

Evaluation of Crohn's disease Activity: comparison of magnetic resonance enterography with conventional colonoscopy, laparotomy and biopsy

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Abstract: Objectives: Magnetic resonance imaging (MRI) represents a noninvasive imaging tool in assessing Crohn's disease activity because of its high soft tissue resolution, multi-planarity and lack of radiation. To evaluate this approach for patients with inflammatory bowel disease, we compared MRI with laparotomy, colonoscopy and biopsy to assess the presence and extent of ten sign of bowel inflammation and define a diagnostic criterion. **Methods:** 41 patients who were suffering from crohn's and had been under colonoscopy or laparotomy and biopsy, were studied with MR Enterography. The existence of 10 sign of Crohn's disease was assessed. **Results:** MRI with regard to the carried -out protocol of this study, led to the proper diagnosis of 19 cases out of the 21 cases of the active Crohn's disease confirmed by laparotomy or colonoscopy and biopsy. Generally, the sensitivity and specificity of MRI were assessed 90.5% and 90% respectively (PPV=95%, NPV=81.8%). The symptoms related to mural involvement of small bowel including mural thickening, enhancement, edema, stratification, multi segmental involvement and comb sign were of high sensitivity and specificity. **Conclusions:** MRI has high sensitivity and specificity for diagnosing Crohn's disease activity and is an excellent imaging modality for assessment of Crohn's disease activity.

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Introduction

Crohn's disease is a chronic inflammatory disease of uncertain etiology. In most cases, it begins from an early age usually in their 20s and 30s and in the course of many years frequently flares and causes many complications for the patient (1). The typical course is one of remissions, relapse, and progression of disease and recurs in 40% to 80% of patients following intestinal surgery, always in the same location within 2 years (2). Crohn's disease can involve any part of the gastrointestinal tract from the esophagus to the anus. The most common sites of involvement include the distal small bowel and the proximal colon; the ileocecal area involvement occurs in approximately 50% of patients, the small bowel alone in 30% to 40% (3) and the colon alone in 20% to 27% (4). An increased risk of small and large bowel adenocarcinoma is likely to be present in patients with Crohn's disease (5, 6), and an excessive rate of lymphomas has also been reported (7). Crohn's disease has certain systemic complications such as arthritis or spondylitis, avascular necrosis caused by corticosteroid therapy, and an increased incidence of

gallstones and nephrolithiasis (5). In a patient with Crohn's, each time the abdominal and gastrointestinal symptoms flare, a noninvasive, low risk and available, repeatable imaging modality is needed to inspect the abdomen and pelvis for possible involvement of the gastrointestinal tract and its extra mural complications. So far, there has not been a single diagnostic gold standard to diagnose the Crohn's disease, and diagnosis of this disease is based upon a combination of clinical, laboratory, histopathologic(epithelioid granulomas ,transmural inflammatory cell infiltrate and absence of identifiable infectious agents), endoscopic findings (Cobblestoning, discontinuous ulceration, fistula)and laparotomy findings (mesenteric lymphadenopathy, bowel wall thickening or induration and serosal involvement showing creeping fat or other inflammatory changes) (8). There are several imaging methods but none of which are able to display all the mural and extramural complications of Crohn's disease together and each has its own disadvantages. For example Small Bowel Follow Through and Enteroclysis, the traditional methods for radiographic

examination of the small bowel are limited by segmentation and flocculation of barium, overlap of bowel loops, unpredictable transit time and the risk of radiation (5). CT Enterography which also uses radiation has a low soft tissue resolution in comparison to MRI and its intravenous contrast has contraindications such as hypersensitivity and nephrotoxicity (1). Techniques such as capsule endoscopy are not available everywhere and are only able to demonstrate mucosal lesion, but transmural and extramural lesion of Crohn's can't be investigated with this method, and in cases of stricture cannot be used because of capsule retention (9). Colonoscopy is a valuable method to assess the activity of Crohn's disease, which demonstrate mucosal lesions of the colon and distal part of terminal ileum, but are limited by occasional failure to reach the proximal part of ileum and jejunum and under the conditions of active inflammation of the intestinal wall; it raises the risk of perforation. Considering all the above points, MRI without radiation, being noninvasive, with high soft tissue resolution and multi-planarity is able to view mucosal, transmural and extramural lesions of Crohn's disease; at the same time other abdominal and skeletal lesion is also showed. And nowadays it is available in many centers. MR Enterography disadvantages include: Lack of MRI technicians familiar with these protocols, Claustrophobia in some patients, Patients with a pacemaker and other metallic prostheses, some patients intolerant to drink intraluminal contrast. In a few studies, MRI has higher sensitivity and specificity in comparison to other techniques such as Enteroclysis, CT Enterography, CDAI (Crohn's Disease Activity Index) and CRP(C-reactive protein) in assessment of Crohn's disease activity. So far studies of Crohn's MRI have generally described their results as either positive or negative and a small number of signs have been evaluated. (10-13). Only in Lasocki and colleagues study, each MRI signs of Crohn's disease activity has been studied and compared with colonoscopy and biopsy (14). More than 10 different MRI signs are listed for Crohn's disease activity in the literature.

