Magnetic resonance enterography: A stepwise interpretation approach and role of imaging in management of adult Crohn's disease

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Abstract

Crohn's disease (CD) is a chronic inflammatory bowel disease that often requires frequent imaging of patients in order to detect active disease and other complications related to disease activity. While endoscopy is the gold standard for diagnosis, it may be contraindicated in some patients and has a limited role in detecting deep submucosal/mesenteric diseases and intra abdominal complications. In recent years, magnetic resonance enterography (MRE) has evolved as a noninvasive, radiation free imaging modality in the evaluation of patients with CD. This review article will focus on role of MRE in imaging patients with CD with emphasis on technical considerations, systematic image interpretation, differential diagnoses, and the role of imaging in deciding treatment options for patients.

Key words: Crohn's disease; fistula; magnetic resonance enterography

Introduction

Crohn's disease (CD) is an inflammatory bowel disease that may involve any area of the gastrointestinal tract from the mouth to the anus. A vast majority of patients have involvement of the small bowel, particularly the terminal ileum. Nearly half of all patients have some involvement of the colon. Patients typically experience diarrhea, abdominal pain, weight loss, and fever. Patients with colonic involvement also suffer from lower gastrointestinal bleeding and perianal complications.[1] Symptoms related to perianal diseases are a frequent complaint of CD patients and include anal fissures, perirectal abscesses, and fistula, which can be seen in up to 26% of patients.[2]

Supportive laboratory data to diagnose CD include elevated serum inflammatory markers such C-reactive protein, erythrocyte sedimentation rate, serum albumin, alpha-1 proteinase inhibitor, and some fecal markers such as fecal calprotectin.[3] However, these markers may also be elevated in infectious conditions such as intestinal tuberculosis.

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Confirmation with an endoscopic procedure with specimen sampling is often performed using ileocolonoscopy, which provides only limited access to the small bowel. Video capsule endoscopy can be used to visualize the entire length of the small bowel but does not have the provision of tissue sampling and is contraindicated in patients with strictures or bowel obstruction. While mucosal disease is well-assessed with endoscopic techniques, submucosal and serosal/mesenteric disease as well as intraabdominal complications cannot be evaluated.

Description of the disease severity, exact location, and associated complications is necessary for appropriate clinical and surgical management. Traditionally, barium studies have been performed to evaluate the upper and lower gastrointestinal tract, but are now used less frequently due to poor sensitivity and specificity.

Computed tomography (CT) remains a common clinical tool in the evaluation of CD and its complications. Because CD patients often undergo multiple studies over the course of diagnosis, they can be exposed to a high cumulative effective dose of radiation.[4,5]

Magnetic resonance enterography (MRE) is a radiation-free alternative to CT and is extremely useful in the management of CD. Usefulness of magnetic resonance imaging (MRI) as an effective modality to evaluate type and severity of inflammatory bowel disease and its comparability with endoscopy has been studied for the past two decades.[6] In an earlier study, MRI of the bowel following conventional small bowel enteroclysis was performed and showed promising results in evaluating small bowel.[7] Follow-up study in patients with CD showed that the efficacy of abdominal MRI after conventional enteroclysis or with an enterographic approach is similar. The use of enterographic examination is less cumbersome compared to conventional or MR enteroclysis, which involves placing a nasojejunal tube to instill the oral contrast.[8]

When compared to conventional endoscopy, MRE has a sensitivity and specificity of 85% and 80%, respectively,[9] and has a good correlation to endoscopy for evaluation of treatment response as well.[10] MRE has similar sensitivity compared to CT enterography for detecting small bowel disease[11] Sensitivity and specificity of MRE compared to histopathology has been reported to be 91% in adults and 94% in pediatric patients,[12] with high accuracy reported in detecting active and fistulizing disease. In addition, MRE has been shown to have higher sensitivity for strictures.[13] CT enterography has, however, been shown to be more sensitive for the detection of mesenteric lymph nodes.[14]

When compared to enteroclysis, MRE has lesser sensitivity for detecting superficial ulcers due to inadequate distention.[15] However, because duodenal intubation is not performed with MRE, it is less invasive and more comfortable for the patient.

High diagnostic accuracy between high resolution MRE and surgical/histopathologic specimens in a series of 49 patients with CD was recently established in a study by Sinha *et al*.[16] The study also showed that contrast enhancement ratio of >1.85 and bowel ulcers are independent and strong predictors of active inflammation.

Technique for Magnetic Resonance Enterography

Patient preparation

Fasting 4–6 hours prior to the examination is recommended in order to improve tolerance of oral contrast. Some authors have advocated the use of rectal enema the morning of the examination because fecal burden obscures colonic disease. Rectal enema has shown to increase the detection of inflammation at the terminal ileum, although this technique is not widely used.[17] Low residue diet may be used for 3–5 days prior to the procedure in order to reduce fecal matter in the colon. A loaded colon can reduce peristalsis and slow the transit of barium through the small bowel.

Bowel distention

Adequate distention of small bowel is very important for the assessment of wall thickening as well as for enhancing mural disease. Bowel distention can be achieved through the use of several oral contrast agents. Biphasic contrast agents that are low in signal on T1 and high in signal on T2-weighted images such as water, polyethylene glycol (PEG), barium sulfate, and mannitol solution are the most commonly used agents.[18,19] Biphasic agents are preferable because the intraluminal low signal on T1-weighted images helps to provide good contrast against the bright enhancing mucosa, following the administration of intravenous contrast. Because of the high rate of absorption of water in the distal small bowel and diarrhea associated with PEG, we use Volumen (0.1% w/v and 0.1% w/w Barium Sulphate suspension, E-Z-EM Canada, Bracco Diagnostics Inc.). Barium, owing to its osmolality, absorbs water from the bowel and slows down bowel transit, and thus has better patient compliance in our experience. Mannitol solution is also reported to be more palatable and causes no diarrhea in comparison to PEG.

Other contrast agents that have been proposed include positive contrast agents with paramagnetic properties. They include solutions containing gadolinium chelates, manganese, and ferrous ions, as well as pineapple and blueberry juices, which are high in signal on both T1 and T2-weighted images.[20] The advantage of positive contrast agents is their ability to better demonstrate wall thickening. The disadvantage is that they may mask subtle

mucosal hyper enhancement after intravenous contrast administration.

