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Use of Advanced Modalities Does Not Guarantee Early Detection of Small-Bowel Crohn's Disease in the Absence of Complications

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Background: This study investigated the approach for detection of small-bowel (SB) Crohn's disease (CD) in the absence of complications at diagnosis using advanced modalities.

Material/Methods: Patients diagnosed with CD in Renji Hospital from 2005 to 2014 were divided into 2 groups by year of diagnosis: 2005 to 2009 and 2010 to 2014. The modalities used and the clinical characteristics of patients were retrospectively examined.

Results: Advanced modalities did not detect higher rate of non-stricturing/non-penetrating disease in 2010 to 2014 than older modalities in 2005 to 2009. Further analysis showed that a stricturing complication was significantly more common in patients with SB CD than in those who had CD with SB and colonic involvement, and the duration from symptom onset to lesion detection was significantly longer in patients with SB CD than in those who had CD with SB and colonic involvement. Fewer patients with SB CD underwent SB capsule endoscopy compared to the other advanced modalities. Abdominal pain (74.4%) was the most common presentation, and 94.0% patients with SB CD presented gastrointestinal bleeding and anemia.

Conclusions: Early detection of SB CD without complications remains difficult even if advanced modalities are introduced. Our hypothesis is that the fecal occult blood test and routine blood test should be administered to patients with abdominal pain or gastrointestinal manifestations. Once the patients are found to have GI bleeding or anemia, they would be further examined according to the guideline and SBCE would be used in the early stage of SB CD.

MeSH Keywords: **Anemia • Capsule Endoscopes • Crohn Disease • Gastrointestinal Diseases**

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Background

Crohn's disease (CD) is a chronic inflammatory disease of unknown etiology. It is characterized by transmural inflammation of the bowel and may involve any section of the gastrointestinal (GI) tract. Stricturing and penetration are the 2 main complications, which markedly affect the patient's quality of life and increase the rate of surgery [1]. Previous studies have shown that the occurrence of complications increases with time, and earlier use of thiopurines and anti-tumor necrosis factor- α monoclonal antibody reduces the need for surgery [1,2]. The current aim of treatment is to minimize complications and reduce the need for surgery. However, diagnosing CD is difficult because there are no specific symptoms or criteria, and much depends on the experience of the gastroenterologist in differentiating CD from other conditions, such as autoimmune disorders, infections, carcinomas, and drug use. Moreover, diagnosis is more difficult in the early stage of disease without complications (e.g., non-stricturing, non-penetrating behavior, B1), especially when only the small bowel (SB) is involved. This is because for many years the part of the SB beyond the duodenum and proximal to the terminal ileum could not be viewed endoscopically and the sensitivity of SB radiography (SBR) is low [3]. In recent years, advanced modalities for investigation of SB disease have become available. At our medical center, SB capsule endoscopy (SBCE) (since 2003), balloon-assisted enteroscopy (BAE) (including single-balloon enteroscopy and double-balloon enteroscopy) (since 2006), computed tomography enterography (CTE) (since 2006), and magnetic resonance imaging enterography (MRE) (since 2010) are now routinely used for detection of SB disease. Carbon dioxide insufflation was introduced in 2011, which improved both the intubation depth and total single-balloon enteroscopy rate [4], and possibly allowed visualization of more SB lesions. Theoretically, these modalities should be helpful in the early detection of SB disease without complications because they are highly sensitive [3,5]. To confirm this hypothesis, we retrospectively analyzed patients with newly diagnosed CD at our medical center between 2005 and 2014, focusing on detection and diagnosis of SB CD.

Material and Methods

Patients

The Research Ethics Committee of Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University approved this study.

Patients diagnosed with CD and whose complete medical data were available were included and classified according to the Montreal system [6]. Diagnosis of CD was based on clinical, endoscopic, histopathological, and radiological findings [7].

Disease location was defined by the maximal extent, including the segmental intestine previously removed surgically. Stricturing (B2) and penetrating (B3) complications had been detected by radiology, endoscopy, or surgery, according to the medical records. If both stricturing and penetrating complications were detected at the time of diagnosis, the complications were classified as penetrating. Patients were excluded if: (1) they could not be classified according to the Montreal system based on their medical data, or (2) they were diagnosed with CD after CD was suspected for 5 years or more. Demographic characteristics, clinical presentations, and modalities used to detect SB CD were analyzed.