In this article we want to study the sensitivity, specificity, positive and negative predictive value of each sign separately including: wall thickness, enhancement, Stratification, mural edema, nodular thickening, stricture, lymphadenopathy, fistulas, Comb sign, and multi-segmental involvement (15, 16), found the most valuable signs in the evaluation of Crohn's disease activity and based on them assessed the sensitivity and specificity of MR Enterography in comparison to histopathology sample was taken during laparotomy or colonoscopy.

Materials and Methods

In this study which lasted from February 2009 to October 2011, The small bowel and colon of 41 known patient of crohn's who had referred to us with exacerbation of gastrointestinal and abdominal symptoms were divided into 8 segments (jejunum, ileum, ileocecal, ascending colon, transverse colon, descending colon, sigmoid and anorectal) and they underwent colonoscopy and the biopsy was taken from the involved segments of colon and terminal ileum, if possible.

Nine Patients underwent surgery due to the complications of the crohn's disease and from their involved segments of jejunum and ileum histopathologic sample was taken and crohn's activity in colon's segments to terminal ileum was determined based on the findings of colonoscopy and biopsy.

The activity of crohn's in the small bowel was also assessed in the patients who underwent surgery based on the findings of laparotomy and biopsy.

Only the patients whose histopathologic results approved of the crohn's disease were included in this study, and those who had the other intestinal diseases like TB or diverticulitis or ulcerative colitis and or were not able to drink the optimal amount of intraluminal contrast were excluded from the study; as a result 31 patients remained in the study. The interval of at least 2 weeks MR enterography was done using a 1.5 Tesla Siemens Avanto scanner (Germany).

Used sequences were both transverse and coronal of half-Fourier acquisition single-shot turbo spin echo (HASTE) technique and true fast imaging with steady-state precession (TRUE FISP) and using fast gradient echo T1-weighted sequences with and without intravenous contrast with 50 seconds scan delay time. Patients were on liquid diet the day before MR Enterography and 50 minutes before imaging gradually drank 1200 to 2000 ml of intraluminal contrast including water and polyethylene glycol (PEG) (Sepidaj, Iran). Immediately before MRI, 20 mg of hyoscine N-butyl bromide was injected to reduce small bowel peristalsis and then imaging was performed. Note that a critical factor for optimal quality of MR Enterography images is distending the bowel lumen with intraluminal contrast In order to achieve this, at first, a T2 HASTE coronal image was taken, and as a rule because bowel lumen was full of intraluminal contrast the protocol of imaging continued; otherwise, the patient would be given more intraluminal contrast so that the bowel lumen would be distended enough. Images were blindly reported by two radiologists independently and each of the eight segments of their bowel was studied separately, regarding the presence of 10 signs of crohn's activity.

MRI findings in each segment were compared with the laparotomy / colonoscopy and biopsy results and findings which were agreed upon by both investigators were accepted. The points of disagreements were examined by both radiologists together again and the consensus results were accepted.

Results

Out of 31 patients 15 were male (48/4%), and 16 were female (51/6%). The patient's age range was from 19 to 58 (33/5±10/6). MRI findings in each involved segment were compared with the results of colonoscopy, laparotomy and biopsy; sensitivity, specificity, positive predictive value and negative predictive value of each sign were analyzed separately (table 1).

Mural thickening of more than 4 mm was considered pathologic, which was seen in 21 patients. 20 of them had active Crohn's and 1 was passive. In the involved segments, minimum mural thickening was 8 mm and the maximum was 13 mm, and the average of mural thickening in active Crohn's was 9.29 mm and in the passive one it was 3.75 mm (Fig. 1). Mural enhancement was considered either equal to or more than the intensity of spleen at same phase (50 second delay time), which was observed in 21 cases (Fig. 1, 2). Stratification was seen in 14 cases, all of which had active Crohn's (Fig. 3). High signal areas in the intestinal wall in the T2 sequence indicating the existence of wall edema were observed in 19 patients (Fig.4).

