

CT enterography and fistulizing Crohn's disease: clinical benefit and radiographic findings

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Abstract

Background: To estimate the clinical benefit of CT enterography (CTE) in patients with fistulizing Crohn's disease and describe the appearance of fistulas at CTE.

Methods: Crohn's patients who had undergone CTE, which diagnosed an abscess or fistula, were identified. A gastroenterologist reviewed clinical notes prior to and following CTE to assess the pre-CTE clinical suspicion for fistula/abscess, and post-CTE alteration in patient management. A radiologist reassessed all fistula-positive cases, which were confirmed by a non-CT reference standard, to describe their radiologic appearance.

Results: Fifty-six patients had CT exams identifying 19 abscesses and 56 fistulas. There was no or remote suspicion of fistula or abscess at pre-imaging clinical assessment in 50% of patients. Thirty-four patients (61%) required a change in or initiation of medical therapy and another 10 (18%) underwent an interventional procedure based on CT enterography findings. Among 37 fistulas with reference standard confirmation, 30 (81%) were extraenteric tracts, and 32 (86%) were hyperenhancing compared to adjacent bowel loops. Most fistulas (68%) contained no internal air or fluid.

Conclusion: CTE detects clinically occult fistulas and abscesses, resulting in changes in medical management and radiologic or surgical intervention. Most fistulas appear as hyperenhancing, extraenteric tracts, usually without internal air or fluid.

Key words: CT—Enterography—Fistula—Crohn's disease—Abscesses

Fistulas are a serious complication of Crohn's disease associated with high morbidity and mortality. The lifetime risk for developing a fistula in patients with Crohn's disease is between 20% and 40%, with the natural history of Crohn's fistulas being one of episodic exacerbation and long episodes of active drainage [1]. Identifying the underlying etiology of a fistula and defining fistula anatomy are key imaging goals that impact patient management. Current options for imaging of fistulas include barium fistulography, small bowel follow-through, fluoroscopic enteroclysis, abdominopelvic CT, CT and MR enterography (CTE and MRE), and pelvic MRI (particularly for perianal fistulas). CTE exploits the high spatial resolution and speed of multidetector CT, using large volumes of neutral oral contrast agents to generate exquisite images of the small bowel wall, lumen, and mesentery.

While barium radiology is widely considered the method of choice in detection of internal fistulas [2, 3], its accuracy is not entirely satisfactory [4, 5]. In contrast, Vogel et al. recently reported on the excellent performance characteristics of CTE in delineating the fistulas and abscesses of penetrating Crohn's disease in a surgical series [6]. CTE has several potential advantages over barium studies in the identification of fistulizing disease. Unlike traditional fistulography, CTE does not suffer from superimposition of bowel loops (e.g., deep in the pelvis) and does not require filling of the fistulous tract with contrast agent, which may be especially important in assessing small fistulous tracts. Furthermore, CTE displays the perienteric mesentery, and retroperitoneal and abdominal wall musculature, typically involved by fistulas. Sinus tracts and abscesses can also be readily characterized by CTE.

Because CTE is increasingly used to detect and anatomically stage small bowel Crohn's disease, fistulizing Crohn's disease and its complications are increasingly

identified by this technique [7–10]. Our purpose was to assess the clinical impact of CTE in the management of patients with fistulizing Crohn's disease and to perform a systematic analysis of fistula appearance at CTE.

Materials and methods

We performed this retrospective study after approval from the Institutional Review Board of Mayo Foundation. CTE was performed on 756 patients between March 2001 and March 2004. Most patients were referred for suspected or complicated Crohn's disease. The spectrum of appearances of active Crohn's and other small bowel disease in this cohort has been previously described [7], but the clinical and radiographic assessment of patients with fistulizing Crohn's herein is entirely unique to this study. A clinical radiologic report was generated at the time of scanning by a gastrointestinal radiologist with experience in interpreting CTE. We retrospectively examined radiology reports to identify patients with radiologic findings of Crohn's disease and fistula or abscess at CTE. A gastroenterologist examined all relevant clinical notes to insure that each patient had a final clinical diagnosis of Crohn's disease and fistula or abscess at the time of CTE.

CTE was performed on each patient in a similar manner. Each patient received 10 mg of oral metoclopramide (Reglan, Pharmaceutical Associates, Greenville, South Carolina) 75 min prior to CT, to increase gastric and small bowel peristalsis. Patients then drank either four 450 mL cups of water, for a total of 1800 mL, or four 375 mL cups of methylcellulose solution composed of 1000 cc water and 500 cc Enterocele Methylcellulose Solution (Lafayette Pharmaceuticals, Ontario, Canada) for a total of 1500 mL. Patients drank the first cup immediately after ingesting metoclopramide and drank subsequent cups 25, 50, and 65 min later. CT examination was performed 75 min after metoclopramide ingestion. Patients received 1 mg of glucagon intravenously immediately prior to scanning. CT was performed using 270 mA, 120 kVp, 0.5 s tube rotation time, 150 mL of intravenous contrast material (Omnipaque, 300 mgI/mL; Amersham Health, Princeton, NJ) at a rate of 4 mL/s, with scanning initiated after a 45- or 70-s delay. Slice thickness was 2.0–2.5 mm with images reconstructed every 1.0–1.25 mm.

