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The Role of Small Bowel Follow Through in Diagnosing Inflammation of the Terminal Ileum in Pediatric Patients

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Abstract

Background—The small bowel follow-through (SBFT) is a non-invasive imaging modality for evaluating terminal ileum (TI) inflammation. The accuracy of this modality in pediatric patients is not well established.

Methods—We retrospectively determined the sensitivity and specificity of SBFT for detecting TI inflammation diagnosed on histology in 93 pediatric patients followed in a single institution.

Results—The mean age at the first study was 12.9 years [range: 1.1-20.9 years]. 45% were female. Twenty-five patients (27%) had abnormal TI's on SBFT. Seventeen patients (18%) had TI inflammation diagnosed by biopsy. The sensitivity of SBFT was 59% and the specificity was 80% for detecting TI inflammation diagnosed on histology. Sensitivity and specificity did not change by demographic factors, final diagnoses, presenting symptoms, or laboratory parameters reflecting the presence of intestinal inflammation.

Conclusions—The sensitivity and specificity of SBFT in pediatric patients were poor and did not vary with demographic factors, final diagnoses, presenting symptoms, or laboratory parameters. Prospective longitudinal studies comparing various imaging modalities (SBFT, magnetic resonance (MR) enterography, and capsule endoscopy) are required to determine which is the most effective tool for evaluating pediatric patients for TI inflammation.

Keywords

Radiology; pathology; histology; inflammation; small bowel

Introduction

The terminal ileum (TI) is the most commonly affected area in Crohn's disease^{1,2}. Intubation and biopsy of the terminal ileum during colonoscopy is considered the gold standard for diagnosing TI inflammation³⁻⁵. Less invasive imaging modalities, such as the small bowel follow-through (SBFT), are also utilized to evaluate for TI inflammation. However, the

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sensitivity of the SBFT for detecting inflammation of the TI in pediatric patients is not well established. We estimated the sensitivity and specificity of SBFT in diagnosing TI inflammation documented by histology of ileal biopsies in children and adolescents with no history of medical treatment for intestinal inflammation.

Materials and Methods

Patient Population

Patients less than age 21 years undergoing both initial SBFT and colonoscopy with intubation and biopsy of the TI between November, 1992 and January, 2008 at UCSF Children's Hospital at the University of California, San Francisco (UCSF) were retrospectively identified and included in the study. Patients were excluded if only one study was performed, if the SBFT and ileal biopsy were performed greater than 10 months apart, or if the patients had prior medical therapy for intestinal inflammation. Ninety three patients met study criteria. This study was approved by the UCSF Institutional Review Board.

Description of Variables

SBFT and histology of the TI biopsy reports were reviewed and dichotomized into normal (absence of inflammatory changes) or abnormal (presence of inflammatory changes). Abnormal SBFT findings included TI thickening, ulcerations, strictures, or fistulas. Abnormal histology included features of acute or chronic inflammatory infiltrates.

Laboratory parameters (obtained $\pm$ 14 days of the date of SBFT or ileal biopsy, whichever came first) included white blood cell count, hematocrit, albumin, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels. Serum albumin levels, hematocrit, ESR, and CRP were dichotomized into normal or abnormal. White blood cell (WBC) count was dichotomized into elevated or not elevated.

Documented patient- and/or parent-reported presenting symptoms of abdominal pain, perianal fissure, anorexia, bloody stool, constipation, diarrhea, fatigue, fever, joint pain, nausea, poor growth, tenesmus, vomiting, and weight loss were dichotomized into present or absent.

Final diagnoses are reported as inflammatory bowel disease (IBD), Crohn's disease (CD), ulcerative colitis (UC), IBD-unspecified (IBD-U), or non-IBD.

Statistical Analysis

Sensitivity and specificity of SBFT for diagnosing TI inflammation documented on ileal biopsies in pediatric patients were estimated, with exact 95% binomial confidence intervals, in the total population and by diagnoses, demographics, year of evaluation, presenting symptoms, and laboratory parameters. Fisher's exact test was used to compare sensitivity and specificity across complementary subgroups. We considered subgroups defined by final diagnosis (CD, UC, IBD-U, non-IBD), procedure date, patient age (<13 years vs ≥ 13 years), gender, race (white vs non-white), presence or absence of presenting symptoms (abdominal pain, diarrhea, bloody stool, weight loss, anorexia, vomiting, fatigue, nausea, fever, constipation, joint pain, tenesmus, poor growth, perianal fissure), and abnormal laboratory parameters (WBC, albumin, ESR, HCT, CRP).