Engorgement of mesenteric vessels (Vasa recta) indicating comb sign was seen in 15 cases (Fig. 1D). Multisegmental involvement a good sign for diagnosing crohn's was seen in 18 patients (Fig. 5).

Mesenteric lymphadenopathy was seen in 13 patients; the minimum diameter of lymph node was 5

mm and its maximum was 9 mm. Nodular wall thickening was observed in 12 patients (Fig. 6), stricture in 7 (Fig. 7) and perianal fistula in 2 (Fig. 8). In one Crohn's patient who was suffering from hip pain, bilateral femoral head avascular necrosis (AVN) due to long term corticosteroid therapy was diagnosed incidentally by MRI.

Discussion

Marked increase in wall thickness and mural enhancement (Fig. 1, 2) had the highest sensitivity and specificity in predicting disease activity and after them wall edema (Fig. 4), multi-segmental involvement (Fig. 5), comb sign (Fig. 1D) and stratification (Fig. 3) had the highest sensitivity and specificity. Although the most specific signs such as stricture (Fig7), fistula (Fig. 8), and nodular wall thickening (Fig. 6) had a lower sensitivity (table 1). Stricture was seen in 7 cases, only 4 of which were active Crohn's disease and in comparison with other signs, had the least sensitivity and specificity (Fig. 7). Intra-peritoneal free fluid which only detected in one patient was not a reliable sign for assessment of Crohn's disease activity (Fig. 8). Based on the results of laparotomy/colonoscopy and biopsy, 21 cases of 31 patients had active disease and based on the results of MR Enterography, 20 cases had active disease. Disease activity in 19 patients were correctly diagnosed and only two MRI result was false negative and one false positive. for defining a diagnostic criterion for crohn's disease activity. If we choose at least presence of three sign from ten sign including wall thickening, enhancement, wall edema, nodular wall thickening, stratification, lymphadenopathy, fistula, stricture, multi-segmental involvement and comb sign, the MRI result will be considered "active disease" and if there are fewer than three of ten sign, the MRI results are considered "in remission".

TABLE 1. Sensivity, specificity, NPV and PPV of each MR Enterography sign

MR Enterography Sign	Sensitivity%	Specificity%	PPV%	NPV%
Wall thickening	95.5	90	95.5	90
Mural enhancement	95.2	90	95.5	90
Multi segmental	85.7	100	100	76.9
Mural edema	85.7	90	94.7	75
Comb sign	71.4	100	100	62.5
Stratification	66.7	100	100	58.8
Nodular wall thickening	57.1	100	100	52.6
Nodal enlargement	57.1	90	92.3	50
Fistula	9.5	100	100	34.5
Stricture	19	70	57.1	29.2