Negative contrast agents with supermagnetic properties such as perfluorooctyl bromide, ferumoxide oral suspension, and oral magnetic particles, which are low in signal on both T1 and T2-weighted images, have also been proposed.[20] The advantages of negative contrast agents is that they provide good delineation of interloop abscesses because the high signal within the abscess stands out in comparison with the low intraluminal signal. The disadvantage of negative contrast agents is that the subtle bowel wall edema, which may only be mildly T2 hyperintense, may not be conspicuous against the low signal of the oral contrast within the bowel.

Scan protocol

Patients are asked to drink the first bottle of Volumen (450 ml) over first 15 min and the next 450 ml over the next 15 min. This is followed by 450 ml of water, thus yielding a total volume of 1350 ml, which has been reported to be an optimal volume for small bowel distention. Dividing the dose over a period of time has been reported to produce more optimal filling and distension of the small bowel.[21] Water helps in the distention of the proximal small bowel as well as reduces the hyperosmolar effects of the barium suspension. Approximately 45 min from the beginning of oral contrast ingestion, imaging is initiated by acquiring single-shot fast spin-echo sequence.

Imaging is performed in the supine position at our institution on Philips 1.5T or Siemens 3T magnet, although imaging at 1.5T is preferred due to greater artifacts on 3T. If adequate contrast distention of the terminal ileum or ileocecal junction is not observed, repeat assessment is made in 10–15 min. Once satisfactory, distention of the small bowel is obtained, as evidenced by contrast in the ascending colon, cine balanced steady-state free precession sequences are performed in the coronal plane from anterior to posterior to evaluate bowel peristalsis. These sequences are also referred to as fast steady state acquisition imaging technique on GE magnet, balanced fast field echo on Philips magnet and true fast imaging with steady-state precession on Siemens magnets. This sequence is relatively motion insensitive but can be prone to chemical shift artifacts, which are more pronounced at 3T imaging. Following the acquisition of cine sequences, intravenous glucagon 0.5 mg is administered to decrease artifacts due to peristalsis. Care should be taken to always administer glucagon after the cine sequences have been performed. Following this, three plane single-shot T2, axial, and coronal balanced steady state free precession, axial fat-suppressed T2 and T1-weighted precontrast and dynamic postcontrast imaging are performed. [Table 1] shows the technique of performing MRE.

Role of diffusion weighted imaging

Acute flare up associated with active inflammatory bowel disease results in increased cellular, decreased freedom of movement of water molecules, formation of lymphoid aggregates, and viscous fluid within the bowel wall, all of which can result in restricted diffusion and corresponding low signal on apparent diffusion coefficient (ADC) maps. Prominent lymph nodes seen on diffusion weighted (DW)-MRI, clustered around segments of small or large bowel may also be indicative of adjacent ongoing bowel wall inflammation and should serve as a clue to evaluate the adjacent bowel in further detail.[22]

Complications of active disease such as abscesses or fistula can also be well-seen on DWI-MRI images with abscess appearing hyperintense rounded lesions and fistula appearing as linear/serpiginous hyperintense signal tracts. DWI-MRI has been found to be sensitive in detecting recurrent disease and assessing response to treatment.[23]

A recent study conducted in a pediatric group of patients has also shown that combination of DWI-MRI and MRE increases accuracy of detecting active disease than either technique used alone.[24]

Image Interpretation: The Stepwise Approach

We follow a structured stepwise image interpretation approach to maintain consistency in reporting. This also helps our referring physicians to quickly locate relevant information from our reports. A summary of our approach is shown in Table 2.

Distribution of contrast and distention of bowel

Adequate contrast distension of the small bowel lumen is necessary for the proper assessment of wall thickening and wall enhancement in patients with CD. Inadequate small bowel distension is a common pitfall, which can both mimic and obscure CD pathology resulting in false-positive and false-negative interpretations, respectively.[25]

The purpose of the coronal single-shot fast spin-echo sequence, which is the initial MR sequence following ingestion of contrast is to ensure adequate distension and distribution up to the terminal ileum, which is the site of common involvement in CD [Figure 1A and B].

Wall thickening, edema, and fat in the wall

Wall thickening: Distended small bowel wall thickness greater than 3 mm is considered abnormal.[18] Typically, abnormal wall thickening in acute inflammatory phase of CD measures >5 mm in thickness. Fat-suppressed balanced steady state free precession imaging is best for evaluating wall thickness.

Table 1: Magnetic resonance enterography technique and protocol

Sequence	Imaging parameters and planes	Pearls and pitfalls
Coronal single-shot fast spin-echo–HASTE (Siemens) SS-TSE (Philips) ↓ Check for adequate distention. If terminal ileum is well distended, then proceed to next sequence	Echo time-80 ms Repetition time-800 ms Slice thickness-5 mm Matrix-384×234 Plane-Coronal	Fast acquisition, which makes it relatively insensitive to bowel motion Provides quick anatomic overview Wall thickening and bowel obstruction are depicted, although the spatial resolution is lower due to rapid acquisition Prone to artifact from flow phenomenon from bowel peristalsis (which can be overcome by intravenous glucagon administration)
Steady state free precession sequences Administer 0.5 mg intravenous glucagon to diminish peristalsis ↓ True FISP (Siemens) and Balanced FFE (Phillips)	Echo time-4 millisecs Repetition time-2 millisecs Slice thickness-5 mm Matrix-320×210 Plane-Coronal	Helps to assess motility in the portions of bowel that appear thickened and to determine if an area of apparent narrowing is transient or fixed High signal-to-noise ratio provides sharp contrast between hypointense bowel wall and intraluminal hyperintense fluid[23] "Black boundary" artifact along bowel wall that may mask small bowel wall lesions
T2-weighted sequence	Echo time-80 ms Repetition time-1250 ms Slice thickness-5 mm Matrix-228×200 Plane-Coronal, axial	Fat suppressed images to distinguish bowel wall edema in acute disease from bowel wall fat in chronic disease
Precontrast volume interpolated T1-weighted thin section gradient echo sequences VIBE (Siemens) and THRIVE (Phillips) ↓ Administer i.v. gadolinium 0.1 mmol/kg body weight	Echo time-1.1 ms Repetition time-3.2 ms Slice thickness-5 mm Matrix-256×154 Plane-Coronal	Important to obtain subtraction imaging as well as to detect preexisting artifactual luminal hyperintensity
Postcontrast T1-weighted gradient echo sequences	Echo time-1.1 ms Repetition time-3.2 ms Slice thickness-5 mm Matrix-256×154 Plane-Coronal, axial Bolus tracking technique Arterial phase-25 s Venous phase-40 s Delayed phase-1 min	Subtraction images are also obtained to differentiate true enhancement from artifactual preexisting enhancement

