Magnetic resonance enterography in Crohn's disease: A guide to common imaging manifestations for the IBD physician

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Abstract
Patients with Crohn's disease (CD) frequently require cross-sectional imaging. Magnetic resonance enterography (MRE) is an accurate tool for assessment of bowel disease and of various complications of CD. The lack of non-ionizing radiation exposure is an important advantage of this imaging modality. Familiarity with common and pathognomonic imaging features of CD is essential for every clinician that is involved in inflammatory bowel disease (IBD) patients' care. This review is aimed to describe the indications for performing MRE in CD, essentials of MRE techniques and typical radiological findings in patients with CD to aid the IBD doctor in daily practice.

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Abbreviations: IBD, inflammatory bowel disease; CD, Crohn's disease; MRI, magnetic resonance imaging; MRE, magnetic resonance enterography; T1/T2-w, T1/T2 weighted; CT, computer tomography; CTE, CT enterography.

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1. Introduction

Crohn's disease (CD) is a chronic inflammatory disease of the intestinal tract that frequently affects young patients. Although CD may involve any part of the digestive tract, small bowel involvement occurs in at least 70% of the patients. As this section of the digestive tract is not easily accessible by conventional endoscopic techniques and because the inflammatory process may penetrate beyond the bowel wall, cross-sectional imaging is frequently employed in CD patients, both for assessing small bowel disease severity and for detection of extra-luminal complications.

Both computed tomography (CT) and MRI enable clear visualization of the entire length of the intestinal tract along with various extra-and intra-intestinal complications such as abscesses, enterovesical and perianal fistulae, perforation and strictures. The diagnostic accuracy of MR enterography (MRE) and CT enterography (CTE) is comparable for diagnosis of CD and its complications. Although CT is still the more commonly employed diagnostic modality in CD worldwide, MRE possesses several important advantages that have lead to a steep increase in its utilization in the recent years.

MRE provides an improved superior soft tissue contrast resolution in comparison to CT, enabling a superior visualization of the inflammatory and fibrotic characteristics of the bowel wall. Recently, diagnostic indices based on MRE-based quantitative assessment of disease severity have been developed. MRIA (magnetic resonance index of activity) is comprised of a formula incorporating wall thickness, edema, ulceration and relative contrast enhancement of the bowel calculated for each bowel segment. This index demonstrated a significant correlation ($r=0.82$, $p=0.001$) with the endoscopic severity index CDEIS (Crohn's disease endoscopic index of severity) with a high accuracy for the detection of disease activity (area under the receiver operating characteristic (ROC) curve 0.891, sensitivity of 81%, specificity of 89%) and for the detection of ulcerative lesions (area under the ROC curve 0.978, sensitivity of 95%, specificity of 91%) in the colon and terminal ileum. Another potentially valuable prognostic tool based on MRE is the Lemann score, aimed at the evaluation of cumulative destructive damage to cause by CD to different segments of the bowel. For each CD location, independent variables including presence of a segment with at least grade 1 (wall thickening $\geq 3$ mm and/or mural stratification without prestenotic dilatation), 2 (wall thickening $\geq 3$ mm and/or mural stratification without prestenotic dilatation), or 3 (stricture with prestenotic dilatation lesion) or surgery; number of segments with at least grade 1, 2, or 3 lesion/surgery; the proportion of segments containing grade 1, 2, or 3 lesion/surgery will also be assessed (if feasible) in the case of small bowel location. The scores of different compartments are integrated into the index. Monitoring of response to anti-inflammatory therapy may become another potential indication for MRE, enabling accurate and non-invasive method of surveillance.

Pelvic MRI is a cornerstone modality in the evaluation of perianal CD due to its capability for providing detailed and high-quality images of the sphincter complex that are essential for evaluation of pelvic disease. Response to therapy in perianal CD can also be monitored by pelvic MRI.

