

Gastroenterology Report, 5(3), 2017, 219–225

doi: 10.1093/gastro/gow037 Advance Access Publication Date: 22 December 2016 Original article

ORIGINAL ARTICLE

Identification of the distinguishing features of Crohn's disease and ischemic colitis using computed tomographic enterography

Min Chen^{1,2}, Erick M. Remer^{1,3}, Xiuli Liu¹, Rocio Lopez¹, Bo Shen^{1,*}

¹Department of Gastroenterology/Hepatology, Cleveland Clinic Foundation, Cleveland, OH, USA, ²Department of Gastroenterology, Zhongnan Hospital of Wuhan University, Wuhan, Hubei, China and ³Section of Abdominal Imaging, Imaging Institute, Cleveland Clinic Foundation, Cleveland, OH, USA

*Corresponding author. The Center for Inflammatory Bowel Diseases, Digestive Disease and Surgery Institute/A31, The Cleveland Clinic Foundation, 9500 Euclid Ave., Cleveland, OH 44195, USA. Tel: +1-216-444-9252; Fax: +1-216-444-6305; E-mail: shenb@ccf.org

Abstract

Background and aims: The differential diagnosis between Crohn's disease (CD) and ischemic colitis (ISC) is important as their clinical management is different. ISC can easily be misdiagnosed as CD, especially in elderly populations. The distinctive radiographic features of the two disease entities have not been investigated. The aim of this study is to assess the utility of computed tomographic enterography (CTE) in the differential diagnosis between CD and ISC.

Methods: Patients with confirmed CD and ISC were identified through an electronic medical record search of the Cleveland Clinic Foundation. Patients who had undergone CTE, with or without concurrent colonoscopy and histopathological specimens, were included in this study. CTE images were blindly re-reviewed by an expert gastrointestinal radiologist. The sensitivities, specificities, accuracies and positive and negative predictive values for each of the CTE findings in differentiating CD from ISC were estimated. Kappa coefficients (κ) were calculated to measure diagnosis agreement between CTE and the reference standard. **Results:** A total of 34 eligible patients were included in this study with 17 having CD and 17 having ISC. In differentiating CD from ISC, the presence of mucosal hyperenhancement and absence of the "target sign" on CTE showed a sensitivity of 100% each for CD, while the two radiographic features yielded a low specificity of 35.3% and 76.5%, respectively. The presence of stricture had a lower sensitivity of 64.7% for the detection of CD but had a high specificity of 100%. In distinguishing CD from ISC, the accuracy of presence of mucosal hyperenhancement and the absence of the target sign achieved an accuracy of 100% for distinguishing CD from ISC. There was a good correlation between CTE and the reference standard for distinguishing CD from ISC ($\kappa = 0.882$). **Conclusions:** CTE appeared to be clinically useful in distinguishing CD from ISC.

Key words: computed tomographic enterography; Crohn's disease; ischemic colitis; differential diagnosis

Introduction

It is clinically important to differentiate between Crohn's disease (CD) and ischemic colitis (ISC). Accurate diagnosis is crucial for

effective clinical management, which in turn may change the disease course. Differentiating between CD and ISC, on the other

Submitted: 9 August 2016; Revised: 25 September 2016; Accepted: 4 October 2016

© The Author(s) 2016. Published by Oxford University Press and Sixth Affiliated Hospital of Sun Yat-Sen University.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/ licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com hand, can be difficult, especially in elderly patients who are at the second peak of the bimodal age distribution of CD. Often, patients have been diagnosed first as having CD based on their clinical presentation, endoscopic and histopathological features but have then had the diagnosis changed to ISC after evaluation of the surgical specimen post colectomy or by their later clinical course [1–4]. Clinical presentations often overlap between CD and ISC. Histopathological features of CD are chronic inflammatory changes including increased mononuclear cell infiltration, crypt distortion and basal lymphoplasmacytosis, which can also be seen in histopathological specimens of ISC. Although the presence of noncaseating granulomas is one of the distinguishing features of CD, it is present in only 30–40% of cases on mucosal biopsy [5,6]. Other endoscopic, histopathological and radiographic distinguishing features for CD or ISC have not been systemically investigated.

