CD) and to correlate disease activity indices with known MRE features of active disease.

Methods This was a retrospective study including 24 patients (median age 11 years, 17 males) with clinically and histologically proven CD who underwent MRE. Two previously validated MRE scores—Magnetic Resonance Enterography Global Score (MEGS) and CD MRI index (CDMI)—were calculated. A correlative analysis was made between the Pediatric Crohn's Disease Activity Index (PCDAI) score and MRE scores as well as individually with each MR variable. Comparison of both the MR scores was made between patients with different disease activity.

Results MEGS and PCDAI scores showed strong positive correlation ($r = 0.724$, $p < 0.001$); CDMI and PCDAI scores showed moderate positive correlation ($r = 0.661$, $p = 0.0004$). There was statistically significant difference in the MR scores between patients grouped by clinical activity. Among individual MR variables, mural thickness and enhancement best predicted the disease activity.

Conclusions MRE-based scores and findings correlate with clinical activity in pediatric CD. Thereby, MRE can be considered a valuable tool in the management of CD, predicting disease activity and offering a potential alternative to endoscopy in monitoring patients during follow-up.

Keywords

- ▶ CD MRI index
- ▶ Crohn's disease
- ▶ MR enterography global score

Introduction

Pediatric inflammatory bowel disease (PIBD) and Crohn's disease (CD) are not rare entities, with 20 to 30% of CD presenting before age of 20 years. Symptoms of PIBD can be nonspecific including growth failure, malnutrition, delayed

puberty, and so forth, other than gastrointestinal symptoms. Treatment goal in PIBD has moved beyond symptom control to mucosal healing and histological control. Thus, treatment strategy depends on accurate assessment of disease location, extent and activity. The gold standard for assessing mucosal

DOI <https://doi.org/10.1055/s-0040-1701328>
ISSN 2581-9933.

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activity is ileocolonoscopy. However, this being invasive and often limited to colon and terminal ileum, clinical scoring like Pediatric Crohn's Disease Activity Index (PCDAI) is often used, especially when reassessing while on treatment.¹ These clinical indices have the disadvantage of being subjective and cumbersome to calculate. Magnetic resonance enterography (MRE) and magnetic resonance (MR) scoring give a better idea of the burden of disease including transmural and extraintestinal involvement and are increasingly used in diagnosis and follow-up of PIBD with good sensitivity and accuracy. The European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) revised porto criteria recommend MRE as the imaging modality of choice in PIBD for diagnosis.²

Most often than not, MR assessment is usually subjective instead of there being quantitative measurements. Rimola et al⁴ proposed and validated the Magnetic Resonance Index of Activity (MaRIA) in adult inflammatory bowel disease (IBD) patients correlating it with endoscopic scoring.³ However, both endoscopy and MaRIA score take only mucosal findings into consideration. Moreover, the proposed MR protocol included colonic preparation and dynamic contrast assessment which may be cumbersome in children. Steward et al proposed the Crohn's Disease Activity Score (CDMI/CDAS) which was a segmental MRI activity score validated against histological scoring, taking into account extraintestinal disease as well.⁵ Based on this score Makanyanga et al developed a global score (MEGS) and compared it with clinical markers of activity like fecal calprotectin, C reactive protein, and the Harvey Bradshaw index (HBI).⁶

All these MR scores have been shown to be good predictors of disease activity in adults. Though there are few studies in assessment of MR enterography in pediatric Crohn's disease,^{7,8} there are no studies in our knowledge that compare the usefulness and validation of these MR scores in pediatric population. The aim of this study is to correlate the MEGS and CDMI scores with clinical activity score (PCDAI) in children.

Materials and Methods

This was a single institutional retrospective analysis of patients with histologically proven CD. All patients who were diagnosed with CD between January 2013 and December 2016, and underwent MRE either for diagnosis or follow-up were included.

Patients

The study included 24 patients who were referred for MRE by the pediatric gastroenterologist for any of the following indications: diagnosis, assessment of disease, evaluation of perianal disease, or response assessment. We had 7 girls and 17 boys with a mean age of 11 years at diagnosis. Patients with inadequate bowel distension and children who already underwent surgery for complications related to CD were excluded because inadequate bowel distension would mask underlying lesion and it would be difficult to analyze the MRI features of the bowel wall in an operated segment.