Table 2: Stepwise approach for interpretation of MRE

Step-wise approach	Key observations
1. Distribution of contrast and distention of bowel	Scout coronal single shot sequences to assess distention Confirm distention of terminal ileum
2. Wall thickening, edema, and fat	Compare between fat-suppressed and nonfat-suppressed T2-weighted images
3. Assessment of Peristalsis	Dynamic cine images to assess for fold pattern and altered bowel motility
4. Disease activity - Early and delayed enhancement	Early enhancement in active disease with comb sign; progressive delayed enhancement in chronic disease
5. Penetrating disease - Fistula and abscess	Star-sign for interloop fistula
6. Fibrostenotic disease - Stricture and small bowel obstruction	Fibrostenosing disease, upstream dilation proximal to a narrowed and aperistaltic segment
7. Colonic assessment	Colonic wall thickening, loss of fold pattern, and fat deposition
8. Extraenteric assessment	Mesentery, fat, and lymph nodes
9. Perianal disease	Axial T2-weighted images through pelvis
10. Bones and other soft tissues	Sacroiliitis, sclerosing cholangitis

MRE: Magnetic Resonance Enterography

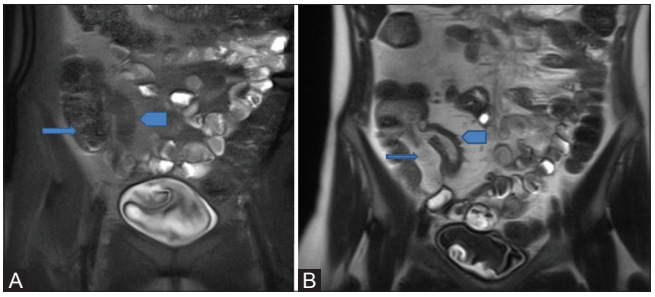

Figure 1 (A and B): (A) Coronal T2-weighted single-shot fast spin-echo images of the abdomen showing inadequately distended small bowel with collapsed terminal ileum (arrow head) and collapsed cecum (arrow). (B) Coronal T2-weighted single-shot fast spin-echo image of the abdomen obtained 15 min after (A) showing oral contrast opacifying a distended terminal ileum which shows loss of normal fold pattern (arrowhead) and contrast seen within the right colon and cecum (arrow)

Wall edema versus Fat: In segments with wall thickening, assessment for edema versus fat in the wall should be made to distinguish active from chronic inflammation, respectively. This is best evaluated by comparing the bowel wall between fat-suppressed and nonfat-suppressed

T2-weighted images. Both mural edema and fat will appear hyperintense on nonfat-suppressed T2-weighted images, whereas mural edema alone will persist as hyperintense wall signal on fat-suppressed T2-weighted sequences, indicating active inflammation. Mural fat will lose signal on fat-suppressed T2-weighted images, suggesting chronic disease.

T2 signal hyperintensity due to mural edema has been shown to correlate moderately with acute inflammation[26,27] compared to bowel ulcers and contrast enhancement ratio of >1.85, which have the highest correlation between active disease and MRI findings [Figures 2A, B and 3].[16]

Assessment of peristalsis

Cine-balanced steady state images are performed to assess bowel motility. In general, normal small bowel loops should show similar rates of peristalsis with greater rate of peristalsis in the jejunum compared to the ileum. Segments of small bowel wall thickening or other areas of suspected CD involvement should be scrutinized on cine images for abnormal or absent peristalsis. Cine imaging also helps differentiate strictures from transient areas of nondistension. Compared to standard MRE without cine, MRE with cine helps to identify significantly more lesions associated with CD.[28] These motility changes have also been shown to correlate with histopathological and inflammatory marker changes, correlating with CD.[29-31]

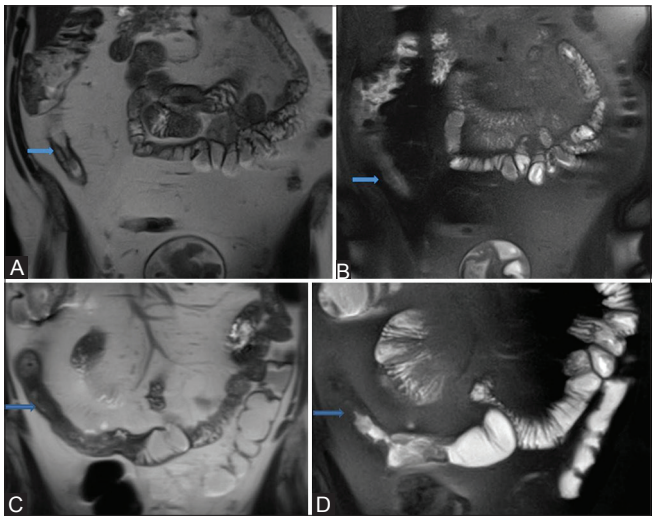

Figure 2 (A-D): (A) Coronal T2-weighted single-shot fast spin-echo image of the anterior abdomen without fat suppression shows a focal segment of bowel wall thickening with loss of normal fold pattern and T2 hyperintense signal, which may be secondary to acute edema or chronic fat deposition in the wall (arrow). (B) Coronal T2-weighted single-shot fast spin-echo image of the anterior abdomen with fat suppression shows persistent high T2 signal (arrow) within the same featureless bowel loop, indicating that this is due to edema, which corresponds to active disease. (C) Coronal single shot fast spin echo image of the anterior abdomen without fat suppression shows high T2 signal (arrow) within a bowel loop. (D) Coronal fat suppressed T2 weighted image of the anterior abdomen shows loss of high T2 signal (arrow) within the same bowel loop, indicating that this is due to chronic fat deposition

CD can present in a variety of subtypes. Active inflammatory disease, fibrostenotic disease, and fistulizing disease are the three most commonly described patterns. The next three steps in image assessment are useful in determining which one of the CD patterns a patient can present with.

