Magnetic resonance enterography (MRE) in Crohn’s disease: How we do it and common imaging findings

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ABSTRACT

Background: Crohn's disease (CD) is a chronic inflammatory bowel disease that can affect children and adults. MRE is the initial imaging modality in assessing it essentially due to its non-invasiveness with lack of ionizing radiation. It can demonstrate both mural and extramural manifestations of CD. So, familiarity with MRE is essential for radiologists and clinicians to assess the clinical management of CD.

Results: A total of 54 patients with proved Chron's disease were included in our study that underwent MR enterography to assess the different imaging features during active or complicated disease stage. Active bowel inflammation was characterized by bowel wall thickening that detected in 46 patients (85%), bowel wall edema in 15 patients (27.8%) and mural wall hyperenhancement in 43 patients (79.6%). Inflammatory mesenteric fat stranding could be detected in 41 patients (75.9%), mesenteric lymphadenopathy in 29 patients (53.7%) and vascular engorgement within the affected mesentery in 39 patients (72.2%). Fistula formation is a feature of penetrating disease with two types of fistulous disease as intra-abdominal (in 9 patients, 16.7 %) and perianal fistula (in 11 patients, 20.4%). The chronic bowel wall inflammation is likely progress to fibrostenotic complications that seen in only two patients (3.7%).

Conclusion: MR enterography is a pivotal diagnostic tool in assessing the common imaging features of Chron's disease as well as its complications.

Keywords: Crohn's disease; Small bowel inflammation; MR enterography.

MANUSCRIPT

BACKGROUND

Chron's disease (CD) is an inflammatory bowel disease, identified by an alternating pattern of relapse and remission [1]. Its highest incidence in the 2nd and 3rd decades of life with a quarter of patients presenting in teenagers [2,3]. CD initiates an acute inflammatory process affecting different parts of the alimentary tract, particularly the terminal ileum and may lead to irreversible injury [4].

Patients with CD typically experience repeated bowel motility, abdominal pain and diarrhoea; while other manifestations as fever, nausea, vomiting and extra-abdominal manifestations (i.e. uveitis, episcleritis, arthritis or erythema nodosum) can be seen in about 25% of involved patients[5-7].

Typically, the affected bowel loop by active inflammation reveals segmental mural wall thickening, intramural edema and sometimes microabscesses with involving its mesenteric border [8,9]. Skip lesions *(alternating inflamed and unaffected segments of bowel loop)* are considered usual features of Chron's disease [10].

Complicated CD presented by stricture development with signs related to bowel obstruction and penetrating disease with abscess and fistulous formation [11]. As CD is a chronic state that can involve various parts of GI tract through time, anti-inflammatory medications is the initial management plan. Surgical intervention is considered for cases resistant to medications or complicated cases [12-14].

The role of imaging in Chron's disease ensued from the need to assess bowel segments inaccessible to optical endoscopy. Generally, barium studies have been done to assess the upper and lower alimentary

tract, but are now used hardly due to poor diagnostic capability, especially in evaluating extramural manifestations [15, 16].

CT enterography (CTE) is a cross-sectional imaging approach to assess the SB loops, through the use of neutral oral contrast with image obtaining after IV contrast administration in the enteric state[17,18]. Due to its wide use in urgent situations, fast image obtaining with facility to estimate mural and extramural bowel manifestations, CTE is considered as an accepted imaging technique for CD assessment [19, 20]. But nowadays, the probable ionizing radiation risks occurred with CT scanning should be considered, especially in pediatric patients and in cases of long-term follow-up[21].

MR enterography (MRE) established as a substitute for CTE to image small bowel in both pediatric and adult patients with CD [22, 23]. MRE enables high-tissue-contrast assessment with perfect diagnosis of the submucosal wall edema, multiparametric data analysis and functional details without ionizing radiation, initiating this approach very applicable for teenager with Chron's disease [24-29].

Additionally, MRE can assess SB segments that cannot be approached by ileocolonoscopy, rule out obstacles such as abscesses and strictures demanding serious interference and also estimate active disease [30-34].

This review aimed to display MRE technique and the typical imaging manifestations of Chron's disease, to aid the clinician in deciding treatment options and to yield a survey of MR imaging in Chron's disease.

