Original Article

Ileal Crohn's disease activity predicted by ruler: CT enterography histopathology correlation

Tamer W. Kassem
Radiology Department, Cairo University, Egypt

ABSTRACT

Objective: The aim of this study was to explore the predictive value of CT enterography-based simple measurement tools for Crohn's disease activity.

Patients and methods: During one and half year duration 54 patients diagnosed with CD were retrospectively evaluated. All patients underwent CT enterography examinations following a preset protocol prior to endoscopic biopsy or surgery. The images obtained were reconstructed using dedicated software and workstations. The length of affected segments was calculated (L) and distance from ileocecal junction till first affected segment was measured (D). Results of CTE examinations were compared with histopathology.

Results: Out of 54 cases, 38 cases had single segment involvement (70.4%) and 16 cases had multiple affected segments (29.6%). The histological inflammatory activity score scored 1 in 10 cases (18.5%), 2 in 25 cases (46.3%) and 3 in 19 cases (35.2%). L varied from 1.4 cm to 20.6 cm while D varied from 0 to 6.7 cm. Spearman rank order correlation coefficient showed a strong uphill linear relationship of L (RHO = 0.663) and weak correlation of D (RHO = 0.222) with the histological inflammatory activity score.

Conclusion: CTE provides accurate data regarding length of affected ileal segments that positively correlated with histopathological score of disease activity.

1. Introduction

Crohn's disease (CD) is a chronic inflammatory process that affects different parts of gastrointestinal tract [1,2]. The prevalence of CD has increased in the last fifty years and despite major advances in understanding its basic mechanisms of inflammation and pathogenesis, its cause remains unknown [1].

CD has extremely variable clinical presentation and exhibits symptoms that vary according to their location, extent, systemic manifestations and potential complications. It exhibits early symptoms in the form of abdominal pain, persistent diarrhea, weight loss, mild fever and extraintestinal manifestations [2].

The diagnosis of CD is based on the analysis of clinical data, complete physical and proctologic examination, endoscopic, radiological, laboratory and histological tests [3]. CT enterography (CTE) and MR enterography (MRE) replaced the intestinal transit and enteroclysis procedures in the evaluation of small intestine. The advantage of CTE is allowing visualization of the whole small intestine, evaluation of the intestinal wall and detection of extraluminal pathological conditions [4–6]. CTE can show changes in bowel wall thickening or enhancement in detail. Segmental mural enhancement, small bowel wall thickening, increased density of mesenteric fat, and engorged vasa recta are correlated with active inflammation [7,8].

Montreal classification [9] with age at diagnosis, location, behavior and CD Activity Index (CDAI) are widely used for disease assessment and therapy stratification. However, these scores are unreliable in differentiating remission and active CD [10]. Currently, endoscopy and biopsy are the gold standard for assessing the inflammatory activity of CD [11].

The aim of this study was to explore the predictive value of CT enterography-based simple measurement tools for CD activity by calculating the length of affected segment or sum of lengths of affected segments.

2. Patients and methods

2.1. Patients

A retrospective study of 54 patients (32 females and 22 males) aged 23–45 years old (with mean age of 34 years old) presenting to
a private specialized medical center with clinical diagnosis of CD coming for assessment by CTE examination between March 2015 and September 2016 was performed. There were no set criteria for referral. Patients had clinical evaluation including medical history. Information regarding laboratory findings and interventional procedures was obtained from all cases. All patients underwent an endoscopic or surgical biopsy within 2 weeks after the CTE examination.

2.2. Methods

CTE examinations were carried out using an Aquilion One 320 scanner (Toshiba Medical Systems, New York, USA), with tube potential set at 120 kV, current at 300 mA, collimation at 2 mm and table movement at 3 mm/s.

After the patients had fasted for at least 8 h, they were informed to drink 1 L of oral contrast (mannitol diluted by 50% with normal water) over 60 min to obtain an optimum distension of the small bowel loops. A 20-gauge cannula was placed at one upper limb. Total amount of 100 ml non ionic contrast material (iopromide, 300 mg iodine per ml, Ultravist 300; Schering AG, Berlin, Germany) was injected with an automatic injector at a flow rate of 3 ml/s. An operator initiated (>120 HU) Smartprep trigger was used to begin scanning from the level of the last dorsal vertebra following short delay time of about 10–15 s after the end of injection. The region of interest from the lower chest till the inguinal region was scanned two consecutive times to obtain images in early arteriographic and venographic phases.