Computed tomographic enterography (CTE) has been extensively used in gastroenterology practice. Previous publications have shown that some CTE features such as mucosal hyperenhancement and bowel wall thickness correlated with endoscopic and histopathological findings of inflammatory CD [7–9]. CTE has also been routinely used to detect postoperative recurrence of CD [10,11]. CTE is also useful in the diagnosis of ISC. One previous study showed that the demonstration of segmental distribution and circumferential bowel wall thickness on CT was the key point in diagnosing ISC after reviewing the CT scans of 54 patients with ISC [12]. However, the capabilities of CTE in the differentiation between CD and ISC have not been extensively studied.

Based on the previous publications and practice pattern in our tertiary care center, we hypothesized that CTE features of the bowel wall (due to underlying pathophysiology) may help differentiate CD from ISC. The aim of this study was to evaluate the utility of CTE in the distinction between CD and ISC.

Patients and Methods

Patients

Patients for this historical cohort study were identified from electronic medical records (EPICARE®). The study was approved by the Cleveland Clinic Institutional Review Board. All patients with ISC who met the inclusion criteria were included in the study. Patients with CD were randomly selected from our patient database from January 2004 to December 2010. The diagnosis of CD or ISC was made based on a combined assessment, before or after bowel resection surgery of: (i) clinical features, (ii) endoscopic findings' (iii) histopathological findings; and (iv) results of follow-up evaluation including response to medical therapy such as corticosteroids, immunomodulators, and/ or antitumor necrosis factor- α (TNF- α) biologics.

Inclusion and exclusion criteria

The inclusion criteria of ISC for this study were as follows: (i) confirmed diagnosis of ISC and (ii) patient history of CTE with or without concurrent colonoscopy and histology specimens. Patients with CD were randomly selected from the Inflammatory Bowel Disease (IBD) registry from January 2004 to December 2010. The exclusion criteria were: (i) other causes of chronic colitis or enteritis such as tuberculosis and (ii) a diagnosis of malignancy in the histology specimens.

Protocol

Patients who met inclusion and exclusion criteria had been evaluated with a standard protocol. Demographic, clinical, endoscopic and histopathological features were evaluated. All patients were followed up to evaluate their clinical course including their responses to medical therapy and their outcomes.

The colonoscopy reports and endoscopy photos were rereviewed by the expert endoscopist (B.S.). The colonoscopic findings were categorized as in remission, mildly active and active. The disease extent was categorized as involvement of the ileum, colon and ileocolon. All abnormal lesions including ulcerations, erythema, stricture and fistula were recorded.

Histopathological re-revaluation was performed on the specimens from colonoscopic biopsy and/or surgical bowel resection. An expert gastrointestinal pathologist (X.L.) evaluated the histology in a blind fashion. The following abnormal histologic categories were recorded: (i) basal lymphoplasmacytosis, (ii) crypt distortion, (iii) pyloric gland metaplasia, (iv) active inflammation, (v) atrophic gland, (vi) edema, (vii) lamina propria hyalinization, (viii) tissue eosinophilia, (ix) mural fibrosis, (x) muscle atrophy, (xi) neural hyperplasia, (xii) granulomas, (xiii) transmural inflammation, (xiv) vascular charge and (xv) fistula or fissuring ulcer.

CTE was performed with a standard institutional protocol. An expert GI radiologist (E.R.), who was blinded to the clinical, surgical, endoscopic or laboratory data, reviewed the CTE images. The following features on CTE were recorded: (i) mucosal hyperenhancement, (ii) the target sign, (iii) lymphadenopathy, (iv) stricture, (v) fistula or abscess, (vi) bowel-wall thickening, (vii) pericolonic infiltration, (viii) pneumatosis and (iv) peritoneal hemorrhage/fluid.

Definitions of variables

Demographic and clinical variables were defined as follows: smoking: consumption of >7 cigarettes per week for at least 6 months at the time of abdominal imaging or colonoscopy; former-smoker: cessation of smoking at least for 6 months; family history of CD: CD in first-degree relatives and regular NSAID use: regular use of NSAID more often than once per week at the time of CTE or colonoscopy.

Colonoscopic variables were defined as follows according to the Simplest Endoscopic Score for Crohn's Disease (SES-CD) [13]: remission: normal mucosa; mildly active: erythema, edema or aphthous or focal ulcers (diameter<0.5cm, ulcerated surface<10%); and active: large or diffuse ulcers (diameter>0.5cm, ulcerated surface>10%) or the presence of stricture.

