

Assessment of Imaging Features of Crohn's Disease with MR Enterography

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ABSTRACT

Background: To evaluate the frequency of pathological findings determined on magnetic resonance (MR) enterography (MRE) in patients with Crohn's Disease.

Methods: A retrospective analysis of the MRE images was made in 34 female and 41 male patients (mean age 41 years) with Crohn's disease. The prevalence of bowel wall (mural thickening, mural edema, mural fat deposits, mucosal enhancement, ulceration, cobblestone appearance, pseudopolyps) and mesenteric fatty tissue alterations (fatty tissue proliferation, mesenteric hypervascularity, enlarged lymph nodes, peri-enteric inflammation, reactive fluid), complications due to penetrating (fistula, sinus tract, abscess) and stenosing processes (fibrotic and inflammatory stenosis, obstruction, dilatation), and involvement of the colon were determined.

Results: The most frequently observed changes in the bowel wall and mesenteric fatty tissue were mural thickening (98.7%) and enlargement of mesenteric lymph nodes (76%), respectively. Stenosis was the most common complication (76%). The most frequently seen pathology of the colon was ileocecal valve thickening and enhancement (74.7%).

Conclusion: MR enterography is a useful imaging modality for the evaluation of changes in both the mesenteric fatty tissue and the bowel wall. As there is no use of ionizing radiation, MR enterography should be the preferred imaging modality during follow-up of patients with Crohn's disease.

Keywords: Crohn's disease, magnetic resonance enterography, imaging features

INTRODUCTION

The small intestine is an extremely difficult part of the gastrointestinal system to visualize with endoscopy. Therefore, enteroclysis and small bowel follow-through series have been used as diagnostic methods for many years.¹ In the past, enteroclysis has been accepted as the standard imaging method in the radiological assessment of small bowel pathologies.¹

Today, magnetic resonance (MR) enterography (MRE) is widely used as a radiological imaging method in the diagnosis, follow-up, evaluation of response to treatment, and determination of possible complications, for Crohn's disease.² Together with developments in radiological imaging technology, the increasing use of computed tomography enterography and MRE allows not only the determination of intraluminal evaluation as in conventional methods, but also of possible mural and extraluminal pathologies.³

MR enterography is a cross-sectional imaging method, which does not include ionizing radiation, can be easily applied, and is tolerated better than conventional methods by patients.⁴ Therefore, it is much more advantageous than techniques based on enteroclysis. As there is no exposure to ionizing radiation, MRE is suitable for use in Crohn's disease, for which frequent follow-up is required and the patient population is in the young age group.⁵

In Crohn's disease, the superficial lesions that begin as lymphoid hyperplasia, erosion, and aphthous ulcers deepen over time, affecting all layers of the intestinal wall.⁶ The disease can be complicated by penetrating lesions such as sinus, abscess, fistula, and tissue changes that narrow or obstruct the intestinal lumen.⁶ Thus, there is a diversity of findings in the small bowel involvement of Crohn's disease. The aim of this study was to determine the frequency of findings detected with MRE in patients diagnosed with Crohn's disease and also to evaluate the

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association of each of the MRE findings with the other findings.

MATERIALS AND METHODS

This retrospective study included a total of 75 patients diagnosed histopathologically with Crohn's disease between July 2011 and December 2014, who were referred to our department for MRE. The patients comprised 41 (54.7%) males and 34 (45.3%) females with a mean age of 41 years (range, 18-78 years). The Local Ethics Committee granted approval for the study.

Following a 6-hour fasting period, all the patients were given 125 mL laxative lactulose solution (Osmolak® 250 mL) which was mixed into 2 L of drinking water, to be drunk within 1 hour. To prevent any artifacts originating from bowel peristalsis, 1 mg Glucagon (Glucagon Hypokit® 1 mg) was applied intramuscularly as a spasmolytic. The MRE examinations were performed on an MR device with 1.5 T magnetic field strength (GE-Optima MR450w). The patients were examined in a supine position using a phase-array body coil. After obtaining standard and heavily weighted T2 images in coronal and axial planes, gadolinium chelate was administered by the IV route and 3D fat-suppressed T1-weighted GE images (LAVA-Flex) were obtained in the precontrast, arterial, venous, and delayed venous phases. The sequences and technical parameters used during the MRE examination are shown in detail in Table 1.