Patients were divided into two 5-year periods – 2005–2009 and 2010–2014 – based on the year of diagnosis.

Statistical analysis

Variables are presented as numbers and percentages. The chi-square test or Fisher's exact test was used to compare categorical variables between groups. The Mann-Whitney *U* test was used to analyze the duration from symptom onset to lesion detection. A two-sided *P* value of ≤ 0.05 indicated statistical significance.

Results

Complications were not reduced by use of advanced modalities

Between January 2005 and December 2014, 511 patients were admitted and newly diagnosed with CD at our medical center; of these, 40 (7.8%) were excluded because they could not be classified according to the Montreal system. Thus, a total of 471 patients with a male-to-female ratio of 1.71: 1 were included. The median age at diagnosis was 30 years (IQR [interquartile range], 23–40 years). No significant differences were found in the rates of stricturing and penetrating complications between the periods of 2005–2009 and 2010–2014 (Table 1). Analysis of the modalities used to investigate the GI tract showed the following results: significantly fewer patients were diagnosed by surgery, and significantly more patients underwent CT, CTE, MRE, and BAE instead of SBR in 2010–2014 (Table 2). The rate at which B1 disease was detected was not higher with the use of these advanced modalities in 2010–2014 ($P=0.269$) (46.2%) than that in 2005–2009 (51.6%). However, significantly more patients had perianal disease in 2010–2014 than in 2005–2009, and the occurrence of stricturing and penetrating complications was significantly lower in the patients with perianal disease than in those without perianal disease (Table 3).

Table 1. Clinical characteristics of newly diagnosed patients: number (percentage).

	Total (n=471)	2005–2009 (n=155)	2010–2014 (n=316)	P value
Age (years) at diagnosis				
A1 (≤16)	25 (5.3%)	9 (5.8%)	16 (5.1%)	0.375
A2 (17–40)	336 (71.3%)	102 (65.8%)	234 (74.1%)	0.063
A3 (>40)	110 (23.4%)	44 (28.4%)	66 (20.9%)	0.071
Location				
L1 (Terminal ileum)	60 (12.7%)	20 (12.9%)	41 (13.0%)	0.983
L2 (Colon)	54 (11.5%)	17 (11.0%)	37 (11.7%)	0.812
L3 (Ileocolon)	204 (43.3%)	71 (45.8%)	133 (42.1%)	0.444
L4 (Upper GI)	9 (1.9%)	3 (1.9%)	6 (1.9%)	1.000
L1+L4	47 (10.0%)	14 (9.0%)	33 (10.4%)	0.631
L2+L4	6 (1.3%)	3 (1.9%)	3 (0.9%)	0.400
L3+L4	90 (19.1%)	27 (17.4%)	63 (19.9%)	0.514
Behavior				
B1 (Non-str/non-pen)	226 (48.0%)	80 (51.6%)	146 (46.2%)	0.269
B2 (Stricturing)	181 (38.4%)	54 (34.8%)	127 (40.2%)	0.262
B3 (Penetrating)	64 (13.6%)	21 (13.5%)	43 (13.6%)	0.986
Perianal disease	102 (21.7%)	23 (14.8%)	79 (25.0%)	0.012

GI – gastrointestinal; non-str – non-stricturing; non-pen – non-penetrating.

Table 2. Modalities used to investigate the gastrointestinal tract: number (percentage).

	Total (n=471)	2005–2009 (n=155)	2010–2014 (n=316)	P value
Gastroscopy	167 (35.5%)	53 (34.2%)	114 (36.1%)	0.688
Colonoscopy	456 (96.8%)	152 (98.1%)	304 (96.2%)	0.280
SBR	97 (20.6%)	68 (43.9%)	29 (9.2%)	0.000
CT	124 (26.3%)	26 (16.8%)	98 (31.0%)	0.001
CTE	280 (59.4%)	60 (38.7%)	220 (69.6%)	0.000
MRI	74 (15.7%)	22 (14.2%)	52 (16.5%)	0.526
MRE	41 (8.7%)	1 (0.6%)	40 (12.7%)	0.000
SBCE	43 (9.1%)	17 (11.0%)	26 (8.2%)	0.332
BAE	196 (41.6%)	53 (34.2%)	143 (45.3%)	0.022
Surgery	38 (8.1%)	26 (16.8%)	12 (3.8%)	0.000
PET	13 (2.8%)	1 (0.6%)	12 (3.8%)	0.063

SBR – small-bowel radiography, including small-bowel follow-through and enteroclysis; CT – computed tomography; CTE – computed tomography enterography; MRI – magnetic resonance imaging; MRE – magnetic resonance imaging enterography; SBCE – small-bowel capsule endoscopy; BAE – balloon-assisted enteroscopy; PET – positron emission tomography.

