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Diagnostic role of computed tomography enterography (CTE) in assessment of intra-mural and extra-intestinal CT findings in active Crohn's disease (CD)

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Abstract

Background: Crohn's disease (CD) is a ruinous bowel disease, which, if left uncured, leads to penetrating bowel complications. Computed tomography enterography (CTE) is nowadays accepted as a principal modality for the assessment of small bowel diseases. The aim of this study is to assess the role of CT enterography in the identification of intramural as well as extra-intestinal CT changes yielding more thorough data about the level and severity of the disease process thus planning appropriate treatment strategy.

Results: From March 2017 to January 2019, 50 patients in Cairo, Egypt, who had clinical manifestations of inflammatory bowel disease, were evaluated by MDCTE. CT image analysis was processed, including anatomical localization of bowel segments affection, assessment of mucosal thickening and hyper-enhancement, and extra-enteric affection. Diagnosis of Crohn's disease (CD) was confirmed by endoscopy and histopathology; mucosal thickening was seen in 42 patients (84%), mucosal hyper-enhancement was seen in 44 patients (88%) while engorgement of vasa recta (comb's sign) was seen in 38 patients (76%).

Conclusion: Although ileocolonoscopy is a proven sensitive method to detect mucosal injury and diagnose disease activity, it is limited by its maximal extent and inability to detect transmural complications as well as limited ability to assess deep bowel wall involvement. CT enterography (CTE) is a valuable technique in diagnostic evaluation of intramural and extra-intestinal involvement in Crohn's disease (CD) during disease activity.

Keywords: CT enterography, Intra-mural, Extra-intestinal, Active Crohn's disease

Background

Crohn's disease is a chronic inflammatory disease affecting the gastrointestinal tract (GIT) with a propensity toward remission and exacerbation. It may affect any segment of the gastrointestinal tract starting from mouth to anus, even sometimes involving multiple discontinuous areas [1].

Crohn's disease, being one of the main subtypes of idiopathic inflammatory bowel disease, is distinguished

by showing chronic, transmural, and often granulomatous, intestinal affection. It mainly involves the small bowel (almost 80% of the cases), with ileocecal region in 50% of the cases [2].

Crohn's disease (CD) is also a ruinous bowel disease, which, if left uncured, leads to penetrating bowel complications [3].

Endoscopies and barium studies are the initial tools for diagnosis and evaluation of the degree of bowel affection in Crohn's disease; however, they are limited in their capacity to demonstrate the transmural and/or extra-intestinal extent of the complications [1].

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Computed tomographic enterography (CTE) has been established as a useful diagnostic method for evaluation of small bowel disease. In CT enterography, multi-slice CT is united with through oral luminal distention of small bowel using neutral enteric contrast material [4].

CT enterography provides a superior evaluation of the entire thickness of the bowel wall and also assess extra-intestinal affection, giving a more complete picture of the degree and severity of the disease [5].

Small bowel inflammation in its earliest phase could be manifested only by subtle mucosal hyper-enhancement on arterial phase images, with little or no wall thickening or enhancement abnormalities in venous phase [6].

With progression of the degree of inflammation, thickening of the bowel wall is usually visualized (together with frank mucosal hyperemia on the venous phase images), with CT evidence of mural stratification ("target" or "double-halo appearance") [7].

The mural stratification commonly reflects the juxtaposition of avidly enhancing mucosa with underlying hypodense submucosal edema in the bowel wall, and in some cases, hyperemia of the serosal surface of the affected bowel wall [8].

Mucosal hyper-enhancement with decreased intramural attenuation gives the image of classic bilaminar mural stratification. While alternating areas of high and low attenuation due to mucosal and serosal hyper-enhancement and low intra-mural attenuation give the tri-laminar mural stratification. Mural hyper-enhancement often involves the mesenteric border of a small bowel loop more than the anti-mesenteric border [9, 10].

Intestinal edema and inflammatory infiltrate may be represented by low intramural attenuation. Mural stratification due to intramural edema is likely more diagnostic of active disease compared to homogeneously enhanced wall, while the presence of intramural fat represents more chronic process [11].

One of the main important signs is the "comb sign" which represents engorgement of vasa recta that penetrates the bowel wall perpendicular to bowel lumen, simulating the appearance of a comb. Comb sign together with increased attenuation of mesenteric fat represents the most specific CT sign for active Crohn's disease [12].

