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Indian guidelines on imaging of the small intestine in Crohn's disease: A joint Indian Society of Gastroenterology and Indian Radiology and Imaging Association consensus statement

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Abstract

The Indian Society of Gastroenterology (ISG) Task Force on Inflammatory Bowel Disease and the Indian Radiological and Imaging Association (IRIA) developed combined ISG-IRIA evidence-based best-practice guidelines for imaging of the small intestine in

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patients suspected to have or having Crohn's disease. The 29 consensus statements, developed through a modified Delphi process, are intended to serve as reference for teaching, clinical practice, and research.

Key words: Biologics; computerized tomography enterography; enterography; imaging; inflammatory bowel disease; magnetic resonance imaging; tuberculosis

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Introduction

The Indian Society of Gastroenterology (ISG) constituted a task force on inflammatory bowel disease (IBD) to describe the characteristics of Indian patients with IBD and to develop Indian guidelines for the diagnosis and management of IBD. The task force published consensus statements on the diagnosis and management in India of ulcerative colitis (UC) and Crohn's disease (CD).[1,2]

Patients with CD need evaluation of the small intestine either by endoscopy or radiological imaging, for determining involvement as well as for monitoring of the disease. Many physicians and gastroenterologists use cross-sectional imaging such as contrast-enhanced computerized tomography (CECT) or magnetic resonance imaging (MRI) for this purpose. However, there are many contentious issues; for example, should one use computed tomography enterography (CTE) or magnetic resonance enterography (MRE); how to image the pelvis in fistulizing disease; which technique to use before instituting biologics. In addition, the most characteristic intestinal lesions in CD, such as luminal narrowing, mucosal enhancement, and wall thickening, cannot be assessed without adequate distension of the intestine, a step often missed out during imaging.

In order to address these and other issues, the ISG-IBD task force together with the IRIA developed a combined ISG-IRIA consensus on imaging of the small intestine in patients with CD.[3] These statements reflect the current recommendations and guidelines for imaging of the small intestine as applicable to patients with CD in India.

Methods

The method employed for development of this set of consensus statements was similar to that used for the earlier consensus statements on UC[1] and CD.[2] Briefly, a modified Delphi process was adopted.[4] Selected authors (BS Ramakrishna, Philip Abraham, Raju Sharma, Vineet Ahuja, Govind Makharia and Saurabh Kedia) generated a list of statements that addressed nine areas:

- Choice of imaging modality
- Evaluation for extent of disease
- Evaluation for activity of disease
- Differentiation between inflammatory and fibrotic stricture(s)
- Evaluation for complications
- Monitoring of activity of disease
- Evaluation for postoperative recurrence
- Optimal imaging modality before starting biologics
- Differentiation of CD from intestinal tuberculosis (ITB).

In each of these areas, issues were determined according to perceived clinical importance, and these were taken up for discussion, revision, voting, and final consensus.

The initial statements were circulated to the members. The first vote was conducted by email, without explanation or justification for the statements. Feedback regarding the statements was collated and the statements were modified wherever required. Literature on imaging in CD, both Indian and international, was collated and copies of full papers and abstracts were circulated to all members by email. Recent guidelines from societies were also included. The revised statements were sent by email to all voting members for a second round of voting. The results of the second round were collated. The third and final round of voting was conducted after a face-to-face meeting held in Mumbai in November 2016, where the group discussed the evidence to support specific statements.

The evidence from literature for each statement, with emphasis on Indian data where available, was presented in sections by RS/VA, UG/RK, NK/SS, KG/DD, GM/DS, ASP/SP, MP/AE, and KSM/SK. Each member then voted using electronic vote pads. The options given for each statement were: (A) accept completely, (B) accept with some reservation, (C) accept with major reservation, (D) reject with reservation, and (E) reject completely. Consensus on a statement was considered achieved when 80% or more of the voting members chose to "accept completely" or "accept with some reservation." A statement was considered refuted when 80% or more of the voting members indicated "reject completely" or "reject with some reservation." Where no consensus was reached, the statement was modified and

a repeat vote was sought. If the repeat vote remained inconclusive, the statement was either deleted or modified after discussion. The participants were then asked to grade the level of evidence and strength of recommendation for the accepted statements, using a modification of the scheme suggested by the Canadian Task Force on Periodic Health Examination [Table 1].[5] The final statements and the level of evidence and strength of recommendation are listed below, along with supporting explanations.

Choice of imaging modality

1. **CTE or MRE are the preferred radiological imaging modalities for evaluation of the small intestine in patients suspected to have CD.**

Voting summary: A (87.1%), B (12.9%), C (0), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

CD is a chronic inflammatory disorder that can affect any part of the gastrointestinal (GI) tract from the mouth to the anal canal.[2] In almost two-thirds of patients, the small intestine is involved, either in isolation or concurrent with colonic involvement.[6] Small intestinal involvement can be unifocal or multifocal.[6] Accurate assessment of extent of the disease has implications on treatment.

Small intestine involvement can be assessed endoscopically (upper GI endoscopy, ileocolonoscopy, push enteroscopy, and capsule enteroscopy) or radiologically.[7] Advantages of endoscopy are direct visualization of the mucosa and access for taking biopsies (except with capsule enteroscopy). Capsule enteroscopy is contraindicated in patients with stricturing disease.[8]

Radiological investigations, including barium studies and cross-sectional imaging (CT and MR), have the advantage of being noninvasive and can assess the entire small intestine. Small-bowel follow-through and small-bowel enteroclysis were the radiologic investigations of choice earlier.[9-11] However, these techniques had their limitations especially with regard to the state of the small intestinal wall and extraluminal features. CTE and MRE have the advantage of not only assessing the intestine but also the extraluminal features, such as abscesses, fistulae, mesenteric changes, and lymph node involvement, all of which have important bearing on the diagnosis and assessment of disease activity.

Several studies have compared the diagnostic accuracy of barium studies with CTE and MRE, and most have concluded that CTE/MRE are better than or at least equal to barium studies for assessment of the intestinal wall in CD.[12-20] CTE/MRE also have better inter-observer agreement than barium studies. Inadequacies of barium studies include suboptimal evaluation of deeply located intestinal loops due to overlap and collapsed intestinal loops distal to a stricture.[12,21,22]

Many studies have shown that the diagnostic accuracy of CTE/MRE is comparable to that of CT/MR enteroclysis (with tube) except for assessment of the proximal small intestine, which is better imaged by enteroclysis.[23-28] Enteroclysis is also not acceptable to many patients because of the discomfort associated with placement of a nasojejunal tube.

In patients with renal failure, when intravenous contrast is contraindicated, or in patients with allergy to contrast agents both for CT as well as MRI, diffusion weighted MRE (DWI-MRE) can be done. DWI-MRE needs intestinal distension but does not require intravenous contrast administration, and its efficacy for detecting small intestinal inflammation has been shown to be comparable to that of gadolinium-enhanced MRI.[29,30] A recent meta-analysis of 1515 intestinal segments for diagnosis and 1066 intestinal segments for assessment of inflammatory severity has shown the sensitivity and specificity of DWI-MRE (in comparison to contrast enhanced MRE) to be 92.9% and 91%, respectively.[31]

In summary, CTE/MRE are the preferred imaging modalities for assessment of the small intestine in patients with CD because their diagnostic accuracy is similar to or better than that of barium studies and their ability to detect extraintestinal features is far superior. CTE/MRE are preferred over CT/MR-enteroclysis because of the patient discomfort associated with the latter and the diagnostic accuracy of both techniques is similar.

Table 1: Quality and grade of evidence

Quality of evidence		Strength of recommendation	
Grade	Description	Grade	Description
I	Evidence obtained from at least one randomized controlled trial	A	There is good evidence to support the statement
II-1	Evidence from well-controlled trials without randomization	B	There is fair evidence to support the statement
II-2	Evidence from well-designed cohort or case control study	C	There is poor evidence to support the statement
II-3	Evidence from comparison between time or place with or without intervention	D	There is fair evidence to refute the statement
III	Opinion of experienced authorities and expert committees	E	There is good evidence to refute the statement

2. CTE is favored over MRE as the baseline investigation in adults suspected to have CD as it provides more consistent quality.

Voting summary: A (80.6%), B (19.4%), C (0), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

CTE and MRE have comparable accuracy in assessment of the small intestine. Several studies have reported that both CTE and MRE detect active inflammation in the terminal ileum with similar sensitivities, up to 90%.[32-35] While CTE is equal to MRE in detecting mucosal enhancement, mesenteric vascularity (comb sign), intestinal wall thickening, and extent of the disease, MRE is superior in detecting intestinal strictures and fistulae.[36-39] MRE is limited by its poor image quality as compared to CTE because of significantly higher motion artefacts and lower interobserver agreement.[40] In resource-constrained countries like India, the use of MRE is also restricted by its cost and limited expertise as compared to that for CTE.

In summary, the comparable diagnostic accuracy of CTE and MRE, more consistent image quality of CTE, its wider availability, and lower cost than MRE, make CTE a favored baseline investigation as compared to MRE, in adults suspected to have CD.[41,42]

3. In children suspected to have CD, MRE is the preferred initial investigation, since CTE entails the risk of ionizing radiation.

