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## ORIGINAL ARTICLE

# Role of CT enterography in assessment of Crohn's disease activity: Correlation with histopathologic diagnosis

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### KEYWORDS

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**Abstract** *Aim:* To evaluate the radiological signs of gastro-intestinal inflammation at CT enterography and to assess its accuracy in determining the degree of activity in patients with Crohn's disease (CD).

*Methods:* CT enterography was performed in 26 CD patients and evaluated for the following parameters: mucosal enhancement, abnormal wall thickening, engorged vasa recta, increased density of the mesenteric fat and enlarged mesenteric lymph nodes. Correlations between CT findings and histopathologic results were made using McNemar test.

*Results:* There was no significant statistical difference in mucosal enhancement and wall thickening between moderate and severe disease ( $P = 0.631$  and  $0.138$ , respectively) whereas engorged vasa recta, fat edema and lymph node enlargement had successfully discriminated between moderate and severe histological findings ( $P = 0.009$ ,  $<0.001$  and  $0.045$ , respectively). Moderate disease was diagnosed correctly by CTE in 50% of cases while severe disease was diagnosed in 100% of cases. When we reconditioned the presence of two CTE severity criteria to diagnose severe disease, the sensitivity to predict moderate disease activity increased to 80%.

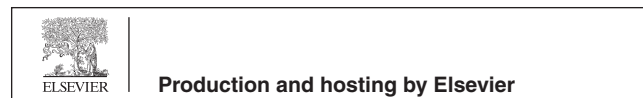
*Conclusion:* CT enterography is a sensitive and specific non-invasive imaging modality for evaluating the degree of activity of Crohn's disease, and should be considered in its diagnostic and management algorithms.

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## 1. Introduction

Assessment of activity in Crohn's disease (CD) is crucial to patient's management and to monitor the effect of therapy. Activity of CD is usually assessed by clinical data, endoscopy, or serum biochemical markers such as erythrocyte sedimentation rate (ESR) and C reactive protein (CRP). However,

endoscopy only assesses the superficial mucosa and does not evaluate the transmural inflammatory process in Crohn's disease. Also inflammatory markers are not fully understood in CD despite their frequent use (1). Although small bowel follow through can define the extent and severity of narrowing, it provides little data on whether narrowing results from inflammation or stricture, and lacks the information about the extra enteric manifestations (2). Computed tomography (CT) is currently used for the detection of possible complications of CD like fistula, abscesses, or stricture/obstruction, but also holds promise in the assessment of disease activity (3). There are many advantages of CT from the patient's perspective compared to small bowel follow through including no tender palpation or change of position, only requires getting on/off the table once, and much less time required (4). CT enterography (CTE) differs from conventional abdominal CT scanning techniques in utilizing multi-detector CT with its high spatial and temporal resolution, thus providing thin slice data that combine the advantages of gastro-intestinal volume challenge with the ability of cross-sectional imaging and multi-planar reformatting to depict extra luminal manifestations of the disease (5). Large volumes of water-attenuation bowel contrast and intravenous contrast improve visualization of the small bowel lumen and wall (6). Abnormal wall enhancement/thickening, increased density and smudging of the mesenteric fat, engorged vasa recta "comb sign" and possibly enlarged mesenteric lymph nodes have been shown to correlate with active inflammation (7,8).

The aim of this work is to assess the accuracy of CTE in detecting the degree of activity in patients with Crohn's disease through the correlation between the histopathologic results and CTE findings of inflammatory activity.

## 2. Patients and methods

This study was carried out in the Radiodiagnosis Department units of Ain Shams University Hospital and in some private centers. The study design consisted of 26 patients (18 males and 8 females) with known CD during the period from June 2010 to November 2011. The average patient's age was 43.4 years (range = 19–69 years). All included patients were referred to further assessment with CTE and an informed consent was obtained from each patient before the study. Determination of disease activity was done by a gastroenterologist through the calculation of the disease activity index (DAI) on the basis of the following data: the number of liquid or very soft stools per week, ratings of abdominal pain and general well-being, hematocrit level, height and body weight, presence of a palpable mass, and presence of complications. Disease was classified as active if the DAI was  $\leq 150$  (9).