Although ileocolonoscopy is a proven sensitive method to detect mucosal injury and diagnose disease activity, it is limited by its maximal extent and inability to detect transmural complications as well as limited ability to assess deep bowel wall involvement [13], so the aim of this study is to assess the role of CT enterography in the identification of intramural as well as extra-intestinal CT changes yielding more thorough data about the level and severity of the disease process thus planning appropriate treatment strategy.

Methods

Ethical consideration

This study was approved by the Ethical Research Committee on March 2017. The ethics committee reference number is not available now.

All patients had provided a written informed consent. The results of this research were only used in scientific purposes and not in any other aims.

Study design

This prospective study included 50 patients (27 males, 23 females) with an age ranged from 25 to 67 years with mean age of 36.8 years; all had clinical manifestations of chronic diarrhea and one or more of the following symptoms: loss of weight, vague abdominal pain, and recurrent vomiting, and referred to MSCT enterography assessment. Diagnosis was confirmed by GI endoscopy and histopathology.

MSCT enterography was done to all patients as requested. The study was conducted between March 2017 and January 2019, in Cairo, Egypt.

Twenty other patients were excluded from this study, 13 patients with positive CTE radiological findings, yet with negative endoscopy results for Crohn's disease ($n=13$, 18.5%), which represent false positive test as well as 7 patients with no CTE radiological findings, yet with positive endoscopy results for Crohn's disease ($n=7$, 10%), which represent false negative test.

Inclusion criteria

Fifty patients with clinical manifestations of chronic diarrhea and one or more of the following symptoms: loss of weight, vague abdominal pain, and recurrent vomiting. They gave positive findings in CTE and confirmed to be Crohn's disease by endoscopy.

Exclusion criteria

Patients with lactose intolerance, pregnant females, patients who could not tolerate ingestion of whole amount of oral negative contrast, patients who gave positive radiological signs of Crohn's disease, yet with negative endoscopy results (13 patients); CTE false positive test as well as patients who gave negative radiological signs of Crohn's disease, yet with positive endoscopy results (7 patients); CTE false negative test.

Methods

All enrolled patients were subjected to the following:

- Full clinical assessment and revision of all patients' laboratory investigations including kidney function tests (blood urea and serum creatinine).

- Revision of all radiological and endoscopic diagnostic investigations was previously done for the patients.
- Patients were scheduled to undergo MSCTE and the results were compared to the GIT endoscopies as well as histopathology results.

CTE technique

- All patients fasted for 8 h prior to the CT examination.
- The night before the examination, a cleaning enema was performed.
- Before scanning, patient ingest a total of 1500~ 2000 mL of 2.5% mannitol solution in 400–500 mL aliquots every 15 min.
- Twenty milligrams of anisodamine was administrated intramuscularly to relax smooth muscle spasm that could mimic bowel wall thickening or abnormal enhancement.
- Perfect luminal distention gave easy and efficient luminal navigation so provided accurate detection and characterization of any small bowel pathologies [14].
- Patients were scanned by using Toshiba Aquilion 64-detector row CT starting from diaphragm and down to ischial tuberosity.
- During scan, 1.5 mL/kg iopromide (ultravist 300, Schering, Berlin, Germany) was injected with a rate of 3–4 mL/s using a power injector.
- Maximal small bowel enhancement on MDCT was obtained to be 50 s after administration of intravenous contrast. We therefore administer contrast intravenously during this enteric phase. Obtaining the enteric phase images started at 35 s after the trigger mark (trigger threshold level was 100 Hounsfield unit (HU) [14, 15].
- CT scan parameters were 120 kV, 200–250 mAs, collimation 64×0.5 mm, slice thickness of 3 mm, and a reconstruction interval of 3.0 mm.
- Automated image reconstruction generate images in all three planes (3-mm thickness), after the volume data acquisition in the axial plane. Multi-planar reformatting (MPR) of the data provides excellent demonstration of enteric and extra intestinal abnormalities.

CTE images analysis

All radiological data were reviewed on a workstation (Vitrea version 3.7). Every computed tomography enterography examination was thoroughly evaluated by two specialized gastrointestinal tract radiologists, 12 and 14 years of experience. Each of them revised the radiological finding individually then compared their findings

Table 1 Clinical presentation of the studied group

Clinical presentation	Number	Percent
Chronic diarrhea	47	94%
Abdominal pain	41	82%
Loss of weight	39	78%
Vomiting	10	20%

NB some patients had more than one clinical symptom

together. Both of them were blinded to clinical and endoscopic findings.

