

Computed Tomography Enterography Demonstrates Association to Histopathological Grading of Small Bowel Crohn's Activity

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ABSTRACT

Introduction: Crohn's disease (CD) is a lifelong, progressive inflammatory condition of the bowel that adversely influences the quality of life. Diagnosis of CD can be challenging, as there is no trusted gold standard diagnostic procedure. Ileocolonoscopy cannot investigate the entire small bowel due to small bowel morphology. Multislice Computed Tomography (MSCT) improves small bowel imaging and has established a crucial role for Computed Tomography Enterography (CTE).

Objective: This study investigated an association between CTE and histopathology in the evaluation of the activity of small bowel CD.

Materials and Methods: A retrospective study was used to collect eligible cases. The sample size was a consecutive sampling of 98 patients with known CD. The patients underwent biopsy by ileocolonoscopy-guided retrograde terminal ileum intubation. Subjects were scanned with CTE for confirmation of the diagnosis, detection of complications, and further evaluation of CD. A Chi-Square test was performed to determine the association between CTE radiological pathological findings and CTE grading.

Results: The peak prevalence of Crohn's activity occurred between the ages of 20–30 years. Definitive clinical presentations of CD include diarrhea, abdominal pain, and weight loss, frequently followed by a chronic deteriorating progression, with distinct variations in the type and severity of symptoms. Fisher exact test showed that there is a statistically significant association between radiological pathological findings of CTE and CTE diagnostic grading of CD (0.05, 2-sided). Moreover, there is a relationship between radiological pathological findings of CTE and histopathological findings.

Conclusions: The CTE radiological pathological findings demonstrate an association with the histopathological findings of CD. The CTE findings may be helpful for the differential diagnosis and planning of treatment strategy.

Keywords: computed tomography enterography, Crohn's disease, histopathology

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disorder that affects different parts of the gastrointestinal tract, most commonly the small bowel [1]. The diagnosis of CD is based on clinical data and radiological, endoscopic, and histopathological analysis [2]. Radiological procedures are an integral part of CD diagnosis and monitoring, in coincidence with ileocolonoscopy investigations. Improved small bowel imaging with developments in Multislice Computed Tomography (MSCT) and use of neutral oral contrast has established a crucial role for Computed Tomography Enterography (CTE). This has resulted in a shift toward the use of CTE imaging versus fluoroscopic examination in the diagnosis and follow up of patients with CD. CTE exhibits high sensitivity for recognition of clinically undetectable CD complications [3].

Comparison of CTE and Magnetic Resonance Enterography (MRE) has confirmed the similar performance of the two procedures for identifying active CD [4]. There is a good correlation among ileocolonoscopy, CTE and MRE findings [5]. The rapidity of the CTE procedure is its advantage over MRE. The short acquisition times of CTE create images free of motion artifacts, which are caused by normal intestinal peristalsis [6]. Accuracy in categorizing disease activity is critical for disease prognosis and evaluation of treatment effectiveness. Ileocolonoscopy is the gold standard for diagnosing and assessing CD activity, but its aggressive nature and associated complications restrict the implementation in CD for long-term patient follow-up. Consequently, CTE is commonly used in clinical practice [7]. Nevertheless, there are insufficient studies related to the grading of lesion activity and quantitative assessment of CTE imaging findings in CD patients [8].

CTE is readily accessible, fast, exhibits high spatial resolution, and is well tolerated by patients. CTE may be superior to MRE in terms of image quality and inter-observer

Table 1. Cross-tabulation of histopathological grading of Crohn's activity versus gender

Gender	Histopathological analysis of Crohn's activity			Total (n=98)	χ^2	P-value
	Mild (n=18)	Moderate (n=42)	Severe (n=38)			
Male	16(88.9%)	23(54.8%)	14(36.8%)	53(54.1%)	13.902	0.001*
Female	2(11.1%)	19(45.2%)	24(63.2%)	45(45.9%)		

* Significant at 0.05 level of Fisher Exact significance (2-sided)

Table 2. Cross-tabulation of histopathological grading of Crohn's activity versus age group