The impact of cumulative radiation exposure associated with recurrent CT examinations is another factor to be borne in mind when choosing between different imaging modalities. CD patients, who often develop symptoms at puberty and in young adulthood, and tend to develop complications requiring urgent interventions, are particularly subject to this kind of radiation exposure. It has been reported that up to 10% of CD patients have been exposed to a potentially harmful levels of radiation exposure defined as $\geq 50$ milli-sieverts (mSv) (equivalent to 5 CT abdomen examinations). Radiation exposure associated with CT imaging may vary significantly. Use of multidetector CT may allow a reduction of 10%–60% in the radiation exposure attributed to efficient detector configuration, automatic exposure controls, improved filters, and image post-processing algorithms. CT enteroclysis facilitated by luminal distention with a contrast agent delivered by a nasoenteric tube allows for a further reduction of the radiation exposure. Recently, low-dose radiation techniques are based on modifications of exposure time, alterations of voltage and amperage and noise-reduction filters. An alternative low-dose technique using concentrated oral contrast (Telebrix 9% instead of the commonly used 3% concentration), no intravenous contrast and a high noise index (MBCT - modified small bowel CT) valuable for depicting strictures and obstruction, along with some features compatible with inflammation, such as mesenteric fat hypertrophy and prominent vasa recta, was described. Although resulting in lower quality images, these techniques are capable of obtaining accurate and diagnostic images.
Importantly, an increased risk of complications may still persist even with lower accumulative doses of radiation. Hence, imaging technique that is not associated with ionizing radiation, such as MRE, is particularly attractive in a cohort of young patients subject to repeated imaging.

2. Magnetic resonance technique for evaluation of small bowel

MRE allows multiplanar imaging of the intestinal tract. Obtaining a diagnostic MRE examination requires adequate distension of the bowel lumina achieved by means of ingestion of oral contrast, reduction of peristalsis by spasmolytics and injection of intravenous contrast material (gadolinium).

Image acquisition is obtained with several sequences. MR enterography imaging protocols vary significantly due to differences in equipment and personal expertise. A more detailed technical description of the MRE sequences is beyond the scope of this review and could be found elsewhere. In addition, a specific sequence can be labeled under different names for different MRI machines, as the manufacturers do not necessarily employ a homogenous terminology for description of the sequences. However, certain basic elements are common to most CD imaging protocols for CD. Fast sequences capable of acquiring T1-w and T2-w images in a single breathhold are crucial for obtaining diagnostic images and reduction of artifacts. In our practice, we use a 1.5 T magnet Signa HDX, General Electric Medical Systems (Wisconsin, Milwaukee, USA), equipped with a phased-array 8-element coil with the following sequences:

- FIESTA-steady state free precession (SSFP) sequence in axial, coronal and sagittal planes;
- FSE (fast spin echo) T2-w sequence with fat suppression, in axial and coronal planes;
- T1-w 2D FSPGR (fast spoiled gradient echo) with fat suppression and breath hold in axial and coronal planes.

T1-w 3D LAVA is performed pre- and 60 s post-intravenous contrast administration with fat suppression and breath hold in axial planes. The same sequence, in the coronal plane, is acquired 120 s after the administration of the intravenous contrast medium.

In T2-w sequence, the positive or biphasic oral contrast agent appears brighter (hyperintense) compared to the darker (hypointense) thickened bowel wall (Fig. 1A), allowing visualization of luminal stenosis and mural thickening. In T1-w sequence ingested contrast agent appears hypointense compared to the bowel wall, and following gadolinium injection, the inflamed wall enhances and appears hyperintense compared to the darker in axial planes. The same sequence, in the coronal plane, is sensitive to alterations in vascular permeability, extracellular, extravascular and vascular volumes and blood flow.

Quantitative analysis of dynamic MRI images was evaluated in small studies for assessment of bowel inflammation and disease chronicity with inconsistent results.