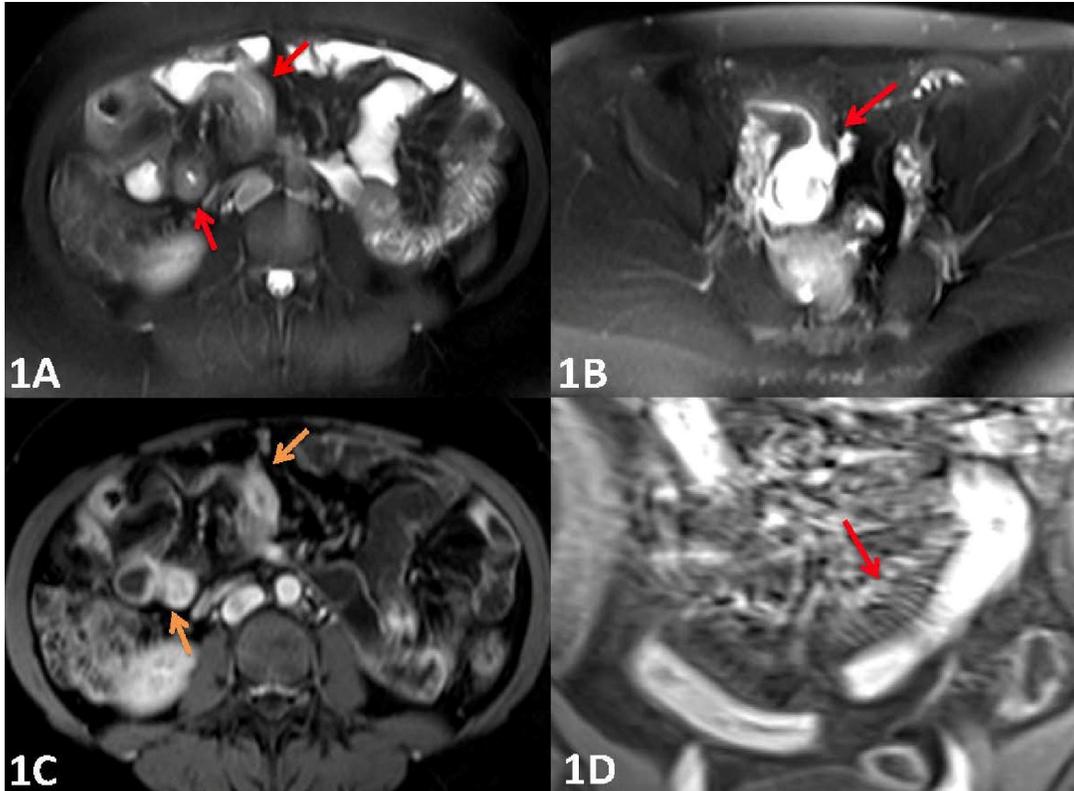


Fig. 1: A and B. Axial T2 HASTE images demonstrate mural thickening, wall edema and transition point (*arrows*). C and D Coronal and Axial post Gd VIBE showed; mural enhancement (*orange arrows*) and comb sign (*red arrow*).

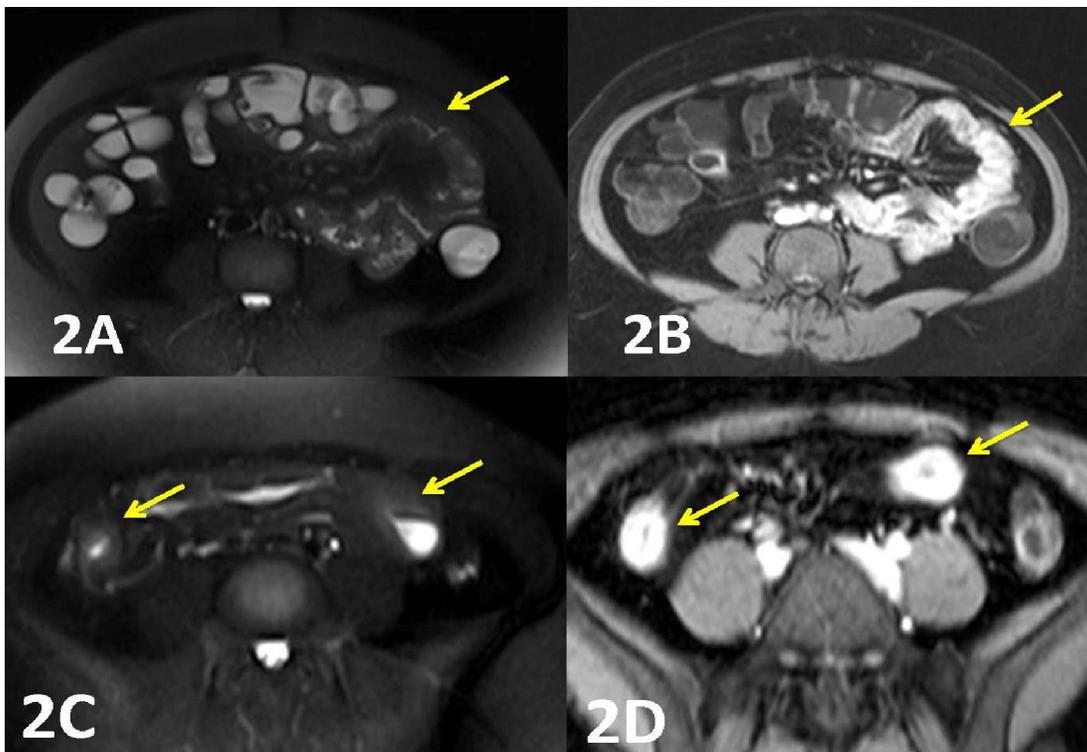


Fig. 2: A and C. Axial HASTE images showing small bowel wall thickening (*arrows*). B and D Axial post contrast VIBE demonstrate mural enhancement (*arrow*).

