Small-bowel imaging in Crohn’s disease: a prospective, blinded, 4-way comparison trial

Craig A. Solem, MD, Edward V. Loftus Jr., MD, Joel G. Fletcher, MD, Todd H. Baron, MD, Christopher J. Gostout, MD, Bret T. Petersen, MD, William J. Tremaine, MD, Laurence J. Egan, MD, William A. Faubion, MD, Kenneth W. Schroeder, MD, PhD, Darrell S. Pardi, MD, Karen A. Hanson, RN, CNP, Debra A. Jewell, RN, John M. Barlow, MD, Jeff L. Fidler, MD, James E. Huprich, MD, C. Daniel Johnson, MD, W. Scott Harmsen, MS, Alan R. Zinsmeister, PhD, William J. Sandborn, MD

Rochester, Minnesota, USA

Background: With the introduction of new techniques to image the small bowel, there remains uncertainty about their role for diagnosing Crohn’s disease.

Objective: To assess the sensitivity and specificity of capsule endoscopy (CE), CT enterography (CTE), ileocolonoscopy, and small-bowel follow-through (SBFT) in the diagnosis of small bowel Crohn’s disease.

Methods: Prospective, blinded trial.

Setting: Inflammatory bowel disease clinic at an academic medical center.

Patients: Known or suspected Crohn’s disease. Exclusion criteria included known abdominal abscess and non-steroidal anti-inflammatory drug (NSAID) use. Partial small-bowel obstruction (PSBO) at CTE excluded patients from subsequent CE.

Interventions: Patients underwent all 4 tests over a 4-day period.

Main Outcome Measurements: Sensitivity, specificity, and accuracy of each test to detect active small-bowel Crohn’s disease. The criterion standard was a consensus diagnosis based upon clinical presentation and all 4 studies.

Results: Forty-one CTE examinations were performed. Seven patients (17%) had an asymptomatic PSBO. Forty patients underwent colonoscopy, 38 had SBFT studies, and 28 had CE examinations. Small-bowel Crohn’s disease was active in 51%, absent in 42%, inactive in 5%, and suspicious in 2% of patients. The sensitivity of CE for detecting active small-bowel Crohn’s disease was 83%, not significantly higher than CTE (83%), ileocolonoscopy (74%), or SBFT (65%). However, the specificity of CE (53%) was significantly lower than the other tests ($P < .05$). One patient developed a transient PSBO due to CE, but no patients had retained capsules.

Limitation: Use of a consensus clinical diagnosis as the criterion standard—but this is how Crohn’s disease is diagnosed in practice.

Conclusions: The sensitivity of CE for active small-bowel Crohn’s disease was not significantly different from CTE, ileocolonoscopy, or SBFT. However, lower specificity and the need for preceding small-bowel radiography (due to the high frequency of asymptomatic PSBO) may limit the utility of CE as a first-line test for Crohn’s disease. (Gastrointest Endosc 2008;68:255-66.)

Modern clinicians have many options available to them for small-bowel (SB) imaging in Crohn’s disease. Barium studies have traditionally been the conventional test for SB radiography in this setting. Barium small-bowel follow-through (SBFT) examinations have previously been shown to be preferable to barium enteroclysis studies in a prospective study involving patients with Crohn’s disease.
disease. Colonoscopy is necessary to assess for colonic involvement, to directly view the terminal ileal mucosa, and to obtain histology, but ileoscopy may not always be technically feasible. CT enterography (CTE) is a newer radiographic technique that has the potential additional advantages of detecting extraluminal complications of Crohn’s disease and aiding the distinction between inflammatory and fibrostenotic stenosis. There have been several prospective studies suggesting significant potential utility of capsule endoscopy (CE) in patients with known or suspected Crohn’s disease. With the introduction of these new imaging procedures, there still remains a considerable amount of uncertainty about their place in algorithms for diagnosis of suspected Crohn’s disease or disease activity assessment in those with known Crohn’s. To circumvent the confounding effects of treatment and natural history, we undertook a prospective blinded study in patients with known or suspected Crohn’s disease, comparing these 4 primary SB imaging modalities over a short duration.

METHODS

Selection of patients

The study was performed between January 1, 2004, and August 1, 2004. Eligible patients included adults aged 18 to 75 years of both sexes who had suspected or known Crohn’s disease. Exclusion criteria from the study included the following: obstructive symptoms defined as postprandial abdominal pain with vomiting; known intra-abdominal abscess, history of non-steroidal anti-inflammatory drug (NSAID) use within 2 weeks, dysphagia, gastroparesis, implantable electromedical devices such as pacemaker or automated intracardiac defibrillator, creatinine ≥ 2.0 mg/dL or hemoglobin < 7.5 g/dL, iodine or metoclopramide allergy, ileostomy or colostomy, history of abdominal radiation therapy, pregnancy, institutionalized or vulnerable adults, patients in need of emergency surgery, and patients with anticipated need for a magnetic resonance imaging scan within 2 weeks. The Institutional Review Board of Mayo Clinic approved the study, and all patients gave written informed consent.