The diagnosis of Crohn's disease and evaluation of its activity were based on the pathologic findings. In most patients the ileo-cecal junction was involved, so in 21 patients an ileo-colonoscopy was performed within one week before CT examination in whom at least the last 10 cm of the terminal ileum was scoped and biopsy was taken. One patient with gastric involvement was diagnosed by gastroscopy. Endoscopic signs of active disease included aphthous ulcers, mucosal erythema and edema, inflammatory nodularity or cobble stoning, spontaneous bleeding and friability. In four patients, the pathological diagnosis was made after segmental small bowel resection for painful fibrotic stricture or subacute obstruction. The severities of acute and

chronic disease by histology were graded based on the greatest severity of inflammation as mild, moderate or severe.

### CTE technique

The patients were instructed to drink an amount of water ranging between 1 and 1.5 l within 2 h prior to the examination according to their tolerance, with one last cup administered immediately before the examination. The CT examinations were performed by at least eight multi-detector scanners (GE Healthcare, Milwaukee, WI, USA). IV contrast (Iopamiro 300; Bracco, Milano, Italy) was given as 100–150 ml at a rate of 4 ml/s using an automatic pump injector via an antecubital or peripheral upper limb vein. Scanning was initiated 60 s after the start of the injection, with 2.5-slice collimation, 3-mm slice thickness, 1.5 reconstruction intervals, and a kV of 140. The images were sent to a workstation where coronal and sometimes sagittal reformats were reconstructed. Viewing of the coronal reformats was more assuring to the viewer in detection of the site of abnormality especially when the involved segments were adequately distended as the transition point between normal and diseased segments could be more easily determined.

The images were reviewed by an experienced radiologist for the following findings: mucosal enhancement, bowel wall thickening ( $> 3$  mm), edema of the mesenteric fat, engorged vasa recta, lymphadenopathy and possible complications like fistula or abscess. Mural enhancement was considered when segmental enhancement of the bowel wall was greater than enhancement of the adjacent bowel loops. Increased density/smudging of the peri-enteric fat was defined by increased inhomogeneous attenuation of the fat as compared with the subcutaneous fat, peri-nephric fat or peri-enteric fat adjacent to normal bowel loops. The comb sign is defined as dilatation of the vasa recta involving the offended bowel loop (10).

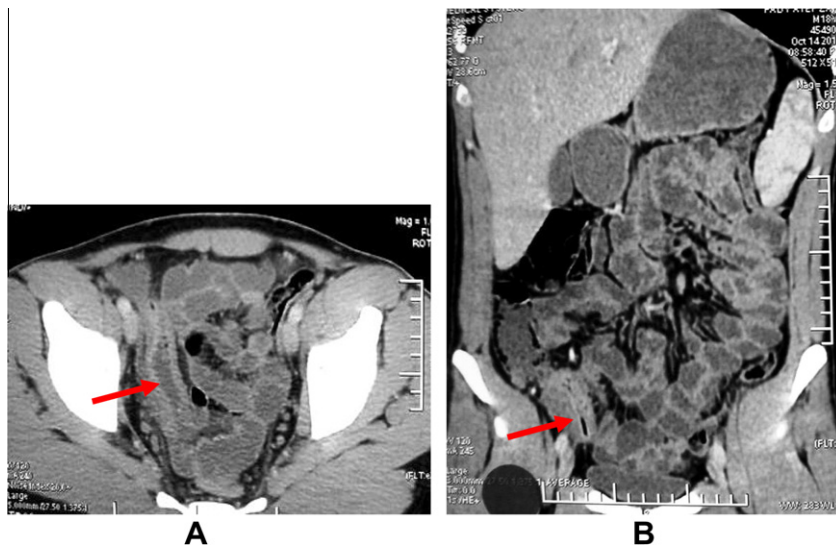
Positive enteral contrast was used in some patients for whom the examinations were done in private centers; however, we were able to enroll these cases in the study because the affected bowel segments were not opacified, and we could reliably assess the degree of mucosal enhancement.

Mild disease was defined at CTE by mucosal hyper enhancement only, while moderate disease was classified as abnormal mucosal enhancement and wall thickening. Severe disease was considered if one or more of the extra-enteric manifestations were detected in addition to the moderate activity criteria (11).