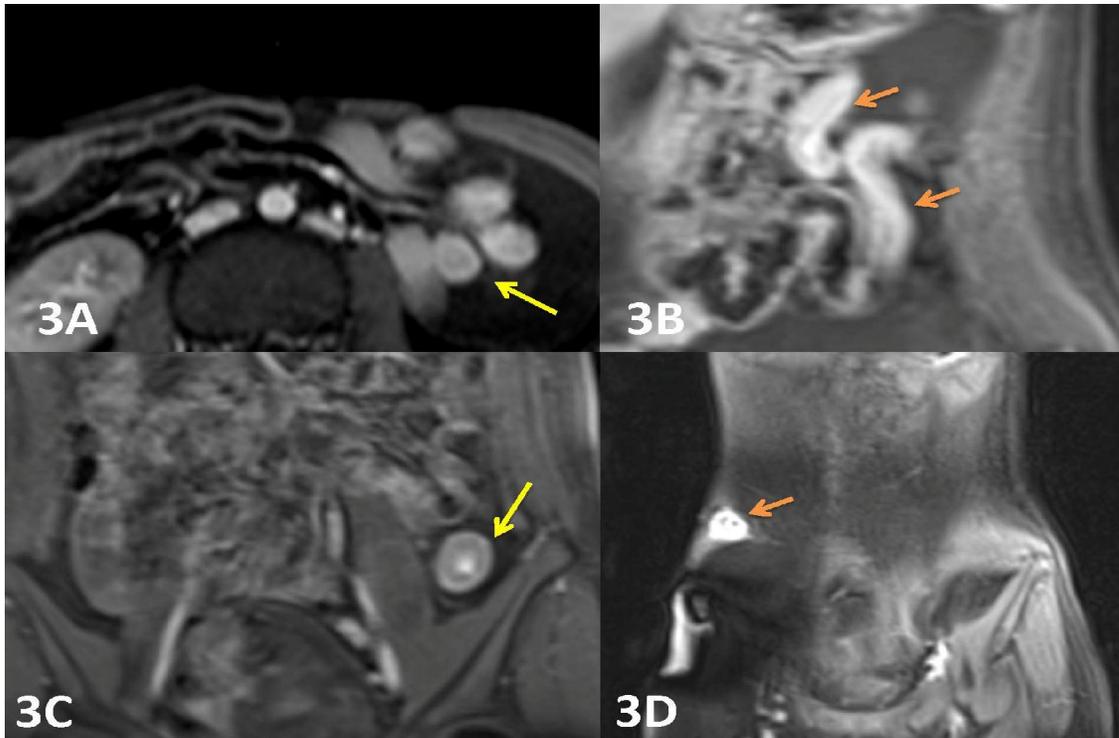


Fig. 3: A-D. Axial and Coronal post contrast VIBE showed: Stratification (*arrow in A and C*) enhancement (*arrow in B*) Comb sign (*arrow in C*) and intense enhancement at ileostomy site due to Crohn's activity (*arrow in D*).

