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Article*

## Comparison of CT Enterography with MR Enterography, and Utility of MRI Severity Index, in Crohn's disease: A Retrospective Analysis

Joshi Harshad<sup>1</sup>, Mehta Nirad<sup>2</sup>, Desai Devendra<sup>1</sup>, Abraham Philip<sup>1</sup>, Gupta Tarun<sup>1</sup>, Joshi Anand<sup>1</sup>

<sup>1</sup>Department of Gastroenterology,

<sup>2</sup>Department of Radiology,

P.D. Hinduja National Hospital,

Veer Savarkar Road, Mahim,

Mumbai-400016, India

Corresponding Author:

Dr Devendra Desai

Email: devendracdesai@gmail.com

### ABSTRACT

**Background:** CT (CTE) and MR (MRE) enterography have not compared in Crohn's disease (CD) in Indian setting. Recently MRI severity index has been developed for objective assessment of inflammatory activity in CD.

**Aim:** To compare CTE with MRE in CD with respect to diagnostic yield and impact on management and evaluate the utility of MRI severity index in CD.

**Methods:** Records of 29 patients (median age 43 years, range 18 - 70 and standard deviation 15.36; 15 female) with CD who underwent CTE and MRE using standard protocols were retrospectively analyzed. Inflammatory activity, stricture detection and costs were compared. The co-relation between clinical activity, biochemical markers (fecal calprotectin, serum C-reactive protein), and the MRI severity index was studied.

**Results:** Fourteen patients had clinically active disease, 15 were in clinical remission. In patients with active clinical disease, MRE identified 14 percent more cases with abnormal imaging findings compared to CTE. Small bowel involvement was detected in 5 patients on CTE, 10 on MRE ( $p=0.133$ ). Ileocolonic involvement was seen in 15 patients on CTE and 19 on MRE ( $p=0.28$ ). Stricture was detected in 2 patients on CTE and 9 on MRE ( $p=0.01$ ). In 17 patients, clinical management was altered based on abnormal MRE findings, giving 58.6% absolute increased yield of MRE over CTE. There was significant correlation between MRI severity index and disease activity ( $r=0.70$ ,  $p<0.0001$ ) and fecal calprotectin ( $r=0.52$ ;  $p<0.003$ ), but not CRP ( $r=0.03$ ;  $p<0.1$ ). Average cost for CTE was Rupees 9214 (INR) and 12121 INR for MRE.

**Conclusion:** MRE was better than CTE in diagnosing stricture in CD. The MRI severity index correlated with clinical activity and fecal calprotectin.

**KEYWORDS:** Inflammatory bowel disease, activity, complications, imaging, stricture.

## Introduction

Crohn's disease (CD) is a chronic inflammatory bowel condition that is characterized by transmural inflammation of the bowel, leading to erosions, ulceration, and sometimes inflammatory or fibrotic stenosis. Enteric sinuses and fistulae and abscess collections are complications of penetrating disease. The European Crohn's and Colitis Organisation (ECCO) recently published a revised consensus on the diagnosis and management of CD.<sup>2</sup> It recommends either computed tomography (CTE) or magnetic resonance (MRE) enterography as standards for assessing the small intestine. Both these modalities can identify inflammatory, penetrating and stricturing disease. A recent study showed that MRE significantly increased the confidence of clinicians for the presence or absence of small bowel disease and changed therapeutic strategy in 61% of patients.<sup>3</sup> In India the use of MRE is increasing but CT scan is still preferred. With MRE, the availability, radiologist's familiarity, the cost and time taken are the issue where as radiation and cost are the issues with CTE.

The following issues need to be addressed while evaluating an imaging modality in CD: (1) safety of the modality, especially where repeated imaging may be necessary and (2) its ability to accurately determine extent of small and large bowel involvement, distinguish active inflammatory from fibrotic stricturing disease, recognize extramural complications, and detect recurrent disease following surgery. There could also be subjective variations amongst radiologists in reporting these findings. An objective scoring system is therefore preferable for maintaining uniformity in reporting.<sup>4-7</sup> Girometti et al.<sup>12</sup> showed that a scoring system (MRI severity index) comprising various MRI findings had diagnostic accuracy of 91%, sensitivity of 93% and specificity of 87% in evaluation of inflammatory disease activity in CD.