METHODS

Patient Enrollment

This prospective survey was accomplished after the approval of research ethics committee. All included cases were patients with histologically proven Crohn's disease who were scheduled to undergo MR enterography for symptom exacerbation. MR enterography scanning was obtained after informed consent from our patients. For those less than 18 years old, informed consent was obtained from a parent. The presence of MRI-incompatible metallic implants, impaired renal function and the inability to undergo MRI without sedation were considered as exclusion criteria.

MR Enterography Technique

MRI examination was performed on a 1.5 T MRI system (GE, Optima 450W, 32 channels) with a body phased-array coil. *Firstly,* the patient is fasted for 4-6 hours. *In adult patients,* oral contrast ingestion of about 1-2 L mixed solution (mannitol, methylcellulose, polyethylene glycol). This hyperosmolar solution is used to obtain an adequate bowel distention. *In pediatric patients,* less oral contrast volume is used & adjusted according to the patient's weight. Mannitol is considered as a biphasic agent that displays low signal intensity on T1-WIs and high signal intensity on T2-WIs. The oral contrast intake was done over a period of 40-60 min at regular intervals prior to the study.

The patient is examined in the prone as well as the supine position. (if abdominal stoma is present). In prone position, better small bowel distension with reducing bowel peristalsis and decrease scan time were obtained. As regard lesion detection and characterization of bowel wall changes in CD, both positions are equal in scanning. The use of spasmolytic as hyoscine butylbromide before the patient is placed on the

table is advised to reduce bowel peristalsis and subsequent motility artifacts.

Typical MRE sequences include balanced steady-state free precession (bSSFP) sequence with single-shot T2-WIs in the coronal plane to obtain motion-free bowel wall assessment, mesenteric structures, such as vessels and lymph nodes and extraintestinal regions; cine motility imaging should be performed before the use of spasmolytic agent by using bSSFP-based sequences in the coronal axis serially from anterior to posterior over 2 min with a 6-10 mm slice thickness to obtain actual bowel peristalasis; axial T2 FS images to assess edematous bowel wall changes and intra-abdominal fluid accumulation; coronal multiphase three-dimensional (3D) T1 FS post-contrast images after IV contrast administration of gadopentetate dimeglumine (Gd-DTPA) to assess bowel wall and mesenteric enhancement and delayed axial T1 FS images to detect complications as fistulae and abscesses.

Diffusion-weighted imaging (DWI) has been recently added to MRE protocol to recognize active bowel wall inflammation and complicated extraluminal collections. No breath hold technique is needed for the DWI sequence.

The pelvic MR protocol by obtaining high-spatial resolution FS and non FS T2-weighted, FS contrast-enhanced T1-weighted and DWI images are dedicated to assess the peri-anal disease.

Imaging Data Analysis

We are going to survey the different imaging features of CD from the uncomplicated acute stage to the acute stage with complications. Pathologic involvement of the small bowel loops and related mesentery seen consensually with signs of inflammation.

Considering the involved bowel loop, the active inflammation of the bowel shows increased wall thickening, intramural edema, segmental hyperenhancement, reduced bowel motility and may be ulceration.

We refer to segmental mural hyper-enhancement as an increase in mural signal intensity on contrast-enhanced images assessed in an uncontracted small bowel segment, comparing it to a normal bowel loop. It can appear as asymmetrical, stratified or homogeneous. *Asymmetrical mural hyper-enhancement* of the affected loop with noticeable involvement of its mesenteric border is an imaging feature specific to small bowel CD. *Stratified mural hyper-enhancement* is described when the submucosa is affected by edematous or inflammatory changes (seen as high T2 signal) with enhanced endoluminal mucosa; this is called a bilaminar pattern, while, the trilaminar pattern is noted with added contrast-enhancing serosa. Lastly, *the homogeneous symmetrical mural hyper-enhancement* is visualized as a regular enhancement of the whole intestinal wall; however, it is not characteristic of CD and may arise from other diseases.

The bowel wall enhancement can be evaluated by two phases during scanning: the enteric phase (45–50 sec. after IV contrast injection) and the portal venous phase (60–70 sec. after IV contrast injection).

