Main Imaging Features of Crohn’s Disease: Agreement between MR-Enterography and CT-Enterography

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ABSTRACT:

Background: Only a few studies have compared the accuracy of magnetic resonance enterography (MRE) and computed tomography enterography (CTE) in the diagnosis of Crohn’s disease and its complications.

Objectives: To compare the sensitivity of MRE and CTE analysis in their ability to detect, sign-by-sign, 10 classical imaging signs of Crohn’s disease.

Methods: The study group comprised 42 biopsy-proven Crohn’s disease patients who underwent both CTE and MRE within an average period of 6 weeks. Agreement between the two modalities in detecting the 10 most significant radiological signs of CD was evaluated using the Kappa index. The sensitivity of MRE and CTE was calculated using a standard of reference composed of all the findings seen by CTE and/or MRE. We analyzed MRE and CTE sensitivity separately in two groups, according to the time interval between the examinations.

Results: Agreement between CTE and MRE was more than 70% in 8 of the 10 signs: mural thickening, phlegmon, stenosis, skip lesions, mucosal stratification, fistula, abscess, and creeping fat. The Kappa level of agreement values for CTE versus MRE varied between substantial for phlegmon and skip lesions; moderate for fistula, creeping fat, abscess and mural thickening; and fair for stenosis and dilatation. CTE detected more findings than MRE, except for creeping fat and fistula. There was no significant difference in the sensitivity of CTE and MRE in the two groups defined by the time interval (time < 1.5 and time > 1.5 months) except for detection of dilatation.

Conclusions: Almost all imaging signs of Crohn’s disease were detected equally well by both modalities regardless of the time interval between examinations. We therefore consider MRE to be reliable for imaging and follow-up in patients with Crohn’s disease who may need recurrent imaging.

KEY WORDS: computed tomography enterography (CTE), magnetic resonance enterography (MRE), Crohn’s disease (CD), imaging signs

Computed tomography enterography (CTE) has been well established as a diagnostic tool in the assessment of bowel disease. It has become the standard imaging technique for many bowel disorders [1] and is considered the primary modality for evaluation of suspected inflammatory bowel disease [2]. The relatively high radiation exposure in CTE is, however, of growing concern when imaging the bowel, especially in young patients and in pregnant women with chronic bowel disease who may have to undergo multiple CT studies. Several publications regarding the high radiation exposure of CTE call for an effort to minimize the number of CT examinations in these patients [3,4].

Magnetic resonance enterography (MRE) does not use ionizing radiation. Proved to be adequately accurate in evaluation of bowel disease, it has been proposed as an alternative diagnostic modality to CTE [4-8]. Recent articles have compared the accuracy of CTE and MRE in suspected Crohn’s disease (CD). These studies focused on the detection of disease activity [9] in the presence of terminal ileitis and of extra-enteric complications [10].

There are scant systematic data comparing the diagnostic accuracy of these two modalities for each individual classical sign of CD. Recently Jensen et al. [11] evaluated the diagnostic yield of CTE and MRE in 50 patients with suspected or known CD. CD was detected with moderate to substantial agreement between the two modalities. The authors evaluated the inter-modality agreement regarding four different small bowel CD radiological signs: bowel wall thickening, bowel wall hyper-enhancement, creeping fat, and stenosis.

In addition, the clinical course often dictates the need for a follow-up study after an initial CTE, but whether MRE can serve as the follow-up examination in this scenario remains uncertain. Thus, the purpose of the present study was to compare the sensitivity of MRE and CTE in the detection of 10 classic imaging features of CD. A secondary objective was to compare the accuracy of MRE according to the time interval between an initial CTE and a follow-up MRE.

PATIENTS AND METHODS

The study protocol was approved by our institutional review board. A total of 203 consecutive patients were referred for MRE during a 4 year period (2005–2009). Only patients with CD established by conventional endoscopic and histologic criteria and who underwent both a CTE and a MRE within a maximal
time interval of 6 months between examinations were included in the study. Patients underwent the two examinations either for evaluation prompted by a change in their clinical condition or prior to operative management.