## 3. Results

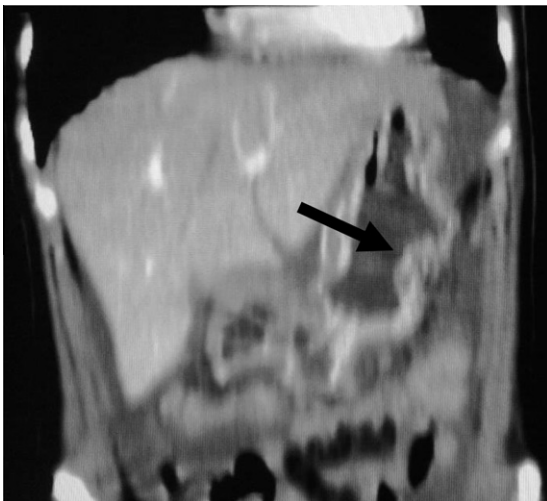
Twenty-six patients were included in the study. There were 18 males and 8 females. Median age was 43.4 years (range 19–69). The patients were on no treatment for three days prior to the CTE study irrespective of the type of treatment. The radiological findings were correlated with the histopathological results for all cases. Sixteen patients were histologically diagnosed with severe disease (61%) while 10 patients were diagnosed as having moderate disease (39%) (Fig. 1).

CTE revealed mucosal enhancement in almost all patients (25 patients; 96%), but not appreciated in one patient with moderately active disease. Wall thickening was present in 24 patients (92%) but not appreciated in two cases with moderate disease activity at endoscopy, one of them was under graded as



**Fig. 1** Moderate degree of diseased activity. A 22 year old male with CD presented with increasing abdominal pain and diarrhea. (A) Axial and (B) coronal CTE show wall thickening and mucosal enhancement at the terminal ileum (arrows).

mild (Fig. 2). Engorged vasa recta were present in 14 patients (53%) and diagnosed by CT as severe inflammation (Figs. 3 and 4); their histopathological results confirmed severity of inflammation in 12 patients, while the other two were diagnosed as moderate. Mesenteric fat edema and smudging were present in 19 patients (73%); histopathological results revealed severe inflammation in 16 of them (Fig. 4) and moderate disease in three patients (Fig. 5). Enlarged mesenteric lymph nodes were present in nine patients (35%); eight of them had severe disease by histopathology (Fig. 3), while the remaining one had moderate disease activity. No gross complications of Crohn's disease like abscess or fistula were encountered in our groups of patients, but four patients with severe disease



**Fig. 2** Mild disease activity at CTE but histologically moderate degree. A 40 year old man with CD presented with abdominal pain and repeated vomiting. CTE coronal reformatted image shows intense gastric mucosal hyper enhancement (arrowed) that was interpreted as mild active disease. However, gastroscopic tissue sampling revealed moderate disease activity.

had fibrotic inflammatory strictures causing pain and subacute obstruction, for whom segmental small bowel resection was done (Fig. 6).

Table 1 shows the association between CT findings and histological findings in our patients' population.

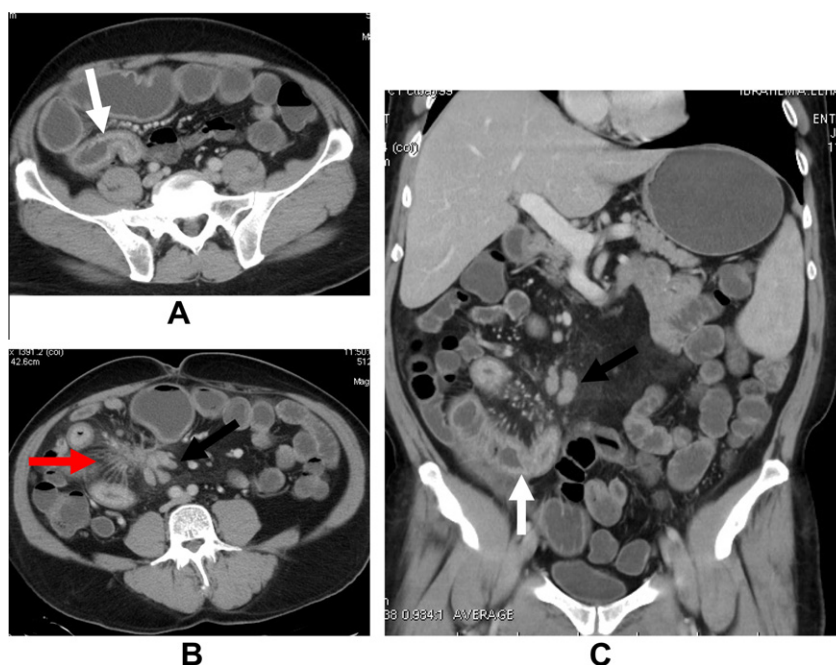
In our study, moderate disease was diagnosed correctly by CTE in 5 out of 10 patients (50%) (Fig. 1). The remaining five patients were diagnosed as severe in four cases where they showed only one sign of severe activity (engorged vasa recta, mesenteric fat edema, or lymphadenopathy) (Fig. 5), and as mild activity in one case that showed only mucosal enhancement (Fig. 2). All patients with severe disease (16 cases) were diagnosed correctly by CTE (100%). Each of them was having at least two criteria of severe disease (Figs. 3 and 4).