Radiographic variables were defined as follows: mucosal hyperenhancement: segmental hyperattenuation of distended bowel loops relative to nearby normal-appearing loops; the target sign: involved bowel wall with 3 concentric rings of high, low and high density; lymphadenopathy: lymph node enlargement; strictures: segment of decreased luminal diameter; and bowel wall thickening: mural thickness of intestinal wall >3mm. In addition, radiographic comb sign was evaluated.

Outcome measurement

The primary outcome of the study was the comparison of CTE features between CD and ISC.

Statistical analysis

Descriptive statistics were computed for all factors. These included medians and percentiles for continuous factors and frequencies for categorical factors. The sensitivities, specificities, accuracies and positive and negative predictive values of CTE variables were calculated. Univariate analysis was used with

Table 1.	Demograph	nic and o	clinical	data
----------	-----------	-----------	----------	------

Factor	Crohn's disease (N = 17)	Ischemic colitis (N = 17)	<i>P</i> value 0.16	
Male gender, n (%)	9 (52.9)	4 (23.5)		
Age, years	47.3±16.9	65.1±15.3	0.003	
Smoking, n (%)*			0.37	
Never	6 (37.5)	10 (62.5)		
Former	5 (31.2)	3 (18.8)		
Active	5 (31.2)	3 (18.8)		
BMI at diagnosis, kg/m ²	23.0±5.0	26.7±6.2	0.06	
Abdominal surgery before diagnosis, n (%)	4 (23.5)	2 (11.8)	0.66	
Family history of IBD, n (%)	4 (44.4)	1 (7.7)	0.34	
Past medical history, n (%)				
Coronary artery disease	0 (0.0)	10 (58.8)	< 0.001	
Chronic obstructive pulmonary disease	2 (11.8)	3 (17.6)	1.00	
Hypertension	4 (23.5)	10 (58.8)	0.08	
Renal failure	0 (0.0)	1 (5.9)	1.00	
Liver failure	0 (0.0)	1 (5.9)	1.00	
Diabetes	0 (0.0)	3 (17.6)	0.23	
Regular NSAID use, n (%)	3 (17.6)	5 (29.4)	0.69	

*Data not available for all subjects.

BMI, body mass index; IBD, inflammatory bowel disease; NSAID, non-steroidal anti-inflammatory drugs.

chi-square or Fisher exact test when any expected cell counts were <5. Kappa coefficients (κ) were estimated to measure diagnostic agreement between CTE and the reference standard. The receiver operating characteristic (ROC) curves were constructed. A P value <0.05 was considered statistically significant. SPSS version 13.0 (SPSS Institute, Chicago, IL, USA) was used in all analyses.

Results

Demographic and clinical characteristics

A total of 34 eligible patients were included in this study, with 17 having CD and 17 having ISC. Demographic and clinical parameters are presented in **Table 1**. There was no significant difference in sex, smoking, body mass index (BMI) or history of regular use of nonsteroidal anti-inflammatory drugs (NASIDs) between the two groups. The mean age of the patients with CD was younger than those with ISC ($47.5\pm16.9 \text{ vs} 65.1\pm15.3 \text{ years}$, P=0.003). Ten (58.8%) patients in the ISC group and none in the CD group had a history of coronary artery disease. Four patients (23.5%) in the CD group had a history of bowel-related abdominal surgery before diagnosis including ileocolonic resection (n = 1), total colectomy with ileostomy (n = 2) and partial small bowel resection (n = 1). In contrast, only two patients in the ISC group underwent non-bowel resection abdominal surgery before the diagnosis (appendectomy).

Endoscopic evaluation

Before inception of the study, colonoscopy was performed in 14 patients with CD and 13 patients with ISC. There was no significant difference in endoscopic disease activity between the two groups. Disease extent and location were different. CD involved the ileocolon in 11 (78.6%) patients and the colon in 3 (21.4%) patients, while all patients with ISC involved the colon in isolated locations. Stricture was more frequent in patients with CD than those with ISC on colonoscopy (50.0% *vs7.7%*, *P*=0.033). None of the patients in these two groups had fistula on colonoscopy (Table 2).