We addressed these issues in this retrospective analysis of data of patients with CD who underwent both CTE and MRE.

## Subjects and Methods

This was a retrospective analysis of patients with CD seen in the Division of Gastroenterology who underwent both

CTE and MRE (within a span not exceeding a week of each other) over 2 years (2014-15). In 29 consecutive patients with Crohn's disease, CTE and MRE were done (within 4 weeks of each other) to assess involvement of small bowel. The protocol was approved by the institution's ethics committee (project number 1078-17-DD). CTE and MRE were evaluated by a single radiologist (NM) who was aware only of the diagnosis of CD but not of clinical and laboratory details. Active disease was defined as presence of symptoms (Abdominal pain or diarrhoea) and positive inflammatory markers; the latter included C-reactive protein (CRP) and fecal calprotectin (FC). CRP > 6 mg/L and FC > 50  $\mu$ g/g were considered abnormal as per our laboratory reference standard.

MR severity index<sup>12</sup> was calculated based on MR findings (Mentioned subsequently)

## CTE Protocol

CTE was performed using a helical 64-MDCT system (Light Speed Pro, GE Healthcare, United Kingdom). A neutral enteric contrast agent (mixture of mannitol, edible gum and water; 1500 mL) was administered orally in aliquots at 60, 45 and 30 minutes before the scan. At 15 min before the scan, participants were given 500 mL of water. Immediately before scanning, patients were given 0.5 mL hyoscine butylbromide (Buscopan®; Boehringer Ingelheim) intravenous over 30 seconds. Contrast-enhanced CT was performed with the following settings: 310 mA, 120 kVp, 0.5-second tube rotation time, detector configuration 16  $\times$  0.625, pitch 0.9375. The IV contrast (150 mL iohexol [Omnipaque 300, GE Healthcare]) was injected at 4 mL/s, and scanning was initiated after a 50-s delay.<sup>8</sup> Images were obtained with 2.5-mm section thickness at intervals of 1.25 mm. Overlapping 2 mm coronal images were reconstructed from overlapping 1.25 mm slices.

## MRE Protocol

MRE was performed using a 1.5-T magnet (Philips, Netherlands). Patients were scanned in the supine position with a 16-channel torso array coil using the following protocol: coronal single-shot fast spin-echo (SSFSE) (TR/

TE 2,000/90; matrix size 256 × 256; slice thickness 5 mm; gap 0 mm), coronal 2D true fast imaging with steady-state precession (FISP) (matrix 193 × 340; slice thickness 5 mm; gap 0 mm), axial SSFSE (2,000/90; matrix 256 × 256; slice thickness 6 mm; gap 0 mm), axial 2D true FISP (matrix 192 × 340; slice thickness 6 mm; gap 0 mm), and axial 2D true FISP with fat suppression (matrix 192 × 340; slice thickness 6 mm; gap 0 mm). Patients were then given 0.5 mL Buscopan® intravenous regardless of whether or not MRE was performed on the same day as CTE. After 0.2 mmol/Kg gadodiamide (Omniscan, GE Healthcare) was administered at 3 mL/s and a 45-s scanning delay, coronal 2D fast spoiled gradient-recalled echo (FSPGR) (TR 150 milliseconds; matrix 320 × 160; slice thickness 6 mm; gap 0 mm), coronal 3D liver acquisition volume acceleration (LAVA) (matrix 384 × 224; slice thickness 4 mm; gap 0 mm), and axial 3D LAVA (matrix 320 × 192; slice thickness 4 mm; gap 0 mm) sequences were performed. Parallel imaging was used for all contrast-enhanced sequences. All sequences were performed during breath-holding.