Voting summary: A (90%), B (6.7%), C (0), D (0), E (3.3%)

Level of evidence: II-2

Grade of recommendation: B

Children are at higher risk for radiation exposure resulting from CT scans (because of higher frequency of exposure related to longer life). One study showed that lifetime attributable risk of radiation from CT scan had mean and maximum values of 0.3% and 12% for cancer incidence and 0.2% and 6.8% for cancer mortality, respectively. CT exposures were estimated to contribute 0.7% of total expected baseline cancer incidence and 1% of total cancer mortality.[43] Therefore, radiation exposure compounds the risk of malignancy in young patients over and above the risk of cancer from CD and exposure to immunosuppressants.[44] In a retrospective study, three-fourths of the radiation exposure in patients with CD was attributed to CT scans, and 7% of patients had significant radiation exposure (>50 mSv/5 year).[45] Another study in children with IBD had shown that CT was responsible for 43% of all radiation exposure and total radiation exposure would be significant by 35 years of age in 60% of children.[46] In another study, although the annual radiation exposure in patients with CD was equivalent to the annual background radiation dose occurring from natural sources in USA, a subset (in the upper quartile of radiation dose) of patients had higher exposure.[47] Two studies showed that patients with CD are at higher risk of radiation exposure in comparison to UC patients.[48,49] Because of these concerns alternative imaging modalities such as MRE should be considered for assessing the small intestine in children with CD.

However, problems associated with MR include noncompliance with breath-holding, motion artefacts, and requirement of general anesthesia in younger children.[50] In a study of 85 children with IBD (age range: 9–18 years) who underwent MRE without sedation, MR was acceptable to most of the children (93%) with adequate distension of intestine and good image quality. The authors of this study concluded that MR is acceptable and can be done without sedation in children more than 9 years of age. This study also gave a protocol for acceptable oral contrast dose as per the patient's age.

If MRE is not available, or if a child is not able to tolerate the MR procedure, CTE may be done as the first-line investigation.[38] However, if repeat imaging is required, these children should be referred to a center where the facility for pediatric MRE is available.

4. CECT or MRI without bowel distension by neutral oral contrast should be avoided (except in presence of intestinal obstruction), as the small intestine cannot be reliably assessed in a collapsed state.

Voting summary: A (93.1%), B (6.9%), C (0), D (0), E (0)

Level of evidence: II-3

Grade of recommendation: B

For optimal detection and characterization of intestinal lesions, the intestinal lumen should be distended optimally since collapsed intestinal loops may give a false impression of wall thickening and abnormal enhancement. Luminal distension with oral contrast allows appropriate assessment of the pathology not only in the intestinal lumen but also in the intestinal wall as well.

An ideal oral contrast agent for distension of the intestine should provide high contrast between the intestinal lumen and the wall, allow evaluation of enhancement of the intestine, should be free from artefacts, and be safe with minimal adverse events and minimal mucosal absorption. Neutral contrasts agents such as diluted mannitol and polyethylene glycol are preferred for distension of the intestine as they

allow better characterization of intestinal wall enhancement with intravenous contrast administration.[22,37] Positive contrast obscures the intestinal wall enhancement obtained with intravenous contrast injection. Use of plain water or normal saline is unsatisfactory as they get absorbed and provide suboptimal distension of the intestine. In patients with intestinal obstruction, since the intestine is already distended up to the point of transition, oral contrast administration is not required and CT scan can be done with the administration of intravenous contrast alone.

5. If CTE or MRE cannot be done because of nonavailability or nonfeasibility, the small intestine can be imaged using conventional CECT with oral contrast or barium meal follow-through/barium enteroclysis.

Voting summary: A (93.2%), B (3.4%), C (3.4%), D (0), E (0)

Level of evidence: III

Grade of recommendation: C

Since radiological imaging is essential for establishing the extent of the disease and complications in a patient with CD, at centers where CTE/MRE is not available, the small intestine can be imaged using conventional CECT abdomen or barium studies including barium meal follow-through or barium enteroclysis[51] [Figure 1].

6. Small intestine contrast ultrasound (SICUS) and contrast-enhanced ultrasound (CEUS) are good modalities for imaging of the small intestine in patients with CD.

Voting summary: A (96%), B (4%), C (0), D (0), E (0)

Level of evidence: I

Grade of recommendation: A

Small bowel ultrasound (US) is an inexpensive and noninvasive imaging modality which has been evaluated in the assessment of small bowel CD. Various USG modalities in the assessment of small intestine include CEUS and SICUS. CEUS involves intravenous administration of microbubble contrast such Sonovue, and SICUS involves small bowel distension with ingestion of an isoosmolar contrast agent such as polyethylene glycol. A recent meta-analysis of 33 studies showed that CEUS had the best accuracy amongst imaging techniques including US, CT, and MR for detection of inflammation and differentiation of fibrotic and inflammatory strictures.[52] However, US had limited accuracy in assessing the extent of the disease as compared to CT and MR.

If available, CEUS is a good modality for imaging of the small intestine in patients with CD; however, the facilities and expertise for this technique are at present not widely available in India.

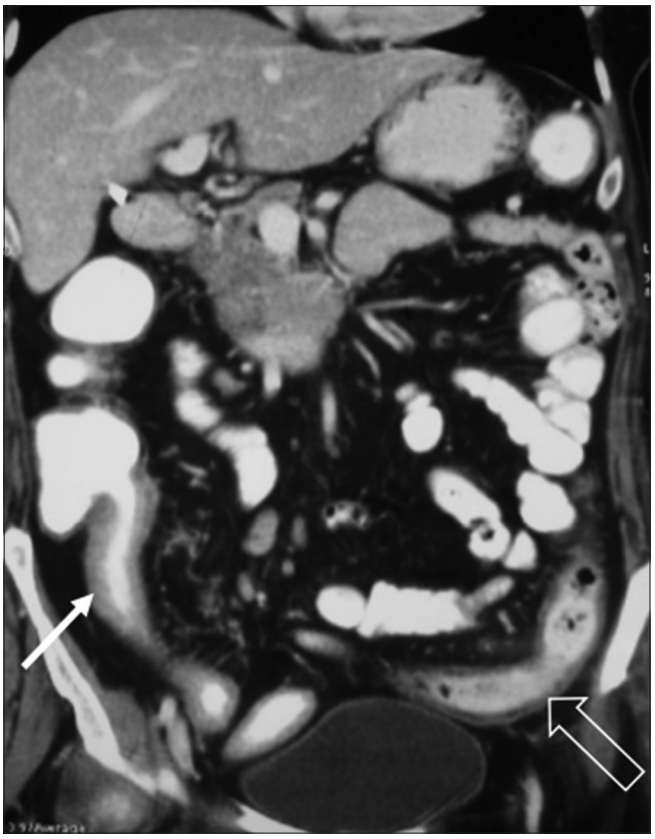

Figure 1: Conventional CT (coronal reformat) using positive oral contrast shows long-segment thickening (arrow) in the terminal ileum without cecal involvement and another noncontiguous ileal segment showing wall thickening (outlined arrow) suggestive of Crohn's disease

Evaluation for extent of disease

7. In all patients with CD, small intestinal imaging and ileocolonoscopy should be performed for determining the extent of the disease.

Voting summary: A (90%), B (10%), C (0), D (0), E (0)

Level of evidence: I

Grade of recommendation: A

As CD can affect the small and large intestine,[6,53] it is important to evaluate the extent of their involvement. The treatment and prognosis of CD are influenced by the extent of involvement of the intestine, which is classified based on the Montreal classification.[54,55]

The colon is best assessed by ileo-colonoscopic examination [Figure 2], which also provides an opportunity to obtain multifocal biopsies for histological and microbiological evaluation.[56]

The small intestine can be evaluated by small-bowel barium studies (enteroclysis or enterography), CTE, MRE, capsule

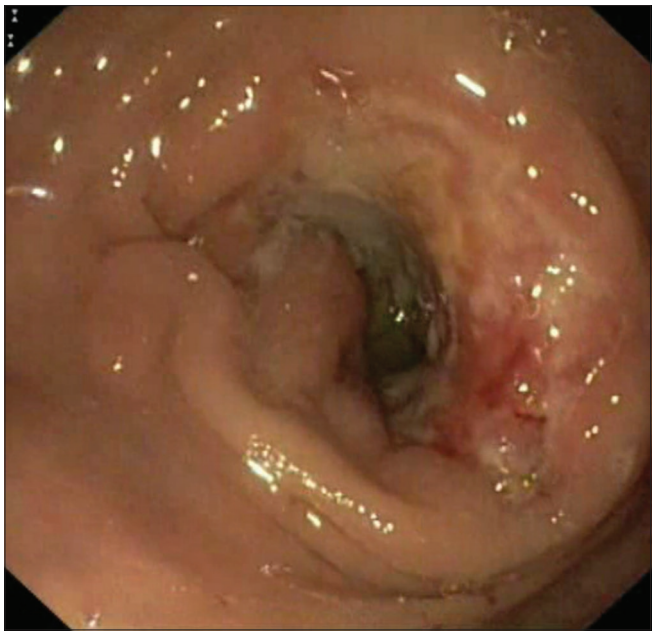

Figure 2: Colonoscopic image of colonic stricture with ulceration (active disease) in Crohn's disease

enteroscopy, double-balloon or single-balloon enteroscopy, and the recently introduced spiral enteroscopy.[56-60]

8. For suspected upper gastrointestinal (UGI) involvement, UGI endoscopy is superior to radiological imaging.

Voting summary: A (90%), B (3.1%), C (0), D (8.7%), E (0)

Level of evidence: III

Grade of recommendation: C

Involvement of the UGI tract (esophagus, stomach, and duodenum) is not uncommon in CD. In a pan-Indian study conducted by the ISG-IBD task force, 23/394 (5.8%) patients with CD had UGI involvement.[6] In another study involving three Indian centers, 26/182 patients (14.2%) had UGI involvement.[53] In a prospective study from Italy, UGI involvement was reported in 16% patients with CD.[61] In pediatric practice, UGI endoscopy with biopsy of even apparently normal mucosa is routinely performed to aid in the diagnosis of CD.[62] Presence of granulomas in the UGI tract, focal cryptitis in the duodenum, and focally enhanced gastritis (in absence of *Helicobacter pylori* infection) supports the diagnosis of CD [Figure 3].[62]

9. If perianal involvement is suspected, MRI of the pelvis and perineum should be the first line of investigation.

Voting summary: A (87.1%), B (9.7%), C (3.2%), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