Table 2 depicts histological activity and CT scan parameters of activity in our patients' population.

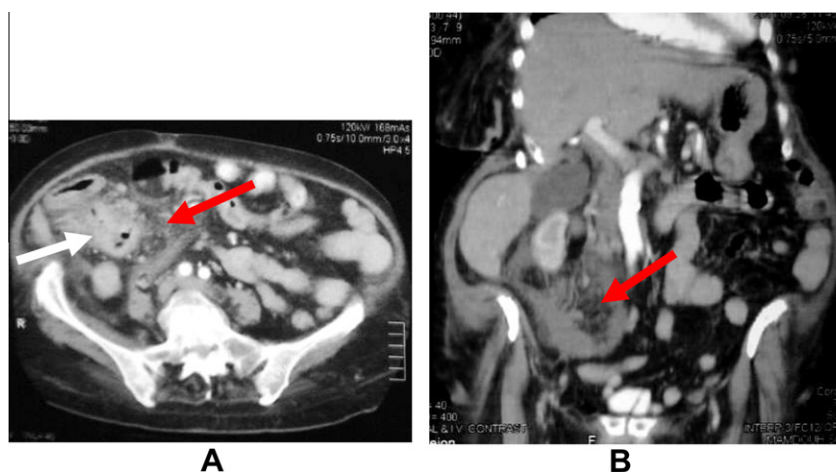
If we consider the presence of any two of the following: engorged vasa recta, fat edema and lymph nodes as "severe" in classification of CTE findings, the correlation with the histological results would be of greater sensitivity (80%) of predicting moderate disease activity (Table 3).

#### 4. Discussion

Crohn's disease (CD) is an incurable chronic condition that can affect any part of the gastro-intestinal tract. Frequently it is manifested by abdominal pain but it is often not clear whether this pain is caused by active inflammation, by stenosis and proximal dilatation, or both. Moreover, there is a high prevalence of extra enteric manifestation of the disease that can significantly alter management plans, including the initiation of antibiotic therapy, surgical referral and/or the use of immunosuppressive or biologic agents (12). Computed tomography enterography (CTE) has been recently applied to the study of Crohn's disease due to its ability to non-invasively differentiate which process is predominant, thus helping the physicians to make more informed treatment decisions for their patients (2,13).



**Fig. 3** Severe degree of disease activity. A 55 year old male with remittent course of CD. Axial CTE cuts (A and B) and coronal reformatted image (C) show wall thickening and mucosal hyper enhancement at the terminal ileum (white arrows), engorged vasa recta producing the comb sign (red arrow), and enlarged lymph nodes (black arrows).



**Fig. 4** Severe degree of disease activity. A 48 year old female with CD. Axial CTE (A) and coronal reformatted image (B) showing wall thickening and mucosal hyper enhancement of the ileal loops (white arrows), engorged vasa recta and increased density of the peri-enteric fat (red arrows).

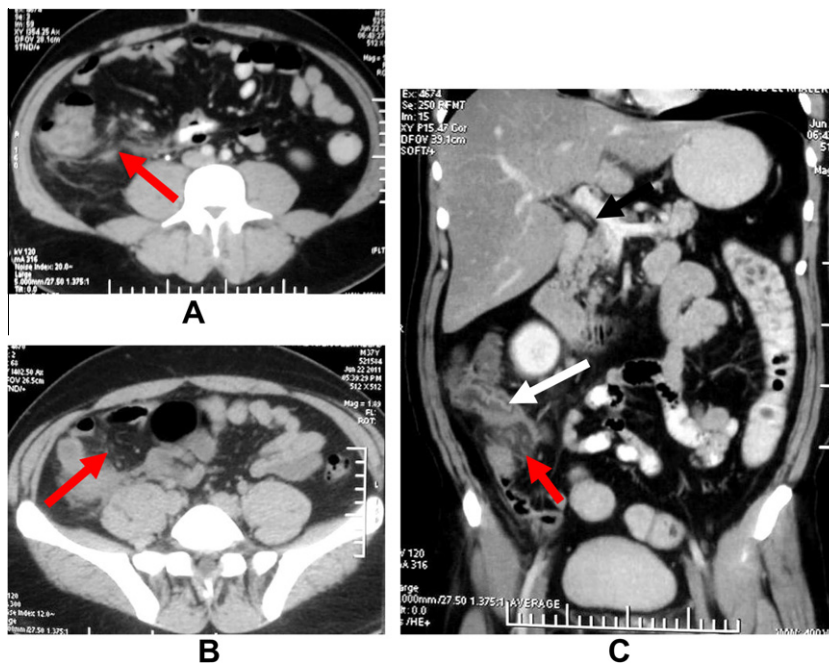
Our study comprised patients clinically proven as Crohn's disease with suspected activity based on CDAI. We considered the CTE findings for activity in the presence of any of the following: mucosal enhancement, bowel wall thickening > 3 mm, edema of the mesenteric fat, engorged vasa recta, and lymphadenopathy.