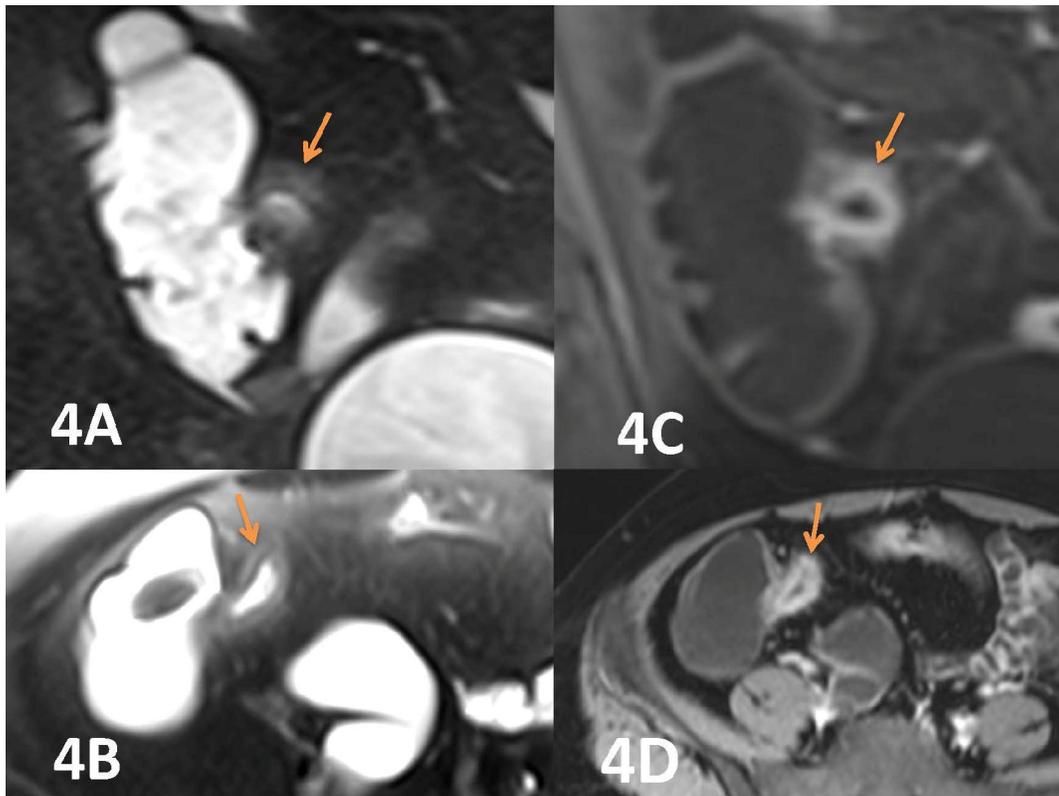


Fig. 4: A and B. Coronal and axial T2 HASTE images showing mural thickening and edema in terminal ileum (*arrow*) C and D. Enhancement at same site (*arrow*).

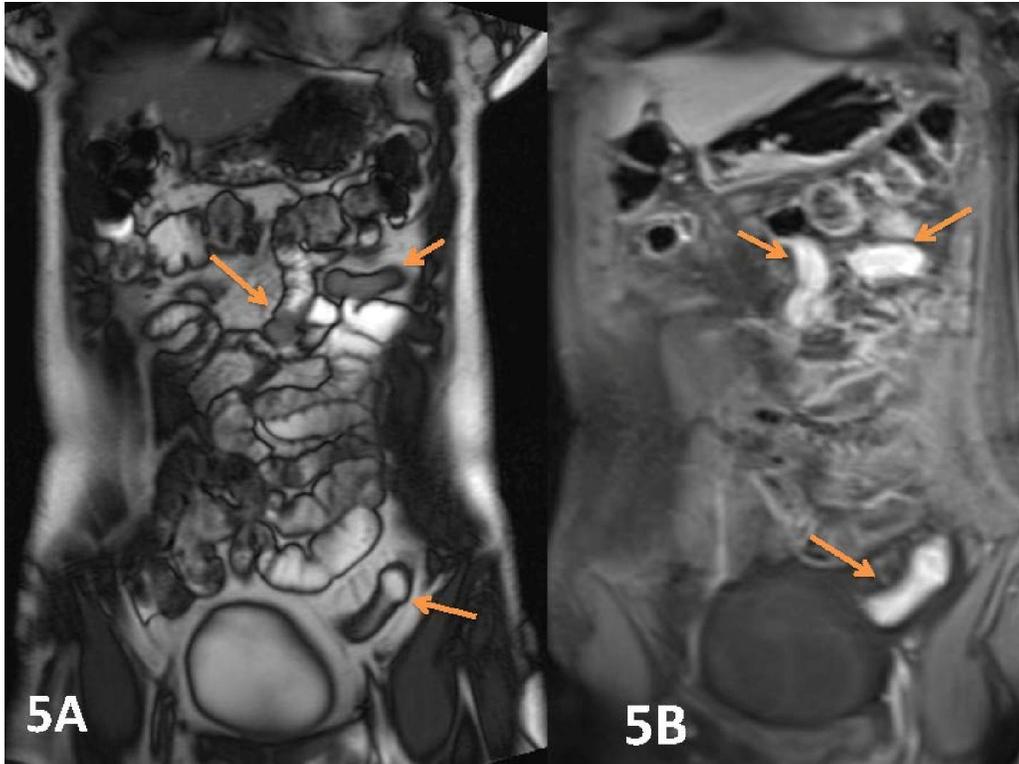


Fig. 5: A. Coronal TRUE FISP image showing mural thickening in three segments. B. Intense enhancement at same locations (*arrows*).