Assessment of clinical benefit of CTE in fistulizing Crohn's disease

In order to determine the contribution of CTE to clinical evaluation of the patient, the medical records for patients with Crohn's disease who underwent CTE and were found to have a fistula/abscess were retrospectively reviewed by a gastroenterologist. First, the clinical notes of the referring clinicians prior to the time of CTE were reviewed to

determine the pre-test clinical suspicion for a fistula/abscess by the ordering physician. The degree of suspicion was characterized as “no suspicion,” “remote suspicion,” “abscess/fistula possible or probable,” and “abscess/fistula definite.” The term “no suspicion” was used when there was no mention of abscess or fistula in the clinical notes or suggestive signs on physical examination. The term “remote suspicion” was used when fistula/abscess was felt to be unlikely but possible based on clinical presentation and mentioned in the clinical notes, or physical signs or symptoms potentially relating to a fistula were present. The term “probable/possible suspicion” was used when new abdominal or rectal pain, a new abdominal or rectal mass, or any other physical signs or symptoms ascribed to a potential fistula were present. The term “definite suspicion” was used when there was an external opening of a fistula visible on physical examination, or active fistula drainage (stool/air) could be observed. Any serum C-reactive protein level obtained within 5 days of the CTE exam was also recorded. In a separate question, the gastroenterologist determined from clinical notes if the fistula was identified on physical examination (i.e., it could have been detected after the CTE was made available to the referring clinician).

Second, the gastroenterologist retrospectively compared the pre-CTE clinical management plan to the post-CTE clinical management plan, taking CTE findings into account. The clinical management plan after CTE was classified for each patient as “no change,” “change in medical therapy,” “change in surgical or percutaneous radiologic intervention,” or “change in medical therapy and surgical or percutaneous radiologic intervention.” “Change in medical therapy” was defined as initiation or increase in the dose of an immunosuppressive agent or the initiation of infliximab or antibiotics. “Change in surgical or percutaneous radiologic intervention” was defined as abscess drainage, either surgically or percutaneously and with or without the introduction of antibiotics.

Assessment of the radiologic appearance of fistulas at CTE

Only those fistulas identified on CTE reports, which could be confirmed using a non-CT reference standard, were selected to undergo visual analysis of radiologic features. The type of non-CT reference standard depended upon fistula type. For enteroenteric fistulas, confirmation was through surgery, fluoroscopic small bowel follow-through, or visualization of the internal opening at ileocolonoscopy within 6 months of CTE. For enterocutaneous fistulas, confirmation was through clinical identification of the external opening and/or confirmation of active drainage during the episode of care when the CTE was performed. For perianal fistulas, confirmation occurred via identification on physical exam, or identification at MRI, exam under anesthesia,

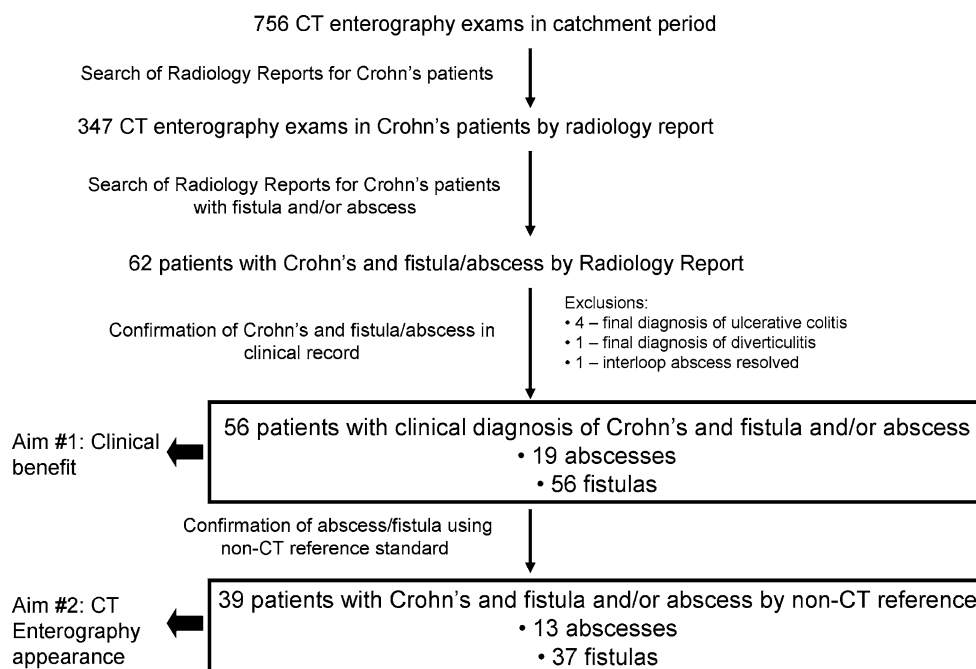


Fig. 1. Selection of CT enterography datasets used to assess the clinical benefit of CT enterography in fistulizing Crohn's disease (Aim 1), and to characterize the appearance of Crohn's-related fistulas at CT enterography (Aim 2).

or endoscopic ultrasound. For enterovesical fistulas, confirmation was through either cystoscopy or surgery. For enterovaginal fistulas, surgical confirmation was used. For abscesses, surgical identification or successful percutaneous radiologic aspiration and drainage were considered confirmation of diagnosis.