To assess increased bowel wall thickness, an adequately distended bowel loop (at least 2 cm in calibre) is needed with wall measurement in the maximum thickness. Mild (4-5 mm), moderate (6-9 mm) or severe (≥10 mm) bowel wall thickness can be done. When bowel wall thickening is more than 15 mm, especially with uneven thickening, neoplastic lesion may be considered.

On FS T2-WI images, intramural bowel wall edema can be identified as a hyperintense signal intensity. Intramural fat, due to

previous intestinal inflammation, also displays high T2 signal intensity, but differs from edema by signal drop in fat-suppressed sequences.

Ulceration of the bowel wall mucosa affected by active CD, seen as a high T2 nidus, with a surrounding rim of moderate signal intensity. Deep and transmural ulcerations may be seen with severe bowel inflammation. The typical "cobblestone" manifestation result from confluent mucosal ulcerations combined with protruding edematous mucosa.

Cine MRE can detect diminished bowel motility in the diseased bowel loop, thus helping to differentiate undistended from inflammed bowel. An inflammatory bowel stenosis should unwrap on cine imaging, while the fibrotic bowel narrowing remains constant with a pre-stenotic dilatation. Establishing the nature of bowel stenosis is of significant therapeutic concern, as an inflammatory bowel stenosis may respond to anti-inflammatory therapy while a fibrostenotic bowel stricture will most likely require surgical intervention.

In CD, the active inflammation of the bowel wall can display restricted diffusion, with high signal intensity on DWI and corresponding low signal intensity on apparent diffusion coefficient (ADC) maps. However, diffusion restriction is a non-specific sign for CD, particularly if the loops are not properly distended.

Regarding the mesenteric involvement, the mesentery is affected in cases with advanced bowel inflammation. Typically, the mesentery may show edematous and inflammatory changes, vascular engorgement, fibrofatty proliferation and enlarged mesenteric lymph nodes. Perienteric inflammation, also defined as "fat stranding" represents an extension of the transmural bowel inflammation and is seen as increased signal in T2-WI and DWI in the mesenteric fat. Mesenteric vascular engorgement are established by dilated the vessels feeding and draining an inflamed

intestinal loop and extend perpendicular to the bowel wall, giving the comb sign. It can be seen in current intestinal inflammation as well as the previous inflammation.

Fibrofatty proliferation; also known "creeping fat" is a result of the acute inflammation, especially with repeated attacks. It can be detected on the mesenteric side or circumferential and visualized as slightly decreased signal intensity on T1-WIs compared to normal fat, due to the inflow of fluid and inflammatory cells.

Mesenteric lymphadenopathy are usually of reactive origin and seen in the mesenteric fat during acute inflammation, presented by enlarged enhanced mesenteric lymph nodes (up to 1-1.5 cm in the short axis).

Regarding the perianal disease, active perianal inflammation is frequent in Chron's disease. Peri-anal fistula is usually following active inflammation with mucosal ulceration in the rectal or anal canal, extending to the perianal skin surface. It is essential to specify if the type fistula (simple or complex) and if there is an associated abscess or not as the fistula management varies.

Penetrating Chron's disease and complications

Penetrating CD involves sinus tract, simple/complex fistula, abscess and free perforation. These findings can be found in about 30% of the affected cases. It is significant to determine if there is penetrating CD or not, as it may need antibiotic therapy and/or drainage before giving biologic medications.

A sinus tract is defined as a blind end tract that extends from the intestinal lumen and then beyond the serosa into the adjacent fatty tissue but does not reach the nearby organs or skin. It appears as a hyperintense blind-ending tracts on T2-weighted images.

A CD-related fistula is a tract that communicates the affected intestinal lumen to another epithelial surface and are named according to

its connected structure, such as an enteroenteric, enterocolic (penetrates into a bowel loop), enterovesical (into the urinary bladder) or enterocutaneous fistula (into the skin). It displays T2 hyperintense signal due to the presence of internal fluid with peripheral rim enhancement and enhanced surrounding soft tissues on postcontrast T1-WIs during active stage. Chronic fistula lack internal T2 hyperintensity due to scarring and fibrous tissue formation.