The MRE images were retrospectively evaluated by a single radiologist. Evaluation was made in respect of changes in the intestinal wall and mesenteric fat tissue, colon involvement, and complications.

Based on the radiological evaluation of the MRE, the behavior of Crohn's disease was subdivided into B1, B2, and B3 subgroups according to the Montreal classification.⁷ Inflammatory disease features such as mural

edema, target sign, lymph node enlargement, and comb sign without stricturing or penetrating signs were considered B1 behavior. The B2 behavior was represented by stricturing with prestenotic bowel dilatation and signs of bowel obstruction. The B3 behavior included a penetrating condition such as an inflammatory mass, an intraabdominal fistula, and/or an abscess.

All the findings were recorded and tabulated.

Statistical Analysis

Data obtained in the study were analyzed statistically using the Statistical Package for the Social Sciences (SPSS) 11.5.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics and frequency and percentage values of MRE findings were calculated. Minimum, maximum, percentage and *n* values were used as descriptive statistics. The association of the presence of each of the MRE findings with the other findings was evaluated statistically. Chi-square and Fisher's exact tests were used to compare independent categorical variables. The results were defined as statistically significant when the respective test statistic had a *P*-value <.05.

RESULTS

The prevalence of the MRE findings is shown in Table 2. The findings were grouped under 4 main headings of intestinal wall changes, mesenteric fat tissue changes, complications, and colon involvement.

The most frequently seen intestinal wall change was wall thickening (98.7%) (Figure 1), the most frequent mesenteric fat tissue change was enlargement in the mesenteric lymph nodes" (76%) (Figure 2), the most common complication was stricture (76%) (Figure 3), and the most common pathological finding in the colon was thickening/enhancement of the ileocecal valve (Figure 4) (74.7%).

The relationship of the presence of each MRE finding with the other findings is detailed in Table 3. The association of mural edema (Figure 1) with mucosal enhancement (*P* < .019), mucosal irregularity (*P* < .003), and enlargement in mesenteric lymph nodes (*P* < .032) was found to be statistically significant. In patients with mucosal enhancement (Figure 2), the association of mucosal irregularity (*P* < .001), the comb sign (increased number of peri-enteric vessels on the mesenteric side of the affected segment) (*P* < .009), enlargement in mesenteric lymph nodes (*P* < .017), and intestinal stricture (*P* < .017) were statistically significant.

MAIN POINTS

- Crohn's disease is an inflammatory bowel disease that progresses with relapses, and MRE is frequently needed in follow-up and treatment.
- The most common sign of MRE in Crohn's disease is intestinal wall thickening (98.7%).
- MRE is a useful and effective imaging method without ionizing radiation to differentiate both intestinal wall and mesenteric tissue findings and to identify complications of Crohn's disease.