In order to examine findings of Crohn's fistulas at CTE, a gastrointestinal radiologist (with 8 years of experience) reviewed the fistula-positive CTE examinations confirmed by the above reference standards. He characterized fistulas anatomically (enteroenteric, enterocutaneous, perianal, enterovesical, enterovaginal). He noted whether or not fistulas appeared as extraenteric tracts and characterized the degree of fistula enhancement (hyperenhancing, isoenhancing, or hypoenhancing relative to nearby bowel loops). The enhancement of perianal fistulas was compared to the external anal sphincter. The presence or absence of internal air or fluid (or both) within the fistulous tract was also noted. He also noted whether or not the fistula arose from a segment of bowel demonstrating typical radiographic signs of active inflammatory Crohn's disease (i.e., segmental mural hyperenhancement, mural stratification, or bowel wall thickening). For abscess, the location of the abscess was recorded, as well as whether or not it appeared to connect to a loop of bowel via a sinus tract, and if so, if the involved bowel loop exhibited radiographic signs of active inflammatory Crohn's disease.

Results

There were 62 patients with a diagnosis of "Crohn's disease" and a finding of "fistula" or "abscess" in the radiology report (Fig. 1). Of these 62 patients, six were

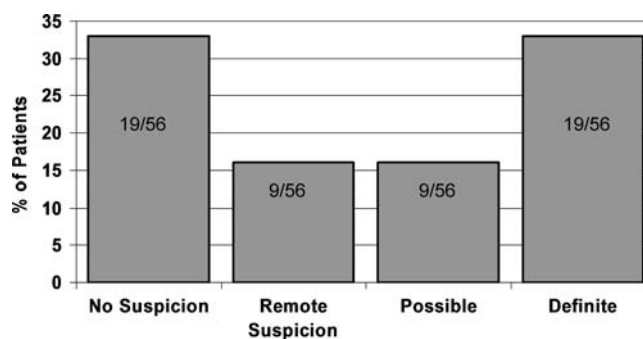


Fig. 2. Clinical suspicion of a fistula or abscess, based on retrospective review of clinical notes and physical exam, as assessed by a gastroenterologist.

excluded because they did not have Crohn's disease (i.e., final clinical diagnosis being ulcerative colitis = 4; diverticulitis = 1; interloop abscess that resolved without treatment = 1). The remaining 56 patients had a final clinical diagnosis of Crohn's disease and comprised the study cohort that underwent further analysis by a gastroenterologist. These patients had 56 fistulas (enteroenteric, 27; perianal, 12; enterocutaneous, 9; enterovaginal, 5; enterovesical, 3) and 19 abscesses (interloop/mesenteric, 10; perianal, 5; subcutaneous/abdominal wall, 2; retroperitoneal, 2).

Clinical benefit of CTE

In half of the patients, there was no suspicion (34%) or remote suspicion (16%) of a fistula or abscess at their pre-CTE clinical assessments (Fig. 2). Fistulas were definitely identified by referring clinicians prior to CTE

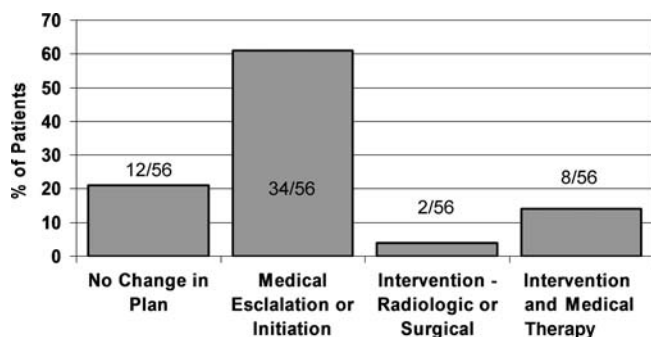


Fig. 3. Alteration in patient management based on CT enterography findings, in patients with fistula or abscess detected on CT enterography, as assessed retrospectively by a gastroenterologist from clinical notes.

in 19 cases on physical exam (34%). In one additional case, a perianal fistula was only noticed after the CTE report described it, and in another case, an external opening that was thought to be healed was reinterpreted as an active fistula. Of the 56 patients with fistula, 23 had a serum C-reactive protein concentration available, of whom 15 (65%) had an elevated C-reactive protein concentration.