2.3. Data analysis and interpretation

2D multiplanar axial, coronal, sagittal and curved reformatted images were reconstructed from the raw data using dedicated software and work stations and read visually. All CTE examinations were performed and evaluated by one staff radiologist with expertise in gastrointestinal imaging. The length of affected segment (L) and the distance between the ileocecal junction and first affected ileal segment (D) were measured using the ruler as a simple measurement tool. In cases of multiple segments affection the sum of their lengths was calculated. If the whole segment could be seen in one plane it was measured directly as one or sum of two measurements (Fig. 1A). In most of the cases the affected segment did not exist in one plane and curved reformatted images were obtained in these cases using the tracking technique. The affected segment was tracked in different planes and cursors was placed from its beginning till its end at a distance interval of 2 mm maximum then it was demonstrated as linear segment before simple measurement by ruler (Fig. 1B and C). The same technique was used in measurement of D in some cases.

Table 1

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Total</th>
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<tr>
<td>Single segment</td>
<td>6</td>
<td>6</td>
<td>4</td>
<td>16 (29.6%)</td>
</tr>
<tr>
<td>Multiple segments</td>
<td>4</td>
<td>19</td>
<td>15</td>
<td>38 (70.4%)</td>
</tr>
<tr>
<td>All</td>
<td>10 (18.5%)</td>
<td>25 (46.3%)</td>
<td>19 (35.2%)</td>
<td>54 (100%)</td>
</tr>
</tbody>
</table>

Fig. 1. Measurements techniques. (A) single segment in one axial plane measured as sum of two linear parts (8.1 + 5.9 = 14 cm), (B) curved reformatted images in coronal and sagittal planes after placement of cursors (L = 10.91 cm), (C) placement of cursors along affected tortuous segment in coronal plane and its demonstration as linear segment prior to length measurement (L = 20.6).
2.4. Histopathological interpretation

The histopathological evaluation of the inflammatory activity in the bowel wall was used as a reference standard. Endoscopic and surgical bowel biopsies underwent fixation. The extent of inflammatory activity was reported by a pathologist blinded for clinical and radiological findings. The evaluation process was based on a semi-quantitative visual 3-point scale: 1 in case of mild inflammation (neutrophils limited to mucosa), 2 in case of moderate inflammation (neutrophils limited to mucosa and submucosa), and 3 in case of severe inflammation (neutrophils affecting the muscularis propria).

3. Results

From March 2015 to September 2016, 54 patients were entered in the study aged on average 34 years (range, 23–45 years). Out of 54 cases, 38 cases had single segment involvement (70.4%) and 16 cases had multiple affected segments (29.6%). According to histological inflammatory activity, the patients were divided into three groups as listed in Table 1. The first group consists of 10 cases (18.5%) with grade 1 histopathological inflammatory activity, 6 cases had single affected segment (Fig. 2) and 4 cases had multiple segments affection (Fig. 3). The second group consists of 25 cases (46.3%) with grade 2

![Fig. 2. 37 years old male patient with terminal ileum CD, histopathological activity grade 1 (arrows). (A) 2D coronal MIP image and (B) 2D axial image. L = 1.6 cm and D = 0.](image)

![Fig. 3. 27 years old female patient with terminal ileum CD, histopathological activity grade 1 (dashed circles). (A) 2D axial images and (B) 2D sagittal images. L = 3 + 3.2 = 6.2 cm and D = 0.](image)
histopathological inflammatory activity, 6 cases had single affected segment and 19 cases had multiple segments affection (Figs. 4–6). The last group consists of 19 cases (35.2%) with grade 3 histopathological inflammatory activity, 4 cases had single affected segment (Figs. 7 and 8) and 15 cases had multiple segments affection (see Table 2).

L varied from a minimum of 1.4 cm till a maximum of 20.6 cm. Spearman rank order correlation coefficient showed a strong uphill linear relationship of L (RHO = 0.663) with the histological inflammatory activity score.

The longest L score (L = 20.6 cm) was detected in a case having single segment affection starting at the ileocecal junction (D = 0) and involving the terminal ileum with histopathological grade of 3 (Fig. 9A). The shortest L score (L = 1.4 cm) was detected in a case having single segment affection at the ileum (D = 3.2 cm) with histopathological grade of 1. These results support the strong correlation between L and disease activity. Sometimes this was not achieved as L recorded 2.8 cm and histological inflammatory activity score was 3 with secondary small bowel obstruction (Fig. 7).