CT enterography findings ranging from subtle mucosal hyper-enhancement, bowel wall thickening, bi-lamellar or tri-lamellar mural stratification, comb sign, and different complications were assessed thoroughly.

Statistical analysis

Owing to the small sample size, all findings were presented as medians, means, and percentages.

Results

This prospective study included 50 patients (27 males, 23 females) with an age ranged from 25 to 67 years (mean age of 36.8 years) confirmed to have Crohn's disease by endoscopy and histopathology. MSCT enterography was performed to all patients and had been processed in a separate workstation.

The clinical presentation of the studied patients is shown in Table 1 and reveals that some patients presented with more than one clinical symptom. However, chronic diarrhea was the main presentation. It was seen in 47 patients (94%), while 41 patients presented with abdominal pain (82%). Followed by 39 patients presented with loss of weight (78%) and 10 patients presented with vomiting (20%).

All patients were scheduled for endoscopy after CTE and diagnosis of disease activity was correlated with both

Table 2 Radiological findings seen in active Crohn's disease on MDCTE

Radiological findings	Number	Percent
Mucosal thickening	42	84%
A (< 4 mm)	33	66%
B (> 4 mm)	9	18%
Mucosal hyper-enhancement	44	88%
Comb's sign	38	76%
Abscess formation	3	6%
Lymph nodes	27	54%
A (< 1 cm)	16	32%
B (> 1 cm)	9	18%
Bowel dilatation	8	16%
Skip lesions	12	24%

endoscopic and histologic findings. Several endoscopic features were described in CD activity. Starting from mild mucosal injury which was characterized by mucosal erythema and edema and with increasing disease activity, endoscopies described progressive mucosal damage ranging from aphthous ulcers, shallow ulcers, up to deep ulcerative lesions. The degree of surface involvement was correlated with disease severity.

We excluded 20 patients, 13 patients with positive CTE radiological findings, yet with negative endoscopy results ($n=13$, 18.5%), which represent false positive test as well as 7 patients with negative CTE radiological findings, yet with positive endoscopy results for Crohn's disease ($n=7$, 10%), which represent false negative test.

The radiological findings which were noted in active Crohn's disease on MDCTE are shown in Table 2.

The most common radiological finding was mucosal hyper-enhancement, which was seen in 44 patients (88%)

(Figs. 1, 2, 3, and 4) followed by mucosal thickening, which was reported in 42 patients (84%) (Figs. 2 and 3). From which 33 patients thickening was >4 mm (66%) while 9 patients was <4 mm (18%). Bilaminar mural stratification was seen in 13 patients (26%) (Figs. 2 and 3) and tri-laminar mural stratification was seen in 8 patients (16%) (Fig. 5).

Engorgement of vasa recta (comb's sign) was seen in 38 patients (76%) (Figs. 1, 3, and 4), lymph node enlargement was noticed in 27 patients (54%) (Figs. 1, 2, 3, and 5). Skip lesions were reported in 12 patients (24%). Abscess formation was seen in 3 patients (6%) (Fig. 5), and bowel dilatation was seen in 8 patients (16%) (Fig. 1).

One case presented with recurrence of clinical symptoms after 12 years from surgical intervention, CT enterography was done and suggested active disease and diagnosis was confirmed by endoscopy and histopathology (Fig. 6).