Data were collected and stored in Microsoft Excel 2002 (Microsoft Corporation, Redmond, Washington). Statistical analysis was performed in STATA, Version 9 (STATA Corporation, College Station, TX).

Results

Demographic information is shown in Table 1. The mean age at the first study was 12.9 years [range: 1.1-20.9 years].

43 patients were diagnosed with IBD. 50 patients carried a non-IBD final diagnosis. The median days between procedures was 9 days (25th percentile= 2 days; 75 percentile = 37 days). The days between procedures did not vary by the order of procedures ($p=.09$). Seventeen patients (18.3%) had inflammation diagnosed by TI biopsies. Of the twenty-five patients (26.9%) with abnormal TI on SBFT, ten (40.0%) had inflammation on TI biopsies. Sensitivity of SBFT was 59% (10/17, 95% CI= 33%-85%), while specificity was 80% (61/76, 95% CI= 70%-89%). Sensitivity and specificity were generally similar across subgroups defined by final diagnoses (Table 2), procedure date, gender, age at first study, race/ethnicity, presenting symptoms, and laboratory parameters. We found weak evidence (Fisher's exact $p=.03$) that specificity was higher in biopsy-negative patients with constipation (15/15, 100%, 95% CI =78%-100%) compared with biopsy-negative patients without constipation (46/61, 75%, 95% CI =63%-86%).

SBFT was performed in 41 patients prior to TI biopsy and in 51 patients after TI biopsy. One patient had a TI biopsy and SBFT on the same day. Sensitivity of the SBFT was 50.0% when it was done prior to TI biopsy and 66.7% when it was done after TI biopsy ($p=.64$). Specificity of SBFT was 66.7% when it was done prior to TI biopsy and 90.5% when the SBFT followed TI biopsy ($p=.02$).

The results presented in Table 2 were similar when patients who underwent the studies greater than one month apart were excluded, decreasing the total number of patients from 93 to 65.

Discussion

Our study of 93 pediatric patients suggests that the sensitivity and specificity of SBFT for the detection of inflammation in the terminal ileum diagnosed by histology are poor in pediatric patients. Furthermore, sensitivity and specificity did not vary with gender, age at first study, race/ethnicity, final diagnoses, or laboratory parameters reflecting the presence of intestinal inflammation. Specificity may be somewhat higher in patients presenting with constipation, which may reflect that constipation is a less common presenting symptom of inflammatory bowel disease. Sensitivity or specificity did not vary with other presenting symptoms.

Sensitivity of SBFT for the detection of TI inflammation diagnosed by histology did not vary by order of procedures. Specificity improved when SBFT followed TI biopsy. This finding most likely represents a selection bias for proceeding with a TI biopsy when SBFT is done first. If the SBFT is positive, a clinician may be more inclined to proceed with TI biopsy; this would select for more patients with a positive SBFT to be included in this study. A patient with a negative SBFT would less likely be captured in this study if it was done prior to the TI biopsy because the clinician may be less likely to proceed with a TI biopsy if the SBFT is negative. This selection can potentially decrease specificity of the SBFT if it is done prior to TI biopsy.

Previous studies have shown widely varying results regarding the accuracy of barium radiography in detecting terminal ileal inflammation^{3, 5-15}. Byrne et al. retrospectively studied 46 patients (age 16-78 years) who underwent SBFT and ileocolonoscopy within two weeks of one another and found that SBFT failed to detect 41% of cases of TI inflammation diagnosed by ileoscopy with biopsy⁵. From a cohort of 121 adults with known Crohn's

disease, Halligan et al. retrospectively studied 23 patients who underwent both SBFT and ileoscopy and reported that SBFT had a 100% sensitivity and 90% specificity for TI disease diagnosed by ileoscopy¹⁵.

Lipson, et al. retrospectively studied 46 pediatric patients with suspected chronic IBD, in which patients underwent ileocolonoscopy and SBFT within a 14 day period³. There was agreement between SBFT and ileal histology in 80% of cases. Authors reported that the sensitivity and specificity of SBFT were 90% and 96%, respectively, for diagnosing Crohn's disease of the terminal ileum. In contrast, our study of pediatric patients demonstrates that the sensitivity and specificity of SBFT for the detection of inflammation diagnosed on TI histology in pediatric patients are poor. Furthermore, sensitivity and specificity did not vary with demographic factors, final diagnosis, or laboratory parameters reflecting the presence of intestinal inflammation. Although specificity improved in patients presenting with constipation, sensitivity and specificity did not change with other presenting symptoms. Furthermore, we examined sensitivity and specificity by combinations of symptoms (data not shown), e.g. abdominal pain, weight loss, and diarrhea, and did not identify any improvement in sensitivity or specificity.