Study design

The study was a prospective, blinded, 4-way comparison trial of CTE, CE, ileocolonoscopy, and SBFT. The diagnostic tests were performed sequentially over 4 days. Patients had the following laboratory tests drawn in addition to any other clinically indicated tests on the first study day: complete blood count (CBC), sedimentation rate, C-reactive protein (CRP), albumin, and creatinine. CTE was performed first by using 2 L of polyethylene glycol (PEG) solution (Braintree Laboratories, Braintree, Mass) consumed over 60 minutes prior to the CT examination. Patients subsequently drank an additional 2 L of PEG solution to complete their bowel preparation for ileocolonoscopy, which occurred on day 2. If no abscess or partial small-bowel obstruction (PSBO) was seen on CTE, patients consumed an additional 1 L of PEG solution the evening prior to their CE on day 3. Patients underwent an SBFT on the final study day. Co-investigators were blinded to the results of the other SB tests until after having interpreted their respective studies. Transcription of all dictations into the medical record was held until after the completion of the SB studies to help maintain blinding, unless a condition that required immediate attention was identified, such as abscess or bowel obstruction. Following each SB imaging procedure, the interpreting physician completed a small-intestine anatomy form, which divided the small-intestine into the duodenum, proximal SB, mid-SB, distal SB, and terminal ileum. The form required identification of all types and severity of lesions present in each small-intestine segment. Each interpreter additionally made one of 4 prespecified global assessments regarding small-bowel Crohn’s disease only: active, suspicious, inactive, or absent. As is common in clinical practice, Crohn’s disease diagnosis by CE was based upon the global assessment of the experienced capsule reader, and diagnosis by other SB imaging modalities was based upon conventional criteria.

CTE

CTE was performed on the first study day in all patients (except for one patient who, for logistical reasons, had the CTE on day 2 after colonoscopy on day 1). CTE was
interpreted at the time of examination by 1 of 5 experienced gastrointestinal radiologists (J.G.F., J.M.B., J.L.F., J.E.H., C.D.J.). All radiologists were blinded to the results of all other imaging studies. CTE examination was conducted on each patient in a similar manner. Each patient was given 10 mg of oral metoclopramide (Reglan, Pharmaceutical Associates, Greenville, SC) 75 minutes prior to CT examination, to increase gastric and SB peristalsis. Oral contrast for CTE examinations consisted of 1500 mL of PEG solution given to the patient 60 minutes prior to the CT examination, supplemented by an additional 500 mL of PEG solution 15 minutes prior to CT examination. One patient consumed 1.8 L of water rather than PEG solution prior to CT due to intolerance (retching).

After being placed on the CT table, each patient was given 1 mg glucagon intravenously (Eli Lilly, Indianapolis, Ind) over 30 seconds. Subsequently, contrast-enhanced CT was performed by using 150 mL Omnipaque 300 (GE Healthcare, Princeton, NJ) injected intravenously at a rate of 4 mL/second, with scanning initiated 70 seconds after the beginning of contrast injection. Scanning was performed on a GE LightSpeed Ultra-8 CT scanner (GE Healthcare, Milwaukee, Wis) by using a field of view to fit, 120 kV, 240 mA, and axial images having a slice thickness of 2.5 mm with a 1.25-mm reconstruction interval.

At the time of examination, radiologist readers determined if patients had an abdominopelvic abscess or PSBO, and notified the study coordinator (who did not participate in the interpretation of other SB studies) if either of these findings was present. PSBO at CTE was defined as segmental SB narrowing accompanied by prestenotic dilation of SB loops and poststenotic nondilation (decompression) of SB loops. Abscesses were defined as extra-intestinal fluid collections circumscribed by an enhancing wall. CT findings indicating active Crohn’s disease included segmental mural hyperenhancement, mural stratification, increased density in the perienteric fat, sinus tract, or fistula. Fibrofatty proliferation and luminal narrowing without hyperenhancement were considered to represent inactive Crohn’s disease.