A simple fistula represents a single tract, whereas a complex fistula results from the presence of more than one fistulous tract. The stellate appearance of fistulas, with spiculated margins is likely as a result of desmoplastic reaction in the surrounding mesenteric tissue.

An abscess is a fluid collection within a thickened enhanced wall (on contrast-enhanced MRE) with or without internal gas foci. Abscesses usually display central restricted diffusion on DWI/ADC imaging, allowing assessing patients with inability to IV contrast administration. Abscesses can occur in the mesentery, peritoneal cavity, retroperitoneum or perirectal and/or perianal region.

Free perforation is a rare complication in penetrating Crohn's disease. It is characterized by free intraperitoneal air and needs surgical assessment to confirm diagnosis.

Eventually, the inflammatory bowel disease may be associated with increased risk of mesenteric venous thrombosis. As thrombosis may occur during acute inflammation, related to the inflamed intestinal loops. It is essential to identify whether the thrombosis is acute or chronic, to determine the need of patient to anticoagulant therapy. Acute thrombosis is associated with distended vein by endoluminal thrombus. In chronic thrombosis, the mesenteric veins may be narrowed or discontinued with difficult assessment, while the collateral mesenteric vessels that occur in chronic cases clearly evident due to ectasia.

Pitfalls

Nevertheless MRE may be more acceptable to patients rather than intubation, inadequate bowel loop distention can be countered frequently with inability to good identify partial bowel strictures. Early mural wall changes of CD may be missed in areas of collapsed bowel loops. Food debris within the bowel lumen may mimic filling defects or polyps; a low-residue diet and fasting before scanning help in eliminating these artifacts. Preceding surgery, especially stricturoplasty, may simulate fibrotic strictures or sharp margin of neoplastic lesion. Survey of these segments in the three imaging planes aids in the differentiation as a lobulated or bi- or trifoliate appearance could be observed in stricturoplasty surgery.

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Statistical Analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Categorical data were represented as numbers and percentages.

RESULTS

A total of 54 patients with proved Chron's disease were included in this study that underwent MR enterography to assess the different imaging features during active or complicated disease stage. Our study included two groups *regarding the age*; adult group (from >18 to 45 years, representing about 38 subjects, 70.4%) and pediatric age group (from 12 to 18 years, representing about 16 subjects, 29.6%). *Regarding the gender,* 29 female subjects & 9 male subjects within the adult group, while the pediatric group included 11 & 5 adolescent girls and boys respectively. **(Figure 1)**

MR Enterographic features of Crohn's disease (CD)

We analyzed our patients by MR enterography and diagnosis of active bowel inflammation or complicated disease was made. Assessment of extra-intestinal CD manifestations and following its progression were also done. A systematic overview of the available patients **(Table 1)** was obtained as following: *Bowel wall thickening* was considered as a sign of active inflammation in about 46 out of 54 patients (85%) and graded into mild (35.2%), moderate (27.8%) and severe (22.2%) thickening as increasing wall thickness associated with increasing disease severity. *Bowel wall edema* was another criterion of active inflammation, found in 15 out of 54 patients (27.8%). Severe inflammatory bowel wall thickening with intramural edema was associated with subsequent luminal narrowing, representing active inflammatory bowel stenosis **(Figure 2)** in CD that detected in about 12 patients (22.2%) within our studied cases.

Mural wall hyperenhancement was a specific sign of active inflammation on dynamic contrast-enhanced images and detected in 43 out of 54 patients (79.6%); that seen symmetrical in 61.1% and asymmetrical in 18.5% regarding the total patients. Active inflammatory

bowel wall also displayed restricted diffusion (on DWI/ADC imaging) in 34 patients (63%) and reduced bowel peristasis (on cine MRE) in 44 patients (81.5%).

Mucosal ulceration is an uncommon MRE finding of active Chron's disease and requires adequate bowel distention for definitive detection. It presented in only 3 of 54 our patients (5.6%).