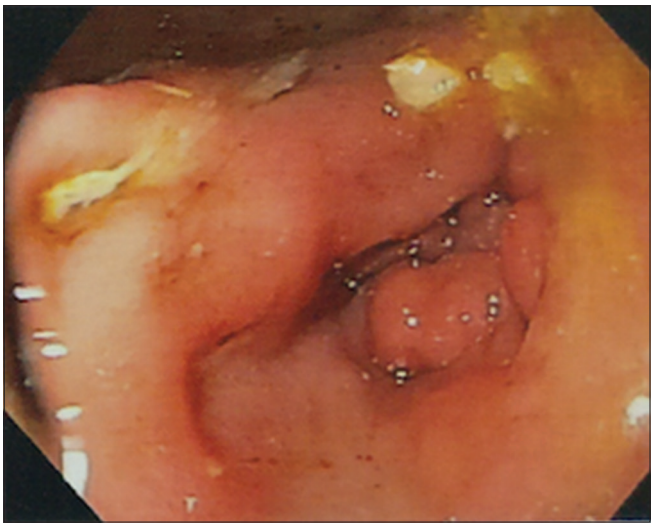

Figure 3: Endoscopic image showing pyloric edema and narrowing in Crohn's disease

In patients with CD, perianal involvement can occur in the form of anal fissure, anal sinus, anal fistula and/or abscesses. In the pan-Indian study, 56/383 (14.6%) patients were reported to have perianal fistula.[6] In the three-center study from India, 31/179 (17.3%) patients had perianal disease.[53] Perianal fistula may be simple or complex.[63] It is important to evaluate the course of fistulae through the anal sphincters, their number, complexity, and the presence of abscess or stricture distal to the opening of the fistulous tract into the intestinal lumen, as these features have bearing on the management and prognosis.

To define these, it is essential to perform cross-sectional imaging. It has been recommended that patients with perianal fistula should undergo at least two of the following: (i) examination under anesthesia, (ii) MRI, and (iii) endoscopic US of the pelvis.[64] Because of the limited availability of expertise in the assessment of anal canal anatomy by endoscopic US, and its limited reliability during acute inflammation of the anal canal/rectum, this modality is generally not preferred. Therefore, MRI of the pelvis and perineum is the preferred first-line investigation for the assessment of perianal fistula in patients suspected or confirmed to have CD.

Evaluation for activity of disease

10. On CTE, the features of active lesion in the small intestine include thickening with abnormal enhancement of the intestinal wall, stratification of layers of the intestine, ulceration (s), mesenteric fat stranding around the involved segment, and comb sign.

Voting summary: A (75%), B (25%), C (0), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

In the clinical setting of acute exacerbation of CD, CTE has been rated as the most appropriate imaging modality by the American College of Radiology appropriateness criteria.[65] However, because of concerns of radiation exposure in the pediatric population, MRE has been judged the most appropriate imaging modality.[65]

The features of active inflammation on CTE include intestinal wall thickening (>3 mm), mural hyperenhancement, mural stratification, ulcerations, higher attenuation in the perienteric fat or mesenteric fat stranding, and engorged vasa recta (comb sign)[66] [Figure 4]. Though mural thickening is the commonest finding (in up to 82% of patients) in active inflammation, it is not specific for disease activity.[67] Mural enhancement is the most sensitive indicator of disease activity and its degree correlates with the severity of the disease.[67,68] It is pertinent to note that collapsed intestinal loops may also show apparent thickening and enhancement. Thus, it is important that evaluation of disease activity on CTE is done after adequate distension of the intestinal loops. Mural stratification or the trilaminar pattern due to the interposed submucosa, while denoting activity, is not a specific feature of CD. Ulcerations are not easily detectable on CTE. Mesenteric fat stranding and the comb sign, when seen in CTE, are the most specific signs of activity of the disease.[69]

Several studies have highlighted the correlation between CTE findings and disease severity based on clinical characteristics, endoscopic characteristics, and level of inflammatory markers of disease activity. In a retrospective study of 72 patients with CD, quantification of the comb sign was done by drawing 20 regions of interest (ROIs) with area of 1 cm^2. Comb sign quantification was done in each ROI and averaged. It was found that the quantitative comb sign predicted disease activity. Setting the cutoff for the quantitative comb sign score at 3.33 led to accuracy of 78% in the arterial phase and 80% in the venous phase for determining disease activity.[70] In another study including 62 patients with CD, increased mesenteric fat density and the comb sign significantly correlated with the Crohn's disease activity index.[71] The grading of activity of CD as perceived on CT, MRI, US, and scintigraphy was assessed in a meta-analysis.[72] CT and MRI showed similar severity grading estimates (86% and 84%, respectively) in per-patient analysis; in the per-segment analysis, CT and scintigraphy did better than MRI and US.

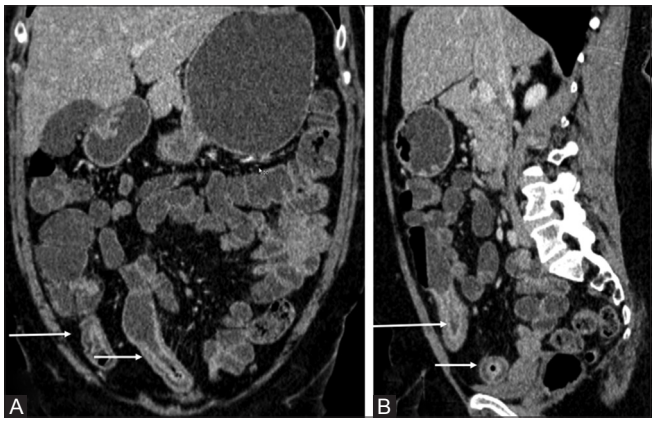

Figure 4 (A and B): Stratified wall enhancement in active CD. Coronal (A) and sagittal (B) reformatted CTE images showing thickening and stratified wall enhancement involving the ileal loops (thin arrow), a sign of active inflammatory stage of CD

11. The characteristic features of active disease on MRE include intestinal wall thickening and hyperintensity of the involved intestinal segment on T2W images, stratified hyperenhancement of the intestinal wall and comb sign on gadolinium-enhanced T1W images, and diffusion restriction on DWI.

Voting summary: A (93.1%), B (6.9%), C (0), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

The imaging characteristics of disease activity with high sensitivity (>80%) on MRE include increased wall thickness, stratified intestinal wall enhancement, and T2 hyperintensity [Figure 5]. The imaging findings of disease activity with high specificity (>90%) include intestinal wall hyperintensity on T2W and mucosal ulcerations. These observations are based on a meta-analysis of 62 studies.[73] Comb sign, though initially described for CTE, is also seen on MRE.

DWI is a useful MR sequence for assessment of disease activity in CD. Differences in the motion of water molecules between different tissues result in image contrast. Actively inflamed bowel wall impedes the movement of water molecules, hence shows diffusion restriction on DWI [Figure 6]. Diffusion restriction can be assessed qualitatively when it is seen as mural hyperintensity on DWI and corresponding low signal on the apparent diffusion coefficient (ADC) map. It can also be assessed quantitatively by drawing an ROI on the ADC map.[74] DWI may circumvent the need for intravenous gadolinium and is very useful for assessment of disease activity in clinical situations when the use of intravenous contrast is contraindicated, such as in those with renal failure. The utility of DWI for evaluation of disease activity in patients with CD was retrospectively evaluated in 36 consecutive patients with active CD.[29] MRE combined with DWI showed a high sensitivity (93.5%), specificity (89.4%), and diagnostic accuracy (92%) in comparison to MRE alone or DWI alone.

Several objective MR scoring systems have been devised to help in the noninvasive assessment of disease activity in

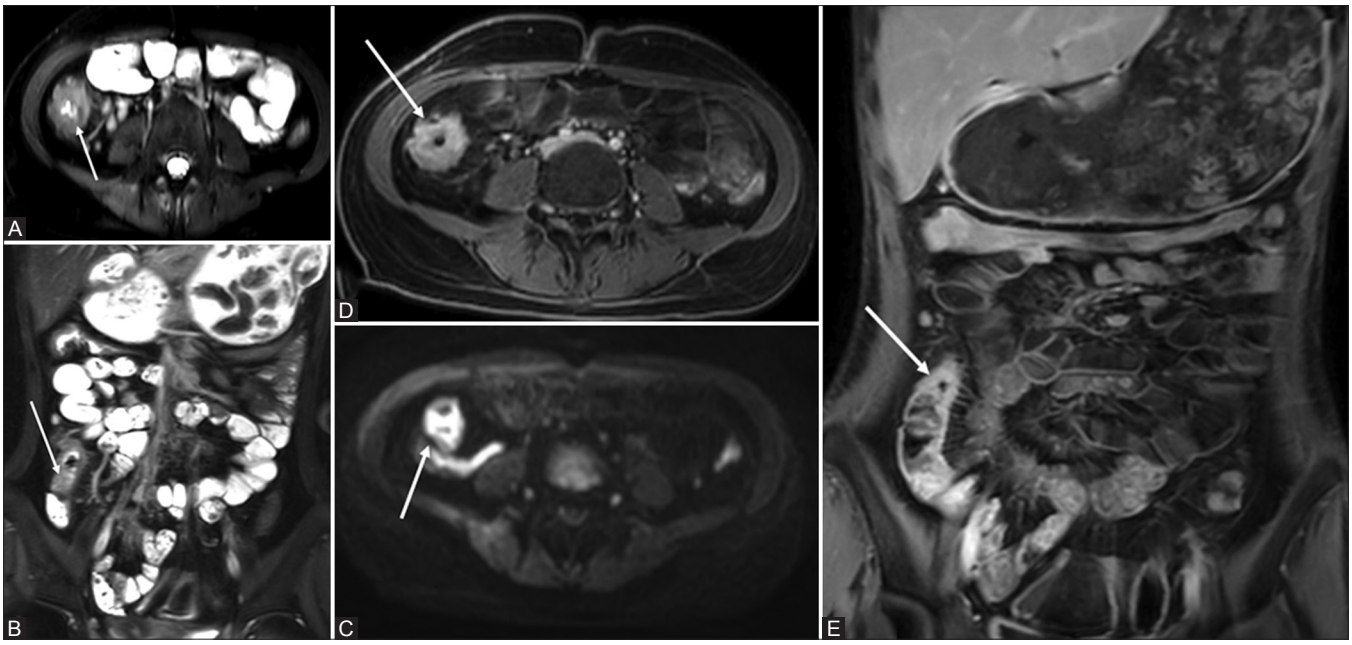

Figure 5 (A-E): Active CD. MRE images showing wall thickening at ileocecal junction (thin arrow) which is hyperintense on T2-weighted images (A and B), shows restricted diffusion on diffusion weighted image (C), and intense enhancement on postcontrast T1 weighted images (D and E). There is associated increased mesenteric vascularity (comb sign) along the mesenteric border of the involved bowel segment. These features are suggestive of active inflammatory stage in CD