Table 1. MR Enterography Sequence Parameters

Parameters	T2-Weighted SSFSE	T2-Weighted SSFSE	T2-Weighted SSFSE Multi-Slice	T2-Weighted SSFSE Thin Multi-Slice	2D FIESTA Cine	T2-Weighted SSFSE Thick-Slice	T2-Weighted SSFSE Multi-Slice	T1-Weighted 3D GE (LAVA-Flex)
Matrix size	320 × 192	320 × 192	320 × 192	320 × 224	224 × 320	480 × 256	320 × 256	440 × 396
Slice thickness (mm)	5.0	5.0	5.0	5.0	6.0	40.0	3.5	3.2
Interslice gap (mm)	0.0	1.0	1.0	1.0	0.5	0.5	0.0	0.0
TR (ms)	1200	1200	1200	Minimum	3.9	Minimum	Minimum	2,1
TE (ms)	85	85	85	100	1.6	Minimum	100	Not open
Flip angle (°)	160	160	160	-	60	-	-	12
Reduction factor	-	-	-	-	2	-	-	2
Slice number	48	67	67	67	24	6	67	76
FoV (mm)	430 × 430	420 × 420	420 × 420	420 × 420	380 × 380	400 × 400	430 × 430	360 × 288
Image plane	Sagittal	Transverse	Transverse	Transverse	Coronal	Coronal	Coronal	Transverse
Bandwidth (kHz)	62.50	62.50	62.50	62.50	100	31.25	62.50	83.33
Respiratory control	Breath-Hold	Breath-Hold	Breath-Hold	Breath-Hold	Breath-Hold	Breath-Hold	Respiratory-Triggered	Breath-Hold
Data acquisition time (min)	0:57	1:20	1:20	1:20	2:33	0:10	1:05	2:18 (0:17)

SSFSE, single-shot fast spin-echo; FIESTA, fast imaging employing steady-state acquisition.

Table 2. The Frequency of Findings of Crohn's Disease Determined on MRE

	MRE Findings	Number of Cases (%)
Intestinal wall changes	Intestinal wall thickness	74 (98.7%)
	Mural edema	63 (84%)
	Mural fat tissue	8 (10.7%)
	Mucosal enhancement	67 (89.3%)
	Mucosal irregularity	54 (72%)
	Cobblestone appearance	1 (1.3%)
	Pseudopolyp formation	3 (4%)
Changes in mesenteric fat tissue	Fat tissue proliferation	27 (36%)
	Comb sign	43 (57.3%)
	Lymph node enlargement	57 (76%)
	Peri-enteric inflammation	14 (18.7%)
	Reactive loculated fluid	4 (5.3%)
Complications	Entero-enteric fistula	20 (26.7%)
	Sinus tract	5 (6.7%)
	Abscess	2 (2.7%)
	Stricture	57 (76%)
	Luminal dilatation	18 (24%)
Colonic involvement	Cecum deformity	31 (41.3%)
	Ileocecal valve involvement	56 (74.7%)
	Mural thickening	24 (32%)

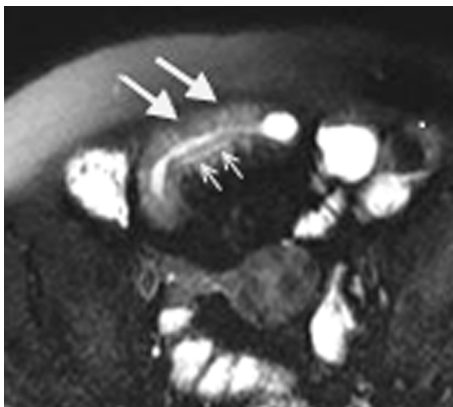


Figure 1. A 46-year old female patient with Crohn's disease followed up for 5 years. Axial fat-suppressed T2-weighted SSFSE MR image shows wall thickening (large arrows) and mural edema as linear hyperintensity (small arrows) in the distal ileum.