Histopathological evaluation

Histopathological specimens were available in 14 patients with CD (3 biopsy specimens and 11 surgery specimens) and 11 patients with ISC (10 biopsy specimens and 1 surgery specimen). Basal lymphoplasmacytosis, crypt distortion, pyloric gland metaplasia, granulomas and mural fibrosis were observed in 92.9%, 92.9%, 92.3%, 64.3% and 57.1% of patients with CD, respectively; however, these features were not seen in any of the 11 patients with ISC. In contrast, atrophic glands and hyalinization of the lamina propria were found only in patients with ISC. The presence of active inflammation, edema and eosinophilia was not significantly different between the two groups. It is not feasible to evaluate the deeper features (e.g. muscle atrophy, neural hyperplasia, transmural inflammation, vascular change, fissuring ulcers and fistula) in colonoscopy biopsy specimens (**Table 3**).

Radiographic evaluation

The presence of mucosal hyperenhancement or stricture and the absence of the target sign were three discriminating variables for differentiating CD from ISC (Figure 1). Mucosal hyperenhancement was seen in all patients with CD, while the feature was observed in only 11 (64.7%) patients with ISC (P=0.02). Stricture was detected on CTE in 11 (64.7%) patients with CD and in none of the patients with ISC (P<0.01). No patients with CD showed the target sign on CT scan, while it was observed in 13(76.5%) patients with ISC (P<0.01). There were no significant differences between the two groups in other CTE variables including lymphadenopathy, fistula/abscess, bowel-wall thickening, pericolonic infiltration, pneumatosis and peritoneal hemorrhage/fluid (Table 4).

The diagnostic accuracy of CTE was evaluated. The sensitivities, specificities, positive and negative predicative values and accuracies of CTE in differentiating CD from ISC are listed in **Table 5**. To differentiate CD from ISC, we found the presence of mucosal hyperenhancement and the absence of the target sign to be the two most sensitive markers with sensitivities reaching 100% of each, but the specificity of mucosal hyperenhancement and the absence of the target sign was only 35.3%

Table 2. Endoscopic data

Factor	Crohn's disease (N = 14)	Ischemic colitis (N $=$ 13)	P value	
Disease activity, n (%)			1.00	
Remission	0 (0.0)	0 (0.0)		
Mildly active	3 (21.4)	4 (31.0)		
Active	11 (78.6)	9 (69.0)		
Disease extent, n (%)			< 0.001	
Ileum	0 (0.0)	0 (0.0)		
Colon	3 (21.4)	13 (100.0)		
Ileocolon	11 (78.6)	0 (0.0)		
Stricture, n (%)	7 (50.0)	1 (7.7)	0.03	
Fistula, n (%)	0 (0.0)	0 (0.0)	1.00	

Table 3. Histopathological data

Factor	Crohn's disease (N = 14)	Ischemic colitis (N = 11)	P value	
Basal lymphoplasmacytosis, n (%)	13 (92.9)	0 (0.0)	<0.001	
Crypt distortion, n (%)	13 (92.9)	0 (0.0)	< 0.001	
Active inflammation, n (%)	13 (92.9)	8 (72.7)	0.17	
Atrophic gland, n (%)	0 (0.0)	8 (72.7)	< 0.001	
Edema, n (%)	4 (28.6)	6 (54.5)	0.19	
Hyalinization of lamina propria, n (%)	0 (0.0)	11 (100.0)	< 0.001	
Eosinophilia, n (%)	3 (21.4)	0 (0.0)	0.10	
Granuloma, n (%)	9 (64.3)	0 (0.0)	< 0.001	
Pyloric gland metaplasia, n (%)*	12 (92.3)	0 (0.0)	< 0.001	
Mural fibrosis*	8 (57.1)	0 (0.0)	< 0.001	
Muscle atrophy*	0 (0.0)	0 (0.0)	_	
Neural hyperplasia*	7 (58.3)	0 (0.0)	_	
Transmural inflammation*	8 (66.7)	0 (0.0)	_	
Vascular change*	3 (25.0)	1 (50.0)	_	
Fissuring ulcer*	6 (50.0)	0 (0.0)	_	
Fistula*	3 (33.3)	0 (0.0)	_	

*Data not available for all subjects.