In addition, we use a multiphase multissection coronal SSFP sequence that covers the entire small bowel and colon in order to follow peristaltic contraction of the bowel. These images may then be displayed as a cine loop to assess bowel motility, stenosis and dilatation. Because of the high image contrast, this type of sequence is also helpful for assessing mesenteric vascularity and lymphadenopathy.

Fat suppression is a sequence depressing the bright signal intensity (white) of the fat allowing for improving visualization of uptake of contrast material and detection of inflammation. It is especially important when contrast material is contraindicated (renal insufficiency, pregnancy).

The acquisition time for an appropriate and diagnostic MRE examination may vary from 16 min to 1 h, usually approximating 20–30 min, depending on the protocols employed.

Three main types of oral contrast agents exist – negative (hypointense on both T1-w and T2-w sequences), positive (hyperintense on both sequences) and the most commonly used biphasic (polyethylene glycol, sorbitol, lactulose etc.), that appear hyperintense on T2-w and hypointense on T1-w images. The contrast agent can be delivered orally or facilitated by a nasojejunal tube (MR enteroclysis). The oral contrast is delivered in large quantities (up to 2 l), usually through an automated pump. Several studies have compared the diagnostic efficacy of oral contrast MRE and MR enteroclysis. In a prospective study of 40 patients with CD, MR enterography compared with MR with oral contrast was statistically better when visualizing superficial abnormalities (p<0.01), and no statistically significant differences were found in assessing the diagnostic efficacy between MR examinations for the depiction of mural stenosis and fistulae. In a prospective study of 48 patients, even though enteroclysis was able to achieve a better distention of the small bowel, the diagnostic accuracy of both techniques was similar. Importantly, enteroclysis is associated with a significant discomfort for the patient and is usually achieved by fluoroscopy that is associated with ionizing radiation.

When using oral contrast, a total volume of 1.5 l is usually ingested, and image acquisition should be performed 40–60 min after the ingestion in order to achieve maximal bowel distention.

Elimination of bowel peristalsis is mandatory to improve image quality, and is achieved by the use of spasmolytics such as glucagon or scopolamine. Reduction of peristalsis is most important for fast gradient-echo sequences performed after the administration of intravenous contrast material and also may help reduce intraluminal flow artifacts (as can be noticed on Fig. 9). In our practice, we administer intravenous glucagon (1 mg) in a 50 ml saline infusion 10 min before the patient is placed on the table, with continued slow drip during the examination to prevent adverse reaction such as nausea and vomiting.

Injection of intravenous gadolinium during the examination is necessary for detection of enhancement of inflamed structures. In our institution, we administer 20–30 ml of gadolinium corresponding to a dose of 10–15 mmol, at a rate of 1 ml/s, followed by a flush of 30 ml of saline
solution. For the same purpose, scopolamine butylbromide (Buscopan, 40 mg IV) can be employed.  

3. Typical manifestations of CD on MRE

3.1. Mural small bowel disease

MRE is very sensitive for recognizing mural small bowel disease. Most common signs of small bowel involvement include bowel wall thickening, mucosal irregularity and mural attenuation. Inflamed bowel wall appears hyperintense on T2-w sequences and enhances after gadolinium injection on T1-w sequences (Fig. 2). However, fibrostenotic lesions may also be associated with a high contrast uptake resulting from increased permeability of the local vasculature. In this case, T2-w fat saturated images may be instrumental in diagnosing active inflammation by demonstration a presence of an edema in active. In the study by Grieser et al., ROC (receiver operating curve) analysis of the total inflammatory score demonstrated an AUC (area under the curve) of 0.93 ($p<0.001$) for T2-activity.