Colonoscopy

Ileocolonoscopy was performed by 1 of 8 experienced gastrointestinal endoscopists (median duration as staff gastroenterologist 10 years, range 1-24 years). All endoscopists were blinded to the results of all other imaging studies. Patients consumed a total of 4 L of PEG solution (2 additional liters of PEG solution after CTE) as preparation for the procedure, which occurred on day 2 (except for the patient noted previously, who had ileocolonoscopy on day 1). Two patients had sodium phosphate colonoscopy preparations instead of PEG solution, due to recruitment into study after already completing this colon preparation in one patient, and patient preference in another patient. One patient who had an ileorectostomy drank 2 L of PEG solution for CTE on day 1 and then had 2 enemas prior to ileocolonoscopy on day 2 to avoid excessive preparation, given the absence of the colon. Intubation and inspection of the terminal or neo-terminal ileum was attempted with all colonoscopies.

CE

CE was performed by using the Given Pillcam SB capsule system (Given Imaging Limited, Yoqneam, Israel). CE studies were interpreted by 1 of 4 experienced capsule readers (T.H.B., B.T.P., C.J.G., E.V.L.). All capsule readers were blinded to the results of all other imaging studies. If no abscess or PSBO was seen on CTE or ileocolonoscopy, patients consumed 1 L of PEG solution the evening prior to their CE on day 3. Patients were on a clear liquid diet after completing the 1-L PEG solution preparation approximately 12 hours prior to the procedure. No prokinetic medications were used. Patients were allowed to drink clear liquids 2 hours after capsule ingestion but not allowed to not eat until after study completion. Data were collected for up to 8 hours. At the time of the study, there existed no standardized criteria of what constitutes active, inactive, or suspicious Crohn’s disease on CE. To simulate what occurs in clinical practice, the global assessment of the individual capsule reader was used to make these determinations.

SBFT

SBFT was performed by a subspecialized gastrointestinal radiologist. Prior to contrast ingestion, a follow-up plain abdominal radiograph was arranged within approximately 2 weeks to confirm capsule passage. SBFT examinations utilized thin barium (60% w/v barium sulfate suspension; Liquid E-Z-paque, EZ EM, Inc, Westbury, NY) as oral contrast, with aliquots drunk at intervals and volumes chosen at the discretion of the radiologist. Frequent, intermittent palpation and fluoroscopic observation were performed until the terminal ileum was adequately assessed. The fluoroscopist issued a written report addressing the presence of fluoroscopic findings of Crohn’s disease at the time of the examination.

A second gastrointestinal radiologist (J.G.F. or J.M.B.), unblinded to the fluoroscopic report, examined spot and overhead SBFT images, and completed study data forms, noting radiologic findings of active Crohn’s disease (ie, mucosal irregularity, aphthous ulcer/erosion, mesenteric border linear ulcer, mucosal cobblestoning, fistula, abscess) and categorizing Crohn’s as present, suspicious, inactive, or absent. In 2 cases, the fluoroscopist completed the SBFT study forms himself.

Questionnaire

After completing all tests, patients completed a study questionnaire on the tolerability of each diagnostic
procedure and the willingness to repeat the procedure in the future.

**Consensus reference standard**

After the results of the 4 studies (CTE, ileocolonoscopy, CE, and SBFT) were recorded for each patient, the findings of all of the studies were reviewed at the conclusion of the study period by a consensus panel of co-investigators representing each diagnostic modality and a referring gastroenterologist, to establish a consensus global assessment of SB Crohn’s disease. If there were discordant results among studies, this discussion necessitated a change of opinion by one or more investigators about the initial interpretation of the findings of one or more studies. More specifically, the investigator representing one of the diagnostic modalities had to concede that a mistake had been made in the initial interpretation of the SB findings with their modality. Thus, the reference standard for assessment of Crohn’s disease activity was the final determination of the consensus panel (ie, active, suspicious for active, inactive, or absent). The consensus criterion standard has previously been used in a prospective trial of tests evaluating perianal Crohn’s disease. After the modified readings were used to establish the consensus reference standard for SB disease, the original interpretation of each study as recorded on the study forms, was used to estimate the performance characteristics of the tests.

In a prespecified primary analysis, the diagnoses of active and suspicious SB Crohn’s disease were grouped together, and the diagnoses of inactive or absent disease were grouped together, for all reported analyses to detect active SB Crohn’s. A prespecified secondary analysis was also performed for detecting the presence of SB Crohn’s disease by combining the categories of active, suspicious, and inactive disease, and comparing this group to the absent category. (However, the latter results were consistent with those of active SB Crohn’s, and are therefore not reported in the Results.)