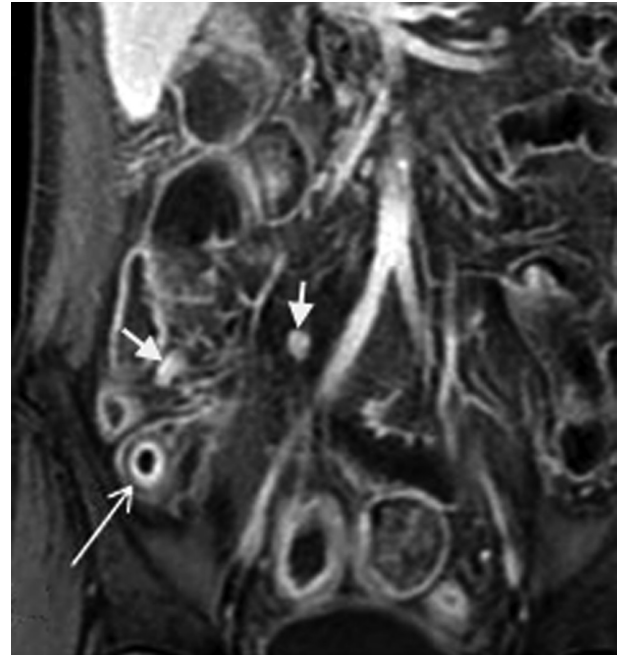


Figure 2. A 57-year-old male patient with Crohn's disease followed up for 4 years. Coronal contrast-enhanced fat-suppressed T1-weighted 3D gradient echo MR images shows mural thickening and mucosal enhancement (long arrow) in the distal ileum. Note the enlarged mesenteric lymph nodes (short arrows) adjacent to the involved intestinal segment.



Figure 3. A 52-year-old female patient with Crohn's disease followed up for 19 years. Coronal contrast fat-suppressed T1-weighted MR image shows ileoileal fistula (asterisk) associated with stricture formation (thin arrow). Note the dilated small bowel (short arrows) proximal to the site of stricture.



Figure 4. A 25-year old patient with Crohn's disease followed up for 2 years. Coronal FIESTA MR image shows ileocecal valve thickening (arrow).

In patients with mural fat deposition in the intestinal wall (Figure 5), and also in cases with intestinal pseudopolyps (Figure 6), the mesenteric fat tissue proliferation (Figure 5) was statistically significantly frequent ($P < .022$ and $P < .043$; respectively). The mesenteric fat tissue proliferation was statistically significantly more frequent in patients with the comb sign ($P < .002$), mesenteric lymph node enlargement ($P < .012$), peri-enteric inflammation ($P < .014$), and reactive loculated fluid ($P < .014$). The coexistence of mesenteric lymph node enlargement ($P < .004$), peri-enteric inflammation ($P < .003$), stricture ($P < .004$), and cecum deformity ($P < .045$) was statistically significantly frequent in patients who had the comb sign (Table 3).

In cases with fistula, cecum deformity ($P < .001$) and colon deformity were determined at statistically significantly higher rates. In cases with cecum deformity, ileocecal valve thickening/enhancement was determined statistically more frequently ($P < .001$) (Table 3).

Based on the radiological evaluation of the MRE, the phenotypic behavior of Crohn's disease in our study is shown in Table 4. The most common disease behavior in our cohort was B1.

DISCUSSION

Crohn's disease is a complex pathological process, for which the lifetime course with frequent relapses cannot be predicted. It is usually seen in a young age group, and because of the need for repeated CT examinations in the follow-up of the disease, exposure to ionizing radiation is inevitable.⁸ Involvement is seen most often in the small bowel, which is the part of the digestive tract for which visualization with endoscopic techniques is limited.⁹

Traditionally, the combination of fluoroscopy and CT techniques has been of benefit in the evaluation of the small bowel in Crohn's disease. In advanced stages of the disease, the enteroclysis method is used, which provides information about the intestinal lumen and mucosal surface, but is limited with respect to extra-enteric complications.^{3,10} CT provides detailed information about the intestinal wall and extra-enteric structures. Despite the diagnostic success, for the reasons stated above, the use of CT techniques is limited in young Crohn's patients who need follow-up imaging.¹¹ MRI provides safe and non-invasive imaging without exposure to ionizing radiation for Crohn's patients.¹²

In the current study, pathological wall thickening was determined in all but one of the patients. Mucosal enhancement was determined in 89% of the patients. In a study of 40 patients with Crohn's disease by Negaard et al.,¹³ the prevalence of MR enteroclysis and MRE findings was compared. The prevalence of intestinal wall thickening was determined as 46% and mural enhancement as 45% on MRE and MR enteroclysis, respectively.¹³ Goldberg et al.¹⁴ evaluated 28 Crohn's patients with CT and compared the findings of conventional barium studies with surgical findings. Intestinal wall thickening was determined in 82% of the patients.¹⁴

In the current study, the prevalence of mucosal irregularity compatible with ulceration was determined as 72%. A cobblestone appearance was determined in 1 patient and pseudopolyps in 4% of the patients. Negaard et al.¹³ calculated ulcer prevalence as 45% on MRE and MR enteroclysis. In a study by Goldberg et al.,¹⁴ no mucosal anomalies (cobblestone appearance, pseudopolyp, or ulceration) were determined with CT.