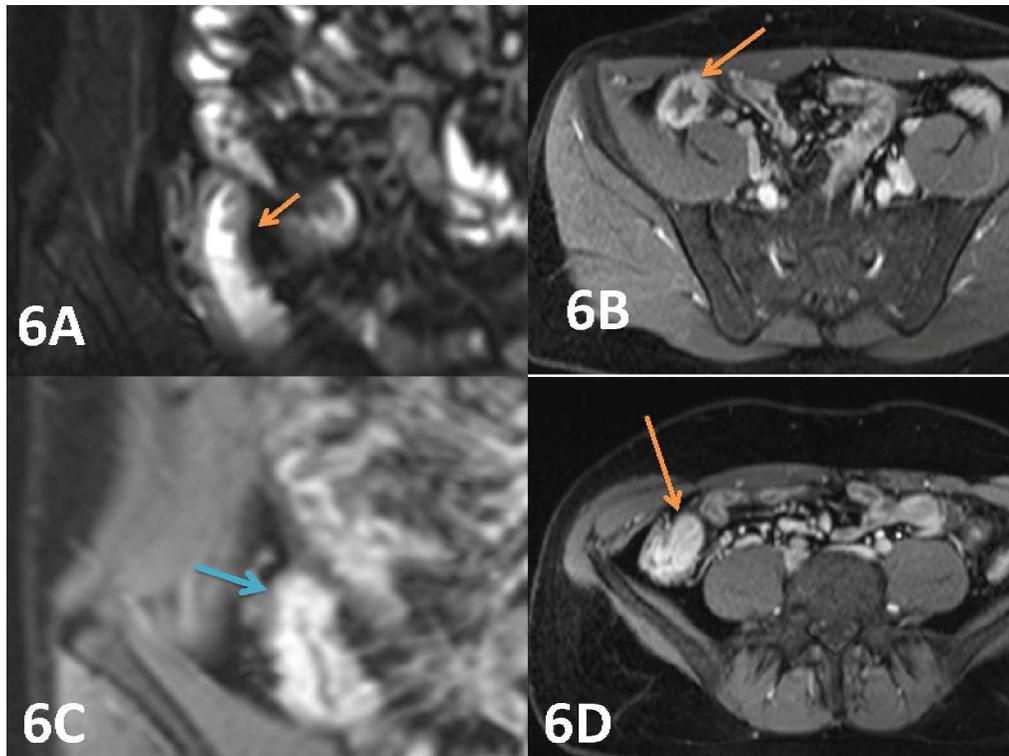


Fig. 6: A. coronal T2 image showing nodular wall thickening. B, C and D demonstrate enhancement of involved segment.

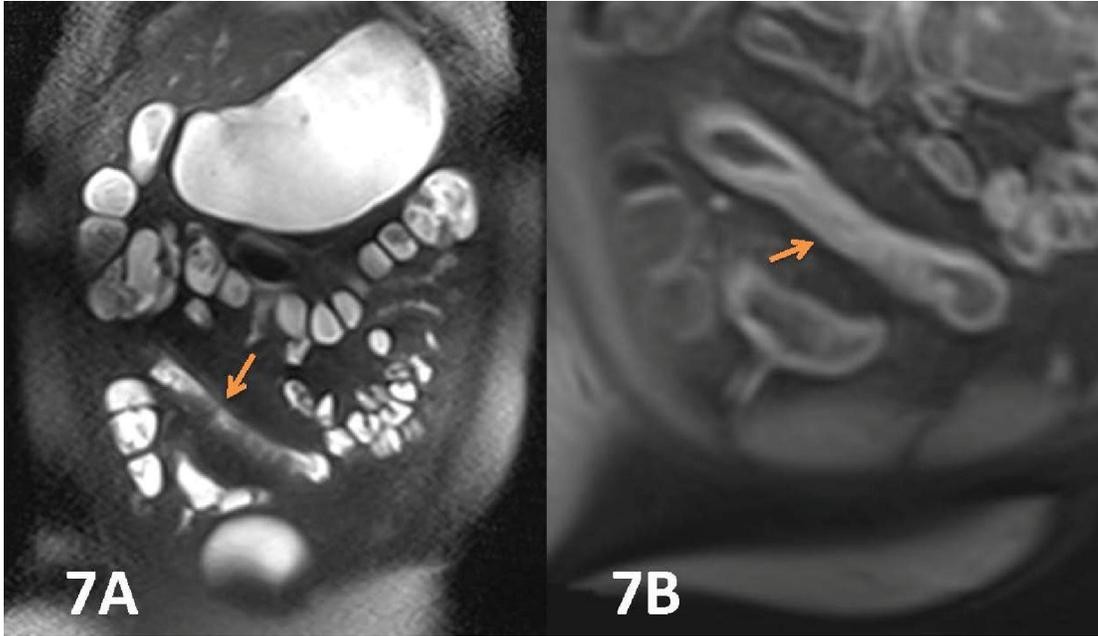


Fig. 7: A. Coronal T2 HASTE and B. Coronal post Gd VIBE images demonstrate Stricture, fixation and thickening of terminal ileum (*arrows*).