**Statistical analysis**

For the primary analysis, the sensitivity of each test was calculated by dividing the number of patients with active or suspicious SB Crohn’s disease based on the consensus criterion standard. The specificity of each test was calculated by dividing the number of patients with negative tests results by the number of patients with inactive or absent SB Crohn’s disease based on the consensus criterion standard. The diagnostic accuracy of each test was calculated by dividing the number of patients with test results in agreement with the consensus criterion standard divided by the number of tests performed. Exact binomial 95% confidence intervals were also reported.

The operating characteristics of each SB examination were compared to those of CE in the subset of patients having both CE and another SB examination. The sensitivity, specificity, and accuracy of CTE, ileocolonoscopy, and SBFT were compared to CE by using McNemar’s test of paired proportions. The combined sensitivity, specificity, and accuracy of all pairs of tests that could be considered were also estimated against the consensus criterion standard. McNemar’s test was used to compare the performances of pairs of tests (CE plus CTE vs ileocolonoscopy plus SBFT, CE plus ileocolonoscopy vs CTE plus SBFT, and CTE plus ileocolonoscopy vs CE plus SBFT). Comparisons of pairs containing a common diagnostic test were not performed. The P values were not adjusted for multiple comparisons.

**RESULTS**

Forty-two patients enrolled in the study (Fig. 1). One patient withdrew for personal reasons before any diagnostic studies were performed and was not included in the analysis. The median age of the 41 patients (81% female) participating in the study was 40.1 years (range 18.9-73.5 years). Forty-one patients underwent ileocolonoscopy. One patient subsequently withdrew for personal reasons and had no further studies. Ileoscopy was feasible in 36 of the 40 colonoscopies. Thirty-eight patients had SBFT examinations after 1 patient exited the study due to a stricture detected on CTE, and 1 patient underwent surgery for a PSBO. Twenty-eight patients had CE studies after 10 patients were excluded for PSBO or abscess, and 2 patients left the study for personal reasons. One capsule study was repeated due to a technical malfunction with the initial examination (no images were obtained), and one capsule was retained in the stomach for the duration of battery life, resulting in no SB images (but the capsule eventually passed spontaneously). Twenty-seven capsule studies were then used for analysis. Table 1 details the combinations of the 4 SB examinations patients received.

The study co-investigators were able to reach a consensus opinion regarding the global assessment of SB Crohn’s disease after unblinding at the conclusion of study in all 41 patients who had one or more SB studies (Table 2). The final clinical diagnoses for all patients, not limited to the SB, are reported in Table 3.

Table 4 reports the sensitivity, specificity, and accuracy of the 4 SB tests individually, with the consensus criterion standard used to classify patient status as either “active” (active plus suspicious) or “inactive” (inactive plus absent). The sensitivity for the detection of active SB Crohn’s disease was 83% for CE, 82% for CTE, 74% for ileocolonoscopy, and 65% for SBFT. The specificity for SB Crohn’s disease was 100% for ileocolonoscopy, 94% for SBFT, 89% for CTE, and 53% for CE. The overall accuracy for SB Crohn’s was 86% for ileocolonoscopy, 85% for CTE, 79% for SBFT, and 67% for CE.

The performance of CTE, ileocolonoscopy, and SBFT were each compared with that of CE (Table 5). There
were 12 patients in each of 3 sensitivity comparisons, and for specificity there were 15 patients, except to compare CE versus SBFT, where only 14 received both examinations. The sensitivity of CE (83%) was not significantly different from that of CTE (67%, P = .63), ileocolonoscopy (67%, P = .69), or SBFT (50%, P = .22). However, the specificity of CE (53%) was significantly lower than that for either CTE (100%, P = .02) or SBFT (100%, P = .02). The specificity of CE (43%) was also significantly lower among the 14 patients having ileocolonoscopy (100%, P = .03). The lower specificity of CE was due to the fact that, in 7 patients, there were findings that led the CE reader to deem the examination either suspicious (n = 5) or “definite” (n = 2) for active Crohn’s disease, but according to the consensus criterion standard, these patients had either no evidence of Crohn’s disease (n = 5) or only inactive disease (n = 2).

The performance characteristics of pairs of SB examinations against the consensus criterion standard were estimated (Table 4). A patient was classified positive for active SB Crohn’s disease if either of the 2 examinations indicated active disease. The sensitivity for combinations of examinations ranged from a high of 100% for the CE and ileocolonoscopy combination to a low of 78% for...
the ileocolonoscopy and SBFT combination. The specificity of examination combinations against the criterion standard ranged from a high of 100% for SBFT plus ileocolonoscopy to a low of 53% for both the CE plus SBFT and CE plus CTE combinations. The overall accuracy of examination combinations against the criterion standard ranged from 89% for both the CTE plus ileocolonoscopy and CTE plus SBFT combinations to 70% for the CE plus CTE and CE plus SBFT combinations.