In our study, the formation of enteric fistula was determined in 20 (26%) patients, and sinus tract in 5 (6%). In the study by Goldberg et al.,¹⁴ fistula and sinus tract formation were found in 32% of the patients. Brunning et al.¹⁵ aimed to measure the prevalence of penetrating disease and

Table 3. The Association of Crohn's Disease Findings on MRE

	MRE Findings	N (%)	P
Mural edema	Mucosal enhancement	59 (93.7%)	.019
	Mucosal irregularity compatible with ulceration	50 (79.4%)	.003
	Mesenteric lymph node	51 (81%)	.0332
Mural fat	Fat tissue proliferation	6 (75%)	.022
Mucosal enhancement	Mucosal irregularity compatible with ulceration	53 (79.1%)	.001
	Comb sign	42 (62.7%)	.009
	Mesenteric lymph node	54 (80.6%)	.017
	Stricture	54 (80.6%)	.017
	Mesenteric lymph node	45 (83.3%)	.017
	Cecum deformity	28 (51.9%)	.003
Pseudopolyp formation	Fat tissue proliferation	3 (100%)	.043
Fat tissue proliferation	Comb sign	22 (81.5%)	.002
	Mesenteric lymph node	25 (92.6%)	.012
	Peri-enteric inflammation	9 (33.3%)	.012
	Reactive loculated fluid	4 (14.8%)	.014
Comb sign	Mesenteric lymph node	38 (88.4%)	.004
	Peri-enteric inflammation	13 (30.2%)	.003
	Stricture	38 (88.4%)	.004
	Cecum deformity	22 (51.2%)	.045
Mesenteric lymph node enlargement	Stricture	47 (82.5%)	.028
Peri-enteric inflammation	Reactive locular fluid	4 (28.6%)	.001
	Entero-enteric fistula	7 (50%)	.043
Entero-enteric fistula	Cecum deformity	15 (75%)	.001
	Colon involvement	11 (55%)	.01
Stricture	Dilatation	18 (31.6%)	.004
Cecum deformity	Ileocecal valve involvement	30 (98.8%)	.001

extra-intestinal pathologies with CT enterography in 357 patients previously diagnosed with Crohn's disease, and reported fistula in 63 (17%) patients, and sinus tract in 7 (2%) cases. The fistulas were determined as entero-cutaneous in 10 (3%) patients, entero-enteric in 34 (9%), enterovesical in 4 (1%), perianal in 9 (2.5%), and recto-vaginal in 2 (0.5%) patients.¹⁵

In the current study, in the examination of the changes in mesenteric fat tissue in Crohn's disease, the prevalence of fatty tissue proliferation was determined as 36%, peri-enteric inflammation as 18%, mesenteric lymph node enlargement as 76%, and mesenteric abscess was determined in 2 patients. In the study by Goldberg et al.,¹⁴ mesenteric fat tissue proliferation was reported as 39%, mesenteric abscess as 25%, mesenteric inflammatory

reaction as 14%, and mesenteric enlarged lymph nodes as 18%. In a study of 18 Crohn's patients with MRI by Holzknecht et al.,¹⁶ the prevalence of mesenteric lymph node enlargement was calculated as 83%, and mesenteric fat tissue hypertrophy as 66%.

Goldberg et al.¹⁴ determined luminal stricture and proximal dilatation in 71% of patients. In the current study, luminal stricture was determined in 57% of the patients, and intestinal dilatation in 18%. Complete bowel obstruction was not determined in any patient. In the study by Negaard et al.¹³ bowel stenosis was determined in 20% of patients on MR enteroclysis and MRE.