Clinical Assessment

Clinical disease activity was assessed by calculating the PCDAI score by the same pediatric gastroenterologist. A PCDAI score of ≥ 30 is considered indicative of moderate/severe disease.

MR Enterography

Imaging was performed on a 1.5 T system (Siemens, MAGNETOM AERA, Germany) with patients in supine position, after 4 to 6 hours of fasting. Oral preparation or bowel cleansing was not consistently used. Contrast images were acquired after administering 0.1 mmol/kg body weight of gadolinium contrast agent. Each imaging series consisted of breath hold (whenever possible) axial, coronal, sagittal single-shot fast spin echo T2-weighted sequences, axial and coronal steady state free precession sequences, and axial and coronal T1-weighted fat suppressed sequences before and after contrast administration. Diffusion-weighted imaging was not consistently performed (► Table 1).

Analyses of MR Enterography and Scoring

The images were reviewed by two experienced radiologists blinded to the patient's clinical scores at the time of scans. In case of any discrepancies a consensus read was performed.

The following MR features were recorded: mural thickness (► Fig. 1), T2 signal intensity (► Fig. 2), degree and pattern of enhancement (► Fig. 5), and perimural edema, and they were quantitatively scored (0–3) as described by Steward et al.⁵

Extramural findings like lymphadenopathy, comb sign (► Fig. 4), abscess, and perianal disease (► Fig. 3) were recorded as present or absent (► Figs. 1–5).

Two previously validated MRE scores, MEGS⁶ and CDMI,⁵ were calculated. The details of the score have been listed in the appendices.

Table 1 MR enterography parameters used in our study

Parameter	HASTE	True FISP	VIBE
Repetition time (ms)	2,000	3.50	4.36
Echo time (ms)	94	1.45	2
Flip angle (°)	150	50	10
Matrix (pixel)	320 × 81	256 × 100	320 × 75
Section thickness (mm)	3.5	3	3
Intersection gap (mm)	0	0	0
Field of view	300–350	300–350	300–350

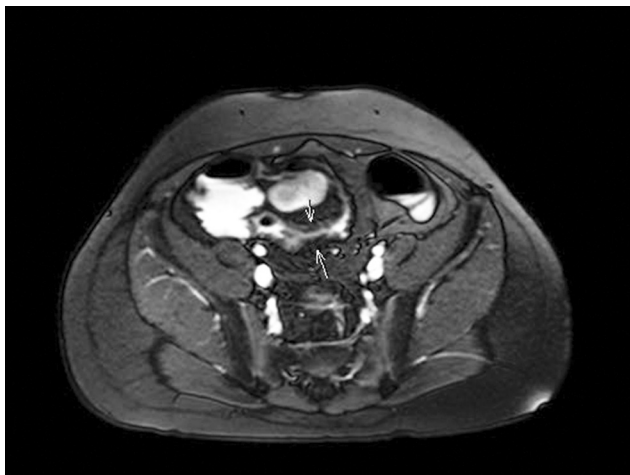


Fig. 1 T1 VIBE fat suppressed axial images shows wall thickening with mucosal enhancement pattern in the terminal ileum.

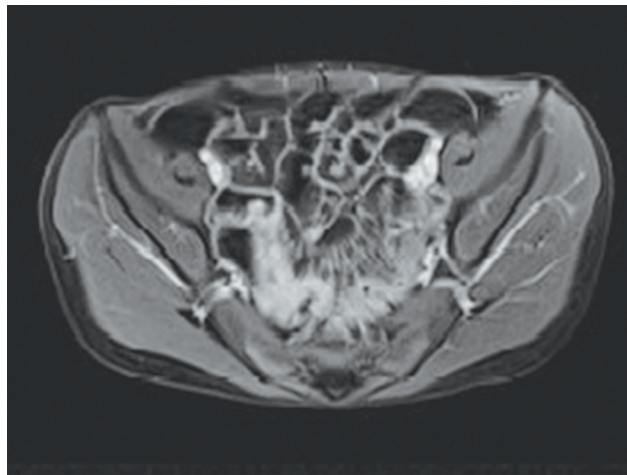


Fig. 4 T1 VIBE fat suppressed axial images of pelvis shows hypervascular appearance of the mesentery—comb sign.