Changes in patient management on the basis of CTE findings, based on the retrospective assessment by the study gastroenterologist, occurred in the majority of patients (Fig. 3). While 12 patients (21%) had no change in management as a result of CTE, 34 (61%) had a change in medical management (dose increase or initiation of new immunosuppressives, infliximab, or antibiotics), 2 (4%) had surgical or percutaneous radiologic intervention alone, and 8 (14%) had combined intervention and changes in medical therapy. Seven of these patients had intervention combined with adjuvant antibiotic therapy, while one patient received immunosuppressive dose increase alone.



Fig. 4. Axial CT enterography image in a 54-year-old man with a 23-year history of Crohn's disease and multiple surgical resections, demonstrating a large enterocutaneous fistula arising from matted loops of distal ileum (arrows). The patient had obvious drainage from fistula site. No active small bowel inflammation was observed at CT enterography or demonstrated clinically. Consequently, the patient was observed.

Among the 34 patients that underwent changes in medical management as a result of CTE findings, antibiotics were initiated in 17 (50%), with five of these patients receiving immunosuppressives prior to the initiation of antibiotics. Immunosuppressives alone were initiated in eight (azathioprine, 5; 6-mercaptopurine, 2; methotrexate, 1), with three of these patients also receiving bridging therapy with oral corticosteroids. Immunosuppressives in combination with infliximab were used in four cases. A weight-based dose increase in immunosuppressives (azathioprine 2–2.5 mg/kg; 6-mercaptopurine 1–1.5 mg/kg) was performed in five cases.

Table 1. CT enterography appearance of different types of fistulas, which were confirmed with non-CT reference standard (i.e., enteroenteric = surgery, fluoroscopy, ileocolonoscopy; enterocutaneous = clinical confirmation; perianal = EUA, MR, EUS, clinical exam; enterovesical = cystoscopy or surgery; enterovaginal = surgery)

Fistula type (number)	Appear as extraenteric tract? (#/total confirmed cases)	Fistula enhancement, compared to adjacent bowel ^a % (#/type)		Internal content of fistula % (#/type)			Arise from inflamed bowel loop
		Hyperenhancing	Isoenhancing	Fluid	Air	Neither	
Enteroenteric (n = 14)	11/14	93%	7%	14%	0%	86%	86%
		13/14	1/14	2/14	0/14	12/14	12/14
Enterocutaneous (n = 8)	8/8	100%	0%	25%	13%	63%	25%
		8/8	0/8	2/8	1/8	5/8	2/8
Perianal (n = 11)	9/11	72%	27%	27%	27%	45%	NA
		8/11	3/11	3/11	3/11	5/11	
Enterovaginal (n = 3)	1/3	67%	33%	0%	33%	67%	0%
		2/3	1/3	0/3	1/3	2/3	0/3
Enterovesical (n = 1)	1/1	100%	0%	0%	0%	100%	100%
		1/1	0/1	0/1	0/1	1/1	1/1
Total (n = 37)	30/37	86%	14%	19%	14%	68%	58%
		32/37	5/37	7/37	5/37	25/37	15/26

^aFor perianal fistulas, fistula enhancement was compared to the external anal sphincter