MRE studies were performed on a 1.5T GE Sigma HDx MR System (USA), version 14. Mannitol 5% (1000 ml) was orally administered 60 minutes prior to the examination. The patient was instructed to drink four doses of 250 ml every 15 minutes. During the last 15 minutes an infusion of 50 ml saline containing 1 mg glucagon was started. MRE scanning included: Axial (Ax), Coronal (Cor), and Sagittal (Sag) Fiesta TR/TE 4.3/1/9 ms, Ax and Cor 2D SSFSE T2w 1680–3200 /92.7 ms, Ax and Cor FSPGR FS BH TR/TE 150/1.3 ms and pre-Gad injection, Ax and Cor LAVA TR/TE 4.2/2.1 ms. At this point, gadolinium (Gd) (0.1 mmol/kg) was injected at 2–3 ml/sec via injector, and 40 sec post-Gad injection, Ax, Cor LAVA fat suppressed TR/TE 4.2/2.1 ms, FOV 32–40 cm, slice width 3.6–6 mm was acquired.

CTE without enteroclysis was performed, using either a 40 slice or 64 slice multidetector CT scanner (Philips Medical Systems, The Netherlands) 70 sec after intravenous injection of 100 ml of contrast media (Iopamiro) at a rate of 4 ml/sec with slice thickness of 2.5–5 mm. Patients received 1 L of either a positive contrast agent (60 ml Iomeron 350 mg iodine/ml, Bracco, Italy) (n=25) or a negative one (n=17), mainly mannitol 5% or lactulose Syrup Avilac Perrigo, Israel (66.7 g lactulose per 100 ml). CTE and MRE studies were reviewed in tandem and in consensus by two board-certified abdominal radiologists with more than 10 years of experience in abdominal imaging. The radiologists interpreted each study blinded to the patient's clinical data. Image analysis of the MRE and the CTE was performed in two separate sessions, 1 month apart, in order to prevent bias.

Ten typical radiological signs associated with CD were evaluated, comprising both mural and extramural findings. Mural findings included: mural thickening (> 3 mm), mural stratification (a differential enhancement pattern of the bowel wall layers depending on the degree and kind of inflammation and fibrosis), presence of skip lesions (multiple simultaneously occurring separate lesions), luminal stenosis, and luminal dilatation (stenosis may be anatomic or functional and is also suggested if the degree of distension of an affected bowel segment remains unchanged during the examination). The extramural findings sought were the presence of phlegmon, fistula, abscess, adenopathy (nodes > 10 mm in diameter, especially if clustered and enhancing), and creeping fat (referring to fatty deposition along the mesenteric border of inflamed bowel segments) [12].

A standard of reference was defined by combining all positive findings seen on either MRE or CTE. This composite standard of reference was designated as CTE+MRE. Positive findings seen in each of the MRE or CTE studies were compared to this CTE+MRE standard of reference.

A separate analysis was performed to determine if the agreement between studies was affected by the time elapsing between them. For this purpose, the study patients were divided into two groups according to the duration of time interval between the MRE and CTE. The first group included patients whose MRE and CTE were performed up to 1.5 months apart, and the second group included patients whose examinations were done with a longer time interval of up to 6 months. The agreement between CTE-MRE findings was then compared between the two groups.

### STATISTICAL ANALYSIS

The radiological signs on the MRE and the CTE studies were compared by calculating the percentages of agreement and disagreement of each of the signs. The level of agreement was evaluated using the Kappa index [13,14] and the sensitivity of MRE and CTE was calculated and compared. As there is no radiological standard of reference for comparison between the modalities, a standard of reference comprising all the findings seen by CTE and/or MRE (CTE+MRE) was used. The sensitivity of MRE and CTE was calculated using this standard of reference. The difference between the sensitivity of MRE in the two time interval groups and the sensitivity of CTE in the two time interval groups was tested using a conservative t-test for proportions.

### RESULTS

Forty-two CD patients (23 males, 19 females, mean age 27.7 ± 9.3 years, range 8–51) underwent both MRE and CTE within a 6 month period (average 1.83 months). The time interval between CTE and MRE in the study group was less than 1.5 months in 23 of the patients and between 1.5 and 6.2 months in the other 19 (regardless of whether the MRE or CTE was the first exam).

The comparable detection rates of 10 common CD radiological signs observed on MRE vs. CTE along with the agreement and disagreement for the detection of each of these signs are shown in Table 1. As shown, there was agreement in more than 70% in 8 of the 10 signs compared: mural thickening [Figure 1], phlegmon, stenosis, skip lesions, mucosal stratification, fistula, abscess, and creeping fat. Agreement was less than 70% in two signs: dilatation and adenopathy.

