

Organic colonic lesions in 3,332 patients with suspected irritable bowel syndrome and lacking warning signs, a retrospective case–control study

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Abstract

Purpose The diagnosis of irritable bowel syndrome is symptom based, and colonoscopy is the most direct way to rule out organic colonic diseases. It is controversial on the necessity of colonoscopy for patients with suspected irritable bowel syndrome and lacking alarm features. This study was designed to verify the organic lesions and discuss the value of colonoscopy in this type of patients.

Methods Colonoscopy of 3,332 patients with suspected irritable bowel syndrome and lacking warning signs from 2000 to 2009 were reviewed. One thousand five hundred eighty-eight patients under 50 years of age who underwent colonoscopy screening for health care in the same period were used as controls. The prevalence of different colonic organic lesions was compared between two groups.

Results Organic colonic lesions were found in 30.3% of the patients with suspected irritable bowel syndrome (1,010/3,332) and 39.0% of the controls (619/1,588). Compared with controls, patients with suspected irritable bowel syndrome had higher prevalence of noninflammatory bowel disease and noninfectious colitis and terminal ileitis, however, had lower prevalence of diverticular disease, adenomatous polyps, and non-adenomatous polyps (all $P < 0.001$).

Conclusions The diagnostic sensitivity of symptom criteria on irritable bowel syndrome without colonoscopy is not more than 69.7% in patients with suspected irritable bowel syndrome lacking warning signs. Though the method of colonoscopy is hard to screen tumor in this type of patients, it is beneficial to uncover some other relevant organic lesions such as terminal ileitis. Colonoscopy should not be refused to suspected irritable bowel syndrome patients without warning signs.

Keywords Irritable bowel syndrome · Rome criteria · Organic lesions · Warning signs · Colonoscopy

Introduction

Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders (FGID) [1, 2]. The prevalence of IBS in the general population is between 5% and 10% in Asia [3], and the adjusted prevalence of IBS is 5.67–11.50% in China [4]. According to Rome III criteria for FGID, IBS has been categorized into three subgroups as IBS with diarrhea, IBS with constipation, and IBS with mixed bowel habits [5]. The clinical characteristics of IBS are recurrent abdominal pain or discomfort associated with improvement after defecation, change in frequency of stool, or change in appearance of stool. Because there are no reliable biological markers associated with IBS, the diagnosis of IBS is empirical and based on IBS-like symptoms. Exclusion of organic disorders is an important practice for the diagnosis of IBS and colonoscopy is usually the most direct way to rule out organic lesions of the lower gastrointestinal tract. Rectal bleeding, anemia, weight loss,

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fever, family history of colon cancer, and age above 50 years are considered the warning signs of severe gastrointestinal disease [5–7]. It is an agreement that patients who meet Rome criteria on IBS with warning signs are strongly advised to perform colonoscopy to rule out severe colonic diseases such as inflammatory bowel disease (IBD) and colorectal cancer [8, 9]. Several studies propose that no further investigations including colonoscopy are needed for individuals aged below 50 years who fulfill Rome criteria on IBS and have no alarm symptoms [10, 11]. A systematic review showed that the pretest probability of inflammatory bowel disease, colorectal cancer, or infectious diarrhea is less than 1% among patients meeting symptom-based criteria for IBS [12]. Negative colonoscopy was not associated with increased reassurance or improved health-related quality of life in IBS patients with IBS <50 years of age [13]. Another study showed that flexible sigmoidoscopy or colonoscopy had high incremental cost-effectiveness ratio on diagnosis of IBS, which constituted the most costly portion (50–75%) of any workup for IBS [8]. So, endoscopy should not be used first to rule out organic disease in the diagnosis of IBS. However, a retrospective analysis showed that colonoscopy findings were abnormal in 51.6% of 622 patients (ages 19–91 years) diagnosed with IBS and if indicated, colonoscopy should not be delayed [14]. There is no consensus so far on whether patients with suspected IBS lacking warning signs need colonoscopy or not. To investigate this into detail, we made a retrospective case–control study on colonoscopy of 3,332 patients with suspected IBS lacking warning signs. We try to answer the questions as below: How many IBS patients are there in the suspected IBS patients lacking warning signs? How many kinds of organic lesions are there in this type of patient? Is it worth to take a colonoscopy for this type of patient?