Age groups	Histopathological analysis of Crohn's activity			Total (n=98)	χ^2	P-value
	Mild (n=18)	Moderate (n=42)	Severe (n=38)			
Less than 20y	2(11.1%)	7(16.7%)	0(0)	9(9.2%)	46.836	<0.001*
20y to 30y	13(72.2%)	24(57.1%)	7(18.4%)	44(44.9%)		
31y to 40y	3(16.7%)	9(21.4%)	8(21.1%)	20(20.4%)		
41y to 50y	0(0)	2(4.8%)	9(23.7%)	11(11.2%)		
More than 51y	0(0)	0(0)	14(36.8%)	14(14.3%)		

* Significant at 0.05 level of Fisher Exact Test (2-sided)

agreement. Nowadays, there are several strategies available to reduce radiation dose exposure with no compromise of diagnostic accuracy. Nevertheless, cumulative radiation exposure of CD patients undergoing repeated CTE needs to be carefully considering. The current study explored the viability of CTE in quantitatively assessing and grading CD activity relative to the histopathological results of ileocolonoscopy biopsies.

MATERIALS AND METHODS

Study Design and Participants

We performed a retrospective study among 98 patients with known or suspected CD, in which CTE was performed to evaluate its possible impact on accurate diagnosis, detection of complications, and consequent guidance for management. The data were collected from the medical records of 98 consecutive patients who had been referred to a gastroenterologist for small bowel evaluation and who underwent biopsy by ileocolonoscopy retrograde terminal ileum intubation. These patients underwent CTE to confirm the diagnosis and for further evaluation of the disease. The study excluded all patients who had suboptimal CTE or ileocolonoscopy and patients who had incomplete medical records.

Protocol for CTE

CTE studies were performed using a 64-slice Siemens SOMATOM Definition AS. Patients abstained from food for at least six hours before the CTE examination without any other bowel preparation. They were instructed to drink 1350 ml of a neutral oral contrast medium solution comprised of Mannitol diluted with water (20%) to obtain good distension of the small bowel. The solution was ingested as follows: 450 ml at 60 minutes; 450 ml at 40 minutes; 225 ml at 20 minutes; and 225 ml at 10 minutes before scanning. An 18-gauge cannula intravenous line was placed in the antecubital fossa.

A dose of 80-100 ml Iohexol injection, a high-iodine concentration contrast agent (OMNIPAQUE 350 contains 755 mg of Iohexol equivalent to 350 mg of organic iodine per ml, GE Healthcare) was injected at a flow rate of 4 ml/s followed by a 40-ml bolus of saline at the same flow rate.

With the patient supine on the examination table, scout images were obtained from the diaphragm superiorly down to

the symphysis pubis inferiorly. Enteric phase images were obtained at 45-50s after initiation of IV contrast. All imaging was performed with 120-140 kV, 200-350 mA, matrix 512 × 512, pitch 0.8-1 and slice collimation 1.25 mm. Axial and coronal images were reconstructed at a slice thickness of 2 mm and an increment of 2 mm using a B20 medium smooth kernel.

Statistical Analysis

IBM SPSS Statistic Version 23.0 (IBM Corporation, New York, USA) was used for data entry and analysis. Several correlations were used to describe the relationships among demographic characteristics, clinical manifestations, and CTE radiological pathological findings versus histopathological grading. $P < 0.05$ was considered to be significant.

RESULTS

Baseline Characteristics

The study included 53 (54.1%) males and 45 (45.9%) females (**Table 1**). The Fisher exact test of independence was used for frequencies of fewer than five observations. This test revealed that gender had a significant influence on the histopathological grading of Crohn's activity (Fisher exact test = 13.902 and $P = 0.001$).

The degree of Crohn's activity among patients was inconsistent. Histopathological analysis of specimens obtained from bowel wall tissues taken through ileocolonoscopy biopsies revealed mild Crohn's activity in 16 (88.9%) male patients versus two (11.1%) female patients. Moderate CD was found in 23 (54.8%) males versus 19 (45.2%) females, and severe CD was found in 14 (36.8%) males versus 24 (63.2%) females.

Age prevalence of Crohn's activity in patients with histopathological grading is listed in **Table 2**. Peak prevalence of Crohn's activity by age group was evident, with the peak occurring between the ages of 20-30 years. Furthermore, the Fisher exact test reveals that the patients' age has a significant incidence of the histopathological grading of Crohn's activity, where the value of the Fisher exact test was 46.836 and $P < 0.001$.