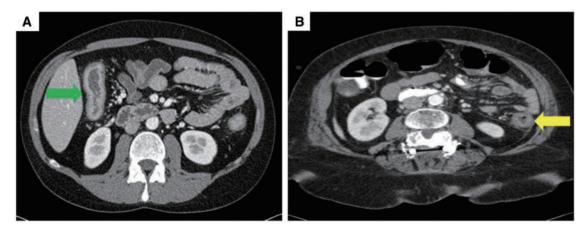


Figure 1. CT scan of abdomen. (A) Crohn's disease with mucosal hyperenhancement (green arrow). (B) Ischemic colitis with the target sign (yellow arrow).

and 76.5%, respectively. The stricture had a lower sensitivity of 64.7% but a higher specificity of 100%. It appears that the presence of mucosal hyperenhancement or stricture and the absence of the target sign were the three most discriminating features for CD and ISC with accuracy of 67.7%, 82.4% and 88.2%, respectively (P<0.01). The ROC curves are shown in **Figure 2**. The combination of the presence of mucosal hyperenhancement and the absence of target sign achieved an

accuracy of 100% for the differential diagnosis. The inclusion of the presence of stricture did not increase the accuracy for the differential diagnosis. Finally, all 17 (100.0%) patients with CD and 15 (88.2%) patients with ISC were diagnosed correctly by the combined assessment of CTE findings (Figure 2). For the differential diagnosis between CD and ISC, there was good correlation between the CTE diagnosis and the reference standard ($\kappa = 0.882$).

Table 4. CT enterography data

Factor	Crohn's disease (N = 17)	Ischemic colitis (N = 17)	P value	
Mucosal hyperenhancement	17 (100.0)	11 (64.7)	0.02	
Lymphadenopathy	3 (17.6)	0 (0.0)	0.23	
Stricture	11 (64.7)	0 (0.0)	< 0.01	
Fistula/ abscess	1 (5.9)	0 (0.0)	1.00	
Bowel wall thickening	16 (94.1)	16 (94.1)	1.00	
Pericolonic infiltration	6 (35.3)	6 (35.3)	1.00	
No target sign	17 (100.0)	4 (23.5)	< 0.01	
No pneumatosis	16 (94.1)	17 (100.0)	1.00	
No peritoneal hemorrhage/ fluid	17 (100.0)	14 (82.4)	0.23	

Table 5. Values for CT enterography features in the distinction between Crohn's disease and ischemic colitis

Factor	True positive	False positive	False negative	True negative	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
Mucosal hyperenhancement	17	11	0	6	100.0	35.3	60.7	100.0	67.7
Lymphadenopathy	3	0	14	17	17.7	100.0	100.0	54.8	58.8
Stricture	11	0	6	17	64.7	100.0	100.0	73.9	82.4
Fistula/abscess	1	0	16	17	0.0	9.1	0.0	100.0	9.1
Bowel wall thickening	16	16	1	1	94.1	5.9	50.0	50.0	50.0
Pericolonic infiltration	6	6	11	11	35.3	64.7	50.0	50.0	50.0
No target sign	17	4	0	13	100.0	76.5	81.0	100.0	88.2
No pneumatosis	16	17	1	0	94.1	0.0	48.5	0.0	47.1
No peritoneal hemorrhage/fluid	17	14	0	3	100.0	17.7	54.8	100.0	58.8
Hyperenhancement and no target sign	17	0	0	17	100.0	100.0	100.0	100.0	100.0
Hyperenhancement and stricture	11	0	6	17	64.7	100.0	100.0	73.9	82.4
Stricture and no target sign	11	0	6	17	64.7	100.0	100.0	73.9	82.4

We also found that the comb sign may not be specific for CD. We retrieved available images in the study (n = 17) and control (n = 16) and rescored. The comb sign was present in 10 patients (58.8%) in the study group and 3 in the control group (18.8%) (P=0.019).

Discussion

Our study showed that CTE is a useful modality for the differential diagnosis between CD and ISC. We found that the presence of mucosal hyperenhancement or stricture or the absence of the target sign were three CTE features distinguishing CD from ISC. When the presence of mucosal hyperenhancement and the absence of the target sign were taken into consideration together in a given case, the accuracy for the differential diagnosis between CD and ISC reached 100%. We also found that there was good correlation between CTE diagnosis and the reference standard (i.e. the composite evaluation of clinical, endoscopic and histopathological features), suggesting that CTE is useful in distinguishing CD from ISC.