## Imaging Findings

Maximum small bowel wall thickness was recorded in millimetres in three small bowel parts – duodenum, jejunum and ileum. Findings indicative of active inflammation on CTE included segmental mural hyperenhancement, increased wall thickness (>3 mm), or presence of extraluminal complication (sinus tract, fistula, abscess).<sup>8,9</sup> On MRE, mural stratification, high T2 mural MR signal, and presence of the comb sign and mesenteric adenopathy were noted as signs of active disease.<sup>10,11</sup>

## MRI Severity Index<sup>12</sup>

The quantitative findings and scores allotted to each parameter in this scoring system were as follows: wall thickness (<3 mm – 0, 3-4 mm – 1, >4 mm – 2), percentage wall enhancement (<70 – 0, 70-99 – 1, 100 – 2), percentage luminal stenosis (<50 – 0, 50-80 – 1, >80 – 2). Amongst qualitative findings, score was 0 for absent and 1 for present. The following variables were studied: mucosal abnormality (ulcer, cobblestoning, mucosal

irregularity), layered pattern of enhancement, mesenteric abnormalities (hyperemia, comb sign), pathologic lymphadenopathy (>10 mm, intense enhancement), fistulae, abscess and distensibility. MRI severity index was cumulative of all scores and was classified as: no activity: 0-1, mild activity: 2-6, severe activity: >7.

## Statistical Analysis

Statistical analysis was done using Microsoft Excel 2007 (Microsoft, Washington, USA) and STATA software (version 10, Stata Corporation, Texas, USA). The primary objective was to determine whether CTE or MRE is better than the other. Sample size was not calculated prior. The secondary objective was to compare MR severity index with clinical disease activity, inflammatory markers and specific MRE features. The 95% exact binomial confidence intervals for these estimates were calculated. Biochemical parameters of inflammation were compared with MRI severity index using coefficient of correlation for paired values.

## Results

Of the 29 patients (median age 43 years, standard deviation 15.36, range 18 to 70; 15 females) analysed, 14 had active disease and 15 were in remission, as defined by clinical features and inflammatory markers. **Table 1** depicts demographic details of these patients: Age, sex, clinical disease activity, fecal calprotectin values and descriptive imaging findings.

CTE vs MRE comparative findings are mentioned in **Table 2**.

On CTE, normal findings were noted in 14. In 15 patients ileocolonic involvement was seen, 5 had additional small bowel involvement and two patients had strictures. Abnormal findings included wall thickening in 13 patients, increased mesenteric vascularity in 5.

On MRE, 19 patients showed definitive intestinal or vascular changes; 10 patients had normal MRE (**Table 1**). Of the 19 patients with abnormal findings, 13 showed long-segment involvement or concentric wall thickening. T2 hyperintensity was noted in 8 patients and mural stratification in four. Comb sign

**Table 1: Demographic details of patients who underwent CTE and MRE (Age, sex, clinical disease activity, fecal calprotectin - FCP and imaging findings).**

No.	Age	Sex	Disease Activity	FCP	CTE Findings	MRE Findings
1	23	m	remission	6	mild TI wall thickening	no wall thickening
2	18	m	remission	35	mild SI enhancement	terminal ileitis, conc. Wall thickening
3	18	m	remission	63	normal	normal
4	26	m	active	858	mild thickening of ilealseg	long segment conc. Thickening, enhancement
5	44	f	active	540	TI thickening, 9 cm long, fat stranding, LN+	T2 hyperintense, T1 hypointense segment of SI
6	63	f	remission	48	normal	normal, no T2 hyperintense segment, no increased vascularity, no nodes
7	23	m	remission	38	Extensive wall thickening of descending colon	conc. Wall thickening sigmoid, adj. soft tissue changes
8	65	m	remission	30	mild small bowel thickening	no thickening, enhancecent rectal wall
9	68	m	active	303	no wall thickening	focal ecc. Wall thickening, narrowing of distal ileum
10	57	f	remission	28	normal	no focal narrowing or thickness, normal vascularity
11	36	f	active	526	subtle wall thickening of Cecum and TI	mild enhancement, subtle wall thickening, increased vascularity
12	31	f	active	746	ti thickening, few LN	mild wall thickening, exagg. Enhanc. ,increased vascularity
13	36	m	active	650	no wall thickening or stenosis	conc. Wall thickening, exaggerated inflamma, increased vascularity
14	32	f	remission	62	mild TI wall thickening	no wall thickening, no increased vascularity
15	43	m	active	640	mild ileal thickening, no abscess, fistula	long segment thickening, subtle stratification, active inflammt.
16	34	m	remission	53	normal	normal
17	45	m	remission	18	distal ileal thickening,	focal circumferential thickening, luminal narrow, no increased vascularity
18	49	f	active	410	no wall thickening, normal vascularity	no increased T1 or T2 hyperintensity, no fistula , abscess
19	44	f	active	480	normal	long seg, wall thickening, multiple focal strictures in SI, increased vascularity, T2 hyperintense
20	38	f	remission	51	normal	normal
21	66	f	active	532	mild ileal clumping, no wall thickness, no fistulae / abscess	mild clumping of SI, no vascularity or LN
22	46	m	remission	15	normal	no increased T1 or T2 hyperintensity, no fistula , abscess
23	70	f	remission	45	mild increased small bowel wall thickness	no T2 hyperintense wall exaggeration, no mesentric vascularity, no nodes
24	51	f	active	568	Mild TI thickening	conc. Wall thick of TI, exaggerated wall enhance, LN+2 cm (uniform)
25	30	f	active	972	long seg. Thickening	mid ilealstricturous narrow, LN+,
26	59	f	remission	200	normal	normal
27	51	f	active	1800	no wall thickening	mild wall thickening, increased enhancement
28	28	m	active	780	no wall thickening	long segment T2 hypointense diffuse enhancement
29	39	m	remission	60	normal	normal