No pair of SB examinations was significantly more sensitive than the combination containing the other two examinations (among the 4 SB examinations), \( P > .05 \) (Table 6). However, each combination of examinations that included CE had a significantly lower specificity (57%) than did the opposite pair of examinations (\( P = .03 \) for each of the 3 comparisons, unadjusted).

Patients completed a questionnaire at the end of the study. All patients swallowed the capsule easily. Ninety-two percent of patients did not experience any pain during the CE study, significantly better than colonoscopy (\( P < .05 \)), but no better than CTE or SBFT (\( P > .05 \)). Ninety-three percent of patients stated they would undergo CE (14%) despite efforts to cleanse with 1 L PEG solution prior to the study. The terminal ileum was examined completely in only 75% of studies. One capsule study had a technical malfunction resulting in no images. In a single patient with suspected Crohn’s disease, CE demonstrated multiple SB erosions when the other 3 SB tests were normal (Fig. 4).

### DISCUSSION

In this prospective, blinded trial, we compared 4 primary small-intestinal imaging modalities in the diagnosis of SB Crohn’s disease. In contrast to the other studies examining the utility of CE in patients with known or suspected Crohn’s disease,22,27,29,33–40 we believe this is the only prospective, blinded trial comparing all 4 primary SB imaging modalities over a short time period, avoiding both treatment and natural history effects. Unlike the “diagnostic yield” reported in most published CE studies, we established a surrogate criterion standard, allowing us to calculate the sensitivity, specificity, and accuracy of each test for diagnosing SB Crohn’s disease. We found that there was no significant difference among CTE, CE, ileocolonoscopy, and SBFT for the sensitivity or accuracy of diagnosing SB Crohn’s disease. CTE and CE demonstrated similarly high sensitivity for SB Crohn’s, which was numerically superior to SBFT and ileocolonoscopy. Although the numerical superiority of CTE and CE was not statistically significant, this may have been due to the limited sample size and potential lack of power to detect a significant difference. Combining diagnostic tests may improve sensitivity, and this is commonly used in clinical practice. We found that the specificity of CE for SB Crohn’s disease was significantly lower than other SB imaging modalities, which lowered its overall accuracy. Our study also indirectly suggests that SB radiologic imaging may be needed prior to CE in suspected or known Crohn’s disease patients, due to the high frequency (17%) of asymptomatic PSBO. When we used an algorithm of performing CTE prior to CE and using a finding of stricture with proximal bowel dilation to preclude ingestion of the endoscopy capsule, we observed no capsule retention.

The finding of a lower specificity of CE for SB Crohn’s disease is not entirely unexpected. “Diagnostic yield” as a measure of the operating performance of a diagnostic test is less than ideal—it merely reports the prevalence of abnormalities detected by a particular imaging modality and does not attempt to determine whether those symptomatic PSBO requiring hospitalization, but the capsule passed within a few days following medical therapy with corticosteroids and infliximab, with symptoms resolving (Fig. 3). Unlike the higher capsule retention rates seen in other studies, we had no retained capsules (confirmed by radiograph) using our diagnostic algorithm.

Chyme significantly limited study quality in 4 patients who underwent CE (14%) despite efforts to cleanse with 1 L PEG solution prior to the study. The terminal ileum was examined completely in only 75% of studies. One capsule study had a technical malfunction resulting in no images. In a single patient with suspected Crohn’s disease, CE demonstrated multiple SB erosions when the other 3 SB tests were normal (Fig. 4).

### TABLE 3. Final overall clinical diagnosis (not limited to the small intestine) in all 41 patients who underwent at least 1 diagnostic test, and in 26 patients who underwent all 4 tests

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>All patients, n (%)*</th>
<th>Patients with all 4 tests, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s disease</td>
<td>30 (73%)</td>
<td>19 (73%)</td>
</tr>
<tr>
<td>Indeterminate abdominal pain</td>
<td>3 (7%)</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>Irritable bowel syndrome</td>
<td>2 (5%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Indeterminate colitis</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Carcinoid</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Submucosal mass, small bowel</td>
<td>1 (2%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Gastroparesis</td>
<td>1 (2%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Indeterminate diarrhea</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total</td>
<td>41 (100%)</td>
<td>26 (100%)</td>
</tr>
</tbody>
</table>

*Percentage of the group undergoing at least 1 SB imaging test.  
| Percentage of the group undergoing all 4 tests. |  

Solem et al
abnormal findings are clinically significant. Most studies reporting “diagnostic yield” do so because the test is not being compared against a reference standard. CE is an extremely sensitive tool for direct visualization of the SB mucosa. As in most diagnostic tests, improved sensitivity typically comes at the cost of decreased specificity. Goldstein et al found that 22% of asymptomatic control patients who denied recent NSAID ingestion had SB abnormalities at CE, with an average of 4 lesions per subject. As several CE findings, such as mucosal erythema, are nonspecific, and do not indicate a diagnosis of active Crohn’s disease by themselves, their inclusion into reference standard assessments of disease activity in SB imaging trials may result in confirmation bias favoring CE.