The distinction between CD and ISC is important, as their treatment and prognosis are different. Corticosteroids, immunomodulators or anti-TNF- α biologics are often used in the management of CD, while supportive management with fluid hydration and avoidance of triggering factors are the mainstay therapy for ISC. Approximately 60–80% of patients with CD may require at least one bowel resection surgery during their lifetime due to disease-related complications or medically refractory disease [14–16]. In addition, postoperative recurrence of CD is common after bowel resection and anastomosis [17].

While ISC is typically treated conservatively, surgical intervention (including bowel resection and revascularization) may be required for those with bowel infarction, perforation or stricture from chronic injury. Recurrence of ISC after surgery is not common [18].

The challenge in distinguishing CD and ISC is well known, particularly in patients older than 50 years of age, as the second peak of the bimodal age distribution of CD can overlay with the age demographics of patients who have ISC. In 1981, Brandt et al.performed a retrospective study evaluating the records of 81 patients over 50 years of age who were diagnosed as CD, ulcerative colitis (UC) or nonspecific colitis [19]. A diagnosis of ISC was made retrospectively in three-fourths of the patients. CD and ISC may share the same risk factors such as consumption of a Western diet, tobacco consumption and NSAID use [20,21]. Although endoscopic evaluation with biopsies remains the major diagnostic tool for all patients suspected of CD or ISC, endoscopic and histopathological features are not specific. CD and ISC may share similar endoscopic features such as rectal sparing, skip lesions and deep ulcers. The characteristic endoscopic findings of ISC include segmental distribution (80% in the left colon, 25% in the splenic flexure and 55% in the sigmoid colon), focal submucosal hemorrhage, red-purple blebs and dusky purple mucosa. Although being suggestive, the colonoscopic features of ISC are often nonspecific and insufficient for making a distinction from CD. The diagnostic value of mucosal biopsy from colonoscopy is also potentially limited by its inherited inability to assess transmural nature in both CD and ISC. As shown in our study, multiple histopathological features such as fissuring ulceration, microangiopathy or fistula could

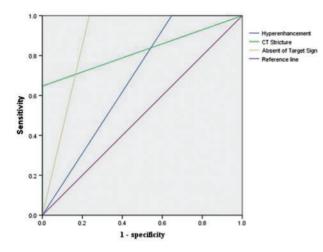


Figure 2. ROC curves for the presence of mucosal hyperenhancement or stricture and the absence of the target sign for distinguishing Crohn's disease from ischemic colitis.

not be evaluated in the specimens from endoscopic biopsy. The histopathological pictures of ISC may show various patterns of acute injury (e.g. mucosal and submucosal hemorrhage, mucosal infarction, granulation tissue and crypt abscesses) as well as chronic injury (e.g. dropout of crypts, lamina propria hyalinization and transmural fibrosis). These ischemia-associated features may overlap those seen in CD [22,23]. One of the distinguishing histopathological features of CD is the presence of noncaseating granulomas. However, these can only be observed in 30–40% of histopathological specimens of patients with established CD [5,6].

The accuracy and effectiveness of CTE in the evaluation of patients with CD or ISC have been validated separately [24,25]. However, the utility of CTE for differentiating between CD and ISC has not been previously investigated. In our study, we found that mucosal hyperenhancement had a high sensitivity (100%) in the diagnosis of CD. It was reported that mucosal hyperenhancement correlated with histopathological findings of active CD [7,8]. The mechanism that mucosal hyperenhancement can help in the differential diagnosis may be due to the fact that mucosal perfusion is usually increased in the acute stage of inflammatory CD [26,27] while being decreased in the colonic wall of ISC. Bowel-wall thickening is also a typical sign of CD, which is found to be correlated with mural inflammation [8]. However, ISC may share the same CTE feature of symmetrical, circumferential thickening of the affected bowel wall with CD. Our study demonstrated that bowel-wall thickening was not a distinguishing feature for either CD or ISC. On the other hand, the target sign, a radiographic feature of mural stratification, refers to visualization of layers of the bowel wall at CTE. In mural stratification, the mucosa and serosa enhance avidly, but the intervening bowel wall can have any of various degrees of attenuation depending on which pathologic process is present. The target sign was more commonly present in ISC. Our results showed that the target sign was detected only in CTE of patients with ISC. The target sign is a useful CTE feature for the differential diagnosis between CD and ISC, but the detection of the sign is not necessarily indicative of active disease because it may occur in a chronic burned-out inflammatory ISC or asymptomatic ISC [28]. CTE features of severe acute ISC include air in the wall of bowel (pneumatosis) or in the intrahepatic portal vein (portal venous gas). ISC can be more reliably diagnosed by the detection of these CTE signs; however, they do not appear

often and exist only in advanced cases of ISC. Therefore, the diagnostic values of these CTE features are limited.