Assessment of active disease: Enhancement characteristics

Active inflammatory disease is characterized by acute exacerbation of clinical symptoms, elevation of acute inflammatory markers, and is often managed medically. Precontrast T1-weighted images are necessary to delineate the segments of small bowel that are already hyperintense and are used to obtain postcontrast subtraction images and confirm areas of true wall enhancement. Normal enhancement of adjacent small bowel loops should be used as a reference when assessing abnormal mural enhancement.

Segments of active CD with transmural inflammation often present with both early submucosal and serosal enhancement.[32] The intervening edematous submucosa will appear less intense giving the bowel a target appearance when viewed in cross-section. This pattern of enhancement is often described as "layered" or "mural stratification," and has been shown to have good correlation with acute inflammation [Figure 4].

Diffuse transmural enhancement is also a pattern, which has been described in CD reflecting the transmural nature of the disease. In addition, enhancement extending into the adjacent mesentery is only seen with active disease. Enhancement may also involve "skip segments" of bowel with normal intervening segments in between areas of active disease. In

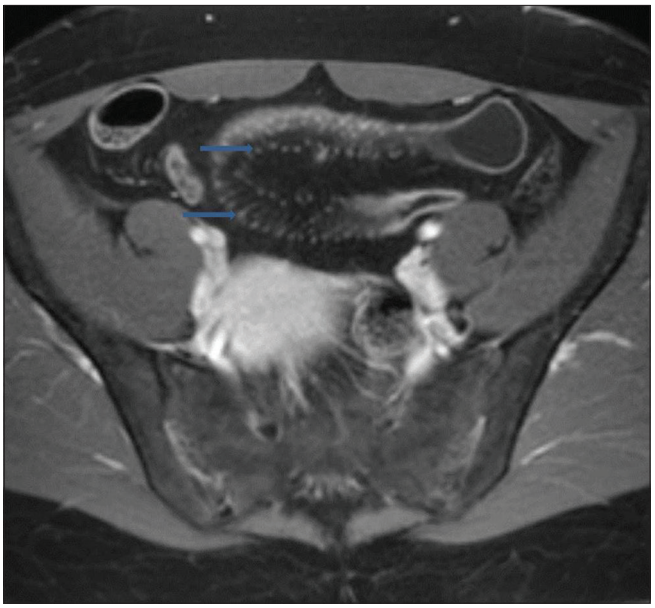

Figure 3: Axial postcontrast T1-weighted image shows the "comb sign" (arrows) with vascular engorgement in the mesentery, a finding suggestive of active disease

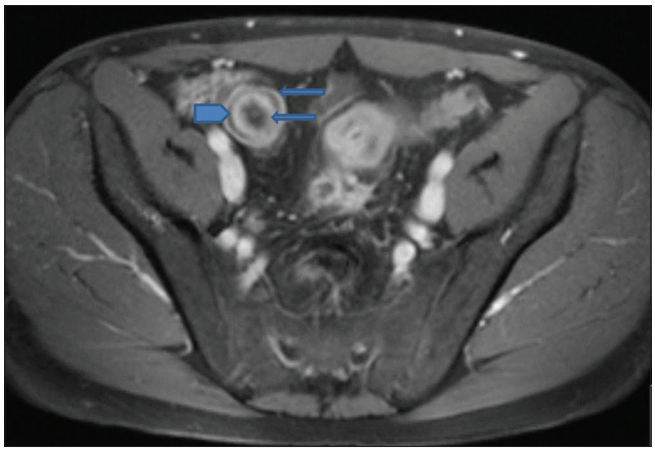

Figure 4: Axial postcontrast T1-weighted image of the abdomen shows the "target" sign or mural stratification with hyperenhancement of the inner mucosa and outer serosa (arrows) and nonenhancing intervening edematous submucosa (arrowheads)

addition to MRE, contrast enhancement using ultrasound has also been studied in CD of the terminal ileum and has shown good correlation with MRE.[33] Enhancement ratios have been studied on CT, MR, and ultrasound studies and show good correlation with acute inflammation. Enhancement ratios of 1.85 and 1.91 have been reported to have strong correlation with advanced transmural inflammation on MR and ultrasound-validated studies [Figure 5A-C].[16]

Table 3 summarizes the differences between acute and chronic disease.

Assessment of bowel ulceration

Both superficial and deep ulcers are another hallmark of active inflammatory disease. Small aphthous ulcers are well-observed on MRE when there is adequate luminal distention. A superficial aphthous ulcer is seen as a central focal area of high T2 signal surrounded by a mound of T2 intermediate signal. Deep transmural ulcers are seen as linear high signal intensity projections into the bowel wall and are best observed on fat-suppressed T2-weighted images. Cobblestone appearance of the mucosa is also associated with areas of deep ulceration alternating with thickened mucosal folds.[34] Deep ulceration can eventually result in penetrating and fistulizing disease.

Gourtsoyiannis *et al.* ranked the product of bowel wall thickness, lymph node enhancement, and intestinal ulcers as having the strongest correlation with active CD.[35] These findings were confirmed by Sinha *et al.* in a large validated study of surgically excised bowel segments compared with MRE [Figure 6].[16]

Assessment of fibrostenosing disease: Stricture and small bowel obstruction

Chronic bowel wall inflammation results in fibrosis and stricture formation, which can lead to small bowel