In the current study, statistical evaluations were made with respect to frequency of coexisting pathological

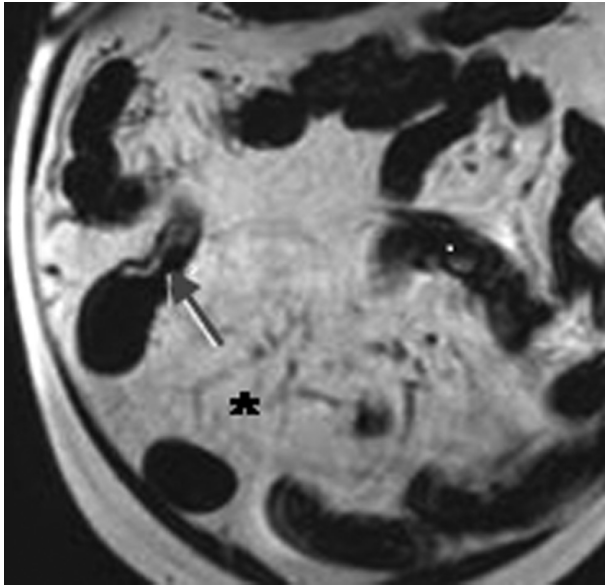


Figure 5. A 64-year-old male patient with Crohn's disease followed up for 10 years. Coronal fat-only image obtained with LAVA-Flex sequence shows intramural fat deposition (arrow) as a hyperintense linear signal in the ileal wall. Also note the mesenteric fatty proliferation (asterisk) in right lower quadrant.

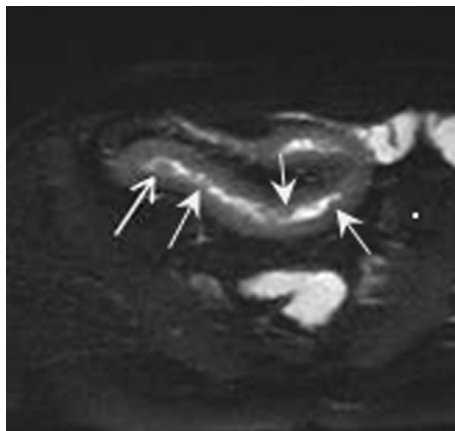


Figure 6. A 37-year-old female patient with Crohn's disease followed up for 10 years. Axial fat-suppressed T2-SSFSE MR image shows pseudopolyps (arrows) extending into the ileal lumen.

Table 4. MRE Findings of the Disease Behavior Based on the Montreal Classification

	B1 (%)	B2 (%)	B3 (%)
Patients (n)	41 (54.6)	11 (14.7)	23 (30.7)
Age $\pm$ SD	40.70 $\pm$ 13.02	40.81 $\pm$ 16.35	42.08 $\pm$ 13.34
Male	21 (28)	6 (8)	14 (18.7)
Female	20 (26.6)	5 (6.6)	9 (12.1)

B1, non-stricturing, nonpenetrating; B2, structuring; B3: penetrating.