Materials and methods

Patients and controls selection

The population under investigation was constituted by suspected IBS group and control group. From 2000 to 2009, 40,778 patients performed colonoscopies in a gastroenterology center in China (Nanfang Hospital, Southern Medical University) and 4,050 patients were consulted for clinical irritable bowel syndrome before colonoscopy. Among these 4,050 patients, 3,332 patients who fulfilled Rome III criteria and lacked warning signs were enrolled in our study and classified as suspected IBS group. Warning signs include rectal bleeding, anemia, weight loss, fever, family history of colon cancer, and onset of the first symptom after 50 years of age [5]. Patients

with any warning signs above were excluded from the research. Among 2,661 patients who underwent colonoscopy for health care, 1,588 patients under 50 years of age who had no major abdominal complaint, such as abdominal pains, diarrhea, or blood in the stool were enrolled as controls. Since age above 50 years and family history of colorectal cancer are two of the warning signs, we exclude the patients with these two clinical features from the control group. Patients who had history of colorectal polyps or had received polyp resection were also excluded from the control group. The demographic feature of the population enrolled and subgroup of suspected IBS patients was recorded.

Colonoscopy diagnosis and classification

The colonoscopy diagnosis was recorded according to the endoscopic descriptions or histological report. Normal colonoscopy finding was defined when total colon was checked and no lesion was found. For easy analysis, the organic colorectal lesions were classified as 13 kinds of diseases according to inflammatory disease, neoplastic lesions (including tumor and polyp), and others. Because terminal ileum always indicates the end region of a colonoscopy and always needs to be observed, terminal ileum disease was classified as a kind of organic disease in this study. The 13 kinds of organic colonic lesions were item by item classified as below: IBD (including ulcer colitis, Crohn's disease, and IBD unclassified [15]), infectious colitis, non-IBD and noninfectious colitis (a variety of inflammatory diseases of the colon, differentiated from IBD and infectious colitis), parasitic infection (including trichuriasis and ascariasis), intestinal tuberculosis, adenomatous polyps, non-adenomatous polyps (including metaplasia polyps, inflammatory polyps, juvenile polyps, and Peutz–Jeghers polyps), malignant tumor (including colorectal cancer, carcinoid, and lymphoma), benign tumor, melanosis coli, diverticular disease, angiodysplasia (including rectal varices, telangiectasia, hemorrhoids, ischemic enteritis, and Behcet's disease), and terminal ileitis (mucous hyperemia, slight ulcer in colonoscopy; histology showing lymphocytes infiltrate in the lamina propria or lymph follicle hyperplasia and excluding Crohn's disease and intestinal tuberculosis).

Statistical analysis

Frequencies and rates of colonoscopy diagnosis in IBS group and control group were accounted and compared by using Pearson chi-square test with continuity correction when appropriate. $P < 0.05$ was considered as statistical significant.

Results

Patients and controls characteristics

During the mentioned period, a total of 4,050 patients performed colonoscopy due to suspected IBS and 3,332 patients without warning signs were enrolled in this study. The demographic and clinical features of suspected IBS group and control group were listed in Table 1. The suspected IBS group was younger and had lower male patients than controls (mean age 34.1 ± 7.8 vs. 38.4 ± 7.3 , $P < 0.001$, 53.7% vs. 67.0% male, $P < 0.001$, respectively). IBS with diarrhea was the prominent subgroup in the suspected IBS group and accounted for 72.5%.

Colonoscopy finding

The colonoscopy finding of patients with suspected IBS and controls were listed in Table 2. Organic colonic lesions were found in 30.3% of suspected IBS patients (1,010/3,332). The five most common organic diseases were IBD (6.9%), non-adenomatous polyps (6.7%), non-IBD and noninfectious colitis (5.7%), terminal ileitis (4.3%), and adenomatous polyps (2.5%). The total colonic lesions rate of controls was 39.0%, which was higher than that of suspected IBS patients ($\chi^2 = 36.747$, $P < 0.001$). The five most common organic diseases in controls group were non-adenomatous polyps (14.7%), adenomatous polyps (6.7%), IBD (6.1%), diverticular disease (3.6%), and terminal ileitis (2.2%). Compared with controls, patients with suspected IBS had higher prevalence of non-IBD and noninfectious colitis ($\chi^2 = 63.371$, $P < 0.001$) and terminal ileitis ($\chi^2 = 13.757$, $P < 0.001$), however, had lower prevalence of diverticular disease ($\chi^2 = 8.596$, $P < 0.05$), adenomatous polyps ($\chi^2 = 49.986$, $P < 0.001$), and non-adenomatous polyps ($\chi^2 = 81.437$, $P < 0.001$).