D varied from a minimum of 0 till a maximum of 6.7 cm. Spearman rank order correlation coefficient showed a weak correlation of D (RHO = 0.222) with the histological inflammatory activity score. This is clearly justified when comparing two cases with CD and ileocecal junction affection (D = 0) having two different histological inflammatory activity scores (Fig. 9A and B).

4. Discussion

CD is a transmural inflammatory process involving the bowel wall and mesentery [12].

The disease activity assessment is important to choose the appropriate line of management and monitor the effects of treatment in follow up studies.
Crohn’s disease activity index (CDAI) scores reflect extra-enteric inflammation rather than enteric inflammation [13].

Endoscopy and biopsy are the gold standard for assessing the inflammatory activity of CD [11]. Small bowel loops are difficult to reach with endoscopy, accompanied by increased risk for bleeding and perforation [14]. Furthermore, endoscopic examination including biopsy is not always immediately available and can be stressful for the patient [11].

Imaging studies are necessary for evaluating the extent of disease and the presence of complications, such as fistula or abscess [13]. CTE has received increasing attention because of its ability to detect small bowel mucosal inflammation, as well as the extraintestinal inflammatory changes [15].

Several studies have reported the imaging features of CTE to be helpful in the diagnosis of active CD, and evaluated whether imaging findings are correlated to disease activity for each CTE finding [16].

Recent studies have reported mural hyperenhancement and increased mural thickness as the most sensitive CT findings of active CD [17].

In a study performed by Park et al. [13] there was moderate correlation between mesenteric fat density, mural hyperenhancement, mural stratification and mural thickenings scoring RHO of 0.548, 0.516, 0.487 and 0.442 respectively after studying 39 patients. This was lower than current study results as RHO scored 0.663 as strong correlation between length of affected segments and histological findings after studying 54 patients.

Paquet et al. [11] studied 42 patients and obtained moderate correlation of mesenteric adenopathy and wall thickness with histopathology as RHO scored 0.54 and 0.40 respectively. They
also obtained weak correlation of mesenteric fat stranding and abscess formation with histopathology as RHO scored 0.33 for each.

In this study another parameter of disease activity estimation was tried. The distance between the ileocecal junction and first affected segment was measured in each case (D). Unfortunately, there was weak correlation with histopathological grades and RHO scored 0.222. This was too far from results obtained by Paquet et al. [11] as the least calculated correlation coefficient was RHO of 0.318 after correlation of comb sign as CTE findings with C reactive protein (CRP) levels.

The added value of CTE findings for inflammatory activity of CD may be important in subjects whose pathology is located mainly in small bowel loops. It gives a total overview regarding diseased segments, extraintestinal abscess formation and extent of luminal perforation which cannot be assessed by endoscopy. It also offers the opportunity for detection of non intestinal manifestations of CD such as spondylarthitis and sacroiliitis.

CTE had limitations as the radiation dose is higher than that from a routine single phase scan. MRI is a good radiation-free non invasive technique that can be used as an alternative for evaluation of CD. The current study focused on ileal involvement; however, the study revealed all small and large bowel segments.

In conclusion CTE provides accurate data about the lengths of affected ileal segments positively correlated with the histological inflammatory activity score and can be considered a good predictor of severity of the disease. It also defines the extraintestinal manifestations and complications. This data is mandatory for clinician to decide and start the appropriate line of therapy till endoscopy and histopathological results become available particularly in acute phase of the disease.

<table>
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<tr>
<th>RHO</th>
<th>N</th>
<th>Inflammatory activity versus</th>
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<tbody>
<tr>
<td>0.663</td>
<td>54</td>
<td>L (length of affected segment or sum of lengths of affected segments)</td>
</tr>
<tr>
<td>0.222</td>
<td>54</td>
<td>D (distance between the ileoceleal junction and first affected ileal segment)</td>
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Table 2
Correlation of L and D with histological inflammatory activity score.

Fig. 8. 33 years old female patient with terminal ileum single segment CD, histopathological activity grade 3 (arrows). (A) 2D coronal image and (B) 2D axial image. L = 10.9 and D = 0.

Fig. 9. (A) 37 years old male patient with ileocecal junction and terminal ileum single segment CD, histopathological activity grade 3 (dashed circle). 2D coronal image. L = 20.6 and D = 0. (B) 31 years old male patient with ileocecal junction and terminal ileum single segment CD, histopathological activity grade 1 (dashed circle). 2D coronal image. L = 19.3 and D = 0.
Conflict of interest

The authors declare that there are no conflict of interests.

References