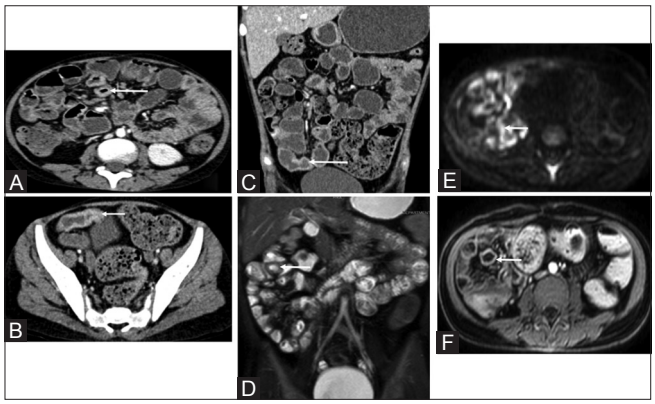

Figure 6 (A-F): Multifocal CD (active). Axial (A and B) and coronal (C) CTE images showing multiple noncontiguous segments of bowel wall thickening (thin arrow). Coronal T2-weighted MRE image (D), diffusion weighted b 800 axial image (E) and postcontrast image (F) confirm the multifocal involvement

CD. The magnetic resonance index of activity (MaRIA) score is based on mural thickness, relative wall enhancement, mural T2 hyperintensity, and ulcers.[75] The Clermont score includes mural thickness, T2 hyperintensity, ulcers and ADC values from the DWI sequence;[76] this score correlates well with the MaRIA score and has achieved excellent results for diagnosing disease activity.[77]

12. While CTE/MRE is good for the assessment of activity disease, mucosal involvement is better assessed by endoscopic examination.

Voting summary: A (87.1%), B (12.9%), C (0), D (0), E (0)

Level of evidence: II-1

Grade of recommendation: B

Direct visualization by endoscopy of the mucosa for active lesions, such as erythema, ulcerations, and friability is best for assessment of the activity of CD. Active lesions in the large intestine can be assessed using colonoscopy, in the terminal ileum by retrograde ileoscopy, in the small intestine by either enteroscopy or capsule enteroscopy, and in the upper GI by UGI endoscopy. CTE is a poor technique for detecting mucosal ulcers. A properly performed MRE may demonstrate moderate to deep mucosal ulcerations (seen as mucosal indentations on an abnormal segment of bowel) to some extent.[78,79] It is often possible to identify discrete deep ulcers, but when there is extensive ulceration or inflammation, ulcers are obscured by diffuse enhancement and mucosal fold thickening.[80] It is hard to see superficial ulcers, mucosal erythema, and mucosal friability on MRE [Figure 7].

Evaluation for differentiation between fibrotic and inflammatory strictures

13. MRE is a preferred imaging modality for differentiation between fibrotic and inflammatory stricture because of its superior contrast resolution and functional information.

Voting summary: A (87%), B (13%), C (0), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

The behavior of intestinal involvement in patients with CD is classified into three distinctive phenotypes: nonstricturing and nonpenetrating, stricturing, and penetrating.[54] As per the European Crohn's and Colitis Organization (ECCO) guidelines on endoscopy in IBD, a stricture in CD is defined as a narrowing of the intestinal lumen.[81] CD is frequently complicated by intestinal strictures[82], with approximately 25% of patients having at least one small intestinal stricture.[83] While the terminal ileum is the commonest site of stricture formation, colonic strictures occur in at least 10% of patients.[83] Patients with CD may present for the first time with the symptom complex of stricturing phenotype; but more often this occurs because of long-standing inflammation.

In addition to stricture detection, differentiation between a predominantly fibrotic stricture and a predominantly inflammatory stricture is of paramount clinical importance, as it has a direct impact on the management of the disease. While patients with active inflammatory strictures are treated with anti-inflammatory drugs, those with fibrotic strictures, if symptomatic, are treated with either endoscopic dilatation or surgical intervention. As per the European Crohn's and Colitis Organization guidelines on endoscopy in IBD,[81] ileocolonoscopy is recommended for the detection of stenosis in the distal ileum and colon, also allowing tissue sampling for dysplasia and cancer. Approximately, 3.5% of colonic strictures demonstrate dysplasia or cancer.[84]

While endoscopic examination can determine disease activity in the mucosa, cross-sectional imaging provides information about the activity in the intestinal wall and perienteric tissues. In the absence of proximal bowel dilatation, the accuracy of detecting a stricture on any imaging technique is deceptive.

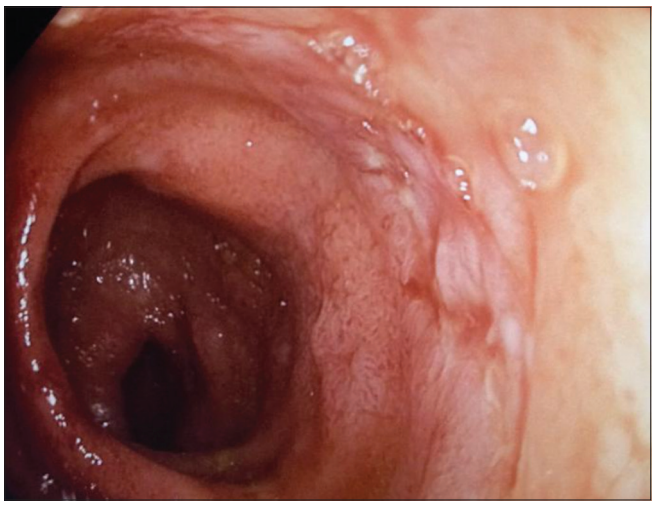

Figure 7: Ileocolonoscopic image showing terminal ileal ulcer in Crohn's disease

While MRE, CTE, and CEUS are used for evaluation of strictures and assessment of transmural and perienteric abnormalities, MRE is the preferred imaging tool for making a distinction between a fibrotic stricture and an inflammatory stricture because of its multiparametric approach, superior contrast resolution, functional information, and lack of ionizing radiation.[85]

14. On MRE, hyperintensity on T2W images and hyperenhancement with stratification of the intestinal wall on postcontrast T1W images are suggestive of inflammatory stricture, whereas hypointensity on T2W imaging and nonenhancing stricture on postcontrast T1W images suggest fibrotic stricture.

Voting summary: A (87.1%), B (12.9%), C (0), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

Strictures in patients with CD can be of three types – inflammatory, fibrotic, and mixed (fibroinflammatory). Various studies have identified and validated the imaging characteristics of active inflammatory stricture on CTE/MRE as: mural thickening >3 mm, deep transmural ulcers resulting in a cobblestone appearance, mucosal fold thickening and hyperemia, mural hyperenhancement and stratification, perienteric inflammation such as engorged and enhancing mesenteric vessels supplying an inflamed intestinal segment (comb sign), and mesenteric edema and enhancement [Figure 8]. In one study, CTE and MRE had similar accuracy for detecting active inflammation.[38] Rimola *et al.*[86] reported that inflammatory strictures were associated with hyperintense signal on T2W images, mucosal enhancement on postcontrast T1W images, ulcerations, and blurred margins. Though T2W imaging may be able to differentiate a predominantly inflammatory (hyperintense signal of the wall) from a predominantly fibrotic (hypointense signal of the wall) lesion,[38,87] occasionally the involved intestinal segment may show a combination of T2 hyperintensity and hypointensity, which indicates the presence of concurrent inflammation in a fibrotic stricture.[88]

The DWI images on MR act as an important surrogate biomarker for identification of inflamed intestinal segments in CD.[29] However, DWI has low spatial resolution and signal-to-noise ratio and is prone to distortion; hence, correlation with the findings on the T2W and postcontrast T1W images is vital.