Bowel wall enhancement was present in almost all our cases (96%). Previous studies done by Choi et al. (14), and Koh et al. (15), using either CT or MRI, have validated the ability of mural enhancement in the terminal ileum to detect active small bowel inflammation. Also bowel enhancement has been used to monitor patients with CD before and after anti-inflammatory therapy (16).

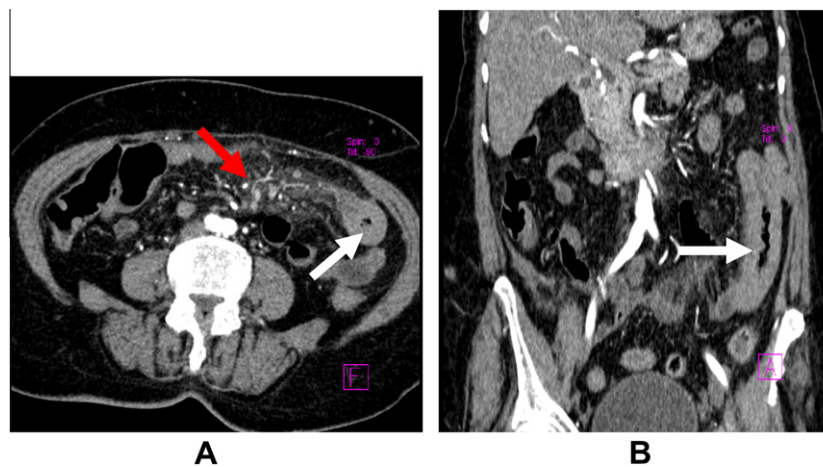
We categorized cases in our study as severe disease in the presence of engorged vasa recta, increased density/smudging of peri-enteric fat or enlarged lymph nodes. Meyers and McGuire (17) referred to tortuosity and dilatation of the ileal vessels as "vascular jejunisation of the ileum" or the "comb sign" noting the occurrence of this finding in patients with active CD. In agreement with them, engorged vasa recta (comb sign) were present in 14 cases in our study (53%) and is correlated with histological inflammation severity in 12 cases (Figs. 3 and 4).

Lee et al. (18) analyzed 33 patients with CD using endoscopic and pathological examination as well as barium enema and abdominal CT, and reported that CRP and length of hospitalization correlated with the presence of the "comb sign".





**Fig. 5** Severe disease activity at CTE but histologically moderate degree. A 43 year old male with remittent course of CD. Axial CTE cuts (A and B) and coronal reformatted image (C) show wall thickening and mucosal hyper enhancement at the ileo-cecal junction (white arrow) with stranding and increased density of the peri-colic fat (red arrows).



**Fig. 6** Severe CD with stricture formation. 31 year old male with active Crohn's disease. Axial CTE (A) and coronal reformatted image (B) show segmental mural thickening of the jejunum at the left lumbar region with luminal narrowing mounting to stricture formation (white arrows). The adjacent mesenteric fat is edematous with engorged vasa recta (red arrow). The stenotic segment was resected and histology confirmed severe active disease.

The presence of hypertrophied mesenteric adipose tissue is another characteristic feature of CD. In our study we assessed the mesenteric fat adjacent to the affected bowel loop for increased density and smudging, which is believed to represent edema and infiltration of inflammatory cells in the peri-enteric fat. Increased fat density was present in 19 patients (75%) of our cases (Fig. 3 and 5) and correlated with the disease severity in 16 of them. Correlating with our radiological findings, Yamamoto et al. (19) recently found significant infiltration of inflammatory cells in hypertrophied mesenteric adipose tissue adjacent to the involved intestine in patients with CD. Inflammatory cells were mainly CD68

positive and CD3 positive T lymphocytes, suggesting that inflamed mucosa and its adjacent mesentery share a common inflammation in CD.