Various mesenteric MR signs in the active disease stage have been delineated in our patients as inflammatory mesenteric fat stranding **(Figure 3)** in 41/54 patients (75.9%), mesenteric lymphadenopathy in 29/54 patients (53.7%) and vascular engorgement within the affected mesentery in 39/54 patients (72.2%). Mesenteric venous thrombosis could be also detected in about 8 patients (14.8%) **(Figure 4)**.

Fistula formation has been reported in about 37% of our patients and is a feature of penetrating disease. Two types of fistulous disease are seen in our study as intra-abdominal (in 9 patients, 16.7 %) and perianal fistula (in 11 patients, 20.4%) **(Figure 5)**. In fact, simple fistula is the foremost intra-abdominal fistula as seen in 8 out of 9 patients (89%) with the remaining one is complex (Entero-entero-cutaneous fistula) **(Figure 6)**. Sinus tract with a blind-end could be also identified in our study in three patients (5.6%).

Other regional complications of CD comprise abscess formation that detected in about six patients (11.1 %), characterized by inhomogeneous content and an enhancing peripheral lesion edge.

The chronic bowel wall inflammation with long-term intestinal injury is likely progress to fibrostenotic complications (bowel stricture with luminal obstruction) that seen in only two patients (3.7%). The chronic disease stage was identified by submucosal fat deposition that can be differentiated from submucosal edema on T2-weighted images by reduced fat signal on fat saturation sequence.

DISCUSSION

This survey defined MR enterography as a potential imaging technique for Crohn's disease assessment. Generally, barium fluoroscopy and enteroscopy have been the traditional methods to detect abnormal bowel findings in patients with Crohn's disease. However, neither tool is sensitive for detecting extramural complications, which need to be ruled out in patients with acute exacerbated attack. Nowadays, CT has become the initial imaging tool to assess Crohn's disease as it can estimate both mural and extramural manifestations of the involved bowel loops [35].

Additionally, CT imaging has common accessibility, multiplanar capability and fast image possession [36]. Recent concern has focused on the ionizing radiation risk associated with CT imaging, especially in Crohn's disease that could be discovered during pediatric age and required repeated follow-up during the disease process. So, MR imaging likely provides the diagnostic CT values without the risk of ionizing radiation [37].

MRE protocol applied in our research was well accepted by the target individuals with scan time extending from 40 to 60 minutes and no persons being ruled out due to an inability to finish the scanning. Approximately, none of our included young patients needed sedation. The capability to do MRE without sedation is a valuable concern facilitating the wide use of this tool in the pediatric age group. We noted that some involved subjects in our study did unable to swallow the needed oral contrast volume. So, adding sugar-free fruit-flavored components to the used oral preparation appreciably improved subject compliance.

As far as we know, this research is to estimate MR enterography as the prime imaging tool in assessing Crohn's disease, especially in

pediatrics. A 2004 survey[38] established high sensitivity and specificity of contrast-enhanced MRI in pediatric patients with inflammatory bowel disease (IBD) with ability to discriminate Crohn's disease from ulcerative colitis, whereas a 2009 survey[39] of MRE in pediatrics with IBD revealed a relation between unusual small-bowel wall enhancement and serum C-reactive protein measures. Both exhibited MRE to be practical in pediatric subjects with IBD.

MR enterography has the ability to distinguish active from non-active bowel inflammation, a significant status during follow-up scanning of CD patients receiving medical treatment. This differentiation is especially serious stated the new approach of biologic therapies selecting certain inflammatory molecules, such as tumor necrosis factor–α, which are more seemingly to be effectual in the active inflammatory stage[40,41].

The ability of MRE to reveal mural wall fibrosis in the affected bowel loop is also appreciated in our work, which is a characteristic sign of fibrostenotic strictures with subsequent bowel obstruction that often need surgical management[42]. *In our study,* bowel stenosis was recognized in about 14 patients as the active inflammatory bowel stenosis was seen in 12 patients with severe submucosal edema (T2 hyperintensity) and the last two patients were likely fibrostenotic in nature with submucosal fat deposition (loss of signal on fat saturation sequence). *Gee et al.*[40] reported that the sensitivity (58.3%) and accuracy (64.9%) of MRE for identifying fibrosis were reduced compared with observing active inflammation. Their data were likely showed that MRE missed mural wall fibrosis as a consequence of superimposed active bowel wall inflammation.