Our study has several clinical implications. If a biopsy shows nonclassic CD in a patient older than 50 years with newly suspected CD. CTE may be used to evaluate for ISC. Special attention should be paid to the CTE features of mucosal hyperenhancement, stricture and the target sign, which can help distinguish the two disease entities. Furthermore, accurate and early diagnosis can ensure the appropriate clinical management. The medical treatment of CD and ISC is totally different. Treating ISC patients with immunosuppressive agents for wrongly diagnosed CD may be catastrophic. Lastly, CTE may be used to distinguish between CD and ISC in CD patients with anastomotic and neoterminal ileum ulcers or strictures following ileocolonic resection. In clinical practice, newly recurred endoscopic ulceration or strictures after bowel resection and anastomosis for underlying CD are often interpreted as being from the recurrence of CD rather than surgery-associated ischemia [17]. However, a differential diagnosis of ISC should also be considered, especially when the endoscopic lesions are confined to the anastomosis. Mucosal ischemia may occur in patients with CD due to inflammatory microvascular occlusion, which may arise from mesenteric vasculitis [29] or be due to hypercoagulability of CD or surgical resection. Surgical ileocolonic resection may compromise blood to the bowel by lengthening the mesentery or by suturing the anastomosis under tension. Angerson et al.used endoscopic laser Doppler flow meter and demonstrated that neoterminal ileal blood flow was inversely related to severity of endoscopic recurrence grade [30].

There were limitations to our study. First, we had a small number of patients in our series. This was due to that fact that CTE was not routinely performed in patients with ISC. Second, there might have been referral bias since this study was performed in a tertiary-care setting. Finally, histopathological reevaluation was not available in all cases. To overcome this shortcoming, we used a combination of clinical, endoscopic and histopathological findings rather than a single test as a reference standard. In addition, the results of follow-up evaluation, including assessment of response to medical therapy, were reliable criteria for ascertaining the accurate diagnosis of CD or ISC.

In conclusion, we found that CTE may provide a useful tool for differentiating CD from ISC, with features of the presence of mucosal hyperenhancement and stricture and the absence of the target sign.

Conflict of interest statement: none declared.

References

- Durando R, Viora T, Rispoli P, et al. Ischemic colitis manifested as Crohn's disease. A case report. Minerva Med 1992;83:567–70.
- Eisenberg RL, Montgomery CK, Margulis AR. Colitis in the elderly: ischemic colitis mimicking ulcerative and granulomatous colitis. AJR Am J Roentgenol 1979;133:1113–8.
- Gan SI, Urbanski S, Coderre SP, et al. Isolated visceral small artery fibromuscular hyperplasia-induced ischemic colitis mimicking inflammatory bowel disease. Am J Gastroenterol 2004;99:2058–62.
- Heer M, Sulser H, Krampf K, et al. Ischemic-granulomatous colitis: a new differential diagnosis from Crohn's colitis. Schweiz Med Wochenschr 1987;117:643–50 (in German).
- 5. Heresbach D, Alexandre JL, Branger B, *et al*. Frequency and significance of granulomas in a cohort of incident cases of Crohn's disease. *Gut* 2005;**54**:215–22.