In a study by Johnson et al. (11), including 35 cases with proven colitis at colonoscopy, sensitivities of CTE for detection of mild, moderate and severe disease were 67%, 90% and 100%, respectively, on the basis of defining mild disease in cases with only mucosal hyper enhancement, moderate disease with mucosal hyper enhancement and wall thickening, and severe disease with moderate activity criteria plus peri-colonic soft tissue stranding, concluding that sensitivity was best for detecting moderate and severe disease.

**Table 1** Association between detailed CT scan findings and histological findings among our 26 Crohn's disease patients.

	Histological findings <i>n</i> (%)		<i>P</i> value
	Moderate ( <i>n</i> = 10)	Severe ( <i>n</i> = 16)	
<i>Detailed CT findings</i>			
Mucosal enhancement	9 (90)	16 (100)	0.631 NS
Wall thickening	8 (80)	16 (100)	0.138 NS
Engorged vasa recta	2 (20)	12 (75)	0.009*
Fat edema	3 (30)	16 (100)	<0.001*
Lymph nodes	1 (10)	8 (50)	0.045*

No statistically significant difference in mucosal enhancement and wall thickening has been found between moderate and severe disease stage as assessed by histopathologic result, while engorged vasa recta, fat edema and lymph nodes had successfully discriminated between moderate and severe histological findings. In other words, mucosal enhancement and wall thickening are not good predictors of histological findings.

\* Significant.

**Table 2** Correlation between CT scan findings and histological findings among our 26 patients with Crohn's disease.

	Histological findings <i>n</i> (%)		<i>P</i> value
	Moderate ( <i>n</i> = 10)	Severe ( <i>n</i> = 16)	
<i>CT scan grading</i>			
Mild disease	1 (10)	0 (0)	0.125
Moderate disease	5 (50)	0 (0)	
Severe disease	4 (40)	16 (100)	

McNemar test  $P = 0.125$ . NS denoting no significant agreement between CT and histologic result when we considered the presence of any of engorged vasa recta, fat edema or lymph nodes as "severe".

**Table 3** Correlation between CT findings and histological findings if we consider the presence of any two of the following: engorged vasa recta, fat edema and enlarged lymph nodes as "severe":

	Histological findings <i>n</i> (%)		<i>P</i> value
	Moderate ( <i>n</i> = 10)	Severe ( <i>n</i> = 16)	
<i>CT-scan grading</i>			
Mild disease	1 (10)	0 (0)	<0.001*
Moderate disease	8 (80)	0 (0)	
Severe disease	1 (10)	16 (100)	

McNemar test  $P < 0.001$  denoting a significant agreement between CT and endoscopic classification of Crohn's disease severity cases when we considered the presence of two of either engorged vasa recta, fat edema or enlarged lymph nodes as "severe".

\* Significant.

In concordance with their study, we found that CTE findings in predicting the degree of activity of CD highly correlated with the histopathological results. When we considered the presence of any of engorged vasa recta, fat edema, or lymph node enlargement to diagnose severe disease, all severe cases were correctly diagnosed (100%). Moderate disease was diagnosed correctly in 50% of cases on the basis of the presence of mucosal hyper enhancement and bowel wall thickening > 3 mm, while 40% were over graded as severe and McNemar test revealed no significant agreement between CT findings and histological results. So we found that if we recondition the

presence of two criteria rather than only one to diagnose severe disease, the correlation with histological results would be of greater sensitivity in predicting moderate disease activity (80%).

Larger studies have also shown that findings of CD at CTE correlated highly with endoscopy. In a study of 96 patients who underwent CTE and ileoscopy, the authors reported that bowel wall thickening and enhancement on CTE correlated significantly ( $P < 0.001$ ) with ileoscopic and histological findings of active CD (16). In our study, there was no statistically significant difference in mucosal enhancement and wall thickening between moderate and severe disease stage as assessed by histology, while engorged vasa recta, fat edema and lymph nodes had successfully discriminated between moderate and severe endoscopic findings with  $P$  value 0.009, <0.001 and 0.045, respectively.

## 5. Conclusion

CT enterography is a sensitive and specific imaging modality for evaluating the small bowel in patients with Crohn's disease, because of its accuracy and non-invasive nature. This study highlights its ability to assess the degree of activity of the disease, rendering it the method of choice to monitor patient's response to treatment, avoiding the risk and inconvenience of endoscopy.

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