Table 3. Behavior of CD in patients with or without perianal disease: number (percentage).

	Patients with perianal disease (n=102)	Patients without perianal disease (n=369)	P value
Behavior			0.000
B1 (n=226)	75 (33.2%)	151 (66.8%)	
B2 (n=181)	21 (11.6%)	160 (88.4%)	
B3 (n=64)	6 (9.4%)	58 (90.6%)	

Table 4. Clinical characteristics of groups A and B: number (percentage).

	SB only group (n = 117)				SB+colon group (n = 300)				P value
	Total	L1	L1+L4	L4	Total	L2+L4	L3	L3+L4	
B1	43 (36.8%)	22 (18.8%)	16 (13.7%)	5 (4.3%)	152(50.7%)	4 (1.3%)	104(34.7%)	44 (14.7%)	0.011
B2	61 (52.1%)	29 (24.8%)	29 (24.8%)	3 (2.6%)	101(33.7%)	2 (0.7%)	69 (23.0%)	30 (10.0%)	0.001
B3	13 (11.1%)	9 (7.7%)	3 (2.6%)	1 (0.9%)	47 (15.7%)	0 (0.0%)	30 (10.0%)	17 (5.7%)	0.234
Total		60 (51.3%)	48 (41.0%)	9 (7.7%)		6 (2.0%)	203(67.7%)	91 (30.0%)	

GI – gastrointestinal; B1 – non-stricturing/non-penetrating; B2 – stricturing; B3 – penetrating.

Table 5. Demographic characteristics and clinical presentations.

	SB only group (n=117)	SB+colon group (n=300)	P value
Sex			0.440
Male	42 (35.9%)	120 (40.0%)	
Female	75 (64.1%)	180 (60.0%)	
Smoking history			0.271
Non-smoker	109 (93.2%)	269 (89.7%)	
Ever smoker	8 (6.8%)	31 (10.3%)	
Gastrointestinal symptoms			
Abdominal pain	87 (74.4%)	219 (73.0%)	0.778
Diarrhea	37 (31.6%)	169 (56.3%)	0.000
Abdominal mass	5 (4.3%)	16 (5.3%)	0.657
GI bleeding	74 (63.2%)	217 (72.3%)	0.924
Overt bleeding	25 (21.4%)	72 (24.0%)	0.568
Occult bleeding	49 (41.9%)	145 (48.3%)	0.235
Nausea and vomiting	29 (24.8%)	41 (13.7%)	0.006
Perianal disease	12 (10.3%)	76 (25.3%)	0.001
Systemic presentation			
Fever (>37.8°C)	59 (50.4%)	100 (33.3%)	0.177
Weight loss	62 (53.3%)	133 (44.3%)	0.000
Anorexia	9 (7.7%)	13 (4.3%)	0.168
Anemia	52 (44.4%)	88 (29.3%)	0.003
Extraintestinal symptoms	3 (2.6%)	32 (10.7%)	0.007

GI – gastrointestinal. Occult bleeding, only fecal occult blood test was positive.

Table 6. Modalities used for SB investigation: number (percentage).

	Total (n=471)	SB only group (n=117)	SB+colon group (n=300)	P value
Gastroscopy	157 (37.6%)	69 (59.0%)	88 (29.3%)	0.000
Colonoscopy	396 (95.0%)	101 (86.3%)	295 (98.3%)	0.000
SBR	93 (22.3%)	30 (25.6%)	63 (21.0%)	0.306
CT	113 (27.1%)	45 (38.5%)	68 (22.7%)	0.001
CTE	241 (57.8%)	54 (46.2%)	187 (62.3%)	0.003
MRE	39 (9.4%)	10 (8.6%)	29 (9.7%)	0.724
SBCE	43 (10.3%)	26 (22.2%)	17 (5.7%)	0.000
BAE	192 (46.0%)	94 (80.3%)	98 (32.7%)	0.000
Surgery	38 (9.1%)	13 (11.1%)	31 (10.3%)	0.376
PET	12 (2.9%)	5 (4.3%)	7 (2.3%)	0.287

SBR – small-bowel radiography, including small-bowel follow-through and enteroclysis; CT – computed tomography; CTE – computed tomography enterography; MRE – magnetic resonance imaging enterography; SBCE – small-bowel capsule endoscopy; BAE – balloon-assisted enteroscopy; PET – positron emission tomography.