**Table 2: Comparison between CTE and MRE in patients with clinical activity.**

	CTE	MRE	Comment
Normal	14	10*	Changed management in 4*
Ileo-colonic involvement	15	19	
Small bowel involvement	5	10	
Stricture	2	9	
Change in phenotype			7 cases (B1 to B2), 5 had increased involvement (L2 to L3)
Change in management		17	16 medication increase, 1 dilatation

\*Four patients had findings on MRE where CTE was reported normal. In all four, immunosuppression was increased (5-ASA in three, azathioprine in one).

**Table 3: Comparison of disease activity and imaging finding (CTE and MRE) abnormality.**

Clinical disease status	Numbers	Abnormal CTE	Normal CTE	Abnormal MRE	Normal MRE
Active	14	8	6	12	2
Remission	15	7	8	7	8

(Agreement of both CTE and MRE was excellent in patients with remission; however MRE identified 4 more patients with abnormal findings who had clinically active disease but were reported normal on CTE).

**Table 4: Cost comparison between CTE and MRE in various Indian cities.**

City	CTE cost (INR)	MRE cost (INR)	Percentage difference
Mumbai (Private)	10750	14350	28.68
Mumbai (Municipal)	1250	2500	66.66
Bangalore	11000	14500	27.45
Chennai	8500	11500	30
Cochin	12000	14000	15.38
Delhi	11000	15000	30.76
Kolkata	10000	13000	26.08

(or increased vascularity) was positive in 6 patients. MRE showed strictures in the two patients who had it on CTE, and identified strictures in seven additional patients ( $p=0.04$ ; Fischer 2x2 table).

Amongst patient who were in clinical remission, CTE and MRE had good agreement in assessment of disease activity on imaging. However, in patients who had active clinical disease – MRE identified 4 more cases with abnormal findings which were reported normal on CTE. (Table 3). In terms of additional pick up rate of active disease, MRE was about 14 percent better over CTE.

More interestingly, a phenotypic change was noted in twelve cases (41%) after MRE: based on Montreal classification, 7 patients had change in behaviour (non-

stricturing to stricturing, B1 to B2) and 5 had change in location (colonic to ileo-colonic, L1 to L2). Amongst 17 patients, clinical management was altered based on abnormal findings on MRE (bowel wall T2 hyperintensity, increased vascularity) that were not seen on CTE, giving 58.6% absolute yield of MRE over CTE. In 16 patients, the dose of medications was increased (azathioprine in ten, 5-ASA in six patients); In one patient CTE showed stricture but MRE could identify it to be likely fibrotic – (no T2 hyperintensity, no increased vascularity) – needed endoscopic stricture dilatation.

There was significant correlation between MRI severity index and disease activity ( $r=0.70$ ,  $p<0.0001$ ; ANOVA) and fecal calprotectin ( $r=0.52$ ;  $p<0.003$ ), but not

CRP ( $r=0.03$ ;  $p<0.1$ ). On MRE, mural stratification, T2 hyperenhancement and comb sign correlated with disease activity ( $r=0.8$ ,  $r=0.6$  and  $r=0.5$ , respectively;  $p<0.002$ ). On CTE, wall enhancement and comb sign correlated with disease activity ( $r=0.5$  and  $0.4$  respectively;  $p<0.003$ ). Median MR Index of severity for patients with Active disease was 6.5 versus 1 for patients in remission.