Clinical Manifestations of CD Patients

The main clinical manifestations of CD patients related to the degree of Crohn's activity are presented in **Table 3**. The

Table 3. Cross-tabulation of histopathological grading of Crohn's activity versus clinical manifestations

Clinical manifestations of CD patients		Histopathological grading of Crohn's activity			Total (n=98)	χ^2	P-value
		Mild (n=18)	Moderate (n=42)	Severe (n=38)			
Abdominal pain	Yes	13(72.2%)	39(92.9%)	36(94.7%)	88(89.8%)	6.046	0.036*
	No	5(27.8%)	3(7.1%)	2(5.3%)	10(10.2%)		
Diarrhea	Yes	16(88.9%)	28(66.7%)	36(94.7%)	80(81.6%)	10.826	0.003*
	No	2(11.1%)	14(33.3%)	2(5.3%)	18(18.4%)		
Hematochezia	Yes	9(50.0%)	27(64.3%)	35(92.1%)	71(72.4%)	14.132	0.001*
	No	9(50.0%)	15(35.7%)	3(7.9%)	27(27.6%)		
Weight loss	Yes	13(72.2%)	23(54.8%)	34(89.5%)	70(71.4%)	12.062	0.002*
	No	5(27.8%)	19(45.2%)	4(10.5%)	28(28.6%)		

* Significant at 0.05 level of Fisher Exact significance (2-sided)

Table 4. Association between CTE radiological pathological findings and CTE grading

CTE radiological pathological findings		CTE diagnosis grading of CD			Total (n=98)	χ^2	P-value
		Absence (n=6)	Mild (n=12)	Moderate (n=44)			
Mucosal vascularity	Yes	0(0)	1(8.3%)	42(95.5%)	16(44.4%)	54.362	<0.001*
	No	6(100%)	11(91.7%)	2(4.5%)	20(55.6%)		
Mucosal hyperenhancement	Yes	4(66.7%)	12(100%)	44(100%)	36(100%)	10.681	0.003*
	No	2(33.3%)	0(0)	0(0)	0(0)		
Intestinal wall thickening	Yes	0(0)	0(0)	0(0)	28(77.8%)	70.165	<0.001*
	No	6(100%)	12(100%)	44(100%)	8(22.2%)		
Engorgement of mesenteric vessels	Yes	0(0)	0(0)	0(0)	21(58.3%)	45.079	<0.001*
	No	6(100%)	12(100%)	44(100%)	15(41.7%)		
Free fluid adjacent to the affected loop	Yes	0(0)	3(25.0%)	11(25.0%)	20(55.6%)	11.728	0.006*
	No	6(100%)	9(75.0%)	33(75.0%)	16(44.4%)		
Inter loop fistulas	Yes	0(0)	0(0)	0(0)	10(27.8%)	16.431	<0.001*
	No	6(100%)	12(100%)	44(100%)	26(72.2%)		
Enlarged lymph nodes	Yes	0(0)	1(8.3%)	9(20.5%)	29(80.6%)	40.857	<0.001*
	No	6(100%)	11(91.7%)	35(79.5%)	7(19.4%)		
Fat abnormalities	Yes	0(0)	1(8.3%)	29(65.9%)	32(88.9%)	36.452	<0.001*
	No	6(100%)	11(91.7%)	15(34.1%)	4(11.1%)		
Abscesses formation	Yes	0(0)	0(0)	0(0)	8(22.2%)	12.312	0.002*
	No	6(100%)	12(100%)	44(100%)	28(77.8%)		
Intestinal Stricture	Yes	0(0)	0(0)	0(0)	14(38.9%)	25.660	<0.001*
	No	6(100%)	12(100%)	44(100%)	22(61.1%)		

* Significant at 0.05 level of Fisher Exact Test (2-sided)

Fisher exact test revealed that abdominal pain, diarrhea, hematochezia, and weight loss were statistically significantly correlated with Crohn's activity. Abdominal pain was the most common clinical manifestation of Crohn's activity, with 88 (89.8%) of the study patients suffering from abdominal pain (Fisher exact test = 6.046 and P = 0.036). Diarrhea was a second common clinical manifestation of Crohn's activity, with 80 (81.6%) of the patients suffering from diarrhea (Fisher exact test = 10.826 and P = 0.003). Hematochezia was prominent in 71 (72.4%) of the study patients (Fisher exact test = 14.132 and P = 0.001). Weight loss was documented in 70 (71.4%) patients (Fisher exact test = 12.062 and P = 0.002).