SBFT is only one of a growing number of radiographic studies that are used to evaluate the TI. The capsule endoscopy has shown encouraging results in adults¹⁰⁻¹⁴, with studies suggesting higher sensitivity of capsule endoscopy compared with SBFT^{11,14}. One study reported a sensitivity of 89.6% and a specificity of 100% of capsule endoscopy for detecting small bowel inflammation suggestive of Crohn's disease¹⁰.

Studies conducted in pediatric patients also suggest that capsule endoscopy may be superior to SBFT in evaluating small bowel inflammation¹⁶⁻¹⁸. Furthermore, Cohen et al. reported capsule endoscopy may lead to reclassification of IBD from UC or indeterminate colitis to definitive Crohn's disease in a cohort of patients diagnosed with IBD between ages 2 and 18¹⁹. Considering the risks of early onset inflammatory bowel disease²⁰, using techniques involving less radiation (e.g., capsule endoscopy and MR enterography) is important to monitor evolution of disease type and activity in young children.

Although CT evaluation of the small bowel is being studied in adult patients^{12,21-24} the utility of CT enterography in pediatric patients is not well established. The amount of radiation exposure is not insignificant²⁵, which raises concern for using this imaging modality in the pediatric population. Magnetic resonance imaging is another imaging modality that may be used to evaluate small bowel disease^{24, 26-28}. Laghi et al. performed a prospective study of 75 pediatric patients (age 8-17 years) with known Crohn's disease, in which patients underwent contrast enhanced MRI of the bowels, and found that MRI had a sensitivity of 84% and specificity of 100% for detecting erosive ileitis, as documented by ileoscopy²⁷. This modality is appealing because of the avoidance of ionizing radiation.

The major limitation of our study is its retrospective study design. The timing and order of SBFT and ileal biopsy were not standardized, but obtained at the discretion of the pediatric gastroenterologist based on clinical indication. The result of one test would naturally influence the provider's decision to obtain the second test. Furthermore, the severity of a patient's symptoms or progression of symptoms may influence the timing and order of the tests. A further limitation of our study includes its relatively small size, which limits the precision of our sensitivity and specificity estimates, as well as power to detect subgroup effects²⁹.

Summary

Our retrospective study shows poor sensitivity and specificity of SBFT to detect inflammation of the terminal ileum in pediatric patients. Large prospective longitudinal studies comparing the utility of SBFT, MR enterography, and capsule endoscopy, with TI biopsy are required in the pediatric population to determine which of these modalities is the most effective tool for diagnosing TI inflammation in children and adolescents.