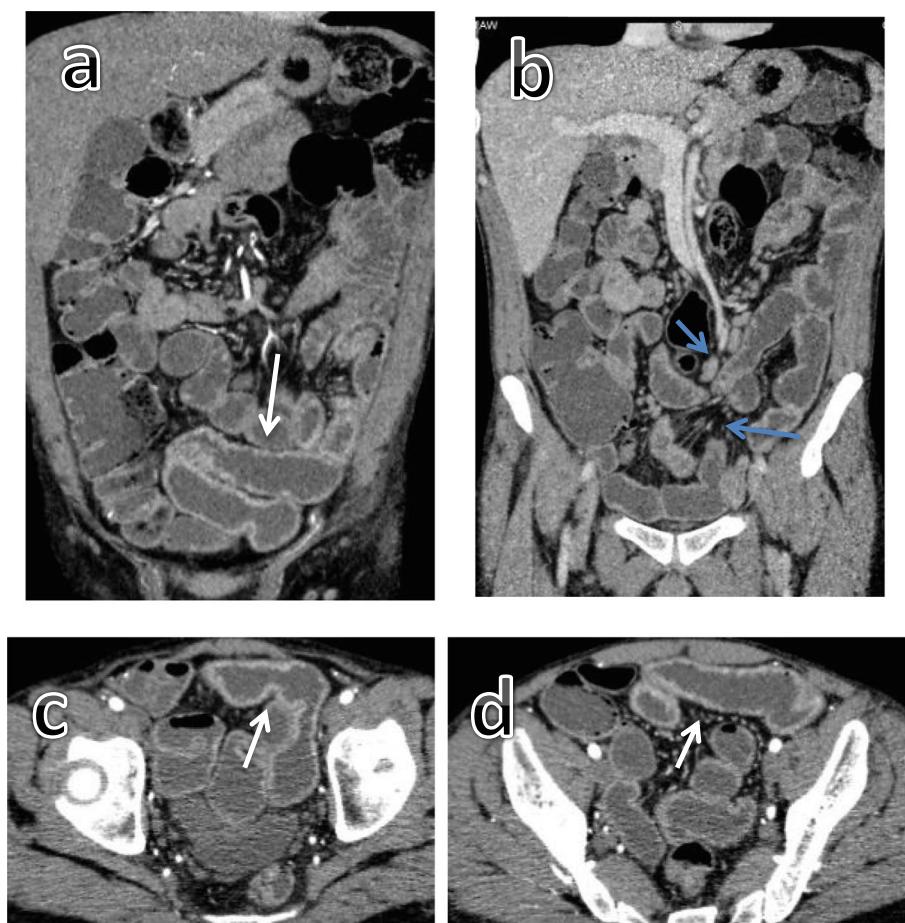


Fig. 1 Male patient 47 years old referred with chronic diarrhea and vague abdominal pain. CTE was done, coronal images (a and b), axial images (c and d) showed hyper-enhancement of segments of ileal loops (white arrows) with skip lesions, bowel dilatation, engorgement of vasa recta (+ve comb's sign), and multiple prominent related mesenteric lymph nodes (blue arrows). Endoscopic and pathological diagnosis was Crohn's disease