Radiological Pathological Findings of CTE Associated with CTE Diagnosis Grading of Crohn's Activity

To explore the relationship between radiological pathological findings of CTE and CTE diagnostic grading of Crohn's activity, the Fisher exact test was used to find the relationship between these two qualitative variables. The results in **Table 4** show that there is an association between radiological pathological findings of CTE and CTE diagnostic grading of CD at the 0.05 level of significance (2-sided).

Regarding CTE image interpretation, mucosal hyper-enhancement was observed in the majority of CD patients (98.0%) (Fisher exact test = 10.681 and P = 0.003). Mucosal hyper-enhancement was observed in all degrees (mild,

moderate, and severe) of CD, while images from two-thirds of patients who classified without CD were interpreted with mucosal hyper-enhancement.

The next common findings were fat abnormalities in 62 patients (63.3%) (Fisher exact test = 36.452 and P < 0.001). Fat abnormalities were prominent in 32 patients (88.9%) with severe CD, followed with 29 patients (65.9%) with moderate CD and only one (8.3%) with mild CD. Mucosal vascularity was a common finding in 59 patients (60.2%) (Fisher exact test = 54.362 and P < 0.001). Among patients with moderate CD, about 42 cases (95.5%) had mucosal vascularity, whereas this was observed in 16 severe CD patients (44.4%) and only one mild CD patient (8.3%).

Enlarged lymph nodes were observed in 39 patients (39.8%) (Fisher exact test = 40.857 and P < 0.001). Enlarged nodes were evident in 29 of severe CD patients (80.6%), in nine of the moderate cases (20.5%) and only one (8.3%) of the mild patients. Free fluid adjacent to the affected loop was seen in 34 patients (34.7%) (Fisher exact test = 11.728 and P = 0.006), 20 of whom with severe CD (55.6%), 7 with moderate, and 7 with mild CD.

The remaining radiological pathological findings of CTE were certain for severe CD patients. Intestinal wall thickening existing in 28 CD patients (28.2%) (Fisher exact test = 70.165 and P < 0.001). These patients represent about 77.8% of the

Table 5. Association between CTE radiological findings and histopathological analysis grading.

CTE radiological pathological findings		Histopathological analysis of CD grading			Total (n=98)	χ^2	P-value
		Mild (n=18)	Moderate (n=42)	Severe (n=38)			
Mucosal vascularity	Yes	1(5.6%)	35(83.3%)	23(60.5%)	59(60.2%)	33.322	<0.001*
	No	17(94.4%)	7(16.7%)	15(39.5%)	39(39.8%)		
Mucosal hyperenhancement	Yes	16(88.9%)	42(100.0%)	38(100.0%)	96(98.0%)	5.341	0.032*
	No	2(11.1%)	0(0)	0(0)	2(2.0%)		
Intestinal wall thickening	Yes	0(0)	0(0)	28(73.7%)	28(28.6%)	66.295	<0.001*
	No	18(100%)	42(100.0%)	10(26.3%)	70(71.4%)		
Engorgement of mesenteric vessels	Yes	0(0)	0(0)	21(55.3%)	21(21.4%)	43.229	<0.001*
	No	18(100%)	42(100.0%)	17(44.7%)	77(78.6%)		
Free fluid adjacent to the affected loop	Yes	3(16.7%)	8(19.0%)	23(60.5%)	34(34.7%)	17.687	<0.001*
	No	15(83.3%)	34(81.0%)	15(39.5%)	64(65.3%)		
Inter loop fistulas	Yes	0(0)	0(0)	10(26.3%)	10(10.2%)	16.016	<0.001*
	No	18(100%)	42(100.0%)	28(73.7%)	88(89.8%)		
Enlarged lymph nodes	Yes	1(5.6%)	13(31.0%)	25(65.8%)	39(39.8%)	21.717	<0.001*
	No	17(94.4%)	29(69.0%)	13(34.2%)	59(60.2%)		
Fat abnormalities	Yes	1(5.6%)	27(64.3%)	34(89.5%)	62(63.3%)	38.639	<0.001*
	No	17(94.4%)	15(35.7%)	4(10.5%)	36(36.7%)		
Abscesses formation	Yes	0(0)	0(0)	8(21.1%)	8(8.2%)	11.978	0.001*
	No	18(100%)	42(100.0%)	30(78.9%)	90(91.8%)		
Intestinal Stricture	Yes	0(0)	1(2.4%)	13(34.2%)	14(14.3%)	18.591	<0.001*
	No	18(100%)	41(97.6%)	25(65.8%)	84(85.7%)		