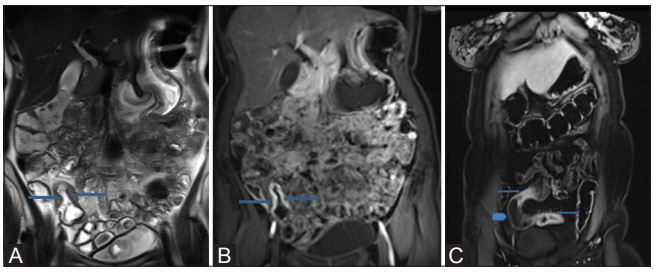

Figure 5 (A-C): (A) Coronal fat-suppressed T2-weighted image showing T2 hyperintense signal within a featureless long segment of small bowel (arrows). Corresponding early postcontrast thin section T1 three-dimensional gradient echo-weighted image (B) shows early post contrast enhancement within the edematous bowel loop, indicating active disease (arrows). (C) Postcontrast thin-section T1-weighted image shows "skip lesions" with hyperenhancement (arrows) and an intervening short segment of normal small bowel in between (arrowhead)

Table 3: Acute versus chronic disease

	Active disease	Chronic disease
True-FISP and T2-weighted images	Bowel wall thickening and edema; mesenteric congestion	May have bowel wall fat, and loss of normal fold pattern with featureless loops
Diffusion weighted images	Positive restricted diffusion	No restricted diffusion
Dynamic motility images	Diminished peristalsis	Diminished peristalsis
Postcontrast images	Early enhancement	Delayed and progressive enhancement

obstruction. Fibrotic segments are seen as fixed areas of thickened bowel wall with luminal narrowing. These segments typically show hypointense signal of the submucosa on T1- and T2-weighted sequences. Because of the presence of fibrous tissue, these segments may show absent, diffuse, or heterogeneous enhancement after contrast administration. Because of asymmetric ulceration and chronic fibrosis on the mesenteric side of the bowel, pseudo sacculations can form on the anti mesenteric side.[36]

One of the major disadvantages of MRE is the poor specificity and sensitivity in the detection of strictures. Although symptomatic strictures may be detected, incipient or partial strictures are often missed on MRE. This is because enterographic technique may not provide adequate distension of the bowel to highlight partial strictures. A "distension-challenge" of the bowel as provided by an enteroclysis examination is better suited to highlight the areas of partial narrowing or strictures [Figure 7A and B].[37]

Cine images are helpful in assessing if an area of thickened bowel with luminal narrowing is fixed or not. If the narrowing is fixed and severe, there will be upstream dilatation of bowel loops and other secondary signs of small bowel obstruction.

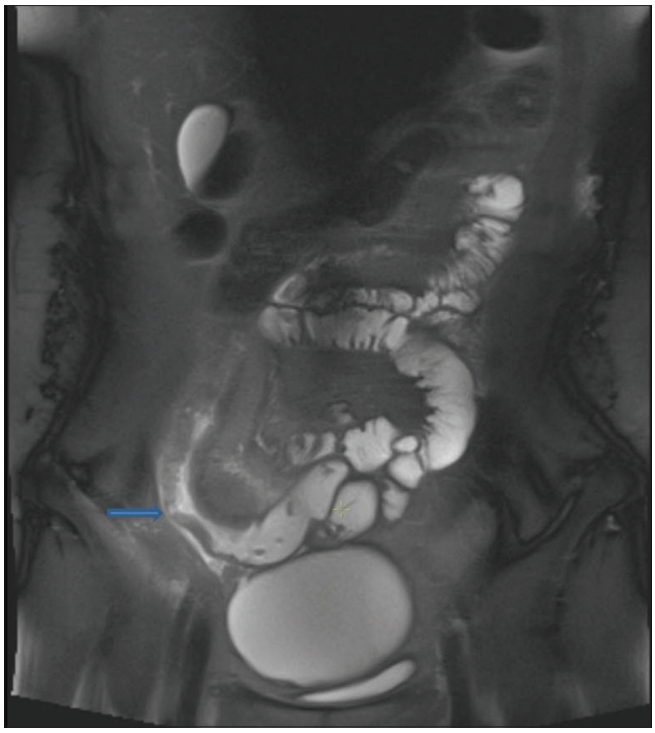

Figure 6: Coronal T2-weighted fat-suppressed single-shot fast spin-echo image of the abdomen shows wall thickening and edema in a small bowel segment with linear area of transmural ulceration (arrow)

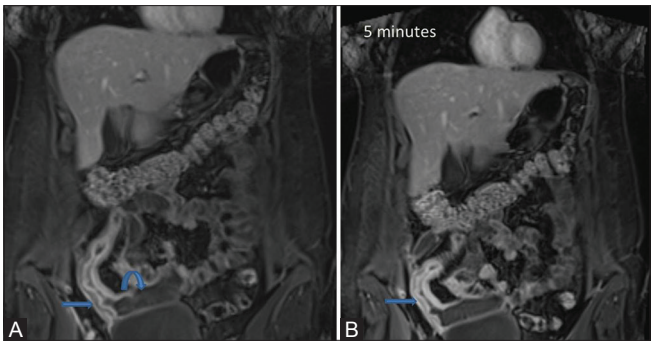

Figure 7 (A and B): (A, B) Coronal post contrast T1 weighted image of the abdomen showing a long segment of small bowel wall thickening and target like pattern of enhancement (arrow) with mild upstream dilatation of the more proximal loops to 3.2 cm (curved arrow), suggestive of stricture (A). The enhancement also progressively increased from early to delayed post contrast imaging (arrows in B), consistent with fibrostenosing disease

Assessment of penetrating disease: Fistula and abscess formation

Fistula formation has been reported in up to one-third of patients with CD and is a feature of penetrating disease.[2] The reported rates of sensitivity of MRE for the detection of fistulizing/penetrating disease range from 83.3–84.4% with a specificity of 100%.[37] Two types of fistulous disease patterns are seen on imaging and include intraabdominal and perianal fistula.

Deep ulceration and transmural inflammation result in the formation of blind-ending fluid-filled sinus tracts with inflammation in the adjacent mesentery. These tracts form small rim enhancing collections, resulting in an abscess. They can also communicate with adjacent inflamed bowel loops, adjacent hollow viscera, or with the abdominal wall. This results in the formation of various types of fistulae such as interloop, enterogastric, enterovesical, enterovaginal, and enterocutaneous fistula [Figure 8].

Small inter loop fistulae can be missed on MRE due to partial volume averaging effects. Larger tracts are best seen on postcontrast and fat-suppressed T2-weighted images. Sagittal sequences are particularly helpful in delineating fluid-filled tracts that extend from the small bowel to the anterior abdominal wall.