Fig. 2 T2 axial turbo spin echo sequence in a known case of Crohn's disease shows wall thickening with increased signal intensity of the involved ileal loop.

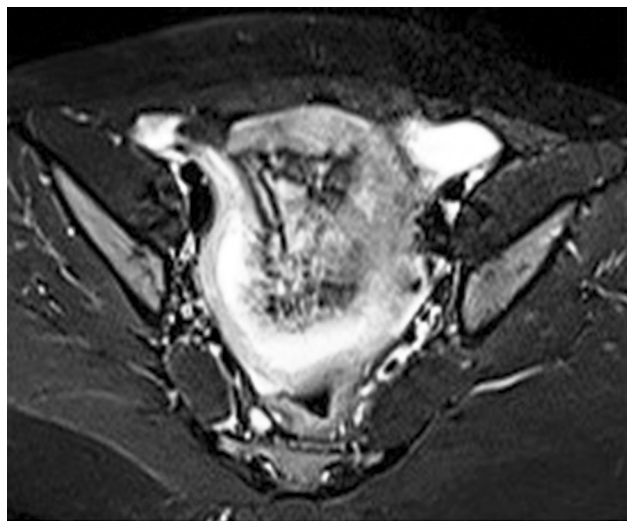


Fig. 5 T2 STIR axial image of pelvis in case of active crohn's disease shows layered pattern of increased signal intensity in a thickened ileal loop.

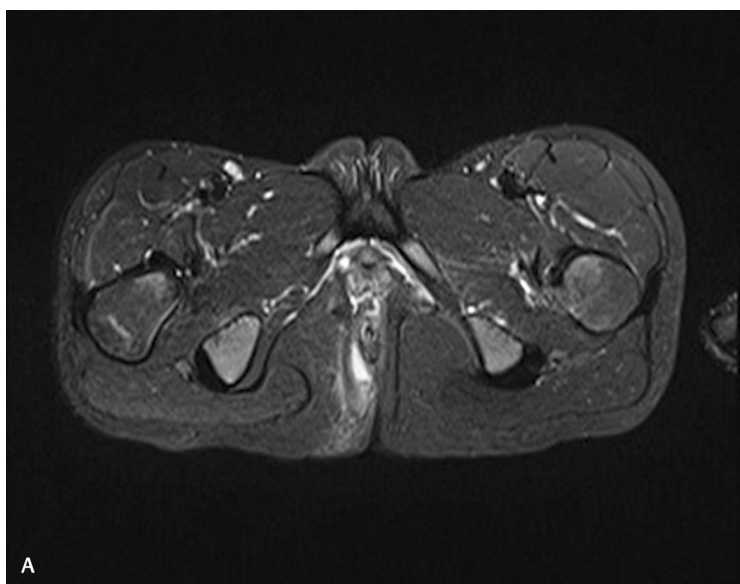


Fig. 3 (A, B) STIR axial and sagittal images of pelvis in a case of penetrating Crohn's disease shows fluid filled linear intersphincteric fistula on right side.

For the purpose of calculating the MEGS score the bowel was divided into eight anatomical segments: jejunum; ileum; terminal ileum; ascending, transverse, descending, and sigmoid colons; and rectum. Individual segmental scores are added together, and then 5 points are added for presence of lymph nodes ≥ 10 mm (short-axis diameter), comb sign, fistula, or abscess. The length of the diseased segment was used to provide a multiplication factor (ranging from 1 to 2) for each segmental score.⁶

For each patient, the MEGS were then calculated as the sum of the scores for all intestinal segments.

Data Analysis

► **Table 2** shows the demographics and clinical data of 24 patients included in the study.

Results

MRI Features

Fifteen had abnormal wall thickening defined as >3 mm, 7 patients (29.2%) had mild (3–5 mm; ► **Fig. 1**) thickening, 2 (8.3%) had moderate (5–7 mm), and 6 (25%) had marked (>7 mm) thickening.

High wall signal intensity on T2-weighted images (► **Fig. 2**) was seen in 17 patients, of which 5 (20.8%) were mild, 11 (45.8%) moderate, and 1 (4.2%) were marked.