Table 1 depicts also the Kappa level of intermodality agreement values (CTE versus MRE). According to the commonly cited scale of Interpretation of Kappa [13,14], the Kappa values varied between substantial (0.61–0.80) agreement for phlegmon and skip lesions; moderate (0.41–0.60) for detection of fistula, creeping fat, abscess and mural thickening; and fair (0.21–0.40) for detection of stenosis and dilatation. Poor (0.01–0.20) agreement was found for adenopathy and less than chance agreement for detection of mucosal stratification.
The rate of positive findings on MRE or CTE as compared to our constructed standard of reference (CTE+MRE) is shown in Figure 2.

In 8 of the 10 signs CTE detected more findings than did MRE, but the difference was not statistically significant. Creeping fat (sign #6) and fistula (sign #8) were the only signs better seen on MRE than on CTE.

The sensitivity of CTE and MRE using the standard of reference (CTE+MRE) was also assessed separately in the group of patients with an interval between CTE and MRE examinations of less than 1.5 months (group 1, n=23) and patients with an interval greater than 1.5 months (group 2, n=19). These results are presented in Table 2.

Comparing the sensitivity for detecting radiological signs between MRE and CTE in the two groups reveals that the detection of creeping fat remained better on MRE than on CTE in the two groups. However, in group 1 (interval < 1.5 months), MRE showed better sensitivity in detecting dilatation than did CTE, while in group 2 (interval > 1.5 months) MRE showed better sensitivity than CTE in detecting fistula. In all other signs, the detection in both groups on CTE was better than on MRE.

Furthermore, the sensitivity of CTE as well as the sensitivity of MRE in the two time interval groups was compared. On CTE no significant difference was found in any of the signs. On MRE, as well, no significant difference was found in any of the signs, except for the detection of dilatation, which was higher in group 1 \[ t(df=40)=2.11, P < 0.05 \].

### Table 1. Agreement and disagreement between CTE and MRE in depicting 10 common imaging signs of Crohn’s disease (n=42)

<table>
<thead>
<tr>
<th>Imaging signs</th>
<th>Agreement n (%)</th>
<th>Disagreement n (%)</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CT = 1 MR = 1</td>
<td>CT = 0 MR = 0</td>
<td>Total</td>
</tr>
<tr>
<td>1. Mural thickness</td>
<td>36 (85.71)</td>
<td>2 (4.29)</td>
<td>38 (90.48)</td>
</tr>
<tr>
<td>2. Phleghmon</td>
<td>18 (42.66)</td>
<td>19 (45.24)</td>
<td>37 (88.10)</td>
</tr>
<tr>
<td>3. Strictures</td>
<td>34 (80.95)</td>
<td>2 (4.76)</td>
<td>36 (85.71)</td>
</tr>
<tr>
<td>4. Skip lesions</td>
<td>22 (52.38)</td>
<td>12 (28.57)</td>
<td>34 (80.95)</td>
</tr>
<tr>
<td>5. Mucosal stratification</td>
<td>33 (78.57)</td>
<td>0 (0.00)</td>
<td>33 (78.57)</td>
</tr>
<tr>
<td>6. Fistula</td>
<td>15 (35.71)</td>
<td>18 (42.66)</td>
<td>33 (78.57)</td>
</tr>
<tr>
<td>7. Abscess</td>
<td>10 (23.81)</td>
<td>21 (50.00)</td>
<td>31 (73.81)</td>
</tr>
<tr>
<td>8. Creeping fat</td>
<td>15 (35.71)</td>
<td>15 (35.71)</td>
<td>30 (71.43)</td>
</tr>
<tr>
<td>9. Dilatation</td>
<td>21 (50.00)</td>
<td>7 (16.67)</td>
<td>28 (66.67)</td>
</tr>
<tr>
<td>10. Adenopathy</td>
<td>14 (33.33)</td>
<td>9 (21.43)</td>
<td>23 (54.76)</td>
</tr>
</tbody>
</table>

**Significant, P < 0.01
CT, MR: 1 = positive, 0 = negative

### DISCUSSION

In our study we found comparable diagnostic yields for MRE and CTE in patients with CD. The agreement between CTE and MRE was evaluated for 10 common imaging signs of Crohn’s disease. Lee et al. [10] found equally high diagnostic accuracies and substantial-to-excellent agreement for detection of CD in the
upper and lower small bowel. However, they evaluated only six signs: three mural (mural stratification, hyper-enhancement, and comb sign) and three extra-enteric signs (fistula, sinus tract, and abscess). Jensen et al. [11], in their meticulous comparison including 50 patients, compared 4 signs and found similar agreement.