Monitoring for mucosal healing on ileocolonoscopy is the traditional approach to assess therapeutic response in patients with CD. MRE-based monitoring and evaluation of transmural healing could be used as an alternative

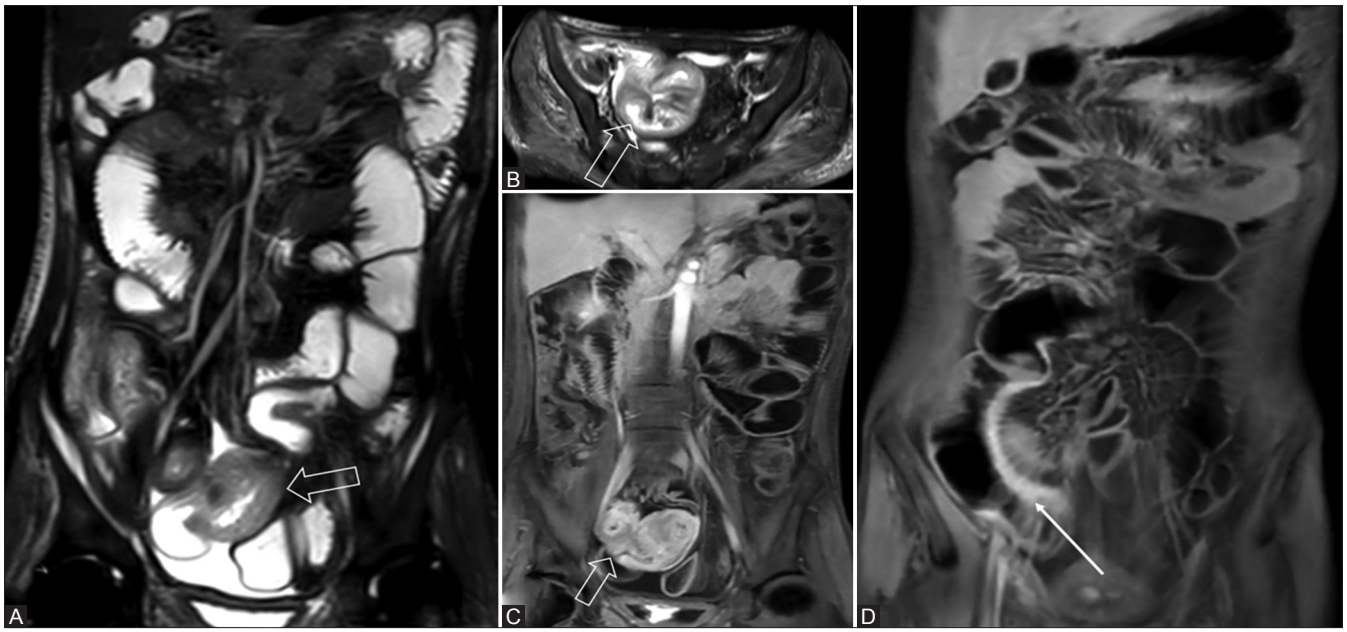

Figure 8 (A-D): Active CD. Coronal MRE (A) and axial T2-weighted images (B) showing segmental wall thickening of a pelvic ileal loop (outlined arrow) which shows T2 hyperintensity (A and B). Coronal postcontrast T1-weighted images (C and D) show stratified mural enhancement, asymmetrical wall thickening involving the mesenteric border of terminal ileum, with intense enhancement (thin arrow). These findings are typical for active inflammatory stage of CD

noninvasive approach to the traditional endoscopically determined mucosal healing. Moy *et al*.[89] investigated MRE findings that could correlate best with mucosal healing as assessed by ileocolonoscopy in 30 pediatric-onset CD patients and showed that an MR index of activity score of less than eight had the highest accuracy for mucosal healing (accuracy 74%; sensitivity 84%; specificity 62%). However, as CD is a transmural inflammatory process, mural inflammation may persist in the presence of mucosal healing.

MRE was significantly more sensitive than CTE in detecting fibrosis in a study by Quencer *et al*.[38] On MRE, fibrotic strictures appear as a persistently narrowed fixed segment, which may or may not be associated with proximal intestinal dilatation, and they demonstrate homogeneously low signal on the T1W and T2W images, inhomogeneous mild mural enhancement, without mural edema or hyperemia, and absence of perienteric or mesenteric inflammation [Figure 9]. Rimola *et al*.[86] evaluated MRI findings in 41 patients with CD who underwent elective surgery and reported that the degree of fibrosis correlated with the percentage of enhancement gain between the 70 s and 7 min scans, the homogeneous pattern of enhancement at 7 min, and the presence of stenosis. The MR feature of percentage of enhancement gain was able to discriminate between mild–moderate and severe fibrosis (markedly higher in segments with intense fibrosis) with a sensitivity of 94% and a specificity of 89%. Fornasa *et al*.,[90] based on T2W and postgadolinium T1 enhancement signal intensities, devised a fivepoint scale for differentiation of a fibrotic stricture from an inflamed stenotic segment. They

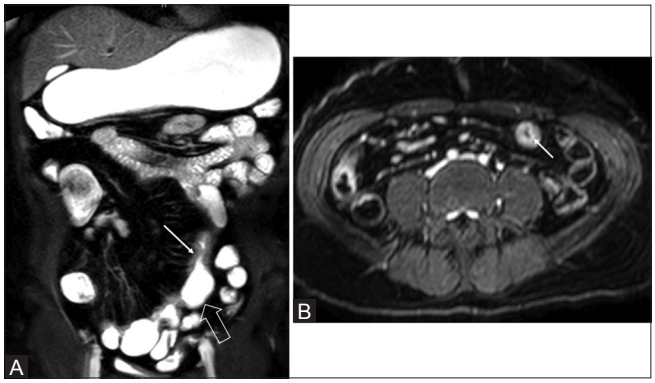

Figure 9 (A and B): Pseudosacculations in fibrotic CD. Coronal T2-weighted image (A) of MRE study showing wall thickening and multiple segments of luminal narrowing involving the ileal loops (thin arrow). Pseudosacculations are seen along the antimesenteric border (outlined arrow). Axial postcontrast T1-weighted image (B) shows homogeneous wall enhancement of the involved loop. These features are characteristic of fibrostenotic stage of CD

reported that using an activity score of 0 or 1, a fibrotic stricture could be diagnosed with 95.8% sensitivity, 100% specificity, and 97.9% accuracy. Pazahr *et al*.[91] showed significantly increased magnetization transfer (MT) ratios in bowel wall segments with fibrotic scarring (35.3 ± 4.0%, $P < 0.0001$) and slightly reduced MT ratios (22.9 ± 2.2%) in intestinal wall segments with active inflammation. The principle behind MT MRI is the exchange of energy between the macromolecules and free water in the surrounding: more the macromolecule in the tissue (which is the case in fibrosis), more transfer of energy to free water protons, resulting in increased MT ratio.

15. Characteristic features of inflammatory stricture on CTE include thickening of the intestinal wall, mural stratification, and hyperenhancement.

Voting summary: A (77.4%), B (19.4%), C (3.2%), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

The features of active CD on CTE include intestinal wall thickening (thickness >3 mm), mural stratification and hyperenhancement, prominent vasa recta (comb sign), and mesenteric fat stranding in the region of the inflamed intestinal wall segment [Figure 10]. Mural hyperenhancement with stratification is the *sine qua non* feature of active CD;[67] however, this feature is not pathognomonic of this condition and may be observed in intestinal tuberculosis, ischemia, and other inflammatory intestinal diseases. In a study on 96 patients, Bodily *et al*.[68] showed a good correlation between disease activity seen on CTE (bowel wall thickening and enhancement) and at ileoscopic examination and histological activity. Prominent vasa recta adjacent to the inflamed intestinal loop (comb sign) and increased attenuation of the mesenteric fat due to transmural extraserosal extension of inflammation are the most specific CT features of active CD.[69] [Figure 11]

16. Characteristics of inflammatory stricture on small bowel ultrasonography include intestinal wall thickening with intestinal hyperemia on Doppler US and intestinal wall enhancement on CEUS.

Voting summary: A (82.8%), B (17.2%), C (0), D (0), E (0)

Level of evidence: II-1

Grade of recommendation: A

CEUS and color Doppler studies are cost-effective noninvasive imaging techniques, which are still underutilized in the work-up of patients with CD in India. A systematic review of 33 studies[52] showed a comparable performance of CEUS, CTE, and MRE for the diagnosis of CD, and CEUS was found to have the highest accuracy in the differentiation between inflammatory stricture and fibrotic stricture. Characteristics of an inflammatory stricture on CEUS include intestinal wall thickening and hyperemia. In a systematic review by Panés *et al*.,[92] CEUS was noted to be an accurate technique for the diagnosis of suspected CD, with sensitivity and specificity of 85% and 91%, respectively, in assessing disease activity. Based on whether the strictured intestinal segment is hypovascular or hypervascular on CEUS, several studies have highlighted the ability of CEUS to differentiate fibrotic from inflammatory strictures.[93,94] While CEUS is a useful imaging technique in the evaluation of the small intestine, expertise for this technique is not widely available yet in India.

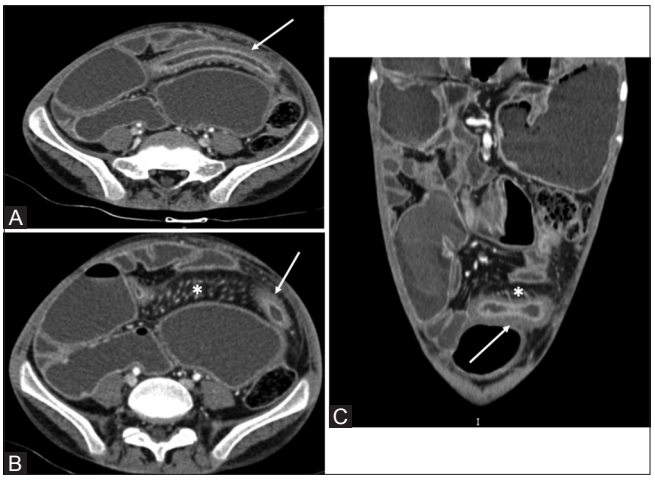

Figure 10 (A-C): Crohn's disease with inflammatory stricture. Axial and coronal CTE images (A-C) showing a narrowed ileal loop with stratified enhancement (arrow) and comb sign (asterisk) causing proximal dilatation

Radiological evaluation for assessment of complications of CD

17. Major complications of CD that require imaging include fistulae, intraabdominal abscesses, intestinal obstruction, intestinal perforation, and malignancy.