Buchman et al used SBFT as a method to detect SB strictures that may lead to retained capsules, and found a 29% incidence of SB strictures in Crohn’s patients, which precluded capsule endoscopy. By using SBFT as a screening examination, they observed 2 episodes of capsule retention (7%). Voderholzer et al compared CE and CTE

---

**TABLE 4. Individual performance estimates of 4 diagnostic tests and all pairs of these tests for active small-bowel Crohn’s disease**

<table>
<thead>
<tr>
<th>SB test</th>
<th>Patients tested, n</th>
<th>Sensitivity (%)</th>
<th>95% CI</th>
<th>Specificity (%)</th>
<th>95% CI</th>
<th>Accuracy (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CE</td>
<td>27</td>
<td>10/12 (83)</td>
<td>52-98</td>
<td>8/15 (53)</td>
<td>27-79</td>
<td>18/27 (67)</td>
<td>46-83</td>
</tr>
<tr>
<td>CTE</td>
<td>41</td>
<td>18/22 (82)</td>
<td>60-95</td>
<td>17/19 (89)</td>
<td>67-99</td>
<td>35/41 (85)</td>
<td>71-94</td>
</tr>
<tr>
<td>Ileocolonoscopy</td>
<td>36</td>
<td>14/19 (74)</td>
<td>49-91</td>
<td>17/17 (100)</td>
<td>80-100</td>
<td>31/36 (86)</td>
<td>71-95</td>
</tr>
<tr>
<td>SBFT</td>
<td>38</td>
<td>13/20 (65)</td>
<td>41-8</td>
<td>17/18 (94)</td>
<td>73-100</td>
<td>30/38 (79)</td>
<td>63-90</td>
</tr>
<tr>
<td>Pairs of Tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CE &amp; CTE</td>
<td>27</td>
<td>11/12 (92)</td>
<td>62-100</td>
<td>8/15 (53)</td>
<td>27-79</td>
<td>19/27 (70)</td>
<td>50-86</td>
</tr>
<tr>
<td>CE &amp; ileocolonoscopy</td>
<td>26</td>
<td>12/12 (100)</td>
<td>74-100</td>
<td>8/14 (57)</td>
<td>29-82</td>
<td>20/26 (77)</td>
<td>56-91</td>
</tr>
<tr>
<td>CE &amp; SBFT</td>
<td>27</td>
<td>11/12 (92)</td>
<td>62-100</td>
<td>8/15 (53)</td>
<td>27-79</td>
<td>19/27 (70)</td>
<td>50-86</td>
</tr>
<tr>
<td>SBFT &amp; ileocolonoscopy</td>
<td>34</td>
<td>14/18 (78)</td>
<td>52-94</td>
<td>16/16 (100)</td>
<td>79-100</td>
<td>30/34 (88)</td>
<td>73-97</td>
</tr>
<tr>
<td>CTE &amp; ileocolonoscopy</td>
<td>36</td>
<td>16/19 (84)</td>
<td>60-97</td>
<td>16/17 (94)</td>
<td>71-100</td>
<td>32/36 (89)</td>
<td>74-97</td>
</tr>
<tr>
<td>CTE &amp; SBFT</td>
<td>38</td>
<td>17/20 (85)</td>
<td>62-97</td>
<td>17/18 (94)</td>
<td>73-100</td>
<td>34/38 (89)</td>
<td>75-97</td>
</tr>
</tbody>
</table>

CTE, CT enterography; CE, capsule endoscopy; SBFT, small-bowel follow-through; 95% CI, 95% confidence intervals.

*Criterion standard is based on consensus diagnosis of active Crohn’s disease or suspicious for Crohn’s disease.