Not all penetrating diseases result in the formation of fluid-filled sinus tracts or fistulae. Desmoplastic reaction incited by transmural inflammation in the mesentery can result in band-like areas of fibrosis, often bridging surrounding small bowel loops in a stellate configuration, also referred to as the "star-sign." These fibrous bands often show delayed progressive enhancement and are an indirect evidence of enteroenteric fistula [Figure 9A and B].[38]

Deep penetrating ulcers can also result in the formation of well-circumscribed peripherally enhancing abscesses, which can be located within the bowel wall (intramural abscess) or decompressed between the bowel loops (inter loop abscess) or into the adjacent mesentery. On T2-weighted images, the detection of interloop abscess may be limited due to similar signal characteristics of intraluminal bowel fluid and fluid within the abscess. Use of negative contrast agents that provide hypointense T2 signal has also been described in order to better delineate interloop abscesses which appear hyperintense compared to the T2 hypointense contrast within the bowel.[39] Timely detection of these abscess is important because it is a contraindication to use of steroids and agents such as antitumor necrosis factor.[40]

Perianal disease

Although obstruction of the perianal glands is the most common cause of idiopathic perianal fistulization, up to 26% of patients with CD can have perianal fistula.[2] Anal glands that lie along the dentate line of the mid anal canal can get obstructed and inflamed, with inflammation extending to the inter sphincteric plane. The inflammation can then track down directly inferiorly into the perianal skin or traverse the external sphincter and then track into the perianal skin.

Although dedicated high resolution imaging of the pelvis is always warranted for detailed evaluation of perianal disease is a patient with CD, axial T2 and postcontrast images provide a gross overview of findings and can be used as a guide to recommend further detailed evaluation [Figure 10].

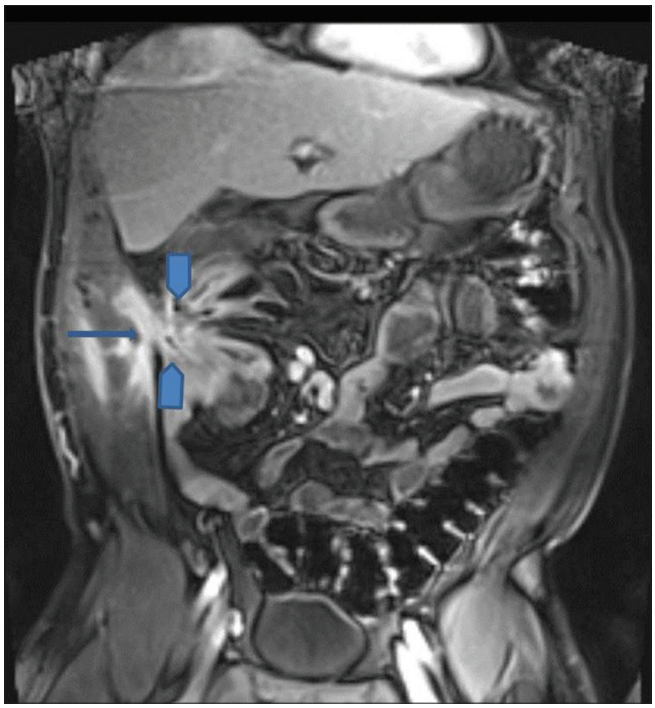

Figure 8: Coronal fat-suppressed three-dimensional gradient echo thin-section postcontrast T1-weighted image through the abdomen shows an enterocutaneous fistula (arrows) between the anterior abdominal wall and multiple tethered small bowel loops, creating the "star sign" (arrow heads) consisting of a stellate pattern of mesenteric enhancement extending between multiple small bowel loops. This is indicative of penetrating/fistulizing disease

The most important objective of assessing perianal fistula on high resolution MRI is to determine sphincter involvement, which would help determine the surgical technique and prevent incontinence. The other important objective is to detect secondary tracts and abscesses that can result in failure and recurrence if undetected or inadequately treated.

Active fistulous tracts appear hypointense on T1 and hyperintense on T2-weighted images due to the presence of fluid and surrounding granulation tissue. With intravenous gadolinium administration, these tracts show peripheral rim enhancement on postcontrast T1-weighted images, with enhancement also extending into the surrounding soft tissues due to increased vascularity. Inactive or chronic fistula lack the T2 hyperintense signal due to presence of scarring and fibrous tissue. Change in T2 signal from hyperintense or hypointense and lack of post contrast enhancement during the course of treatment of a fistula are predictors of good treatment response [Figure 11A and B].[2]

Assessment of colon

Because of the ease and feasibility of colonoscopy as well as the potential for the obscuration of subtle superficial lesions due to high fecal residue, colonoscopy remains the gold standard and is more often performed for assessment of features such as superficial aphthous ulcers. Features

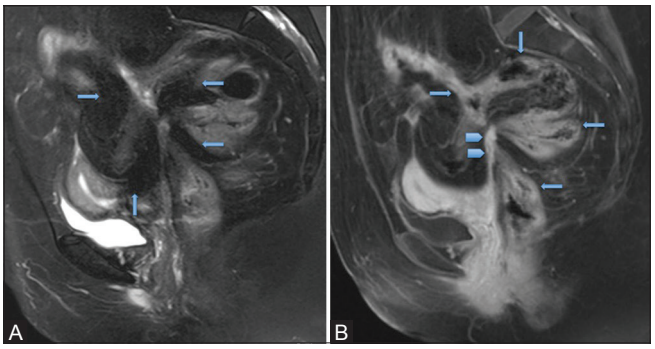

Figure 9 (A and B): (A) Sagittal T2-weighted image showing multiple small and large bowel loops tethered to each other in the pelvis (arrows). (B) Corresponding sagittal postcontrast T1-weighted image shows multiple tethered loops (arrows), with linear enhancement between the loops indicative of inter loop fistulization (arrowheads)

of large intestinal CD, which are similar to small bowel disease such as bowel wall edema and mucosal hyper enhancement, can be seen on routine MRE sequences as well. T1 hyperintense signal from fecal residue within the colon may interfere with the assessment of mucosal hyperenhancement. Use of subtraction imaging in these situations is helpful in preventing false positive results. MRE can also be helpful in detecting the penetrating disease of the colon and extramural complications as well [Figure 12A and B].