Table 2 Clinical and demographic data

Age in y median (range)	11 (5–17)
Gender, n (%)	
Male	17 (70.8%)
Female	7 (29.2%)
Disease location, n (%)	
Isolated small bowel	11 (45.8%)
Ileocolonic	4 (16.7%)
Colonic	3 (12.5%)
Terminal ileum	2 (8.3%)
Associated with perianal fistula	2 (8.3%)
PCDAI median (range)	22.5 (0–65)
MEGS median (range)	15.25 (0–53)
CDMI median (range)	7.5 (0–13)
Extramural features	
Lymph nodes	10 (41.7%)
Comb sign	12 (54.2%)

Table 3 Detailed report of PCDAI, MEGS, and CDMI scores

Descriptive statistics	No.	Minimum	Maximum	Mean	Standard deviation
Age in years	24	5	17	11.05	2.958
PCDAI	24	0	65.0	20.833	18.9627
MEGS	24	0	53.0	17.881	15.1821
CDMI/CDAS	24	0	13	7.00	4.012

Abbreviations: CDMI/CDAS, Crohn's Disease Activity Score; MEGS, Magnetic Resonance Enterography Global Score; PCDAI, Pediatric Crohn's Disease Activity Index.

All cases with abnormal wall thickening had mural enhancement of varying degrees.

Marked enhancement was seen in 9 (37.5%) cases.

Enhancement pattern was recorded as mucosal ($n = 5$) transmural/homogenous ($n = 9$) and striated ($n = 6$).

PCDAI scores ranged from 0 to 65 (median 22.5) while the MEGS and CDMI scores ranged from 0 to 53 and 0 to 13, respectively (► **Table 3**).

► **Figure 6A** shows the correlation of MRE scores with PCDAI. The MEGS and PCDAI scores showed strong positive correlation ($r = 0.724$, $p = <0.001$, $r^2 = 0.5237$). CDMI and PCDAI scores showed strong positive correlation (► **Fig. 6B**; $r = 0.661$, $p = 0.00043$, $r^2 = 0.4367$). Individual MRI features were correlated with the PCDAI scores where wall thickness showed a strong correlation ($r = 0.792$, $p = <0.001$; ► **Fig. 7A**), wall T2 signal showed a weak correlation ($r = 0.499$, $p = 0.02123$) (► **Fig. 7B**), and wall enhancement showed a moderate positive correlation ($r = 0.5463$, $p = 0.0104$; ► **Fig. 7C**; ► **Table 4**).

Pattern of enhancement showed a weak correlation ($r = 0.394$, $p = 0.07726$). Extramural features like presence of lymph nodes and comb sign ($r = 0.338$) showed weak correlation to PCDAI score (► **Table 5**).

Patients were grouped according to their clinical activity (PCDAI scores) into group A score <30 ($n = 16$, having mild activity) and group B score 30 and above ($n = 8$, having moderate to severe disease; ► **Table 6**).

The MEGS and CDMI scores ranged from 0 to 28 (median = 14.50) and 0 to 10 (median = 4.50), respectively, in group A and from 19 to 59 (median = 20.5) and 7 to 13 (mean = 11.50) in group B, respectively (► **Fig. 7d**). There was a statistically significant difference in the scores between the two groups by using both *t*-test as well as Mann–Whitney test (nonparametric) ($p < 0.05$).

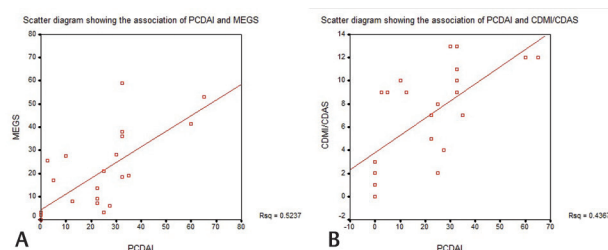


Fig. 6 Correlation between PCDAI with MEGS and CDMI scores. (A) Scatter diagram showing strong positive correlation between the MEGS and PCDAI scores. (B) Scatter diagram illustrating CDMI and PCDAI scores with strong positive correlation ($r = 0.661$, $p = 0.00043$, $r^2 = 0.4367$).