Voting summary: A (100%), B (0), C (0), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

Internal fistula and abscess formation are grouped under penetrating disease and they are considered as major complications of CD[54] that can occur during the course of the disease.[82] A third of patients with CD develop fistulae and abscess.[95] Another study showed presence of penetrating disease at the time of presentation in 15% of patients with CD.[53] As disease progresses, the rate of complications is also expected to increase. Symptoms of penetrating disease are nonspecific and clinical examination alone is not sufficient to detect these complications; approximately half of the fistulizing complications detected on imaging are missed on clinical examination alone.[96]

CTE and MRE are optimal for detection of complications of CD. Fistulae are seen as linear hyperdense structures with or without branching on CECT[96] or as T2 hyperintense lesions on MRI. They show intense enhancement after contrast administration.[97] Abscess is seen as fluid collection with peripheral enhancement with or without air pockets.[97]

Although intestinal obstruction is most commonly seen in long-standing CD, it can sometimes be the initial

presentation of the disease. The segment upstream to a strictured segment is dilated with a definite point of transition.[98] Imaging findings of perforation peritonitis are extraluminal air, free fluid in abdomen or collection.[99]

The risk of developing small intestinal as well as colorectal malignancies is higher in long-standing CD.[100] Mass lesion involving a focal area with loss of mural stratification, extraserosal soft tissue, and associated enlarged lymph nodes are features suspicious for malignancy.

18. CTE and MRE have comparable diagnostic yield for detection of enteroenteric, enterocolic, enterovesical, and rectovaginal fistulae.

Voting summary: A (92.7%), B (7.3%), C (0), D (0), E (0)

Level of evidence: I

Grade of recommendation: A

Internal fistulae in patients with CD may be enteroenteric, enterocolic, enterovesical, rectovaginal, or enterocutaneous.[101] Presence of internal fistulae indicates active disease and they are seen as hyperdense linear structures on CT and hyperintense structures on T2W MRI images.[92] They cause mesenteric fat stranding and wall thickening of the involved intestinal loops. Complex enteroenteric fistulae cause tethering of multiple bowel loops to a single point, giving a stellate appearance on cross-sectional imaging [Figure 12].

The pooled sensitivity and specificity of CTE and MRE for the detection of fistula are 70% and 97% and 76% and 96%, respectively.[39,102] The sensitivity and specificity of ultrasonography in detecting nonperianal fistulae are 71% and 96%, respectively;[103] its accuracy depends on the location of the fistula.

19. CT and MR have comparable diagnostic yield for detection of intraabdominal and pelvic abscesses.

Voting summary: A (90.3%), B (9.7%), C (0), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

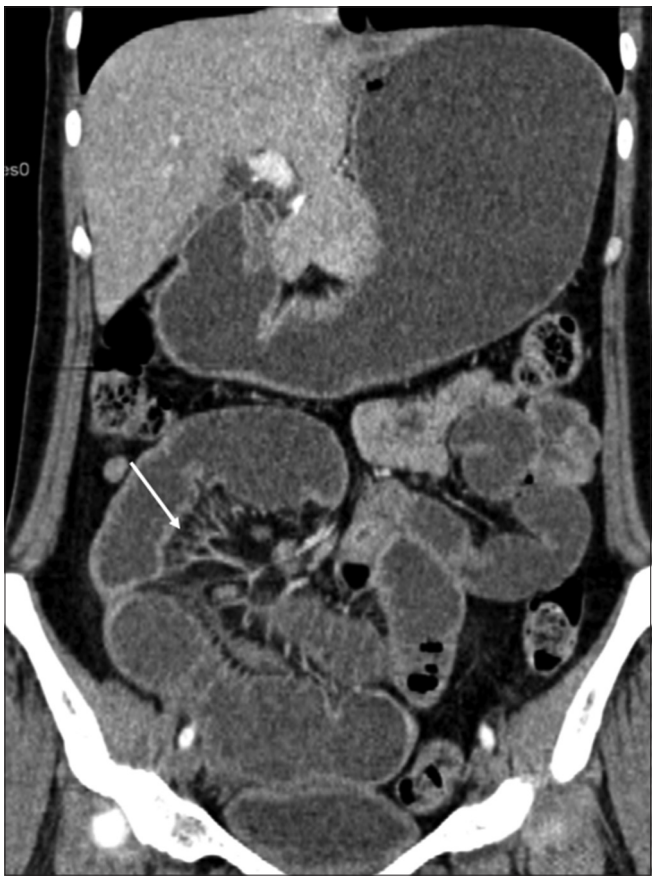

Figure 11: Comb sign in active CD. Coronal CTE image showing a segment of dilated ileal loop with increased mesenteric vascularity (comb sign) (thin arrow) in CD. Comb sign is a marker of active inflammatory stage of CD. Small subcentimeter homogeneous lymph nodes are also noted

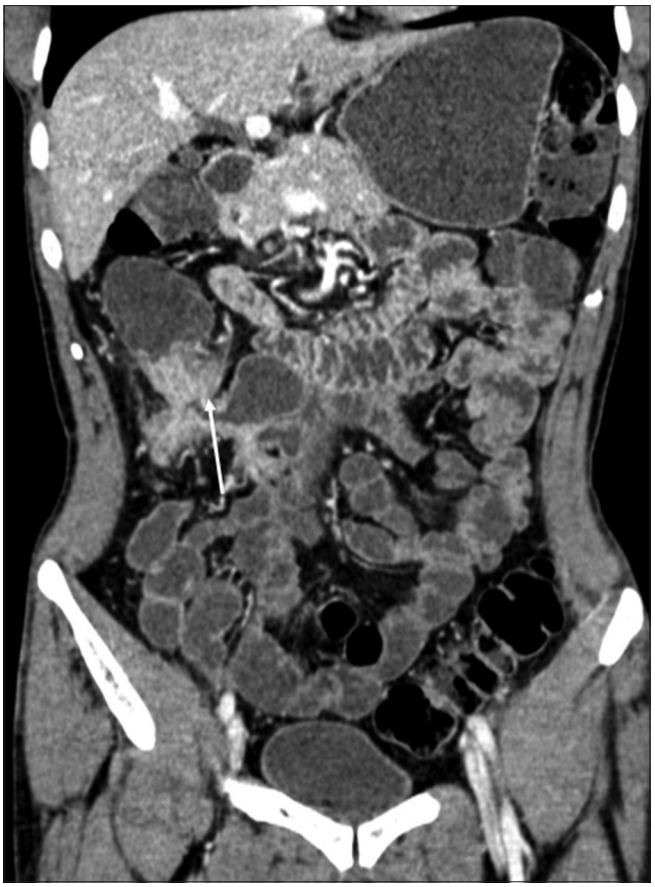

Figure 12: Fistulizing stage of CD. Coronal CTE image showing abnormal thickening, distorted stellate configuration, and communication between the small bowel loop and the ascending colon (thin arrow) suggestive of enterocolic fistula

Intraabdominal abscess formation is a sign of active disease. On US examination, abscess is seen as a hypoechoic collection with varying amounts of internal echoes.[103] On CT, it is seen as a hypodense collection with peripheral enhancement usually in the vicinity of an involved intestinal segment.[39,103] CT scan is the best modality to show air pockets within intraabdominal abscesses.[103] The surrounding mesentery may also show features of inflammation. On MR, abscesses are seen as T2 hyperintense collections, which enhance peripherally after contrast administration.[39] On DWI, abscess shows diffusion restriction, which differentiates it from fluid within intestinal loops. DWI is particularly useful when administration of contrast is contraindicated.

The accuracy of CT and MR in diagnosing intraabdominal abscesses is comparable. The reported sensitivity and specificity of CT and MR for detecting abscess are 84% and 97% and 86% and 93%, respectively.[92] US of the abdomen can be used as an alternative modality if intraabdominal abscess is suspected. It has a reported sensitivity and specificity of 84% and 93%, respectively.[103] US has the added advantage that it lacks radiation and the machine can be taken to the bedside. However, the modality is operator dependent and depends on the location of the abscess: deep-seated abscesses in the pelvis can be missed on US.

20. Perianal fistula should be defined as simple or complex type. The extent (supra- or infralevator), routes and activity of the fistula and any associated perianal abscess should be defined.

Voting summary: A (80.6%), B (3.3%), C (0), D (0), E (16.1%)

Level of evidence: II-2

Grade of recommendation: B

Perianal fistulae can be classified as simple or complex type based on their location, number of openings, involvement of adjacent structures, and complications.[63] Simple fistulae are generally located below the levator ani, have single opening, and are not associated with surrounding abscesses. Complex fistulae are generally supralevator in location, may have multiple openings and/or multiple ramifications of the fistulous tracts, can be complicated by abscess (es), and may involve adjacent structures. The management of perianal fistulae depends on the type of fistula, activity of the fistula, associated complications, and the activity of the disease in the intestine.[104,105]

Traditionally, examination under anesthesia has been used to evaluate perianal fistulae.[64] Currently, pelvic and perineal MRI, transperineal US and endoanal US are used for this purpose.[64] Imaging is used to delineate the extent of the fistula (number of openings, ramifications, extent and relationship with sphincter), and to detect abscess formation and associated complications[106] [Figure 13]. MRI is accurate in diagnosing and delineating the extent of fistulae, with sensitivity and specificity of 81% and 100%, respectively.[107] It is also excellent in delineating abscesses and their relationship with adjacent structures such as sphincters. The length of a fistulous tract on MRI can be a predictor of prognosis.[107]

While endoanal US is able to detect a fistulous tract and abscesses with reasonable accuracy,[108] it is invasive and may not be suitable especially during acute perianal disease. Endoanal US may also not be feasible in the presence of anal canal stenosis. Transperineal US is another valuable technique that is inexpensive and noninvasive. It has excellent agreement with MRI findings in the classification of the type of fistulae, but has poor sensitivity for detection of abscesses.[109]