In a study by Rimola et al., a significant correlation with disease activity as represented by CD endoscopic index of severity (CDEIS) was demonstrated for segment wall thickness ($p=0.007$), relative contrast enhancement (calculated using a formula incorporating wall signal intensity before and after gadolinium injection) ($p=0.01$), presence of edema ($p=0.02$) and ulcers ($p=0.003$) on MRE. However, correlation of clinical and MRE staging of CD is associated with certain areas of uncertainty. A systematic review by Horsthuis et al. has demonstrated that MRE was accurate for grading frank disease 91% of the cases, but in only 62% of the patients with mild disease or remission, overstaging patients in remission in 38% of the cases. These discrepancies could be explained by the lack of gold standard stemming from inherently different nature of the diagnostic methods employed (ileocolonoscopy being capable of visualizing only the luminal surface as opposed to MRE's ability to evaluate all the layers of the bowel wall along with extraluminal pathology), in addition to a lack of defined cutoff points for differentiation of different stages of the disease, and the subjective selection of the bowel segments for disease activity.
analysis. In addition, the included studies tended to include mostly patients with frank active disease rather than patients with mild or inactive disease.  

Additional signs of mural disease may include ulcerations, "cobble stone" appearance characteristic of multiple continuous bowel wall ulcerations (Fig. 3) and stratification of the bowel wall (heterogeneous enhancement of the layers of the abdominal wall with hyperintense appearance of the mucosa and the serosa, and hypointense appearance of the muscularis layer on T1-w sequence) (Fig. 4), the latter reported to be associated with histologically proven acute bowel wall inflammation in several studies. However, this enhancement pattern was demonstrated to be also associated with fibrostenotic lesion.

Figure 2  Terminal ileitis: inflamed mucosa. T1-w (A) pre- and (B) post- gadolinium injection with enhancement of terminal ileum (arrow).

Figure 3  Mural thickening with mucosal irregularity, ulcers and enhancement. (A) Coronal view T1-w post-gadolinium injection demonstrating irregular enhancement of the mucosa mimicking "cobble stone appearance" with deep ulceration and enteroenteric fistula (arrow). (B) FIESTA: Mural thickening due to inflammation causing luminal narrowing (arrowhead).
3.2. Extramural manifestation of bowel disease

Substantial mural disease may be associated with extra-mural involvement that is characterized by several pathognomonic signs.

Mesenteric vascular engorgement ("comb sign," Fig. 5), usually resulting from increased inflammatory activity, can be seen as high-signal intensity parallel lines oriented perpendicular to the longitudinal access of the affected bowel wall on T1-w contrast-enhanced images, frequently adjacent to a bowel segment showing signs of active disease. On FIESTA (fast imaging employing steady state acquisition) and T2-w sequences the comb sign can be seen as black line on the white mesenteric fat background (Fig. 10A).

Fat wrapping ("creeping fat," Fig. 6) can be described as a mass effect caused by proliferation of mesenteric resulting in a displacement of intra-abdominal viscerae or vascular structures. Fat wrapping is usually asymmetric and tends to appear more frequently on the mesenteric side of the bowel wall. The hypertrophic fat is best seen on steady state acquisition (FIESTA sequences), as also seen in Fig. 1A and D.

Mesenteric lymphadenopathy presenting as enlargement, hyperenhancement and edema of the lymph nodes on the T1-w sequences post-gadolinium injection, as seen in Fig. 7, is highly pathognomonic for active CD. Nodal edema resulting from inflammation is better demonstrated on fat-suppressed images. Alternatively, non-enhancing lymphadenopathy may imply a different etiology such as malignancy or chronic infection such as tuberculosis or histoplasmosis.

3.3. Mural colonic disease

Inflammation of the colonic wall can also be clearly demonstrated on MRE. The signs of colonic mural disease such as bowel thickening, mucosal ulcerations and mural enhancement are analogous to those of small bowel disease. Long-standing severe mucosal inflammation of the colonic mucosa may appear as polypoid structures (Fig. 8).