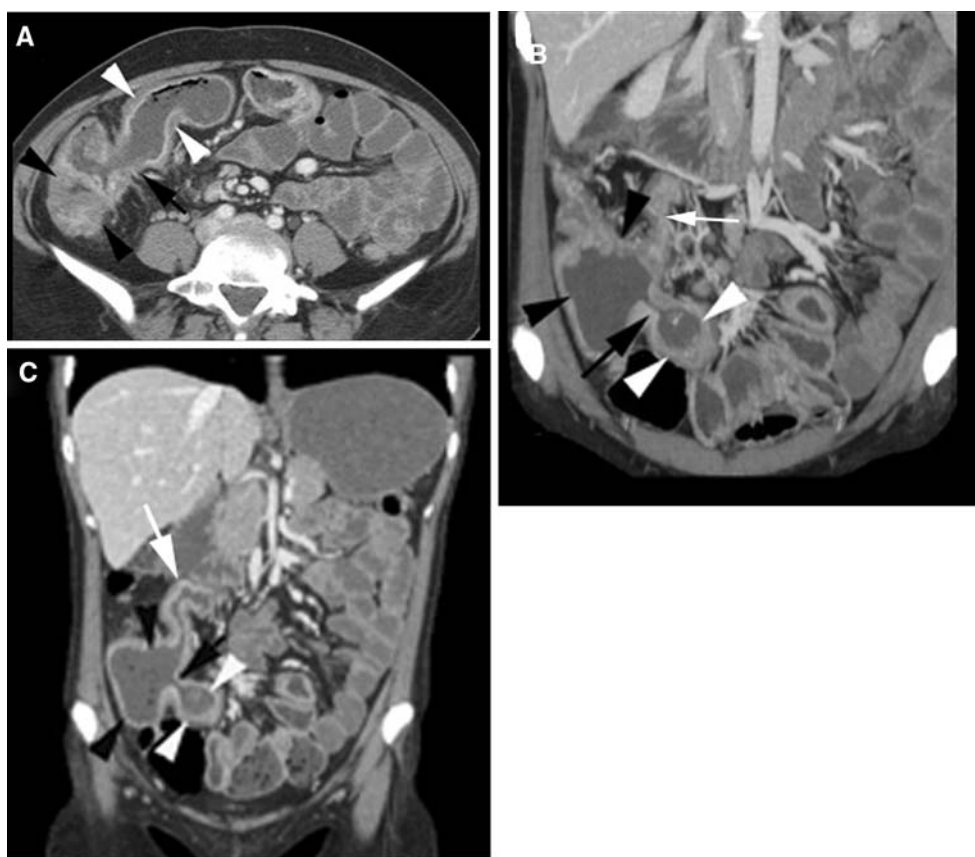


Fig. 5. Axial CT enterography image in a 30-year-old woman with malabsorption and weight loss. **(A, B)** Axial and coronal reformatted CT images demonstrate a large ileocecal fistula (*black arrow*) arising from an ileal loop with Crohn involvement (*white arrowheads*; wall thickening, segmental hyperenhancement). The cecum (*black arrowheads*) is also inflamed and demonstrates wall thickening and stranding the pericolic fat. **(C)** A second coronal reformatted image shows an inflamed and decompressed terminal ileum (*white arrow*) superior to the fistula. Fistulas of this size are often treated surgically, and this patient underwent distal ileal resection and right hemicolectomy. The patient's fistula was confirmed by ileocolonoscopy and further surgery.

Appearance of Crohn's fistulas at CTE

Thirty-nine patients had 13 abscesses and 37 fistulas identified at CT enterography confirmed using a non-CT reference standard (Table 1). Thirty fistulas (81%) appeared as extraenteric tracts. The large majority (86%) were hyperenhancing compared to adjacent bowel loops, and most arose from actively inflamed large or small bowel. Five fistulas (14%) were isoenhancing, with half of these being perianal fistulas. No air or fluid was seen in 25 fistulas (68%).

Enteroenteric and enterocutaneous fistulas

Most confirmed enteroenteric and enterocutaneous fistulas appeared as extraenteric tracts (11/14 and 8/8, respectively; Fig. 4) and were hyperenhancing (13/14 and 8/8, respectively; Fig. 5). Most of these fistulas contained neither internal air nor fluid (Table 1). With larger fistulas, the fistulous tracts were filled with fluid (Fig. 5). Smaller fistulas did not contain any fluid or gas (Fig. 6). Most confirmed enteroenteric fistulas (86%; 12/14) arose from a bowel segment that exhibited CT signs of active Crohn's disease, while only two confirmed enterocutaneous fistulas (25%; 2/8) arose from a bowel segment exhibiting CT findings of active disease. Not

surprisingly, enteroenteric fistulas comprised the largest anatomic group of fistulas without a reference standard confirmation (i.e., 14 were confirmed, 13 were not).

Perianal fistulas

Perianal fistulas usually appeared as hyperenhancing extraenteric tracts, and sometimes contained internal air or fluid. Some patients had associated perianal abscesses (Fig. 7). Perianal fistulas were more likely to contain internal air (3/11; 27%) or fluid (3/11; 27%).

Enterovesical and enterovaginal fistulas

Although a direct fistula tract was observed in some patients, secondary signs of inflammation, such as a thickened bladder or vaginal wall or a small locule of intravesical or intramural air at the site of fistula insertion in the bladder or vagina, were generally relied upon (Fig. 8).

Abscesses

Abscesses appeared as fluid collections with hyperenhancing rims (Fig. 9). Abscesses were seen in multiple locations (interloop/mesenteric, 7; perianal/perirectal, 2;