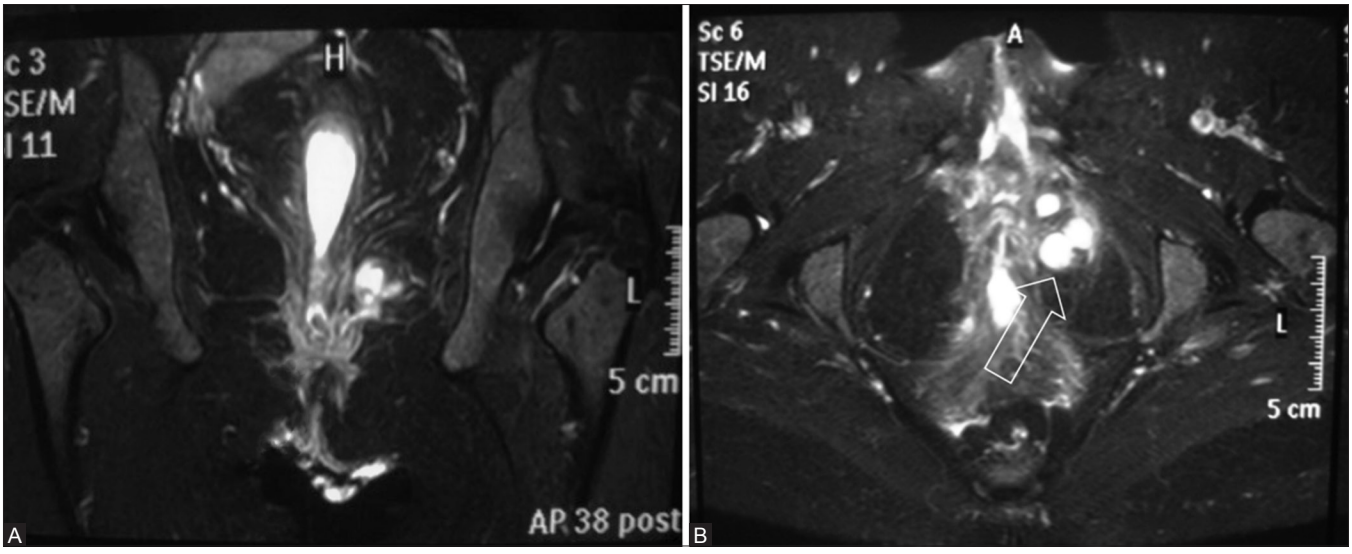

Figure 13: Perianal fistula in CD. T2-weighted coronal (A) and axial (B) images showing complex fistulous tract and collections (arrow) in the left ischioanal fossa. Fistula and sinus tracts are markers of inflammatory stage in CD

21. MR is the preferred modality for follow-up evaluation for complications of CD.

Voting summary: A (93.2%), B (3.4%), C (3.4%), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

The use of CTE for follow-up imaging at multiple time points increases the cumulative radiation dose, which is the most important reason for the use of MRE or US although CTE has diagnostic accuracy comparable to MRE.[110–112]. US can be used depending on the site and type of involvement.

Evaluation for monitoring of activity of disease

22. In the appropriate clinical setting, cross-sectional imaging can supplement clinical parameters, inflammatory markers, and endoscopic characteristics for monitoring the activity of CD.

Voting summary: A (75.9%), B (24.1%), C (0), D (0), E (0)

Level of evidence: III

Grade of recommendation: C

The frequency and time interval at which imaging should be repeated for assessment of disease activity is not well established and should be based on clinical features and inflammatory markers. Mucosal healing, and not just remission of clinical symptoms, should be the aim of therapy in patients with CD. Mucosal healing is characterized by endoscopic remission in addition to clinical remission and has been associated with better long-term outcomes including higher rates of steroid-free clinical remission and lower hospitalization rates and surgeries.[113,114] To document this, cross-sectional imaging can be used along with inflammatory markers and endoscopy.[115] Segments of the intestine that are not accessible by endoscopy should be assessed using cross-sectional imaging.

23. While MRE and CTE are comparable for monitoring of disease activity, MRE is preferable because of lack of radiation risk.

Voting summary: A (86.7%), B (10%), C (3.3%), D (0), E (0)

Level of evidence: I

Grade of recommendation: A

Since MRE is free of ionizing radiation, it should be preferred over CTE for repeated assessment of disease activity in the small intestine.[116] In a systematic review and meta-analysis including 290 patients with CD from six studies,[35] the pooled sensitivity and specificity for MRE in detecting active small intestinal CD were 87.9% (95% confidence interval, CI, 81.8, 92.5) and 81.2% (95% CI: 71.9, 88.4), respectively; corresponding figures for CTE were 85.8% (95% CI: 79.2, 90.9) and 83.6% (95% CI: 75.3–90.1), respectively. There was no incremental yield of MRE over CTE. In another meta-analysis of 19 articles, there was comparable efficacy of CTE and MRE in grading CD in the per-patient analysis.[72]

24. CEUS can be used for monitoring of disease activity.

Voting summary: A (75.9%), B (20.7%), C (3.4%), D (0), E (0)

Level of evidence: II-1

Grade of recommendation: B

CEUS involves the use of specialized software and US contrast agents (gas-filled microbubbles of size 2–6 microns) injected intravenously. These microbubbles act as echo enhancers and increase signal from blood. They have been used to evaluate enhancement patterns and assessment of vascularity of lesions in solid organs such as liver and pancreas.

Studies have been performed to evaluate the efficacy of CEUS in determining activity and quantification of disease activity in patients with CD on follow-up.[94] In active CD, increased angiogenesis results in increased intestinal wall perfusion. On CEUS, several patterns of intestinal wall enhancement have been described in patients having active CD. In a meta-analysis of eight studies including 332 patients with CD, disease activity as assessed by CEUS had pooled sensitivity of 94% (95% CI 0.87, 0.97) and pooled specificity of 79% (95% CI 0.67, 0.88).[117]

Evaluation for postoperative recurrence

25. MRE is preferred over CTE for detection of postoperative recurrence of disease in the small intestine.

Voting summary: A (75.9%), B (24.1%), C (0), D (0), E (0)

Level of evidence: II-2

Grade of recommendation: B

Although there is no study comparing the efficacy of different imaging modalities for the evaluation of recurrence of CD in postoperative patients, MRE has the advantage of being radiation free. Ojea *et al.* reported that MRE, in comparison to ileocolonoscopy, had sensitivity, specificity, and positive and negative predictive value (PPV and NPV) of 100%, 60%, 92.6%, and 100%, respectively, for the assessment of postoperative recurrence.[118] In another study, there was moderate degree of concordance between MRE and

ileocolonoscopy for assessment of postoperative recurrence. By classifying patients into high grade and low grade groups, based on severity of the recurrence and need for surgery, concordance was excellent (k = 0.87), with 85% sensitivity, 100% specificity, 100% PPV, and 76.9% NPV. In a study including 30 patients suspected to have recurrence of CD, who underwent MRE and colonoscopy, a new severity-based MR score (0–3) was compared with the endoscopic Rutgeerts score.[119] The mean observer agreement for total score was 77.8%. The level of agreement increased to 95.1% when scores above or below the MR score of 2 were compared.

In another study including 32 patients with CD who underwent surgery, CTE was used to detect recurrence using a previously validated score and compared with ileocolonoscopy using Rutgeerts score.[120] Good correlation was observed between the two modalities (r = 0.782, P < 0.0001).

Evaluation before instituting biologics

26. CECT chest may be added to radiograph of the chest, interferon gamma-release assay (IGRA**), and tuberculin skin test (TST) as screening tests for latent tuberculosis prior to starting biologic therapy.**

Voting summary: A (84.6%), B (15.4%), C (0), D (0), E (0)

Level of evidence: II-3

Grade of recommendation: C

Latent tuberculosis is defined as a state of persistent mycobacterial viability and immune control with no evidence of clinically manifesting active tuberculosis.[121] Currently, there is no universally acceptable gold standard for the diagnosis of latent tubercular infection. One of the major reasons for this is the wide disparity in the prevalence of tuberculosis in developed versus developing countries.

Latent tubercular infection is usually diagnosed by either the TST or interferon gamma-release assay. TST may be falsely positive in individuals vaccinated with Bacillus Calmette Guerin vaccine BCG) at birth and may be falsely negative in individuals who are on immunosuppressants.[122,123] Interferon gamma-release assay was introduced with the assumption that its specificity would be higher vis-à-vis TST, but several recent studies have suggested that it is equally prone to false-negative results in patients who are on immunosuppressants.[124] These facts have been validated by several reports of reactivation of tuberculosis in patients exposed to biologics who had tested negative for latent tubercular infection prior to the initiation of the biological therapy.[125,126] The reactivation is characterized by disseminated tuberculosis in more than 25% of patients, with a significantly high mortality rate reported in the initial study by Keane *et al*.[127] Thus, there is a pressing need for improving the sensitivity of diagnostic tests for latent tubercular infection especially in regions of the world where tuberculosis is endemic.

Chest radiography is poor in detecting small lung nodules and mediastinal nodes.[128] CECT of the chest is an excellent modality for the diagnosis of tuberculosis. Features suggestive of latent tuberculosis on CECT chest include pleural thickening, fibrotic scarring, calcified nodules, and calcified hilar or mediastinal lymphadenopathy.[129,130] A recent study from Shanghai showed that 23% of patients with inflammatory bowel disease had radiological abnormalities suggestive of latent tubercular infection on CECT of the chest.[131] The commonest abnormality identified was pleural thickening in 55 of the 102 (54%) patients who had abnormal CECT chest. The concordance rate between CECT chest and IGRA (T spot) was 75%. The authors strongly recommended the usage of CECT chest as a supplementary test in combination with IGRA for screening for tuberculosis in countries having a high prevalence of tuberculosis.