Extra enteric assessment: Mesentery, fat, and lymph nodes

Mesenteric edema is a well-known feature of CD, and in combination with bowel wall edema and enhancement, suggests active disease. Engorgement of the mesenteric vessels (vasa recta) results in the "comb sign," which is seen as multiple parallel hyperintense lines that are perpendicular to the bowel wall. The hypervascularity, dilatation, and tortuosity of the vasa recta have a higher association with active disease.[41]

Hypertrophy of the mesenteric fat, also called "fat wrapping" or "creeping fat" is seen usually along the mesenteric border of the bowel wall and can cause mass effect on mesenteric vasculature and separation of bowel loops. Although fibro fatty proliferation is only seen in long standing cases of CD, when present, it is considered a specific sign for CD. It is unclear if the fibro fatty proliferation is a driving force for inducing inflammation because of its propensity to produce hormones or if it is reactive to the existing chronic inflammation in CD.

Enlarged lymph nodes are commonly seen in the mesenteric root as well as in the right lower quadrant. They usually show homogeneous enhancement after contrast administration. These features are important in differentiating lymph nodes of CD from other infectious causes of lymphadenopathy such as tuberculosis where nodes may be necrotic and show central low density.

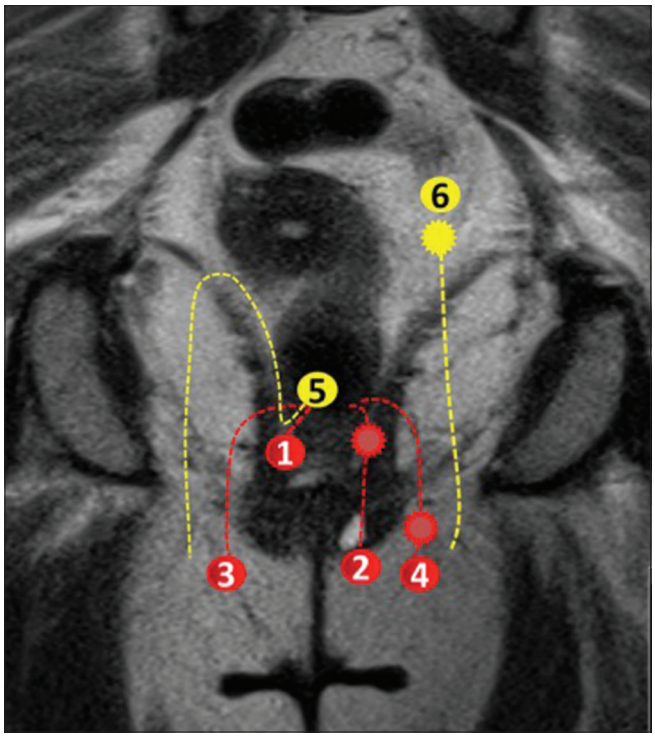

Figure 10: Schematic representation of perianal fistula according to St. James University classification system. (1) Simple linear inter sphincteric fistula (2) Intersphincteric fistula with inter sphincteric abscess or secondary fistulous track (3) Transsphincteric fistula (4) Transsphincteric fistula with abscess or secondary track within the ischioanal or ischiorectal fossa (5) Supralevator disease (6) Extrasphincteric disease

Assessment of bone and other organs

Extraintestinal manifestations such as spondyloarthropathy and ankylosing spondylitis had previously been reported in 9.9 to 45% patients with inflammatory bowel disease, with no significant differences reported between frequency of occurrence in ulcerative colitis and CD.[42] Axial involvement in the form of sacroiliitis and/or ankylosing spondylitis may be present in up to 5–22% patients with CD and 2–6% patients with ulcerative colitis.[43] No definite association has been shown between the presence of sacroiliitis and presence of active bowel inflammation.

Although MRE is not the ideal modality to detect bony changes, some bony manifestations such as sacroiliitis may be well-visualized on MRE which includes coronal and axial views of the sacroiliac joints.

Sacroiliitis presents as bilateral, often symmetric joint involvement. Active inflammation is best seen on fat-suppressed coronal T2-weighted images as bone marrow edema on both sides of the joint. Joint effusion can also be seen on coronal fat-suppressed T2-weighted images, which are routinely included in the enterography protocol. Chronic features such as subchondral fat deposition and sclerosis are best seen on coronal T2-weighted nonfat-suppressed single-shot fast spin-echo sequences.[44]

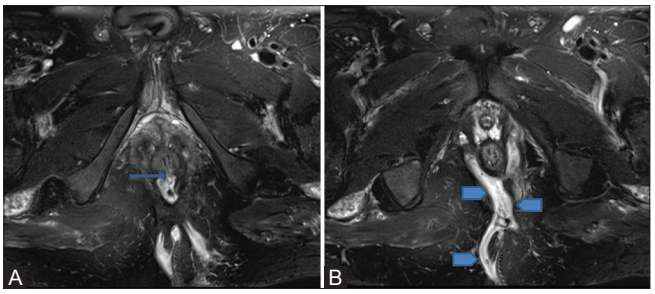

Figure 11 (A and B): (A, B) Axial fat-suppressed T2-weighted images of the pelvis showing a linear transsphincteric fistula at the 6 o' clock position of the anal canal (arrow in A). Multiple T2 hyperintense fluid filled intercommunicating tracts are seen extending in a horseshoe shaped configuration around the anal canal (arrow heads in B)

Extra intestinal manifestations involving the hepatobiliary system are common in patients with inflammatory bowel disease. Primary sclerosing cholangitis is one of the most common biliary manifestations and occurs more commonly in patients with ulcerative colitis than CD. The percentage of patients diagnosed with ulcerative colitis that have primary sclerosing cholangitis ranges 2.4–7.5%.[45] Although dedicated MRCP sequences are not performed, a gross assessment and screening of the liver for multifocal intra and extrahepatic biliary dilatation and stricturing, which are hallmarks of primary sclerosing cholangitis, can be made on axial T2-weighted sequences obtained during routine enterography and further recommendations for dedicated MRCP can be provided.