Table 7. Modalities that detected ileal lesions first: number (percentage).

	Total (n=108)	L1 (n=61)	L1+L4 (n=47)	Total (n=293)	L3 (n=203)	L3+L4 (n=90)	P value
Colonoscopy	22 (20.4%) ^a	12 (19.7%)	10 (21.3%)	116 (39.6%) ^a	81 (40.0%)	35 (38.9%)	0.000 ^a
SBR	7 (6.5%)	5 (8.2%)	2 (4.3%)	32 (10.9%)	22 (10.8%)	10 (11.1%)	
CT	23 (21.3%) ^b	16 (26.2%)	7 (14.9%)	16 (5.5%) ^b	13 (6.4%)	3 (3.3%)	0.017 ^b
CTE	14 (13.0%) ^c	7 (11.5%)	7 (14.9%)	70 (23.9%) ^c	51 (25.1%)	19 (21.1%)	0.000 ^c
MRI	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.7%)	1 (0.5%)	1 (1.1%)	
MRE	0 (0.0%)	0 (0.0%)	0 (0.0%)	13 (4.4%)	9 (4.4%)	4 (4.4%)	
SBCE	23 (21.3%) ^d	9 (14.8%)	14 (29.8%)	5 (1.7%) ^d	1 (0.5%)	4 (4.4%)	0.000 ^d
BAE	11 (10.2%)	7 (11.5%)	4 (8.5%)	23 (7.9%)	14 (6.9%)	9 (10.0%)	
Surgery	7 (6.5%)	5 (8.2%)	2 (4.3%)	15 (5.1%)	11 (5.4%)	4 (4.4%)	
PET	1 (0.9%)	0 (0.0%)	1 (2.1%)	1 (0.3%)	0 (0.0%)	1 (1.1%)	

SBR – small-bowel radiography, including small-bowel follow-through and enteroclysis; CT – computed tomography; CTE – computed tomography enterography; MRI – magnetic resonance imaging; MRE – magnetic resonance imaging enterography; SBCE – small-bowel capsule endoscopy; BAE – balloon-assisted enteroscopy; PET – positron emission tomography.

Clinical characteristics of SB CD

Stricture disease has been reported as a complication of small intestinal disease [8]. Patients with SB involvement were divided into 2 groups: the SB only group and the SB+colon group (Table 4). Obstruction occurred in 24 (20.5%) patients in the SB only group, a rate that was significantly higher than

that in the SB+colon group (28 [9.4%]; $P=0.002$). The duration from symptom onset to lesion detection was significantly longer in the SB only group (median, 12 months; IQR, 3–48 months) than that in the SB+colon group (median, 5 months; IQR, 0–24 months) ($P<0.001$).

Figure 1. Modalities used for diagnosis of small-bowel Crohn's disease. SBCE – small-bowel capsule endoscopy; BAE, balloon-assisted enteroscopy.

Table 8. Modalities that were the first to detect upper gastrointestinal disease: number (percentage).