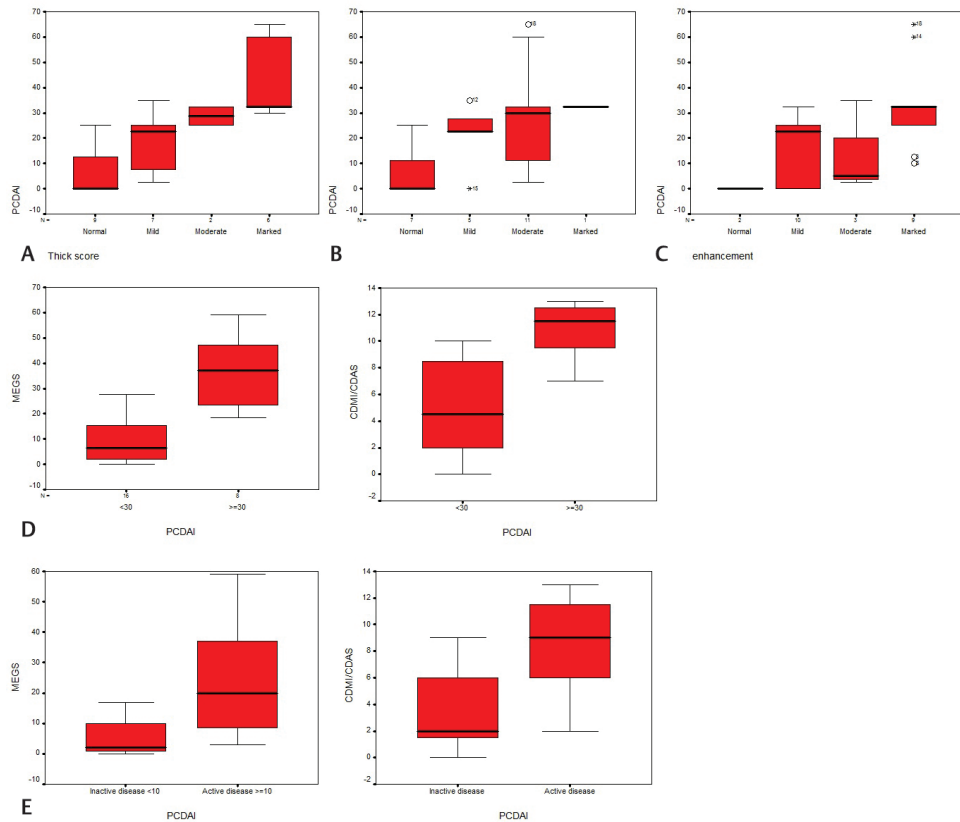


Fig. 7 Correlation between MRE features and PCDAI scores: (A) Wall thickness showed strong correlation ($r = 0.792, p = <0.001$). (B) Wall T2 signal showed weak correlation ($r = 0.499, p = 0.02123$). (C) Wall enhancement showed moderate positive correlation ($r = 0.5463, p = 0.0104$). Correlation between PCDAI groups with MEGS and PCDAI scores: (D) Statistically significant difference in the scores between the two groups by using both t-test as well as Mann-Whitney test (nonparametric) ($p < 0.05$). (E) Correlation between groups C and D with MEGS and PCDAI scores.

Table 4 Correlation between PCDAI with MEGS and CDMI scores

		PCDAI	MEGS	CDMI/CDAS
PCDAI	Pearson correlation	1	0.782 ^a	0.637 ^a
	Sig. (2-tailed)	NA	0.000	0.002
	N	24	24	24
MEGS	Pearson correlation	0.782 ^a	1	0.891 ^a
	Sig. (2-tailed)	0.000	NA	0.000
	N	24	24	24
CDMI/CDAS	Pearson correlation	0.637 ^a	0.891 ^a	1
	Sig. (2-tailed)	0.002	0.000	NA
	N	24	24	21

Abbreviations: NA, not applicable; PCDAI Pediatric Crohn's Disease Activity Index; MEGS, Magnetic Resonance Enterography Global Score; CDMI, Crohn's Disease MRI Index; CDAS, Crohn's Disease Activity Score

^aCorrelation is significant at the 0.01 level (2-tailed).