* Significant at 0.05 level of Fisher Exact significance (2-sided)

severe CD group. Engorgement of mesenteric vessels was seen in 21 patients (21.4%) (Fisher exact test = 45.079 and $P < 0.001$), which represent about 58.3% of the severe group. Disease complications were classified into intestinal stricture, inter loop fistulas, and abscess formation. Intestinal stricture was evident in 14 patients (14.3%) (Fisher exact test = 25.660 and $P < 0.001$) representing 38.9% of severe cases. Inter loop fistulas were seen in 10 (10.2%) CD patients (Fisher exact test = 25.660 and $P < 0.001$) representing 27.8% of the severe subjects. Abscess formation was seen in 8 patients (8.2%) (Fisher exact test = 12.312 and $P = 0.002$) representing 22.2% of the severe group.

Radiological Pathological Findings of CTE Associated with Histopathological Diagnostic Grading of Crohn's Activity

To test the relationship between radiological pathological findings of CTE and grading based on histopathological analysis, the 2-sided Fisher exact test was used. The results presented in **Table 5** show that there is a relationship between radiological pathological findings of CTE and histopathological findings at the 0.05 level of significance. Thus, all CTE radiological pathological findings are good predictors of histopathological findings relevant to CD.

DISCUSSION

In agreement with our results, Costea et al. [9] reported that the gender distribution of CD is about 56.4% male and 43.6% female. In general, the frequency of CD is similar in males and females. This pattern is reversed with pediatric CD, which has a higher incidence in pediatric males than in females [10].

Age descriptions of early and elderly onset CD within the literature diverge and frequently depend on clinical practice due to the age of referral from pediatric to adult CD care. Besides, a dilemma in patient characteristics, diagnostic criteria, access to diagnostic modalities, and hence variation in the ability to capture altogether CD patients might bias and confound associations. Specific studies indicated that elderly

patients were more likely to have a colonic disease and less likely to have ileocolonic CD when matched with the younger age groups [11,12]. In accord with our results, European reports have shown an increasing prevalence of CD in the age group 20 to 30 years [13,14]. Furthermore, similar studies confirm that the vast majority of patients with CD are frequently diagnosed in the same age group [15,16].

The clinical manifestations of CD are important in the investigation of CD patients in that they can predict CD activity. Sands [17] reported that diarrhea is the most common presenting symptom of CD. According to Jaffe et al. [18], the definitive clinical presentation of CD is abdominal pain, weight loss, and diarrhea. Clinical signs and symptoms of patients with CD are essentially correlated with diagnostic modalities as well as laboratory test results [19]. Dos Santos et al. [20] reported the clinical manifestations of CTE and revealed that the main clinical manifestations were abdominal pain (85%), diarrhea (70%), weight loss (64%), and hematochezia (55%).

Interpretation of CTE images with attention to the radiological pathological findings of CD is essential to judgment of Crohn's activity grading. Radiological pathological findings such as mucosal hyper-enhancement, intestinal wall thickening, fat abnormalities, and extraintestinal features are consistent with active small bowel CD [21]. A study done by Choi et al. [22] revealed that mucosal hyper-enhancement and intestinal wall thickening were predictive of active CD. Intestinal wall thickening in CD refers to a wall thickness of greater than 3 mm under conditions of an optimal CTE procedure with a good distended bowel loop [23]. Intestinal wall thickening is the most frequent finding observed with CTE for CD patients (up to 82% of patients) [24].

Among these radiological pathological observables, a combination of mucosal hyper-enhancement and intestinal wall thickening is the most sensitive CTE finding signifying active inflammatory CD [6,25]. While these studies suggested that intestinal wall thickening correlated best with Crohn's activity, another study has suggested that mucosal hyper-enhancement may be an extra sensitive sign [26]. The comb sign refers to engorged vasa recta that infiltrate the bowel wall

perpendicular to the bowel lumen, suggesting the appearance of a comb [24]. Mesenteric fat abnormalities together with the comb sign were reported to be the most specific CTE finding for active CD [27]. Chiorean et al. [28] identified that CTE findings of comb sign and enlarged mesenteric lymph nodes were strongly correlated with Crohn's activity.