Cost comparison amongst the two modalities in various Indian cities is shown in **table 4**. The percentage change in costs between CTE and MRE amongst seven cities varied between 15 to 66 percent (with average of 32 percent, standard deviation 16 percent), MRE was costlier than CTE.

## Discussion

Overall MRE was about 14 percent better at identifying abnormal radiologic findings compared to CTE, in clinically active patients with almost equal agreement in patients who are in clinical remission. Interestingly, our study showed that in 17 patients MRE changed management compared to CTE (additional yield of 58.6%). Based on CTE no patient had change in management. To our knowledge, no Indian study has compared MRE and CTE in IBD. We found that amongst CTE findings bowel wall thickness and increased mesenteric vascularity correlated best with disease activity. Amongst MRE findings, mural stratification, T2 hyperenhancement or mural stratification and comb sign correlated best with active Crohn's disease. MRI severity index was confirmed to be a useful indicator of active clinical disease.

CT is more widely available and is less time-consuming than MRI. The diagnostic utility of CT in Crohn's colitis was investigated in two studies.<sup>15,16</sup> Sensitivity and specificity were compared with ileo-colonoscopy findings as gold standard; they ranged from 60% to 90% and 90% to 100%, respectively. MRI also provides useful information in colonic CD, although mild disease may not be detected. Per-patient analysis<sup>15,17-20</sup> showed high sensitivity and specificity, ranging from 78% to 100% and 46% to 100%, respectively. A meta-analysis comparing the accuracies of ultrasonography, MRI, leukocyte isotope scintigraphy, CT, and positron emission tomography for diagnosis in patients with suspected or

known inflammatory bowel disease (IBD), mainly CD, 21 concluded that the mean sensitivity estimates on a per-patient basis were high and not significantly different among the imaging modalities (90%, 93%, 88%, and 84% for US, MRI, leukocytescintigraphy and CT, respectively. Mean per-patient specificity estimates were 96% for ultrasonography, 93% for MRI, 85% for leukocyte scintigraphy, and 95% for CT. CT and MRI had similar diagnostic accuracy for imaging IBD.<sup>21</sup> Although limited, data show that MRE changed management in about 60% of cases.<sup>15</sup> In our study, MRE changed management in 58% of cases.

The percentage change in cost between CTE and MRE ranged between 15 to 66 percent (with average of 32 percent, standard deviation 16 percent), MRE was costlier than CTE. The MRI severity index, which incorporates various qualitative and quantitative parameters, is an objective score to identify active inflammation. In the study by Girometti et al.,<sup>12</sup> the MRI severity index had shown diagnostic accuracy of 91%, and sensitivity and specificity of 93% and 87%, respectively, in evaluation of active inflammation on MRE. In our study, we noted good correlation between the MRI severity index and clinical disease activity as well as inflammatory markers.

Earlier studies<sup>13</sup> found that in the depiction of mural thickness and hyperenhancement, MRE was superior to CTE. In contrast, Schmidt et al.<sup>14</sup> showed better inter-observer agreement and sensitivity for bowel wall thickening and enhancement on CTE when compared with MRE. In our study, MRE features of mural stratification and bowel wall T2 hyperintensity independently correlated with clinically active Crohn's disease. As for CTE, bowel wall enhancement and comb sign had positive correlation with active CD.

Our study had limitations. Only twelve of our patients had undergone recent ileo-colonoscopy. In the rest, disease activity was based on clinical disease status and inflammatory biomarkers. Although studies have considered ileo-colonoscopy as the gold standard in ileo-colonic disease, this modality can obviously not assess disease activity in the rest of the small bowel. Secondly, the two modalities (CTE and MRE) were not performed on the same day in our study.

In summary we found that MRE significantly

diagnosed more strictures than CTE and also helped in management decision-making, in addition to identifying more patients with abnormal findings who are clinically active. This came at an additional cost of 32 percent more for MRE. The MRI severity correlated with disease activity and may be incorporated in clinical practice for follow up.

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