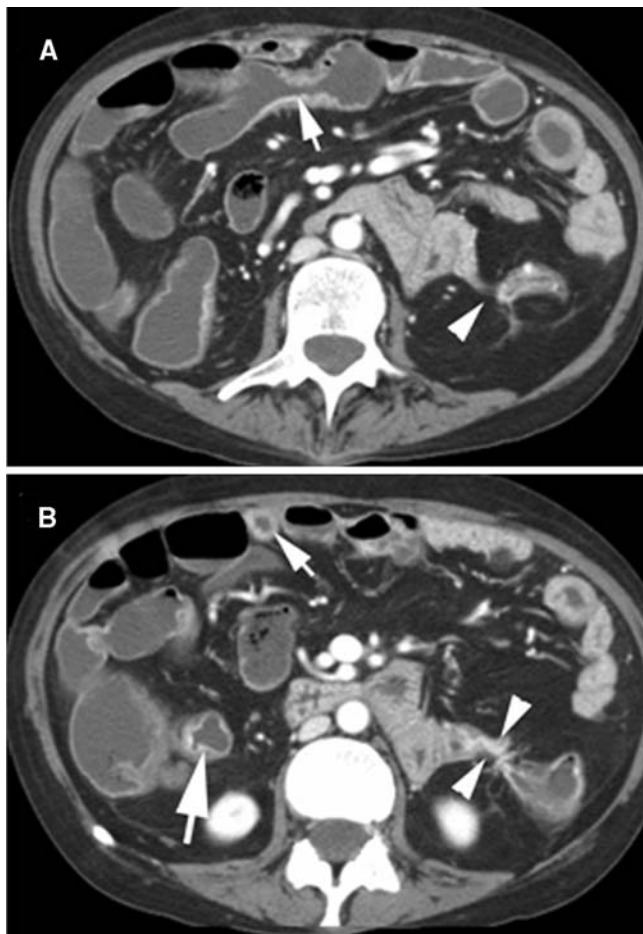


Fig. 6. Axial CT enterography images in a 46-year-old man with 32-year history of ileocolonic Crohn's disease. **(A, B)** Contiguous axial CT enterography images demonstrate multiple jejunal and ileal loops with CT findings of Crohn's disease (*arrows*), including the terminal ileum (*large arrow*). A short, hyperenhancing jejunocolic fistula is identified in the left upper quadrant (*arrowheads*). The patient was treated with bowel rest, total parenteral nutrition, azathioprine, and infliximab. The fistula tracts were confirmed by barium follow-through. The patient had incomplete colonoscopy due to stricture that limited further evaluation.

subcutaneous abdominal wall, 2; retroperitoneal, 2). Nine abscesses (69%) appeared to connect to bowel, with most of these bowel segments (89%) demonstrating CT findings of active Crohn's inflammation.

Discussion

Approximately 20% of Crohn's patients at our institution demonstrate penetrating Crohn's disease at CT enterography. We found that CT enterography is particularly beneficial in this subset of patients, primarily because clinical signs and symptoms of fistulizing Crohn's are protean and do not predict penetrating disease.

There was either no clinical suspicion (34%) or remote clinical suspicion (16%) in half of the patients with fistulas and abscess prior to CTE. In those patients in whom CRP was available, it was normal in 35% of cases. Moreover, we found that 61% of patients underwent a change in medical therapy (initiation or dose escalation) following detection of penetrating Crohn's disease on CTE, and another 18% of patients underwent surgical or percutaneous radiologic intervention following CTE.

We also characterized the radiographic appearance of fistulas at CTE when the fistulas could be confirmed with a non-CT reference standard. Most fistulas appeared as extraenteric tracts; the majority of these were hyperenhancing compared to adjacent bowel loops. This hyperenhancement likely reflects ongoing inflammation in the fistulous tract itself.

Not all fistulas demonstrated the most common appearance of hyperenhancing, extraenteric tracts. Non-hyperattenuating tracts were occasionally observed and sometimes reflected fistulas arising following surgery (Fig. 4). We also observed some perianal and enterovesical fistulas without hyperenhancement of the fistulous tract, perhaps reflecting chronicity. Rectovaginal fistulas were poorly demonstrated at CT imaging. Fluoroscopic or MR examination may be preferred in these clinical scenarios.

Treatment for fistulizing Crohn's disease depends upon symptoms and occasionally the site and extent of fistulous involvement [11, 12]. In addition to fistula identification, radiologists should describe the location of a fistula (by its proximal and distal connections), its extent (i.e., number of tracts), the presence and location of abscesses, enteric involvement by inflammatory Crohn's disease (e.g., proctitis in patients with perianal fistulas), and other superimposed conditions important in guiding appropriate management decisions [13]. Complicating features such as superimposed abscess formation, small bowel obstruction, and location proximal to a stricture, which may help predict the efficacy of medical, image-guided, or surgical management, should also be described. In our experience, many enteroenteric, enterocutaneous, and perianal fistulas can be treated successfully with modern medical therapies [14, 15]; however, enterovesical and enterovaginal fistulas often require surgical treatment [16].

Our study has several weaknesses. It is retrospective and identified patients via a radiologic database, so that our patient cohort is skewed toward a population of patients with radiographically identifiable fistulas and abscesses. We did not estimate the performance (i.e., sensitivity, specificity) of CTE for identifying fistulizing disease; however, Vogel et al. performed this analysis in a surgical series and found that CT enterography was able to detect patients with fistulas with an accuracy of 94% [6]. While their primary aim was to