	Total (n=56)	L4 (n=9)	L1+L4 (n=47)	Total (n=96)	L3+L4 (n=90)	L2+L4 (n=6)	P value
Gastroscopy	9 (16.1%)	1 (11.1%)	8 (17.0%)	60(0.0%)	0 (0.0%)	0 (0.0%)	
Colonoscopy	0 (0.0%)	0 (0.0%)	0 (0.0%)	18 (18.8%)	17 (18.9%)	1 (16.7%)	
SBR	6 (10.7%)	2 (22.2%)	4 (8.5%)	19 (19.8%)	16 (17.8%)	3 (50.0%)	
CT	5 (9.0%)	3 (33.3%)	2 (4.3%)	6 (6.3%)	5 (5.6%)	1 (16.7%)	
MRI	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.1%)	0 (0.0%)	
CTE	15 (26.8%)	1 (11.1%)	14 (29.8%)	27 (28.1%)	27 (30.0%)	0 (0.0%)	
MRE	1 (1.8%)	0 (0.0%)	1 (2.1%)	6 (6.3%)	5 (5.6%)	1 (16.7%)	
SBCE	15 (26.8%)e	1 (11.1%)	14 (29.8%)	7 (7.3%)e	7 (7.8%)	0 (0.0%)	0.001 ^e
BAE	3 (5.4%)	1 (11.1%)	2 (4.3%)	5 (5.2%)	5 (5.6%)	0 (0.0%)	
Surgery	1 (1.8%)	0 (0.0%)	1 (2.1%)	6 (6.3%)	6 (6.7%)	0 (0.0%)	
PET	1 (1.8%)	0 (0.0%)	1 (2.1%)	1 (1.0%)	1 (1.1%)	0 (0.0%)	

SBR – small-bowel radiography, including small-bowel follow-through and enteroclysis; CT – computed tomography; CTE – computed tomography enterography; MRE – magnetic resonance imaging enterography; SBCE – small-bowel capsule endoscopy; BAE – balloon-assisted enteroscopy; PET – positron emission tomography.

Demographic characteristics and clinical presentations were compared (Table 5). Significantly more patients in the SB only group had anemia (44.4%) and nausea/vomiting (24.8%). Obstruction was significantly more common in patients with nausea/vomiting (69.0%) than in those without these symptoms (45.5%) ($P=0.028$). Abdominal pain was the most common symptom in both groups, followed by GI bleeding; in fact, occult bleeding, which was only positively detected using a fecal occult blood test without visible blood loss, was considerably

more common than overt bleeding. In the SB only group, 16 (30.8%) patients with anemia had positive results in the fecal occult blood test. A total of 110 (94.0%) patients had GI bleeding and anemia.

Modalities for investigation of SB involvement

The modalities used to investigate SB involvement were compared, showing that significantly more patients in the SB only

group underwent gastroscopy, CT, SBCE, and BAE, while significantly more patients in the SB+colon group underwent colonoscopy and CTE (Table 6). In the SB only group, lesions were first detected by colonoscopy in 20.4% patients, by CT in 21.3% patients, and by SBCE in 21.3% patients. In the SB+colon group, lesions were first detected by colonoscopy in 39.6% of patients. GI lesions were detected using other modalities in no more than 10% of patients in both groups.

In a subsequent analysis, we examined the use of different modalities for initial detection and diagnosis of SB CD. Ileal involvement was first detected by colonoscopy and CTE in significantly more patients with L3 and L3+L4 involvement than in those with L1 and L1+L4 involvement. In contrast, it was detected by CT and SBCE in significantly more patients with L1 and L1+L4 involvement than in those with L3 and L3+L4 involvement (Table 7). The diagnosis of L1 and L1+L4 involvement was made from BAE, colonoscopy, and SBCE findings; in particular, BAE diagnosed more patients than the other modalities did (Figure 1).

Upper GI CD was detected using different modalities, and no particular modality was best for this purpose (Table 8), even though SBCE revealed L4 and L1+L4 involvement (26.8%) in significantly more patients than the number in which it revealed L2+L4 and L3+L4 involvement (7.3%) ($P=0.001$). Only 9 patients were diagnosed with L4 involvement.

Discussion

Prospective studies have shown that advanced modalities have better sensitivity than conventional SBR for detection of SB involvement in CD [9–11]. Therefore, it is to be expected that the rates at which ileal CD and upper GI disease are detected in the early stage will be higher with the use of these modalities. Our findings revealed that these advanced modalities did not detect higher rates of B1 disease (Table 4), and the rate at which stricture was detected at diagnosis was not lower than that with the older modalities. Since the probability of a stricturing complication increases with disease duration and occurrence of a stricturing complication is associated with SB involvement and the absence of colonic involvement [12], we detected the duration from symptom onset to lesion detection and showed significantly longer duration in the SB only group than in the SB+colon group, which suggested that shorter the duration would decrease the rate of stricturing complication.