3.4. Stenotic disease

The accuracy of MRE for detection of stenosis in CD has been well established, with a pooled sensitivity and specificity of 88% and 95%, respectively. Bowel stenosis usually appears as a thickened and enhanced segment adjacent proceeded by a markedly distended segment ("prestenotic dilatation"). Establishing the nature of stenosis (whether predominantly active inflammatory vs. fibrostenotic) is of great therapeutic interest, an inflammatory stricture may potentially respond to...
anti-inflammatory treatment while a fibrostenotic stricture will probably require surgical or endoscopic intervention (Fig. 9). The ability of MRE to obtain high spatial resolution with visualization of distinct enhancement patterns may be useful for guiding therapy in stenotic CD. In a study by Fornasa et al., evaluation of inflammatory activity as defined by T2-w signal intensity and post-gadolinium T1-w enhancement in patients with small bowel stricture has allowed reliable differentiation between active inflammatory and fibrostenotic strictures, with 96% of patients diagnosed with active inflammatory stricture achieving short-term response to anti-inflammatory therapy. De Vescovo et al. demonstrated an association of layered enhancement (mucosa and serosa) of the bowel wall with active histological inflammation, as opposed to homogenous enhancement characteristic of fibrosis (Fig. 4).

3.5. Penetrating disease

MRE allows accurate diagnosis of penetrating complications of CD. Current ECCO guidelines recommend either CT or MRE for diagnosis of intra-abdominal complications of CD, with a pooled sensitivity of 76% and specificity of 96%-99% comparable to the accuracy of CT.

3.6. Fistulae

Different types of intra-abdominal fistulae can be detected in CD patients by MRE. An enteroenteric fistula may appear as an enhanced sinus tract between adjacent bowel loops (Fig. 3). A "star sign" (Fig. 1) represent a conglomerate of inflamed bowel loops interconnected by multiple fistulous tracts (fig). Detection of enterovesical (Fig. 9) and enterovaginal (Fig. 10) fistulae is challenging, and may be facilitated by appearance of an air bubble in the urinary bladder or vagina that are usually air-free, commonly in a proximity to a diseased bowel loop (Fig. 11).

3.7. Abscesses

Abscesses appear as fluid collections encapsulated by an enhanced wall discontinuous with bowel lumen, which may also contain air (Fig. 12). Several studies have evaluated the accuracy of MRE for diagnosis of intra-abdominal abscesses in CD, with pooled sensitivity of 86% and specificity of 93% which is similar to the reported pooled accuracy of CT. MRI may facilitate percutaneous guided drainage of the abscess and is useful for post-drainage follow-up.
3.8. Thrombotic complications

Inflammatory bowel diseases are associated with an increased risk of thromboembolic complications, such as deep venous thrombosis, pulmonary embolism and portal or mesenteric vein thrombosis. Long-standing mesenteric vein thrombosis may appear as a cutoff of the mesenteric vein (rat-tail sign). Liver infarcts may accompany mesenteric vein thrombosis caused by pylephlebitis. Mesenteric/portal vein thrombosis may result in portal hypertension accompanied by ascites and varices (Fig. 13).

3.9. MRE in pregnant women with CD

MRE is invaluable when cross-sectional imaging is indicated in a pregnant patient (Fig. 14), as CT is associated with ionizing radiation potentially harmful for the fetus. Although there are limited data suggesting fetal safety of magnetic resonance examinations, this modality is usually avoided in the first trimester. Intravenous gadolinium compounds cross the placenta and may be demonstrated in the fetal circulation and should be used judiciously.46

3.10. Postsurgical complications and recurrence

Abdominal surgery could be associated with a multitude of intra-abdominal complications such as anastomotic leaks, abscesses (Fig. 12), stoma-associated complications (Fig. 15) and bowel obstruction. MRE, although not always readily available in these frequently urgent settings, still comprises a possible alternative to CT imaging for these patients. MRE could be also instrumental in monitoring post-operative disease recurrence, with a good correlation of an MR-based score with an endoscopic Rutgeerts score.47

Figure 8  Descending colitis with mural thickening. (A) T1-w post-gadolinium injection. (B) FIESTA. Notice mural thickening (arrows) and pseudopolyps (arrowheads).