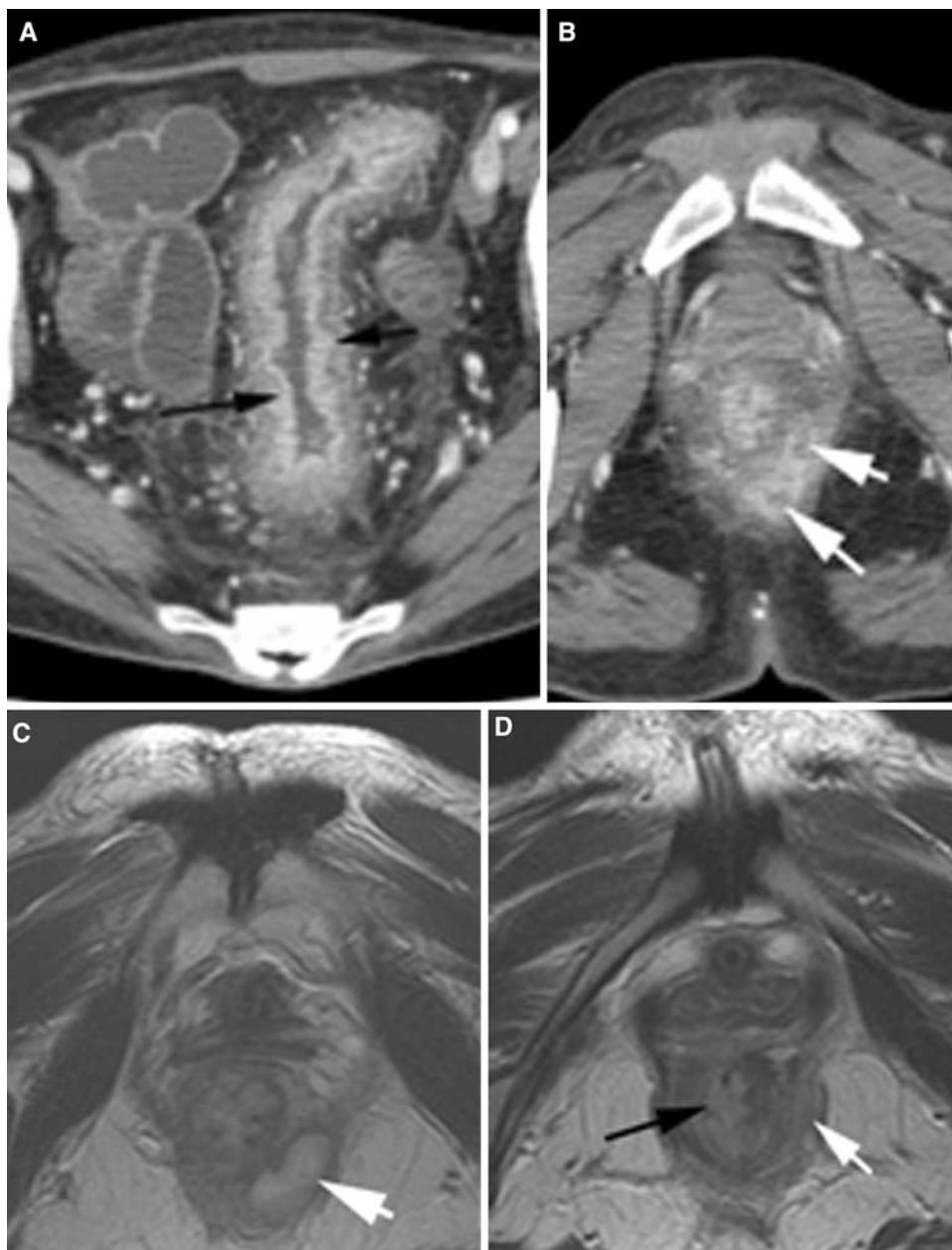


Fig. 7. This 19-year-old woman had sudden onset of diarrhea and right lower quadrant pain. Axial CT enterography images show active rectosigmoid Crohn's as manifested by mural hyperenhancement, wall thickening, and comb sign (**A**, *black arrows*) and an abscess in the posterior anal space (**B**, *white arrows*). Corresponding fast spin-echo MR images demonstrate the perianal abscess (**C**, *white arrow*). In addition, the MR shows a fistulous connection of the abscess to the anus (**D**, *black arrow*). The patient was placed on antibiotics, azathioprine, and infliximab, with eventual resolution of symptoms.

assess the performance of CTE in detecting different types of penetrating disease and not to describe the radiographic appearance of fistulas, their pictorial examples are consistent with our description. Additionally, we did not compare the performance of CTE to other imaging modalities such as small bowel follow-through or MR enterography. Nevertheless, we believe that these weaknesses are acceptable given that our purpose was to estimate the clinical benefit of CTE in patients with fistulizing disease and systematically describe the radiographic appearance of fistulizing Crohn's disease at CTE in patients with confirmed fistulas. We are not aware of such a description in the radiologic literature.

As CTE has been a first-line modality in the diagnosis and staging of Crohn's disease, we are identifying increasing numbers of patients with fistulizing Crohn's disease; therefore, we sought to estimate the contribution of CTE to this challenging group of patients. We believe larger prospective studies will validate our conclusion of the benefit of CT enterography in Crohn's disease.

In conclusion, CTE can detect clinically occult fistulizing Crohn's disease. This detection results in changes in patient management in the majority of cases. Fistulas generally appear as hyperenhancing, extraenteric tracts, often without internal air or fluid. When abscesses are present, sinus tracts are often seen connecting to inflamed bowel loops.