In the SB+colon group, colonoscopy first detected colonic lesions in 82.7% of patients; in the SB only group, no one modality was best, although colonoscopy is recommended as the best modality to detect ileal-involved diseases [13]. Colonoscopy first detected significantly more ileal lesions of L3 and L3+L4 than

that of L1 and L1+L4 (39.6% vs. 20.4%) (Table 7), which was much lower than shown in a prospective study (80.0%) [14]. We think the difference arose from the fact that the previous studies did not separate L3 from L1 disease. Although BAE is not recommended as the first-line procedure for SB CD evaluation [13], since the procedure is complex and has a low rate of completion, which limits its widespread use, the percentage of patients who underwent BAE (80.3%) was similar to that of colonoscopy (86.3%). Frequent use of BAE also suggested the limited role of colonoscopy.

SBCE is recommended as the initial modality for investigating SB in the absence of obstructive symptoms or stenosis when gastroscopy and colonoscopy are inconclusive [14]. It is reported SBCE is more sensitive than radiologic imaging (CTE or MRE) for the detection of proximal SB disease, and it detected significantly more cases of isolated upper GI disease in white patients [15–18]. In our study, it was the only modality that was best for detecting both L1 (Table 7) and L4 (Table 8) disease. In the SB only group, significantly more patients underwent SBCE than in the SB+colon group, even though significantly more patients had obstructions. However, SBCE first detected SB lesions in 21.3% of patients, a rate similar to that of colonoscopy (20.4%) and CT (21.3%), while fewer patients underwent SBCE (28.2%) compared to colonoscopy (86.3%) or CT (38.5%), which may be partly explained by the high prevalence of the stricturing complication. Another possible reason was that the examination of SBCE was vastly more expensive than colonoscopy and CT. We believe that in the future, an increasing number of patients will accept SBCE because health insurance covers the examination in China. CTE or MRE, as a noninvasive and less sensitive examinations, can be used to evaluate intestinal penetration/obstruction before SBCE [19].

In investigating SB using SBCE before the occurrence of stricture, we tried to find the alarming clinical manifestation of SB CD. Abdominal pain was the most common presentation, and use further examinations could not be decided on from subjective symptoms. In the SB only group, significantly more patients presented with nausea and vomiting, which were associated with obstruction complication. Further, significantly more patients were found to have anemia, and GI bleeding (30.8%) was a common cause. A total of 63.2% of patients had GI bleeding, including 21.4% patients with overt GI bleeding, and they probably did not know how long they had chronic occult bleeding before developing overt bleeding. In our study, 94.0% of patients with SB CD had GI bleeding and anemia, which were indications for further GI examinations. Our hypothesis is that if the fecal occult blood test and routine blood test, which are the 2 cheapest and simplest examinations available in every hospital, had been performed in patients who experienced abdominal pain and other GI manifestations, GI bleeding or anemia would have been discovered,

and, according to the guideline, SB lesions could have been detected at the early stage of CD. In recent years, fecal calprotectin and lactoferrin were increasingly being used as markers of active GI inflammation, but they are not correlated with ileal disease [20]. In Kelvin's population-based study [12], B1 disease was detected in 81.4% of patients and L1 disease was detected in 42.5% of patients. The lower rate of complications in this previous study could be explained by earlier disease presentation, better awareness, and better access to health-care services. We hope our findings will improve the awareness of clinicians at a time in which the incidence and prevalence of CD are increasing in China.

This study has certain limitations. First, it was a retrospective study and some factors associated with CD status were not evaluated. Because only inpatients were enrolled, selection bias could not be ruled out; these patients were likely to have higher rates of complications and more aggressive clinical courses than outpatients (since patients with probable CD needed hospitalization during the 5-year follow-up). Second, the SB only group sample size was small, and all patients

were from a single institution (diagnostic modalities at other medical centers may be different). Third, the study spanned a 10-year period, over which different doctors were involved in diagnosis and treatment.

Conclusions

Our results revealed that advanced modalities did not detect a higher rate of B1 disease than older modalities, possibly because the duration from symptom onset to lesion detection was significantly longer in patients with SB CD. Our results also revealed that 94.0% of patients with SB CD had GI bleeding and anemia. Our hypothesis is that the fecal occult blood test and routine blood test should be administered to patients with abdominal pain and other GI manifestations. Once the patients were found to have GI bleeding or anemia, they would be further examined according to the guideline and SBCE would be used in the early stage of SB CD. Our hypothesis needs to be confirmed a large prospective clinical trial.

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