findings on MRE. For example, in patients with mural edema, the most common accompanying findings were ulceration, mucosal enhancement, and mesenteric lymph node involvement. It is known that mural edema is usually present in acutely inflamed bowel segments.¹² Increased mucosal enhancement may be one of the earliest signs of active inflammation, and can be accompanied by ulceration.¹⁷ Lymph node enhancement is also accepted as a finding of active inflammatory disease.¹² Therefore, the coexistence of these findings helps us to report with certainty that the disease is in the active stage. We also determined that mucosal enhancements were mostly accompanied by findings of ulceration (mucosal irregularity), comb sign, lymph node enlargement, and stricture. A comb sign also indicates an acute exacerbation in patients with Crohn's disease.¹⁸ In patients with a comb sign, not all bowel obstructions are the result of fibrotic strictures. In active disease, the areas of spasms and luminal contractions due to severe mucosal ulceration may mimic strictures.¹² In this study, both the fat deposition in the intestinal wall and intestinal pseudopolyps were statistically significantly frequent in cases with mesenteric fat tissue proliferation. All of these MRI findings are evidences suggesting that the disease is in a chronic phase. Although the deposition of mural fat may occur as a normal variant, it is generally secondary to chronic bowel inflammation.¹⁹ Pseudopolyps associated with Crohn's disease are probably the most common inflammatory-type polyps that occur in the small intestine. They usually develop on the background of chronic ileitis. Fat tissue proliferation extending from the mesenteric attachment of the bowel and partially covering the inflamed bowel loop is mostly seen in chronic disease.¹⁷ In those determined with fibrofatty tissue proliferation, the accompanying findings were primarily the comb sign, followed by lymph node enlargement, peri-enteric inflammation, and reactive loculated fluid. When fibrofatty tissue proliferation is associated with engorged mesenteric vessels (comb sign), it is considered pathognomonic for the disease and highly specific for active Crohn's disease.¹⁷ We also noted that fistula formation, peri-enteric inflammation, cecum deformity, ileocecal valve thickening, and coexistent colonic involvement, which are usually seen during chronic Crohn's disease, were associated statistically more frequently.

The Vienna classification was found insufficient to classify penetrating forms of Crohn's disease,⁷ because, perianal disease accompanied by perianal fistula and abscess has a different prognosis from the intraabdominal penetrating phenotype. For this reason, it has been modified

into the "Montreal classification," by adding a modifying (p) factor to the Vienna classification.⁷

The clinical significance of this classification is that there is a good agreement between the disease behavior described in the behavior (B) score and the therapeutic approaches. The B1 phenotype represents an inflammation that is often adequately treated by non-surgical approaches. The stricture form (B2 phenotype) requires endoscopic or surgical treatment in many cases. However, surgery is often required in the treatment of penetrating disease (B3 phenotype). Schill et al.²⁰ reported MRE findings and Crohn's disease B phenotype in 76 patients with surgical correlations. They noted that MRE was an excellent imaging modality to correctly assess the Montreal classification-based disease behavior.²⁰ In our study, we could perform the B phenotype according to the Montreal classification in all patients on the basis of MRE findings. MRE findings were not insufficient in any of our study patients while deciding B behavior. These results can be interpreted as being indicative of MRE being an appropriate imaging method for timely diagnosis of stricturing or penetrating complications of Crohn's disease and for deciding on interventional or surgical treatment.

One of the important limitations of this study is its small sample size. Another limitation is the retrospective nature and single-center design of the study. However, these limitations are acceptable and do not diminish the purpose of the study. Multicenter, prospective studies with larger samples are needed.

In conclusion, in this study, we found that some of the MRE findings were more frequently associated. Although some of these findings may be seen in other diseases, their combined presence is an extremely specific indicator for diagnosis and stage of the disease. In routine practice, the MRE method is preferred more in the follow-up of the disease rather than in diagnosis. Using this method, active inflammation and complications can be seen without the use of ionizing radiation.

MRE is a suitable imaging method for accurately identifying Crohn's disease behavior according to the Montreal classification, and helps clinicians to decide the therapeutic approach. However, MRE is preferred in Crohn's disease not only because it does not include ionizing radiation, but also because it provides multiplanar cross-sectional imaging, it has high soft tissue contrast resolution,

and allows detailed and simultaneous evaluation of the changes in both the intestinal wall and in mesenteric tissue. Moreover, adverse reactions to the contrast agent administered are rarely seen.

Ethics Committee Approval: The Local Ethics Committee granted approval for the study. Date: January 12, 2015, No: 01-12-15.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.E.; Design – A.E., M.O.; Supervision – A.E., M.O., M.T.; Resource – M.O., Ç.M.A.; Materials – M.O., A.E.; Data Collection and/or Processing – M.O., A.E.; Analysis and/or Interpretation – M.O., Ç.M.A., A.B.B.; Literature Search – M.O., Ç.M.A., A.B.B.; Writing – M.O., A.E.; Critical Reviews – A.E., M.T.

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