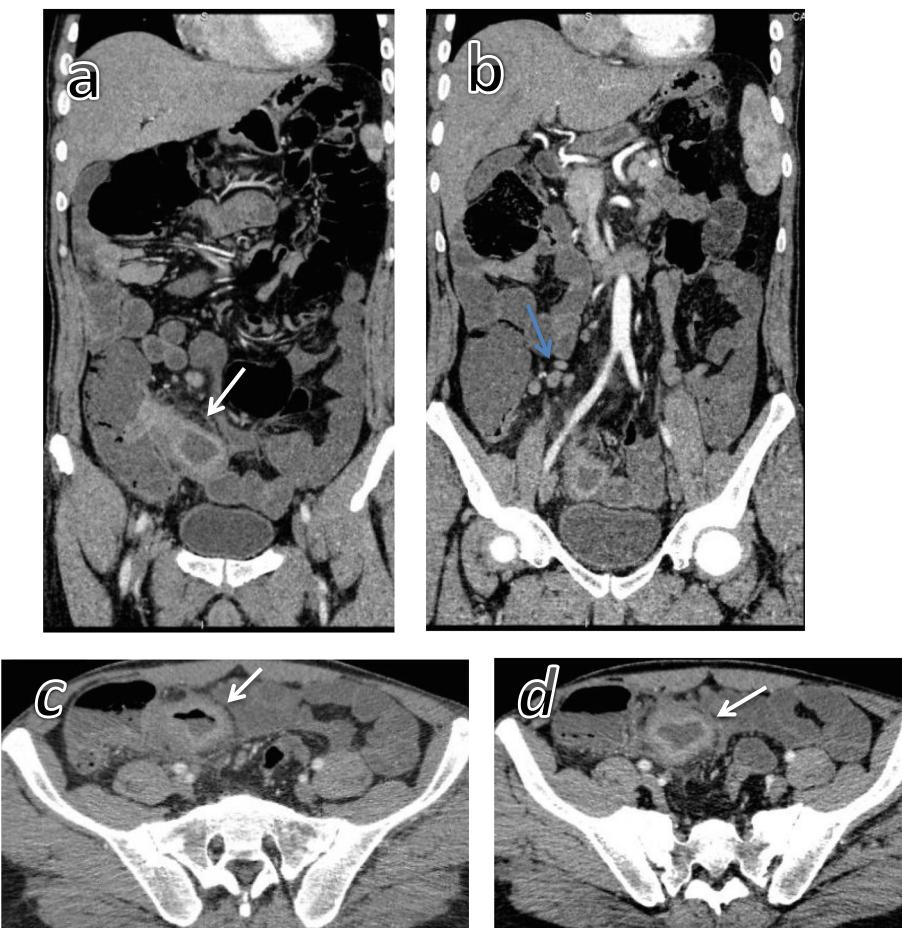


Fig. 2 A 41-year-old male patient referred with chronic diarrhea and abdominal pain (right iliac fossa region). CT enterography was done, coronal images (a and b), axial images (c and d) showed bilaminar mural stratification of the terminal ileum with mucosal hyper-enhancement and submucosal hypodense edema (white arrows) associated with smudging of surrounding mesenteric fat planes and few prominent regional mesenteric LNs (blue arrow) denoting active disease process. Diagnosis was confirmed by endoscopy and histopathology

Discussion

Although ileocolonoscopy is a proven sensitive method to detect mucosal injury and diagnose disease activity, it is limited by its maximal extent and inability to detect transmural complications as well as limited ability to assess deep bowel wall involvement [13].

Several imaging methods including computed tomography (CT), magnetic resonance (MR), and ultrasound (US) were described as essential tests for assessing different mural changes as well as extra-intestinal disease complications [13].

As modern imaging techniques have been improved to detect and quantify mucosal injury, CT enterography (CTE) was described as an imaging modality for small bowel disease assessment over the recent years and has a main role in the diagnosis and evaluation of patients with inflammatory bowel disease (IBD) with a performance comparable to ileocolonoscopy [16].

In current study, we did not use positive oral contrast as it would obscure subtle mucosal changes seen in mild/early disease such as mucosal hyper-enhancement, which is a matching study done by Schindera ST et al. [17] who also stated that positive oral contrast agent (containing iodine) is not routinely used for CTE.

In this study, we observed that the earliest radiological finding of Crohn's disease activity at CTE was mucosal hyper-enhancement, which was also described by Min JP and Joon SL [16], who suggested that mural hyper-enhancement is a sensitive finding in detecting early disease activity. It is very important to compare the bowel loops with similar degree of distension because normal collapsed loops show greater attenuation than distended bowel loops.

As the disease progresses, mural thickening was noticed combined with mucosal hyper-enhancement and that was also noticed by Booya et al. [9] who stated that mural