Similarly, patients were grouped into two groups group C, PCDAI 1 to 10 (inactive disease [$n = 8$]), and group D, PCDAI 10 and above (active disease of varying severity [$n = 16$]). The MEGS and CDMI scores ranged from 0 to 26 (median = 13.5) and 0 to 9 (median = 5), respectively, in group C and from 3 to 59 (median = 28.5) and 2 to 13 (median = 6.5), respectively, in group D (► **Table 6**).

The difference in MR scores between these two groups was also statistically significant. There were two cases where the PCDAI was less than 10 but MRE score showed activity. This patient continued to have active disease on treatment without remission and went on to have hemicolectomy.

Table 5 Correlation between MRE features and PCDAI scores. Comprehensive correlation between PCDAI and MRE features

MRE features	Pearson correlation coefficient (r)
Wall thickness	0.792 ^a
T2 wall signal	0.499 ^b
Wall enhancement	0.546 ^b
Pattern of enhancement	0.394
Lymph nodes	-0.082
Comb sign	0.338

Abbreviations: MRE, magnetic resonance enterography; PCDAI, Pediatric Crohn's Disease Activity Index

^aCorrelation is significant at the 0.01 level (2-tailed).

^bCorrelation is significant at the 0.05 level (2-tailed).

Table 6 Correlation between PCDAI groups with MEGS and PCDAI scores. Groups divided according to PCDAI score

	Group A	Group B	Group C	Group D
PCDAI	<30 mild activity	>30 moderate to severe activity	<10 inactive disease	>10 active disease
No. of studies (n)	16	8	8	16

Abbreviations: MEGS, Magnetic Resonance Enterography Global Score; PCDAI, Pediatric Crohn's Disease Activity Index.

Discussion

As pediatric IBD cases are being diagnosed more and more, the need for an accurate objective test to assess disease activity is paramount. This is even more important when reassessing patients on treatment. Treatment goal of CD is to achieve the best possible histological control and hence evaluation of mucosal activity is important. Clinical activity indices have the drawback of relying on subjective symptoms. Endoscopy remains the gold standard but is invasive and poorly tolerated in children with the added disadvantage of not being able to assess the proximal small bowel at all times.⁹ Besides, extraintestinal disease is not assessed and information about actual disease burden is limited. Even though MRE is shown to have good performance in evaluating PIBD, the description and interpretation of MRE findings is not standardized.^{7,8} There is limited agreement in the available literature as to which MRI feature best correlates with disease activity. The best way to do this would be a universally validated MRI score which incorporates different intestinal and extraintestinal findings and is simple enough to be incorporated by radiologists in their routine reporting. Various MR based scoring systems described have been validated only in adults so far. There have not been many studies comparing known MRE scores with PCDAI scores.

The main focus of our study was to correlate two previously validated MRE scores with clinical activity index. The global MEGS score has already been validated by Makanyanga et al against fecal calprotectin and CRP in adults.³ However, they found no significant correlation with HBI clinical score. When Steward et al developed the CDMI score they showed significant correlation between the MR score and histological acute inflammatory scores (AIS).⁵

Our main finding was that there is strong positive correlation between both CDMI and MEGS with PCDAI score. However MEGS has higher correlation compared to CDMI (► **Table 4**).

When we grouped our patients based on clinical activity, we found that the MR scores among the groups were also correlating. This proves that MRE based scoring is as good as clinical scoring especially when following up patients on treatment to predict disease activity and to confirm disease remission.

Limitations and Recommendations

Our study population was limited. However, this study can still serve as a preliminary analysis with reproducible results.

We correlated the MR scores only with clinical scoring which has a subjective nature. There was no correlation with any histopathological scores.

Another limitation of our study was that bowel preparation and MR protocols were not consistent within the study population. Similarly in cases which had no or inadequate bowel preparation, inadequate distension may have masked small mucosal lesions or ulcerations.

This emphasizes the need for a large multicenter study with standardized protocols and consistent imaging parameters, bowel preparation, and sequences.

Keypoints

Studies comparing PCDAI scores and MRE scores are lacking in pediatric population. MRE scoring of crohn's disease can help predict disease activity compliment clinical indices potentially replacing endoscopy.

Conflict of Interest

None declared.

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