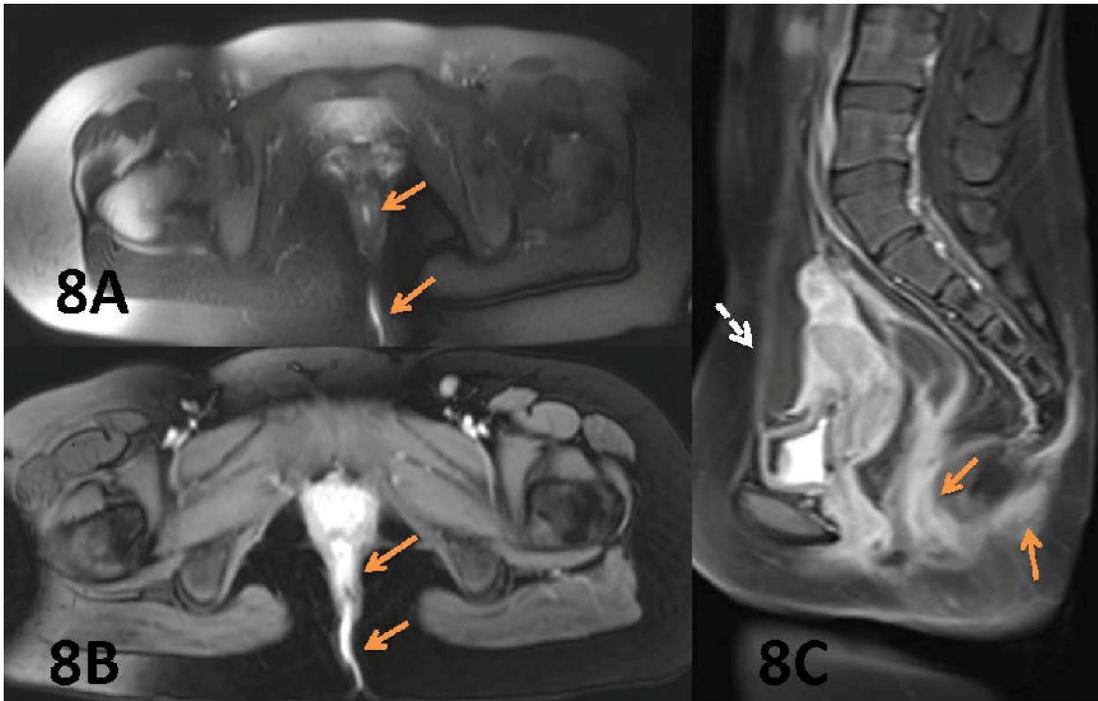


Fig. 8: Axial T2-weighted image (A) show the perianal fistulous track (*orange arrow*). Post-contrast axial and coronal images (B and C) demonstrate enhancement of the track (*orange arrow*) and intraperitoneal free fluid (*white arrow*)

Based on this criterion MRI Sensitivity and specificity in the evaluation of Crohn's disease activity, was respectively 90/5 and 90 percent, and its positive predictive value and negative predictive value in comparison with colonoscopy/laparotomy and

biopsy were 95 and 81 percent. If we choose presence 4 of those 10 sign as a criterion for disease activity, MRI Sensitivity and specificity was respectively 90/5 and 100 percent, it's PPV and NPV was 100 and 83.3 percent. In the research done by Lasocki and

colleagues, like ours, sensitivity and specificity of each of the signs of MRI were studied separately and the results of their research had a thorough compatibility with ours as well. A number exceeding 3 or 4 was considered active and accordingly ppv = 95% and npv = 100 % are reported. They had not studied comb sign, while this sign had high sensitivity and specificity in our study. They had also considered free fluid as a sign of the activity of Crohn's, which lacked high sensitivity and specificity for Crohn's. They had studied and analyzed signs like wall edema, fat edema, and serosal blurring separately, but in our research, the mentioned signs were considered as a single sign.

Conclusion

The results of our study confirm that MR Enterography is a valuable imaging modality for diagnosing active Crohn's. The most specific MRI signs are Stratification, Comb sign, multi segmental involvement, fistula, and nodular wall thickening. The most sensitive MRI signs are increase in wall thickness, enhancement, mural edema, multi segmental involvement, comb sign and stratification. Presence of three or four sign from ten sign is a good criterion for determining Crohn's disease activity. Stricture is not a reliable sign for diagnosing active Crohn's disease.

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