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References

1. Gollop JH, Phillips SF, Melton LJ III, Zinsmeister AR. Epidemiologic aspects of Crohn's disease: a population based study in Olmsted County, Minnesota, 1943–1982. *Gut* 1988 Jan;29(1):49–56. [PubMed: 3343012]
2. Puntis J, McNeish AS, Allan RN. Long term prognosis of Crohn's disease with onset in childhood and adolescence. *Gut* 1984 Apr;25(4):329–36. [PubMed: 6706211]
3. Lipson A, Bartram CI, Williams CB, Slavin G, Walker-Smith J. Barium studies and ileoscopy compared in children with suspected Crohn's disease. *Clin Radiol* 1990;41:5–8. [PubMed: 2297969]
4. Zwas FR, Bonheim NA, Berken CA, Gray S. Diagnostic yield of routine ileoscopy. *Am J Gastroenterol* 1995;90:1441–3. [PubMed: 7661166]
5. Byrne MF, Power DG, Keeling AN, Kay E, Murray FE, Patchett SE. Combined terminal ileoscopy and biopsy is superior to small bowel follow-through in detecting terminal ileal pathology. *Dig Liver Dis* 2004 Feb;36(2):147–52. [PubMed: 15002824]
6. Carlson HC. Perspective: the small bowel examination in the diagnosis of Crohn's disease. *AJR Am J Roentgenol* 1986 Jul;147(1):63–5. [PubMed: 3487232]
7. Tribl B, Turetschek K, Mostbeck G, Schneider B, Stain C, Pötzi R, Gangl A, Vogelsang H. Conflicting results of ileoscopy and small bowel double-contrast barium examination in patients with Crohn's disease. *Endoscopy* 1998 May;30(4):339–44. [PubMed: 9689505]
8. Marshall JK, Cawdron R, Zealley I, Riddell RH, Somers S, Irvine EJ. Prospective comparison of small bowel meal with pneumocolon versus ileo-colonoscopy for the diagnosis of ileal Crohn's disease. *Am J Gastroenterol* 2004 Jul;99(7):1321–9. [PubMed: 15233672]
9. Meyers SG, Ruble PE, Ashley LB. The clinical course of regional ileitis. *Am J Dig Dis* 1959;4:341–51. [PubMed: 13649641]
10. Dubcenco E, Jeejeebhoy KN, Petroniene R, Tang SJ, Zalev AH, Gardiner GW, Baker JP. Capsule endoscopy findings in patients with established and suspected small-bowel Crohn's disease: correlation with radiologic, endoscopic, and histologic findings. *Gastrointest Endosc* 2005 Oct; 62(4):538–44. [PubMed: 16185968]
11. Eliakim R, Suissa A, Yassin K, Katz D, Fischer D. Wireless capsule video endoscopy compared to barium follow-through and computerised tomography in patients with suspected Crohn's disease--final report. *Dig Liver Dis* 2004 Aug;36(8):519–22. [PubMed: 15334771]
12. Hara AK, Leighton JA, Heigh RI, Sharma VK, Silva AC, De Petris G, Hentz JG, Fleischer DE. Crohn disease of the small bowel: preliminary comparison among CT enterography, capsule endoscopy, small-bowel follow-through, and ileoscopy. *Radiology* 2006 Jan;238(1):128–34. [PubMed: 16373764]
13. Triester SL, Leighton JA, Leontiadis GI, Gurudu SR, Fleischer DE, Hara AK, Heigh RI, Shiff AD, Sharma VK. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. *Am J Gastroenterol* 2006 May;101(5):954–64. [PubMed: 16696781]
14. Costamagna G, Shah SK, Riccioni ME, Foschia F, Mutignani M, Perri V, Vecchioli A, Brizi MG, Piccicocchi A, Marano P. A prospective trial comparing small bowel radiographs and video capsule

endoscopy for suspected small bowel disease. *Gastroenterology* 2002;123:999–1005. [PubMed: 12360460]