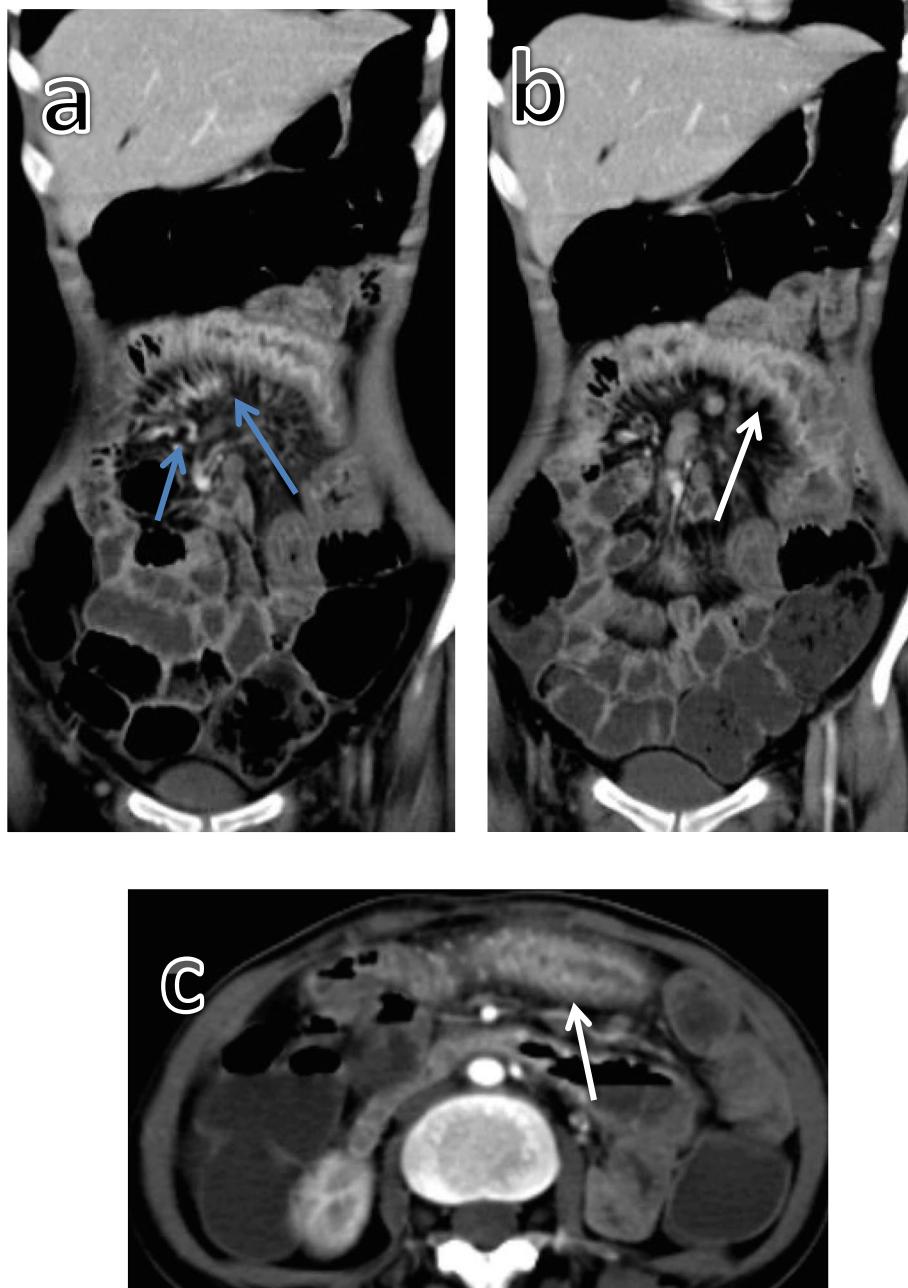


Fig. 3 A 22-year-old female patient referred with chronic diarrhea, abdominal pain, and weight loss. CT enterography was done, coronal images (a and b), axial image (c) showed a long segment of jejunal and proximal ileal loops circumferential mural thickening and hyper-enhancement with submucosal edema giving bilaminar mural stratification pattern (white arrows). Associated engorgement of vasa recta (comb's sign) (blue arrow) and prominent mesenteric lymph nodes (images a and b) were seen. Endoscopy and biopsy confirmed active Crohn's disease

thickening and hyper-enhancement are the most diagnostic computed tomography enterography (CTE) findings that suggest active inflammatory Crohn's disease.

Bilaminar mural stratifications refer to mucosal hyper-enhancement and decreased intra-mural attenuation. In current study, it was seen in 13 patients (26%) while trilaminar mural stratification refers to alternating high and low attenuation areas that occurs due to mucosal and

serosal hyper-enhancement with low intramural attenuation. It was seen in 8 patients (16%). Low intramural attenuation can represent edema, inflammatory infiltrates, or fat. Hara et al. [11] concluded that intramural edema represented by mural stratification is much more indicative of active disease as compared to homogenously enhanced intestinal wall. However, Madureira AJ [18] stated that mural stratification is not specific for Crohn's disease