Imaging for differentiation between CD and intestinal tuberculosis

27. CTE/MRE complements other modalities in differentiation between ITB and CD.

Voting summary: A (76.9%), B (23.1%), C (0), D (0), E (0)

Level of evidence: II-1

Grade of recommendation: A

In countries where tuberculosis is endemic, the closest differential diagnosis of CD is ITB. Both CD and ITB have overlapping clinical, endoscopic, histological, and radiological characteristics, which makes differentiating them a challenging task.[132-138] While clinical characteristics alone cannot differentiate the two diseases, endoscopic examination is limited by its invasiveness and poor access to segments of the small intestine other than distal ileum or proximal jejunum. Although certain histological and microbiological features such as caseating granuloma or a positive mycobacterial culture are considered the gold standard,[139] they are seen in only a small subset of patients having ITB.

CTE/MRE can image the entire small intestine along with delineation of extraintestinal manifestations such as lymph node and mesenteric changes, which helps in differentiating these two diseases and hence they complement other investigations in differentiation between CD and ITB. Recently, a model based on radiological characteristics on CTE has been reported to show good specificity (90%) and PPV (80%) for differentiation between CD and ITB.[140] A study from China showed an increase in the diagnostic accuracy

from 66.7% to 95.2% when radiological characteristics on CTE were combined with colonoscopic characteristics for differentiation between CD and ITB.[141] Another study from China showed that the sensitivity, specificity, diagnostic accuracy, PPV and NPV of a mathematical regression model based on composite clinical, endoscopic and CTE characteristics were 97.8%, 96.8%, 97.6%, 98.9%, and 93.7%, respectively for differentiation between CD and ITB.[142] Similarly, MRE has also been shown to be useful in the evaluation of CD and ITB and thus may be useful in their differentiation[78,143] [Figure 14].

28. Presence of lymph nodes greater than 1 cm in size with central necrosis favors a diagnosis of ITB over CD.

Voting summary: A (92.3%), B (7.7%), C (0), D (0), E (0)

Level of evidence: II-1

Grade of recommendation: A

Regional lymphadenopathy has been described in more than 80% of patients with ITB.[144,145] The size of these nodes varies from 0.6 cm to 4.5 cm, with mean of 1.8 ± 3.3 cm.[144-146] The presence of hypoenhancing area within the node along with peripheral enhancement suggests caseation in the lymph nodes and occurs in 40% to 67% of them.[144,147] Thus, presence of lymph nodes larger than 1 cm with central necrosis in the clinical setting of ulceroconstrictive disease suggests a diagnosis of tuberculosis, as necrotic nodes are not seen in patients with CD [Figure 15].

Necrotic lymph nodes, although considered diagnostic of ITB, are not pathognomonic as they may be seen in other conditions such as metastasis (from primary cancer in the head and neck or gall bladder), lymphoma, pyogenic infection, and Whipple's disease.[148] Hence, other factors should also be taken into consideration for making a diagnosis of tuberculosis. In contrast to larger size of lymph nodes in patients with tuberculosis, the lymph nodes in patients with CD are smaller (mean size 0.9 mm) and show homogeneous enhancement on CECT.[146] In a recent meta-analysis of six studies (612 patients; 417 CD, 195 ITB) evaluating the role of CT in differentiation between CD and ITB, lymph nodes with necrosis was reported to have the best specificity (100%) and diagnostic accuracy (odds ratio: 30.2).[149]

29. Presence of skip lesions (>3), long-segment involvement (>3 cm), comb sign, fibro-fatty proliferation, left colonic involvement, and asymmetric thickening favor the diagnosis of CD over ITB.

Voting summary: A (87%), B (13%), C (0), D (0), E (0)]

Level of evidence: II-2

Grade of recommendation: B

While involvement of the intestine is characteristically discontinuous in patients with CD, discontinuous lesions are well described in patients with ITB as well. In a recent study from India, radiological features that were more common in patients with CD as compared to ITB were involvement of the left colonic segment (22% vs 6%),

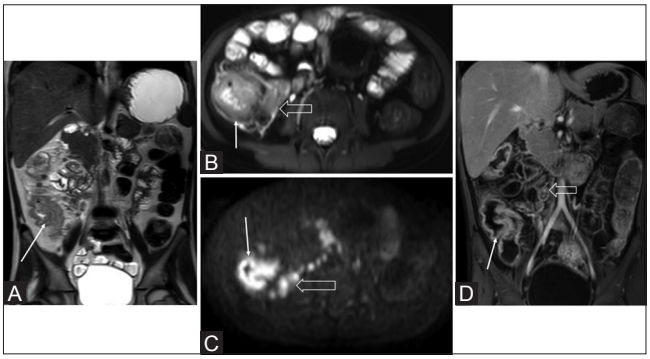

Figure 14 (A-D): Ileocecal TB. T2-weighted MRE images (A and B) showing wall thickening that is hyperintense involving the ileocecal region (thin arrow) with enlarged regional lymph nodes (outlined arrow). The wall thickening and enlarged nodes show diffusion restriction on diffusion weighted b 800 image (C) and hyperenhancement on postgadolinium image (D) along with necrotic enlarged lymph nodes

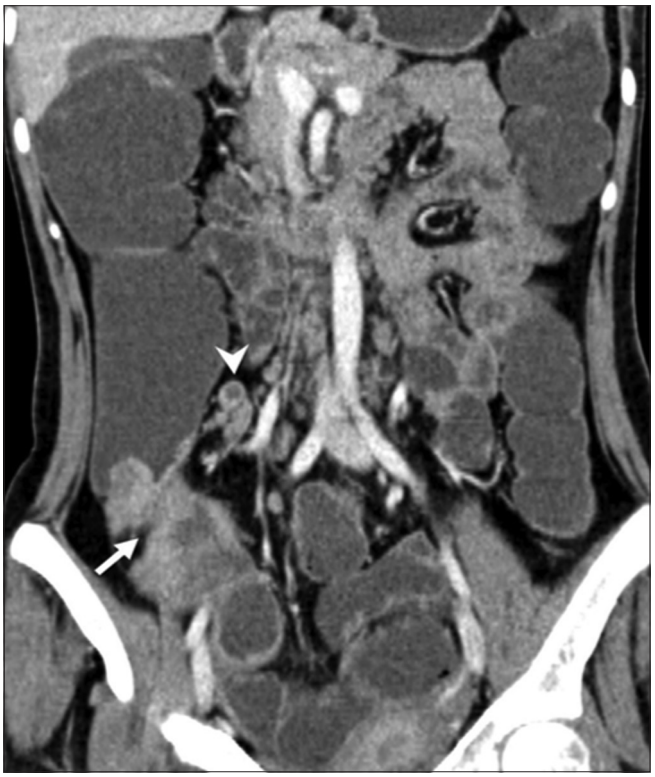

Figure 15: Coronal contrast-enhanced CT enterography image showing short-segment wall thickening and enhancement of ileocecal junction and cecum (arrow) with adjacent mesenteric necrotic lymph node (arrow head)

long-segment involvement (69% vs 28%), presence of skip lesions (63% vs 42%), and presence of comb sign (44% vs 20%). On the other hand, involvement of ileocecal area (70% vs 43%), shorter length of involvement, and presence of lymph nodes larger than 1 cm (20% vs 2%) were more common in ITB.[140] A predictive model based on three characteristics (ileocecal area involvement, larger lymph nodes, and long-segment involvement) had good specificity (90%) and PPV (80%) in differentiating CD from ITB. In a study from China, asymmetric wall thickening, segmental intestinal involvement, comb sign, and mesenteric fibro-fatty proliferation were significantly more common in patients with CD than in those with ITB. Segmental small intestinal involvement and comb sign were independent predictors of CD, and adding these features to colonoscopic findings significantly improved the accuracy of the diagnosis.[141] Park *et al.*, in addition to confirming these findings, also showed that focal (<5 cm) segmental involvement of the intestine occurred in 100% and 56% of patients with ITB and CD, respectively.[150] In a meta-analysis of six studies, comb sign and skip lesions were reported to have the best diagnostic accuracy, with sensitivity, specificity, and diagnostic odds ratio of 82%, 81%, 21.5 and 85%, 76%, 16.5, respectively.[149] Characteristics such as fibro-fatty proliferation, asymmetric bowel wall thickening, and left colonic involvement were observed to be very specific for CD, with specificity reaching up to 90%. Similar findings were also reported recently in another meta-analysis.[151] Studies have also shown that involvement of the descending colon, sigmoid colon, and rectum is significantly more common in patients with CD than in those with ITB.[140,142,151]

In addition to these features, two studies evaluated the role of visceral fat quantification in the differential diagnosis of CD and ITB.[152,153] In the study from India, 75 patients were included in a derivation cohort; visceral-to-subcutaneous fat ratio had sensitivity and specificity of 81% and 82%, respectively in differentiating CD from ITB. These results were validated in a prospective cohort yielding similar sensitivities and specificities.[152] Therefore, visceral fat quantification on CT may be a useful marker for differentiation between CD from ITB [Figure 16].

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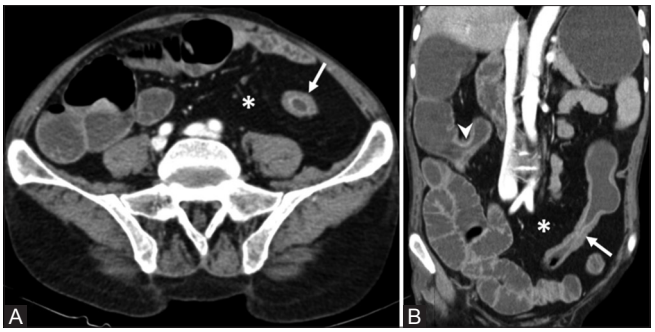

Figure 16 (A and B): Axial (A) and coronal (B) contrast-enhanced CT enterography images showing long-segment wall thickening and mucosal enhancement of descending colon (arrows) with increased visceral fat (asterisks). Another short-segment involvement of ileocecal junction is noted (arrow head)

Conflicts of interest

There are no conflicts of interest.

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