Figure 9  Bowel obstruction. (A) Coronal T1-w post-gadolinium injection: enhancing inflammatory stricture in the distal ileum (arrow). (B) Coronal FIESTA: fibrostenotic stricture causing marked distention of ileal loops. Notice the artifact on (A) secondary to increase peristaltic proximal to stenosis.
Figure 10  Enterovesical fistula appearing as mural thickening with air in the urinary bladder. (A) FIESTA. (B) T1-w post-gadolinium injection. (A) Coronal view: distal ileitis with mural thickening (arrow) adjacent to the urinary bladder. Notice comb sign (arrowhead). (B) Axial view: bubble of air in the urinary bladder (arrowhead) consistent with pneumaturia secondary to the enterovesical fistula.

Figure 11  Rectovaginal fistula secondary to proctitis with mural thickening. T1-w post-gadolinium injection. (A) Sagittal view of thickened rectum (arrow) with perirectal fat hypertrophy (star). Notice air bubble between the rectum and the vagina (arrowhead). (B) Axial view demonstrating air in the vagina (arrowhead) and the fistula tract from the rectum (arrow).

Figure 12  Abscesses (arrows). (A) FIESTA: coronal view, abscess following resection of appendix involved by Crohn's disease in a pregnant patient. (B) Axial view T1-w post-gadolinium injection: abdominal wall abscess. Notice enhancement of abscess capsule and necrotic nonenhancing fluid (pus) and adjacent inflamed ileal loop in the pelvis (arrowhead).
3.11. Perianal disease

MRI is a cornerstone modality in evaluation of pelvic and perianal CD (Figs. 16 and 17). When compared with surgical examination under anesthesia, the sensitivity and specificity of MRI for detecting fistula tracks were 100% and 86%; for abscesses, 96% and 97%; for horseshoe fistulas, 100% and 100%; and for internal openings, 96% and 90%, respectively. In the study by Beets-Tan et al., additional information leading to modification of the surgical procedure was obtained in 40% of the patients with perianal CD who were previously evaluated by endoanal ultrasound. A combination of these two modalities may further increase the diagnostic accuracy. Pelvic MRI may also play an important role in monitoring anti-TNF therapy in perianal CD.

4. Limitations of MRE studies

Several important limitations of MRE in comparison to CT imaging should be acknowledged. CT provides superior overall image quality with better spatial resolution, requiring a significantly shorter acquisition time (8–10 s for CTE and 20–30 min for MRE). MRI is not suitable for claustrophobic patients, although recently utilization of open MRI machines for these patients has been reported. In many countries, MRI scanners are currently less accessible and significantly more costly, especially in the smaller and more peripheral centers.

Despite these limitations, MRE possesses a diagnostic accuracy similar to CTE sparing the exposure to non-ionizing radiation, and thus should be preferred when possible,
especially in patients requiring repeated examinations. In perianal CD, MRI is the diagnostic modality of choice due to its superior soft tissue visualization enabling accurate diagnosis and staging of perianal fistulae.48,49

5. Summary

MRE is an imaging modality that is growing in usage and importance in CD diagnosis and follow-up. Clinicians caring for these patients should be familiar with MRE techniques, as well as with the limitations and strengths of this modality as outlined in the present review. Moreover, because this modality is likely to become even more prevalent as a diagnostic imaging tool for evaluating CD patients in the near future, clinicians may find it increasingly useful to acquaint themselves with the appearance of the different radiological features of the disease on MRE, as provided in this practical guide. Improved familiarity and understanding of the strengths and limitations of this imaging modality by the clinician will facilitate better inter-disciplinary co-operation with the radiologist for both in the choice of the imaging modality and in the interpretation of the results obtained and will hopefully lead to improved patient’s care and outcome.

Conflicts of interest

Dr. Ben-Horin has received lecturer fees from Abbott and Schering Plough. Prof. Eliakim has received lecturer fees from Abbott. Other authors have no conflicts of interest to declare.
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