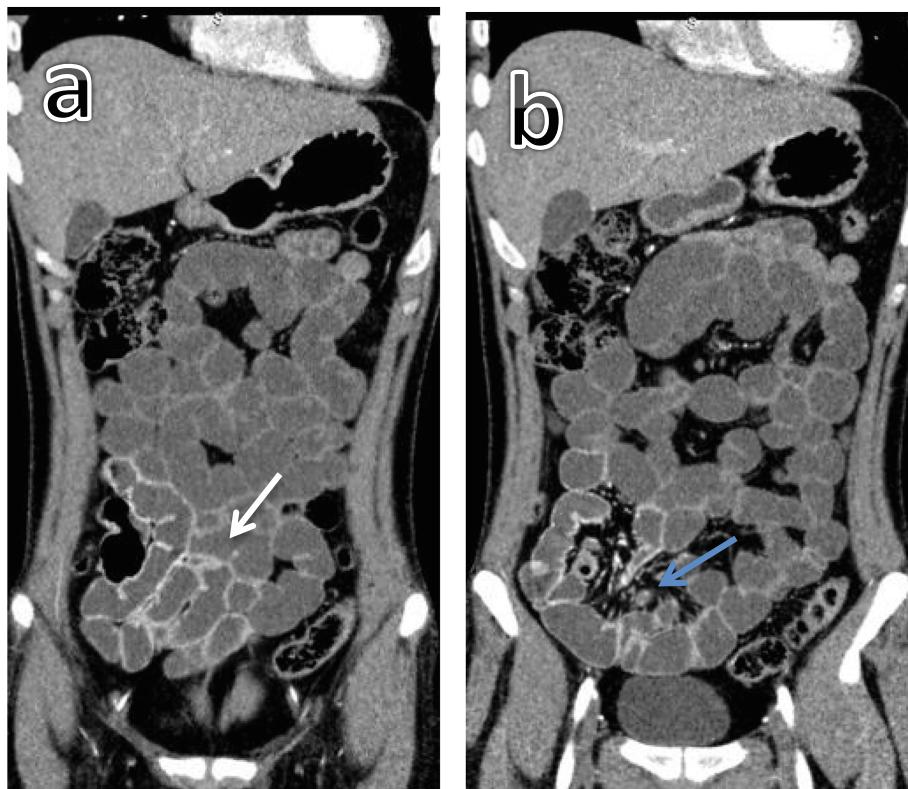


Fig. 4 A 30-year-old male patient referred with loss of weight, chronic diarrhea, and vague abdominal pains. CT enterography was done, coronal reformatted images (a and b) showed hyper-enhancement of distal ileal loops (white arrow) with engorgement of vasa recta (+ve comb's sign) (blue arrow) denoting early active Crohn's disease and that was confirmed by endoscopy and histopathology

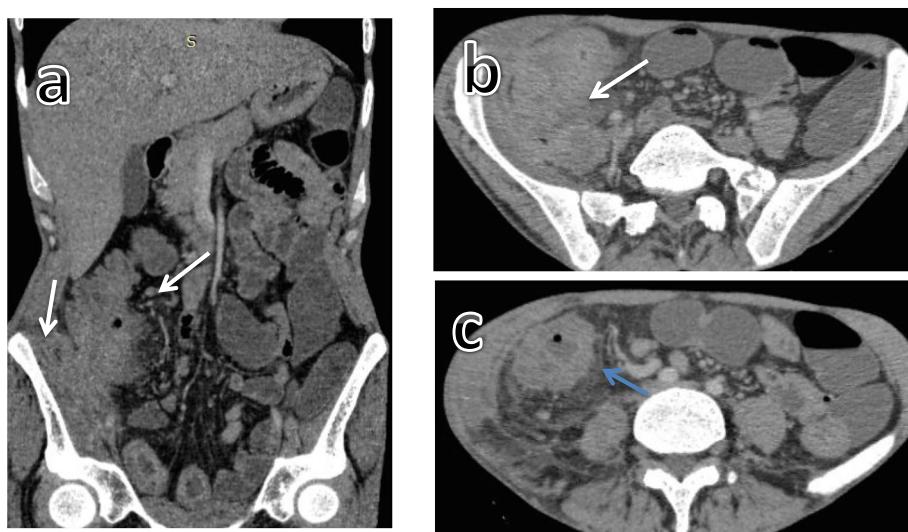


Fig. 5 Male patient 43 years old presented with fever, right iliac fossa pain, and chronic watery diarrhea. Coronal reformatted CT enterography image (a), axial CT enterography images (b and c) show circumferential mural thickening and hyper-enhancement of the cecum and the ascending colon, tri-laminar mural stratification could be noticed (image c) (blue arrow). Marked smudging of surrounding fat planes with extension of inflammatory process to surrounding structures is detected with associated abscess formation. Notice the swollen edematous ilio-psoas muscle being inseparable from inflamed adjacent bowel segments with multiple enlarged enhancing regional lymph nodes (images a and b) (white arrows). Endoscopy and biopsy revealed active Crohn's disease