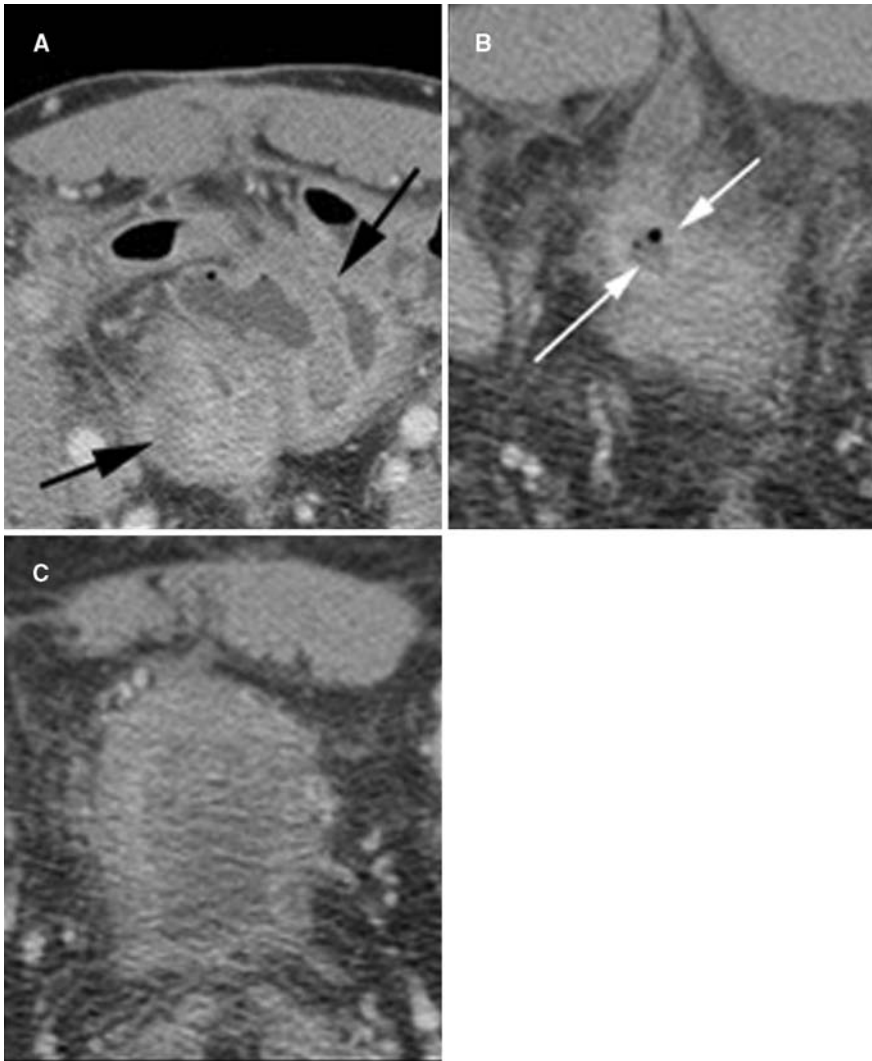


Fig. 8. A 55-year-old man with recurrent UTIs and a prior colectomy for inflammatory bowel disease. **(A)** Axial CT image shows several inflamed small bowel loops and associated phlegmon (*black arrows*) superior to the bladder. An enhancing fistulous tract containing air (*white arrows*) is seen extending caudally **(B)**. The bladder wall is diffusely thickened, consistent with recurrent infection **(C)**. The fistula was removed surgically. The patient had active Crohn's based on ileoscopy and pathology.

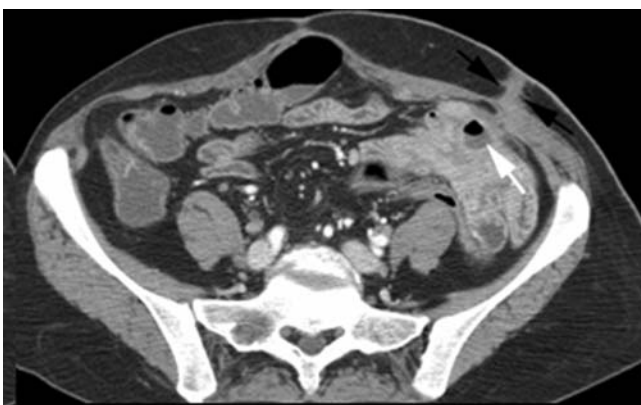


Fig. 9. A 52-year-old female with 20-year history of ileocolonic Crohn's disease, status-post multiple resections. Axial CT enterography image shows a small abscess (*white arrows*) and enterocutaneous fistula (*black arrows*) arising from some matted small bowel loops in the left lower quadrant. The patient had active Crohn's disease based on ileoscopy and pathology. The patient's fistula and abscess were seen at surgery and were removed.

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