We found less agreement between CTE and MRE in depicting dilatation and adenopathy, while creeping fat and fistula were better seen on MRE than on CTE. These findings do not correspond to those of Fiorino et al. [15] who did not find any difference in fistula detection and found good agreement between the modalities regarding detection of abdominal nodes and perivisceral fat enhancement.

When we compared the sensitivity of each modality to itself (CTE to CTE and MRE to MRE) in the two time-interval groups in order to check whether the time interval is a factor, no difference was found in the rate of detection of signs except for the detection of dilatation, which was more prominent in the group with a time interval of less than 1.5 months. A possible explanation is that patients with active disease had repeated examinations within a short time interval and the dilatation of the bowel had resolved in the later study.

Therefore, we can state that even if there is a time interval of up to 6 months we can still compare two different examinations (CTE and MRE) accurately. Only bowel dilatation might not be consistent.

These observations are important for gastroenterologists in deciding whether to refer their patients to CTE or MRE for the diagnosis and follow-up of CD. The present analysis of detailed imaging signs demonstrates that MRE can detect 8 of 10 signs of CD, thereby supporting its usefulness for the diagnosis and follow-up of CD patients. Taken together with its lack of ionizing radiation, MRE may be considered the examination of choice for this purpose. This contention is consistent with the findings of Lee et al. [10], who reported comparable sensitivity of CTE and MRE in the detection of terminal ileitis. CTE and MRE were similar in their capability to discern active inflammation as well as extra-enteric complications in the small bowel.

Several limitations of our study should be acknowledged. This retrospective study included a relatively small number of patients (n=42), although it was still larger than most previously reported studies comparing the accuracy of MRE and CTE [6,7]. Schmidt and colleagues [16] reported 50 patients with various bowel diseases [16]. Jensen et al. [11] reported a group of 50 patients, some of whom had no active disease.

Another drawback is the fact that some patients had an interval of up to 6 months between the two modalities compared. This could potentially affect the reliability of the comparison. We found, however, that the time interval did not alter the classical radiological signs detected by the different techniques. A fair to substantial agreement for most of the imaging findings tested was found. Another limitation is the fact that there were two methods for performing CTE: patients receiving either positive (n=25) or negative oral contrast agent (n=17). This difference in
the technique of acquisition could interfere with the possibility of evaluating enhancement, but we did not include the enhancement as a sign, choosing instead the stratification that can be seen with both techniques.

In conclusion, the diagnostic accuracy in detecting the 10 most common imaging signs of Crohn’s disease is comparable between MRE and CTE. The two modalities are comparable even when up to 6 months have elapsed between the two studies. These data support MRE as a reliable imaging modality for CD, and is especially useful in preventing radiation overexposure in this young population who are often in need of recurrent imaging.

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References

Immunogenetics of mice and men

Species undergo different selective forces, and those that drive immunity are of special interest because they may affect studies of human health. Webb and co-researchers investigated the differences between human and mouse for 456 protein-coding gene families involved in innate immunity. Of these, 2 genes in humans and 35 genes in mice exhibited signatures of positive selection. Examining the evolutionary distance between mice and humans, they further identified many genes likely to be under positive selection in the primate and murid lineages. These changes, for the most part, appear to have been fixed within humans and mice, respectively, demonstrating the different evolutionary trajectories that immune genes have taken during evolution.

Capsule

A CRISPR view of genes responsible for tumor metastasis

Large tumors metastasize more often than small tumors. Is this simply because large tumors release a greater number of malignant cells into the circulation? Or is it because the genetic changes in tumor cells that drive them to proliferate rapidly are the same as those that promote their metastatic behavior? To explore this question, Chen and group designed a screen based on a genome-editing technology called CRISPR-Cas9 to identify genes that, when inactivated, enhance tumor growth, lung metastasis, or both in mice. The small set of inactivated genes found in metastatic lesions largely overlapped with the set found in late-stage primary tumors, implying that functional loss of these genes drives both growth and metastasis.

Capsule