---

**TABLE 5. Comparison of sensitivity and specificity between capsule endoscopy and 3 other diagnostic tests for active small-bowel Crohn’s disease**

<table>
<thead>
<tr>
<th>SB test</th>
<th>Sensitivity (%)</th>
<th>P-value</th>
<th>Specificity (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE</td>
<td>10/12 (83)</td>
<td>ref</td>
<td>8/15 (53)</td>
<td>ref</td>
</tr>
<tr>
<td>CTE</td>
<td>8/12 (67)</td>
<td>.63</td>
<td>15/15 (100)</td>
<td>.02</td>
</tr>
<tr>
<td>Ileocolonoscopy</td>
<td>8/12 (67)</td>
<td>.69</td>
<td>14/14 (100)</td>
<td>.03</td>
</tr>
<tr>
<td>SBFT</td>
<td>6/12 (50)</td>
<td>.22</td>
<td>15/15 (100)</td>
<td>.02</td>
</tr>
</tbody>
</table>

CTE, CT enterography; CE, capsule endoscopy; SBFT, small-bowel follow-through; 95% CI, 95% confidence intervals.

*Criterion standard is based on consensus diagnosis of active Crohn’s disease or suspicious for Crohn’s disease.

Using McNemar’s test for paired proportions, testing performance compared to the CE examination, unadjusted for multiple comparisons.

---

**TABLE 6. Selected comparisons of sensitivity and specificity between pairs of small-bowel examinations**

<table>
<thead>
<tr>
<th>Sensitivity (%)</th>
<th>P-value</th>
<th>Specificity (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE &amp; ileocolonoscopy</td>
<td>12/12 (100)</td>
<td>8/14 (57)</td>
<td></td>
</tr>
<tr>
<td>CTE &amp; SBFT</td>
<td>9/12 (75)</td>
<td>.25</td>
<td>14/14 (100)</td>
</tr>
<tr>
<td>CE &amp; CTE</td>
<td>11/12 (92)</td>
<td>8/14 (57)</td>
<td></td>
</tr>
<tr>
<td>SBFT &amp; ileocolonoscopy</td>
<td>9/12 (75)</td>
<td>.63</td>
<td>14/14 (100)</td>
</tr>
<tr>
<td>CE &amp; SBFT</td>
<td>11/12 (92)</td>
<td>8/14 (57)</td>
<td></td>
</tr>
<tr>
<td>CTE &amp; ileocolonoscopy</td>
<td>9/12 (75)</td>
<td>.63</td>
<td>14/14 (100)</td>
</tr>
</tbody>
</table>

CTE, CT enterography; CE, capsule endoscopy; SBFT, small-bowel follow-through; 95% CI, 95% confidence intervals.

*Criterion standard is based on consensus diagnosis of active Crohn’s disease or suspicious for Crohn’s disease.

Using McNemar’s test for paired proportions, unadjusted for multiple comparisons.
in 56 patients with known Crohn’s disease.\textsuperscript{27} CTE was performed prior to CE, and 27% of patients were precluded from CE because of strictures.\textsuperscript{27} They used stricter criteria for excluding patients from CE (ie, stricture < 1-cm luminal diameter with no proximal SB dilation required), but still experienced one episode of capsule retention (2%) requiring removal from the jejunum with push enteroscopy, and one episode of symptomatic PSBO requiring high-dose corticosteroid therapy before spontaneous passage.

Our results are somewhat at variance with other studies comparing CE and CTE in patients with known or suspected Crohn’s disease.\textsuperscript{22,27,29} A meta-analysis of these 3 studies suggested that the prevalence of abnormalities detected on CE was 38% higher than that of CTE.\textsuperscript{41} However, this value was significantly higher than CTE only for the subgroup of patients with known Crohn’s disease. We believe the differences in study results are due to a number of factors. In one of these studies,\textsuperscript{22} the enteric contrast used apparently was a positive agent (30% Telebrix), not

---

**Figure 2.** A, B, C, Computed tomography enterography in a 43-year-old woman with Crohn’s disease, depicting asymptomatic PSBO due to multiple segments of actively inflamed jejunum, precluding ingestion of endoscopy capsule. Axial and 2D multiplanar reformatted images depict both luminal narrowing caused by active inflammation (with segmental hyperenhancement mural stratification, *arrows*) and prestenotic bowel dilation (*arrowheads*).
a negative/neutral contrast agent, as used in our study. Use of a positive contrast would diminish the operating characteristics of CTE, as it would not take advantage of the differences in attenuation between the bowel lumen and bowel wall. Furthermore, our study was the only one of these that met both of the following criteria: there existed a range of diagnostic uncertainty (recruitment of both known and suspected Crohn’s), and the readers of each

Figure 3. A, B, C, D, SB ulceration and stenosis in the patient who experienced a highly symptomatic PSBO shortly after capsule ingestion, resulting in hospitalization for several days. E, CTE demonstrated approximately 50 cm of actively inflamed ileum with mural enhancement and stratification (arrows), but without any proximal SB dilation (arrowhead). The symptoms resolved and the capsule eventually passed after steroid and infliximab treatment.
modality were blinded to the results of the other modalities. Furthermore, in our study, all patients underwent all imaging modalities after informed consent had been obtained; in other words, the decision to perform certain tests, or even enroll patients, was not dependent upon the results of other tests.