Pitfalls of Magnetic Resonance Enterography Examination

Nondistended bowel

A commonly encountered problem in patients with CD is the inability to drink and retain contrast. This causes inadequate distention and can falsely cause the appearance of bowel wall thickening and apparent enhancement.

Hyperintense signal in the bowel wall on precontrast imaging

Fecal material can sometimes show T1 hyperintense signal along the interface between the bowel wall and mesenteric fat and can obscure mural enhancement. Use of postcontrast subtraction images aids in distinguishing true pathologic enhancement from artifact. This is shown in Figure 13A-C.

Black boundary artifact

On nonfat-saturated steady state free precession sequences, due to the chemical shift phenomenon, a black boundary artifact can be seen along the bowel wall in voxels where fat and water coexist. This can be mistaken for bowel wall thickening. One of the ways to overcome this is to use fat suppression as well as to correlate the abnormal appearing bowel loop with corresponding fat-suppressed T2-weighted sequences as well.

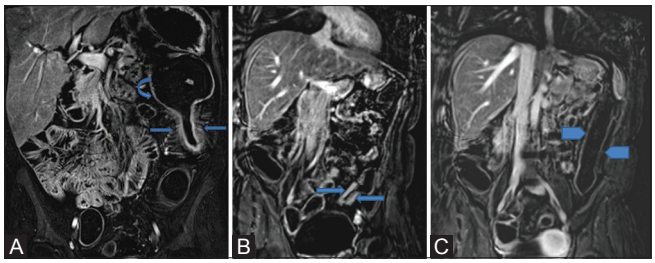

Figure 12 (A-C): (A) Coronal postcontrast fat-suppressed three-dimensional T1-weighted image showing a featureless segment of mid descending colon with wall thickening and enhancement (arrows) and mild upstream dilation (curved arrows), suggesting stricturing. Note the mesenteric vascular engorgement consistent with "comb sign." (B, C) Contiguous coronal postcontrast fat suppressed three-dimensional T1-weighted images showing early post contrast enhancement within the distal descending colon (arrows in C) with a mildly dilated featureless proximal descending colon (arrowheads in C), consistent with lead pipe colon

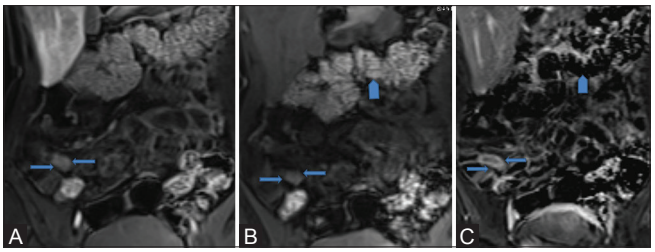

Figure 13 (A-C): (A) Coronal postcontrast T1-weighted image showing T1 hyperintense signal within the terminal ileum, suggesting enhancement related to active disease (arrow). (B) Corresponding Coronal precontrast T1-weighted image also showing T1 hyperintense signal within the terminal ileum, thus making it difficult to determine if the enhancement is true enhancement or not (arrow). Note the T1 hyperintense signal within the colon (arrow head) (C) Corresponding coronal postcontrast T1-weighted image with subtraction, confirming that the enhancement is a true enhancement and not artifactual from preexisting T1 hyperintense signal in the bowel wall (arrow). Note the suppression of T1 hyperintense signal in the colon with subtraction imaging (arrow head)

Differential Diagnoses

Tuberculosis of the intestinal tract is a granulomatous disease that has several overlapping features with CD. Although tuberculosis has a higher incidence in developing countries, increasing incidence of tuberculosis is now seen in Western countries with the reemergence of human immunodeficiency virus. At the same time, there is emergence of CD in many tropical countries where incidence previously was low. The combination of these factors warrants accurate distinction between the two. Prompt and accurate diagnosis of tuberculosis is also important to prevent morbidity and reduce dissemination of infection. Distinct clinical, radiologic, endoscopic, and pathologic differences exist between the two diseases.[46]

While terminal ileal region is involved in both conditions, tuberculosis involves the ileocecal valve with contiguous mucosal thickening, resulting in a patulous valve in the more chronic stage. Tuberculosis also results in short, concentric strictures with smooth margins and transversely oriented ulcers compared to CD, which causes long, eccentric strictures and longitudinally oriented ulcers with deep fissuring.

Role of Imaging in Clinical Management

Medical management of CD involves the use of several classes of drugs, with oral 5-amino salicylates or sulfasalazine being one of the first line of treatment. In patients who do not respond well, other options such as oral steroids and immunosuppressive drugs such as tumor necrosis factor alpha inhibitors are used. Assessment of response to therapy is, however, challenging; a present, endoscopic evaluation due to its ability to directly visualize and follow-up individual bowel segments and to perform biopsy at suspicious sites remains the gold standard for detecting treatment response. However, because of its invasive nature, endoscopy is generally reserved for those patients who remain symptomatic despite treatment. Because of its noninvasiveness, MRE in recent years has shown to be an effective way of assessing response to medical therapy. A prospective study of 96 patients with active disease and ulcers who underwent both endoscopy and MRE at baseline and at 12 weeks following therapy showed that MRE was 90% accurate in detecting ulcer healing and 84% accurate in detecting remission compared to endoscopy.[47]

Conclusion

Diagnosis of CD is usually made based on combining endoscopic, imaging, and histopathologic findings. Distinction from tuberculosis is difficult especially in endemic areas and may even need a trial of antitubercular treatment in some patients. In terms of imaging, however, MRE is a valuable tool in the diagnosis and management of patients with CD. Multiple studies have proven MRE to correlate well with CTE, endoscopy, and histopathology in patients with CD. In clinical studies, MRE has been used to successfully manage CD in medical and surgical settings. Patients with CD undergo multiple imaging evaluations throughout the course of their disease, consequently making MRE's lack of radiation a significant advantage over CT. MRE also has the advantage of enhanced tissue contrast, multiple different sequence options, and the ability to perform functional imaging. A structured imaging protocol and reporting template is valuable in diagnosis and management of patients with CD. While CT retains its role in the emergency setting, MRE should be the chosen method in diagnosis and treatment monitoring in patients with CD.

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Conflicts of interest

There are no conflicts of interest.

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