Extra-enteric complications of CD are accurately identified by CTE. The most common of these complications include inter loop fistulas and abscess formation [29]. Variability of Crohn's activity assessed by CTE radiological pathological findings is reliant on whether the activity is a result of acute or chronic inflammation and whether there are complications such as inter loop fistulas, intestinal stricture, or abscess formation. In a study of CD patients who underwent CTE and ileocolonoscopy, mucosal hyper-enhancement and intestinal wall thickening on CTE correlated highly significantly ($P = 0.001$) with histopathological findings of active CD [30].

Concerning our results, preliminary studies suggested that mucosal hyper-enhancement, intestinal wall thickening, enlarged mesenteric lymph nodes were correlated significantly with histopathological findings of active CD [21,26,31]. A study by Patel et al. [32] explored the radiological findings correlated to clinical manifestation and ileocolonoscopy appearances. They reported that intestinal wall thickening and mucosal hyper-enhancement showed a positive correlation with clinical severity ($P < 0.05$) and identified a statistically significant correlation with ileocolonoscopy severity ($P < 0.0001$).

A comparative study carried out by Hashimoto et al. [33] compared CTE radiological findings of CD patients with a different diagnostic approach. Their study revealed a strong correlation ($P < 0.001$) between CTE radiological findings and mucosal surface. In particular, CTE appeared to be a valuable diagnostic technique for the assessment of the mucosal healing pattern in CD.

Park and Lim [34] reported that extra-enteric complications of CD are distinguished by CTE. The accurate detection of abscesses and inter loop fistulas have high significance not only because it alters the disease management decision but also can affect the surgical approach. Peng et al. [35] investigated the accuracy of new spectral CT generation in assessment Crohn's activity in comparison to conventional CT. The results showed that bowel wall hyper-enhancement, on comb sign, intestinal wall thickness, and normalized iodine concentration increased significantly ($P < 0.01$) with ileocolonoscopy severity.

In concordance with our results, a recent study by Cheng et al. [8] explored the viability of CTE in the quantitative evaluation of CD activity. They reported that intestinal stricture among active mild, moderate, and severe groups was statistically significant (Chi-square test = 13.3 and $P < 0.001$). Similarly, mesenteric hyper-vascularity (comb sign) was statistically significant (Chi-square test = 9.3 and $P = 0.005$). The difference in mucosal enhancement among inactive, mild, moderate and severe groups was significantly different in patients without CD activity and the mild groups (Chi-square test = 15.7 and $P = 0.001$). The difference between the group showing no CD activity and moderate-severe groups was statistically significant (Chi-square test = 14.1 and $P = 0.003$). Moreover, the supplementary comparison showed that wall thickening was statistically significant ($P = 0.002$) between the absent CD activity and the mild groups, and statistically significant ($P < 0.001$) between the inactive and the moderate-severe groups.

In this context, despite extensive availability in clinical practice, the performance of CTE relative to ileocolonoscopy as a diagnostic method as well as measures to evaluate treatment response in CD are important subjects to be investigated. Our results agree with a recent prospective study [36] designed to evaluate the correlation between CTE pathological findings and ileocolonoscopy disease activity. That study revealed that CTE findings significantly correlated with those of ileocolonoscopy. Ileocolonoscopy at one year follow up significantly correlated with improvement in mucosal hyper-enhancement ($P = 0.004$), mesenteric fat abnormality ($P = 0.001$), comb sign ($P = 0.004$), and inter loop strictures ($P = 0.008$) in CTE.

CONCLUSION

Demonstration of radiological pathological features of CD in CTE images is crucial to determine Crohn's activity grading. These features are reliable predictors that support the histopathological features of CD. The current study highlights CTE's capability to assess the presence, severity, and extent of CD and its complications that is not available from clinical and ilicolonoscopy evaluation. Furthermore, our study establishes a common expectation for the use of CTE in patients with small bowel CD, as well as agreed-upon radiological imaging findings. Finally, the study suggests that CTE would be the method of choice for follow up, preoperative guidance in the planning of a treatment strategy, and monitoring the patient response to treatment.

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