The facility of MR enterography to discriminate chronic fibrosis from fibrosis with concurrent active inflammation is clinically significant and implies that MRE can aid patients with CD, especially teenager with

obstructing bowel stenosis to receive firstly medical treatment (with associated active condition) before surgical management [43].

If the results of MR imaging affect clinician management, this is a remarkable aspect. *Mendoza et al.*[44] noticed that MR supported decision-making in more than 50% of involved patients, especially when biological therapy and surgery were applied. *Messaris et al.*[45] exhibited that 69% of patients had transfer to medical and/or surgical management after therapists were given MR findings. Similar studies have revealed that MR findings guide surgical procedures to managing Crohn's patients[46].

In conclusion, CD is a composite disease and imaging plays a crucial role in describing it, using the ultrasound, CTE and MRE with the last-mentioned modality serves as the gold standard of our study offering both structural and functional information without the risk of ionizing radiation. In order to get a perfect evaluation, MRE must be achieved by a meticulous protocol with efficient patient preparation followed by certain dedicated sequences. The radiologist's attempt must be directed to CD assessment with reporting its extension, the degree of activity and the potential complications, identifying the most accurate medical and/or surgical management for each patient.

LIST OF ABBREVIATIONS

MRE; Magnetic resonance enterography. **CD;** Chron's disease. **CTE;** Computed tomography enterography. **SB;** Small bowel. **bSSFP;** balanced steady-state free precession. **Gd-DTPA;** Gadopentetate dimeglumine. **DWI;** Diffusion weighted imaging. **ADC;** Apparent diffusion coefficient.**SPSS;** Statistical Package for Social Science.

Declarations:

Ethics Approval and Consent to Participate: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Institutional Review Board (IRB)" of National Liver Institute Menoufia University and with the Helsinki Declaration of 1964 and later versions. Committee's reference number is unavailable (NOT applicable). Informed consent was obtained before the study.

Consent for publication: All patients included in this research gave written informed consent to publish the data contained within this study.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions: **RAA, MAA and RAM** writing the research, selection of research cases, prepare the figures for cases demonstration and review of the research. **MSA,** assess cases for initial diagnosis. **HSE,** assesses in cases selection and carried out cases on workstation. "All authors read and approved the final manuscript".

Competing interests: The authors declare that they have no competing interests.

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FIGURE LEGENDS

Figure 1: Distribution of the studied cases (n = 54) according to age range (12-18 and >18-45 years old).

Figure 2: Active inflammatory stricture in a patient with Crohn's disease. Axial T1W Fat Sat post-contrast showing severe mural wall thickening and enhancement **(white arrow)** affecting distal ileal loops. Skip lesion is noted in adjacent bowel loop **(Back arrow).**

Figure 3: Fibrofatty proliferation in a patient with Crohn's disease. Coronal T2W showing eccentric fibrofatty proliferation **(white arrows)** adjacent to thick wall small bowel segment **(black arrow)** with mild lumen narrowing and mild upstream dilatation

Figure 4: Chronic mesenteric venous occlusion in a patient with Crohn's disease. Coronal T1W Fat Sat post-contrast showing chronic mesenteric occlusion of the right ilio-colic vein with multiple dilated mesenteric venous collaterals **(white arrows)**.There is diffuse striated mural wall enhancement of the distal ileum **(Back arrows).**

Figure 5: 13-years old female with Crohn's disease and perianal disease. **A&B** Coronal T2 Fat Sat. **C.** Axial T1 Fat Sat post-contrast showing complex trans-sphincteric branching perianal fistula. **D.** Clinical examination showing the perianal fistula.

Figure 6: Active Crohn's disease, complicated by Complex (Entero-entero-cutaneous) fistula. **A.** Coronal T1 post-contrast Fat Sat, showing active inflammation, mild wall thickening and enhancement of the distal ileal loops, associated with mesenteric combing. **B&C.** Coronal and axial T1 post-contrast Fat Sat showing complex entero-entero-cutaneous fistula. **D.** axial DWI showing diffusion restriction of the complex fistula.

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