- Pierik M, De Hertogh G, Vermeire S, et al. Epithelioid granulomas, pattern recognition receptors, and phenotypes of Crohn'sdisease. Gut 2005;54:223–7.
- Chiorean MV, Sandrasegaran K, Saxena R, et al. Correlation of CT enteroclysis with surgical pathology in Crohn's disease. *Am J Gastroenterol* 2007;**102**:2541–50.
- Bodily KD, Fletcher JG, Solem CA, et al. Crohn Disease: mural attenuation and thickness at contrast-enhanced CT Enterography–correlation with endoscopic and histologic findings of inflammation. Radiology 2006;238:505–16.
- 9. Colombel JF, Solem CA, Sandborn WJ, et al. Quantitative measurement and visual assessment of ileal Crohn's disease activity by computed tomography enterography: correlation with endoscopic severity and C reactive protein. Gut 2006;55:1561–7.
- Soyer P, Boudiaf M, Sirol M, et al. Suspected anastomotic recurrence of Crohn disease after ileocolic resection: evaluation with CT enteroclysis. Radiology 2010;254:755–64.
- 11. Mao R, Gao X, Zhu ZH, et al. CT Enterography in evaluating postoperative recurrence of Crohn's disease after ileocolic resection: complementary role to endoscopy. *Inflamm Bowel Dis* 2013;**19**:977–82.
- 12. Balthazar EJ, Yen BC, Gordon RB. Ischemic colitis: CT evaluation of 54 cases. Radiology 1999;211:381–8.
- Daperno M, D'Haens G, Van Assche G, et al. Development and validation of a new, simplified endoscopic activity score for Crohn's disease: the SES-CD. Gastrointest Endosc 2004;60:505–12.
- 14. Sands BE, Arsenault JE, Rosen MJ, et al. Risk of early surgery for Crohn's disease: implications for early treatment strategies. Am J Gastroenterol 2003;98:2712–8.
- 15. Picco MF, Zubiaurre I, Adluni M, et al. Immunomodulators are associated with a lower risk of first surgery among patients with non-penetrating non-stricturing Crohn's disease. Am J Gastroenterol 2009;104:2754–9.
- Mekhjian HS, Switz DM, Melnyk CS, et al. Clinical features and natural history of Crohn's disease. Gastroenterology 1979;77(4 Pt 2):898–906.

- Rutgeerts P, Geboes K, Vantrappen G, et al. Predictability of the postoperative course of Crohn's disease. *Gastroenterology* 1990;99:956–63.
- Glauser PM, Wermuth P, Cathomas G, et al. Ischemic colitis: clinical presentation, localization in relation to risk factors, and long-term results. World J Surg 2011;35:2549–54.
- 19. Brandt L, Boley S, Goldberg L, et al. Colitis in the elderly. A reappraisal. *Am J Gastroenterol* 1981;**76**:239–45.
- 20. Hou JK, Abraham B, El-Serag H. Dietary intake and risk of developing inflammatory bowel disease: a systematic review of the literature. *Am J Gastroenterol* 2011;**106**:563–73.
- 21. Moszkowicz D, Mariani A, Tresallet C, et al. Ischemic colitis: The ABCs of diagnosis and surgical management. J Visc Surg 2013;**150**:19–28.
- 22. Mitsudo S and Brandt LJ. Pathology of intestinal ischemia. Surg Clin North Am 1992;**72**:43–63.
- 23. Price AB. Ischaemic colitis. Curr Top Pathol 1990;81:229-46.
- 24. Al-Hawary MM, Kaza RK, Platt JF. CT enterography: concepts and advances in Crohn's disease imaging. Radiol Clin North Am 2013;51:1–16.
- 25. Romano S, Romano L, Grassi R. Multidetector row computed tomography findings from ischemia to infarction of the large bowel. *Eur J Radiol* 2007;**61**:433–41.
- 26. Spalinger J, Patriquin H, Miron MC, et al. Doppler US in patients with crohn disease: vessel density in the diseased bowel reflects disease activity. Radiology 2000;217:787–91.
- Hulten L, Lindhagen J, Lundgren O, et al. Regional intestinal blood flow in ulcerative colitis and Crohn's disease. Gastroenterology 1977;72:388–96.
- 28. Balthazar EJ. CT of the gastrointestinal tract: principles and interpretation. AJR Am J Roentgenol 1991;156:23–32.
- 29. Wakefield AJ, Sawyerr AM, Dhillon AP, et al. Pathogenesis of Crohn's disease: multifocal gastrointestinal infarction. *Lancet* 1989;**2**:1057–62.
- Angerson WJ, Allison MC, Baxter JN, et al. Neoterminal ileal blood flow after ileocolonic resection for Crohn's disease. Gut 1993;34:1531–4.