15. Halligan S, Saunders B, Williams C, Bartram C. Adult Crohn disease: can ileoscopy replace small bowel radiology? *Abdom Imaging* 1998;23:117–21. [PubMed: 9516495]
16. Guilhon de Araujo Sant'Anna AM, Dubois J, Miron MC, Seidman EG. Wireless capsule endoscopy for obscure small-bowel disorders: final results of the first pediatric controlled trial. *Clin Gastroenterol Hepatol* 2005;3:264–270. [PubMed: 15765446]
17. Argüelles-Arias F, Caunedo A, Romero J, Sánchez A, Rodríguez-Téllez M, Pellicer FJ, Argüelles-Martín F, Herrerías JM. The value of capsule endoscopy in pediatric patients with a suspicion of Crohn's disease. *Endoscopy* 2004;36:869–873. [PubMed: 15452782]
18. Thomson M, Fritscher-Ravens A, Mylonaki M, Swain P, Eltumi M, Heuschkel R, Murch S, McAlindon M, Furman M. Wireless capsule endoscopy in children: a study to assess diagnostic yield in small bowel disease in paediatric patients. *J Pediatr Gastroenterol Nutr* 2007;44:192–197.
19. Cohen SA, Gralnek IM, Ephrath H, Sariipkin L, Meyers W, Sherrod O, Napier A, Gobin T. Capsule endoscopy may reclassify pediatric inflammatory bowel disease: a historical analysis. *J Pediatr Gastroenterol Nutr* 2008 Jul;47(1):31–6. [PubMed: 18607266]
20. Heyman MB, Kirschner BS, Gold BD, Ferry G, Baldassano R, Cohen SA, Winter HS, Fain P, King C, Smith T, El-Serag HB. Children with early-onset inflammatory bowel disease (IBD): analysis of a pediatric IBD consortium registry. *J Pediatr* 2005;146(1):35–40.
21. Bodily KD, Fletcher JG, Solem CA, Johnson CD, Fidler JL, Barlow JM, Bruesewitz MR, McCollough CH, Sandborn WJ, Loftus EV Jr, Harmsen WS, Crownhart BS. Crohn Disease: mural attenuation and thickness at contrast-enhanced CT Enterography--correlation with endoscopic and histologic findings of inflammation. *Radiology* 2006 Feb;238(2):505–16. [PubMed: 16436815]
22. Wold PB, Fletcher JG, Johnson CD, Sandborn WJ. Assessment of small bowel Crohn disease: noninvasive peroral CT enterography compared with other imaging methods and endoscopy—feasibility study. *Radiology* 2003;229:275–281. [PubMed: 12944602]
23. Mako EK, Mester AR, Tarjan A, Karlinger K, Toth G. Enteroclysis and spiral CT examination in diagnosis and evaluation of small bowel Crohn disease. *Eur J Radiol* 2000;35:168–175. [PubMed: 11000559]
24. Lee SS, Kim AY, Yang SK, Chung JW, Kim SY, Park SH, Ha HK. Crohn Disease of the Small Bowel: Comparison of CT Enterography, MR Enterography, and Small-Bowel Follow-Through as Diagnostic Techniques. *Radiology*. 2009;10.1148/radiol.2513081184
25. Jaffe TA, Gaca AM, Delaney S, Yoshizumi TT, Toncheva G, Nguyen G, Frush DP. Radiation doses from small-bowel follow-through and abdominopelvic MDCT in Crohn's disease. *AJR Am J Roentgenol* 2007 Nov;189(5):1015–22. [PubMed: 17954634]
26. Durno CA, Sherman P, Williams T, Shuckett B, Dupuis A, Griffiths AM. Magnetic resonance imaging to distinguish the type and severity of pediatric inflammatory bowel diseases. *J Pediatr Gastroenterol Nutr* 2000;30:170–4. [PubMed: 10697136]
27. Laghi A, Borrelli O, Paolantonio P, Dito L, Buena de Mesquita M, Falconieri P, Passariello R, Cucchiara S. Contrast enhanced magnetic resonance imaging of the terminal ileum in children with Crohn's disease. *Gut* 2003;52(3):393–7. [PubMed: 12584222]
28. Darbari A, Sena L, Argani P, Oliva-Hemker JM, Thompson R, Cuffari C. Gadolinium-enhanced magnetic resonance imaging: a useful radiological tool in diagnosing pediatric IBD. *Inflamm Bowel Dis* 2004;10(2):67–72. [PubMed: 15168803]
29. Leeflang MM, Deeks JJ, Gatsonis C, Bossuyt PM, Cochrane Diagnostic Test Accuracy Working Group. Systematic reviews of diagnostic test accuracy. *Ann Intern Med* 2008 Dec 16;149(12):889–97. [PubMed: 19075208]

Abbreviations used in this paper

SBFT	Small Bowel Follow Through
TI	terminal ileum

MR	magnetic resonance
UCSF	University of California San Francisco
ESR	erythrocyte sedimentation rate
CRP	c- reactive protein
WBC	white blood cell
IBD	inflammatory bowel disease
CD	Crohn's disease
UC	ulcerative colitis
IBD-U	inflammatory bowel disease unspecified

Table 1

Demographics

	N	%
Male	51	55%
Female	42	45%
Age 0-12	47	51%
Age 13-20	46	49%
Caucasian	59	63%
Asian/Pacific Islander	11	12%
African American	5	5%
Other	17	18%
Unknown	1	1%

Table 2
Sensitivity and Specificity of SBFT for Detection of TI Inflammation by Final Diagnoses

	N	N biopsy positive	Sensitivity	Confidence Interval	p-value	N biopsy negative	Specificity	Confidence Interval	p-value
ALL	93	17	0.59	(0.33, 0.85)		76	0.80	(0.70, 0.89)	
FINAL DIAGNOSIS									
IBD	43	17	0.59	(0.33, 0.82)	-	26	0.77	(0.56, 0.91)	.76
Non-IBD	50	0	-	-	-	50	0.82	(0.69, 0.91)	
Crohn's disease	23	17	0.59	(0.33, 0.82)		6	0.50	(0.12, 0.88)	
Ulcerative colitis	19	0	-	-	-	19	0.84	(0.60, 0.97)	.23
IBD-U	1	0	-	-	-	1	1.00	(0.03, 1.00)	