The primary limitation of this study was the use of the consensus panel clinical diagnosis as the reference standard assessment. Because no criterion standard for the diagnosis of Crohn’s disease exists, we believe the consensus clinical diagnosis best approximates how this diagnosis is actually made in clinical practice. Crohn’s disease is a clinical diagnosis based upon a comprehensive evaluation including clinical presentation, SB radiographic imaging, endoscopic findings, and histology. The concept of using a consensus diagnosis when no criterion standard diagnostic test exists has been used previously in a study examining the sensitivity of diagnostic tests (magnetic resonance imaging, examination under anesthesia, and endoscopic ultrasound) for perianal fistulas in Crohn’s disease.42 This method unfortunately requires that the results of all imaging tests will be included in the determination of the consensus clinical diagnosis with which it is being compared. However, we believed this was necessary because clinical symptoms and serologic markers cannot reliably estimate or predict the presence, severity, or location of active Crohn’s disease. Submitting all patients to exploratory laparoscopy or laparotomy for a criterion standard confirmation is obviously invasive and impractical. Moreover, a meta-analysis of several studies suggests that CE may be more sensitive at diagnosing SB Crohn’s disease than other imaging modalities.41 This unique situation warrants inclusion of CE in the consensus clinical diagnosis, to minimize incorrectly labeling lesions seen on CE but not the other imaging modalities as false positives. Neither laparotomy nor laparoscopy are routinely used for diagnosing Crohn’s disease in standard clinical practice, but rather these interventions are reserved for complications of Crohn’s that are not amenable to medical therapy. Additionally, surgery may detect gross findings of Crohn’s disease but may miss mucosal lesions that could be clinically significant.

Figure 4. A, B, C, D, SB ulcers on capsule endoscopy in the single patient found to have active SB Crohn’s disease on CE despite all other imaging studies being normal (3.4%).
As a result of our study, we have adopted the following diagnostic algorithm for evaluating SB Crohn’s disease. CTE and ileocolonoscopy are first-line combined tests, with a combined sensitivity of 84% and specificity of 94% for active Crohn’s disease. CTE has high sensitivity, similar to CE, but with superior specificity. Furthermore, CTE detects extraluminal intestinal complications (eg, fistulas and abscesses) and may help distinguish inflammatory from fibrostenotic strictures, facilitating therapeutic decisions while avoiding potential risks of retained capsules. Ileocolonoscopy stages the extent of disease and obtains necessary histology. SBFT should be considered as an alternative to CTE based upon local expertise or other extenuating circumstances such as iodine allergy or renal insufficiency. CE should subsequently be performed if the clinical suspicion for Crohn’s disease remains high despite a negative evaluation.

DISCLOSURE

The following authors report that they have no disclosures relevant to this publication: C. A. Solem, T. H. Baron, C. J. Gosstou, B. T. Petersen, W. J. Tremaine, L. J. Egan, W. A. Faubion, K. W. Schroeder, D. S. Pardi, K. A. Hanson, D. A. Jewell, J. M. Barlow, J. E. Huprich, W. S. Harmsen, A. R. Zinsmeister, W. J. Sandborn. The following authors report actual or potential conflicts: W. S. Harmsen, A. R. Zinsmeister, W. J. Sandborn. The following authors report actual or potential conflicts: K. A. Hanson, D. A. Jewell, J. M. Barlow, J. E. Huprich, L. J. Egan, W. A. Faubion, K. W. Schroeder, K. W. Schroeder, D. S. Pardi, T. H. Baron, C. J. Gosstou, W. J. Sandborn, B. T. Petersen, W. J. Tremaine. The following authors report actual or potential conflicts: E. V. Loftus, Jr, received consulting fees from Given Imaging in the 12 months prior to implementation of the trial. J. G. Fletcher and C. D. Johnson receive grant support from GE Healthcare, the manufacturer of the multidetector CT scanner and the iodinated intravenous contrast used for CT enterography exams. J. L. Fidler has an NIH grant, in which GE Healthcare is an external collaborator. Supported in part by Given Imaging and the Mayo Foundation for Medical Education and Research.

REFERENCES

correlation with endoscopic and histologic findings of inflammation. Radiology 2006;238:505-16.