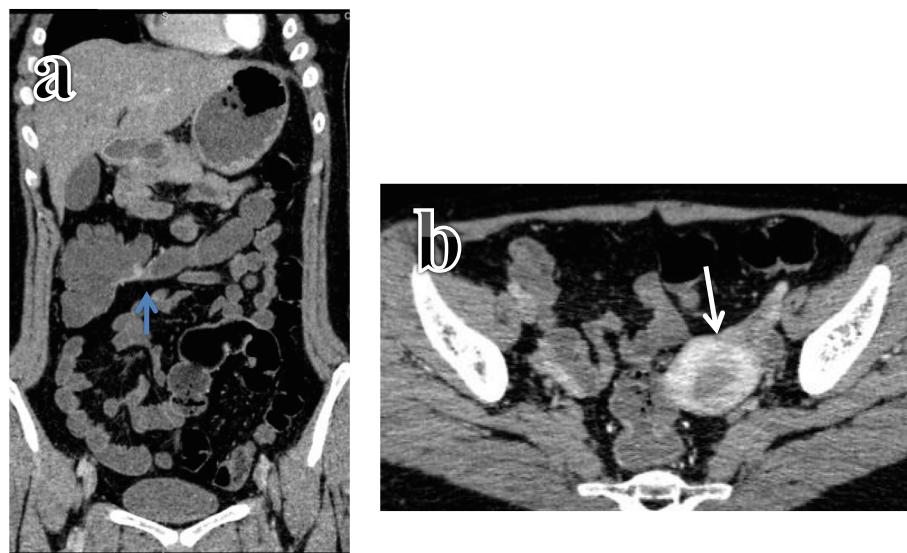


Fig. 6 A 29-year-old female patient (known case of Crohn's disease) operated upon 12 years ago (right hemicolectomy and ileotransverse anastomosis). Referred with chronic diarrhea and generalized abdominal pain. CTE was done (a) coronal image, (b) axial image showed a short segment of the ileal loop showing circumferential mural thickening and hyper-enhancement with smudging of surrounding fat planes (image b) (white arrow) (denoting disease activity). Hyper-enhancement at anastomotic site was seen (image a) and was described in endoscopy as a small ulcer (blue arrow)

and may be also seen with other small bowel diseases, such as ischemia, ulcerative colitis, and radiation enteritis. Inflamed bowel segments are commonly absent at endoscopy and histopathologic analysis. Trilaminar enhancement is often identified more with MR enterography than in CT enterography, probably due to the superior contrast resolution at MR enterography [10].

Engorgement of vasa recta "comb sign" refers to congested vasa recta that penetrate the small bowel wall perpendicular to bowel lumen, simulating the appearance of a comb; it is another indicator of disease activity and was found in 38 patients (76%) in this study. Colombel et al. [12] also described increased attenuation of the mesenteric fat in combination with the "comb" sign are common CT findings seen in active Crohn's disease. The "comb sign" is also reported to be associated with higher C-reactive protein (CRP) levels than for patients with normal vasculature [12].

Extension of the inflammatory process across serosal surface into adjacent mesentery or structures leads to fistula, sinus tract, and/or abscess formation. In this study, three cases showed abscess formation as an extra-enteric complication of active Crohn's disease. Detection of extra-intestinal complications is very important as it affects the decision to treat medically or surgically, and it also affects the method of surgical approach either laparoscopic or open. Booya et al. [19] also reported the importance of detection of clinically unsuspected penetrating disease on CTE examinations as it leads to alteration in therapy regimen in up to 61% of patients with Crohn's disease.

CTE is not also used to assess medical treatment response, which manifests as decreasing mural hyper-enhancement, bowel wall thickening and improvement of the engorged vasa recta, but it also can detect disease recurrence after remission or even after surgical treatment. In this study, one case which was surgically treated represented with recurrence of clinical symptoms including abdominal pain and diarrhea, CTE showed segment of mural thickening and enhancement suggesting disease activity and that was proved by endoscopy results. Wu et al. [20] also reported that CTE findings have high correlation with clinical symptoms before and after treatment.

Although CT enterography (CTE) is optimized to detect intestinal damage and extra-intestinal findings and complications, this study faced some limitations such as limited number of patients, lack of radiological correlation with treatment protocols, and the obtained radiological findings are not specific to Crohn's disease so some cases gave false positive results and were not pathologically proved to be Chron's disease by endoscopy and histopathology.

Conclusion

Computed tomography enterography (CTE) is an established technique for the assessment of active Crohn's disease as it offers the identification of intramural and extra-intestinal CT findings aiding in differentiating between active and fibrotic disease thus planning suitable treatment strategy either medical or surgical.

Abbreviations

CD: Crohn's disease; CT: Computed tomography; CTE: CT enterography; GIT: Gastro intestinal tract; HU: Hounsfield unit; IBDs: Inflammatory bowel diseases; IV: Intravenous; MDCT: Multi-detector computed tomography; MR: Magnetic resonance; MSCT: Multi-slice computed tomography; MSCTE: Multi-slice computed tomographic enterography; US: Ultrasonography

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Authors' contributions

MG and RM have designed this study together. MG contributed to the data collection, RM contributed to data analysis. MF and RM contributed to data processing. MF and RM shared in writing the manuscript together. The authors read and approved the final manuscript.

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Availability of data and materials

Data available within the article or its supplementary materials.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethical Research Committee of Faculty of Medicine Cairo University in Egypt on March 2017. The ethics committee reference number is not available.

A written consent was taken from all patients accepting to participate in our research work.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declared that they have no competing interests.

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