There was no difference in the prevalence of IBD, malignant tumor, benign tumor, parasitic infection, infectious colitis, angiodysplasia, and intestinal tuberculosis between suspected IBS group and control group. Colorectal cancer was the main malignant disease in both groups. There were seven and six colorectal adenocarcinoma found in suspected IBS group and control group. A patient with

lymphoma was found in control group. No carcinoid was found in both groups.

Discussion

Rome diagnostic criteria on FGID give gastroenterology physicians a good tool to diagnose IBS [5, 16]. It seems to show reasonable sensitivity and specificity in diagnosing IBS [11, 17]. However, the diagnosis of IBS still remains a challenge to rule out relevant organic disease. The present study revealed normal colonoscopy finding in 69.7% of 3,332 patients with suspected IBS lacking warning signs. Since patients with microscopic colitis always have normal colonoscopy finding, we cannot rule out this kind of disease in the present study. Microscopic colitis encompasses two similar albeit distinct entities: lymphocytic colitis and collagenous colitis. Three characteristics of microscopic colitis are chronic watery diarrhea, normal or minimal abnormal of colonoscopy, and special histopathology alteration of colonic mucosa [18]. Because patients with diarrhea-predominant IBS may have similar symptoms to the patients with microscopic colitis, several researches showed there was an overlap between the two diseases [19–22]. Microscopic colitis is rarely reported in China and gastroenterology physicians do not pay much attention to it while performing the colonoscopy. In this study, we only find two cases of biopsy on colonic mucosa when the colonoscopy finding was normal in the patients with suspected IBS. We believe the missed diagnosis of microscopic colitis was inevitable in this retrospective study because of having no relevant biopsy on the patients with suspected diarrhea-predominant IBS. So, our results showed that the diagnostic sensitivity of symptom criteria on IBS without colonoscopy is not more than 69.7% in suspected IBS patients lacking warning signs.

Patients with small polyps or early colorectal cancer may not have any symptoms. In this study, we found that there was no significant difference on the colonoscopy finding of benign or malignant tumor between suspected IBS patients and controls. Nevertheless, the prevalence of adenomatous polyps and non-adenomatous polyps were significant higher in controls than those in suspected IBS patients.

Table 1 Demographic and clinical characteristics of the suspected IBS patients and the controls

SIBS suspected irritable bowel syndrome

^a Having significant difference between control group and SIBS group ($P < 0.001$)

	<i>n</i>	Male	Age ($\bar{x} \pm s$)
SIBS group	3,332	1,789 (53.7%)	34.1 ± 7.8
IBS with diarrhea (%)	2,416 (72.5%)	1,279 (52.9%)	34.8 ± 7.6
IBS with constipation (%)	540 (16.2%)	297 (55.0%)	35.6 ± 6.9
IBS with mixed bowel habits (%)	377 (11.3%)	213 (56.5%)	33.8 ± 6.8
Control group	1,588	1,064 (67.0%) ^a	38.4 ± 7.3 ^a

Table 2 Colonoscopic finding in patients with suspected IBS patients and controls

	SIBS	Percentage (%)	Controls	Percentage (%)	Chi-square (χ^2)	<i>P</i>
Normal	2,323	69.7	969	61.0		
Organic lesions	1,009	30.3	619	39.0	36.747	<0.001
IBD	229	6.9	96	6.1	1.193	0.275
Ulcer colitis	13	0.4	8	0.5		
Crohn's disease	6	0.2	3	0.2		
IBD unclassified	210	6.3	85	5.4		
Infectious colitis	28	0.8	14	0.9	0.022	0.883
Non-IBD and noninfectious colitis	191	5.7	14	0.9	63.371	<0.001
Parasitic infection	10	0.3	2	0.1	0.721	0.396 ^a
Trichuriasis	8	0.2	2	0.1		
Ascariasis	2	0.1	0	0.0		
Intestinal tuberculosis	2	0.1	1	0.1	0	1.000 ^a
Terminal ileitis	144	4.3	35	2.2	13.757	<0.001
Adenomatous polyps	84	2.5	106	6.7	49.986	<0.001
Non-adenomatous polyps	223	6.7	233	14.7	81.437	<0.001
Metaplasia polyps	156	4.7	134	8.4		
Inflammatory polyps	59	1.8	90	5.7		
Juvenile polyps	5	0.2	4	0.3		
Peutz–Jeghers polyps	3	0.1	5	0.3		
Malignant tumor	7	0.2	7	0.4	1.286	0.257 ^a
Colon cancer	5	0.2	4	0.3		
Rectal cancer	2	0.1	2	0.1		
Lymphoma	0	0.0	1	0.1		
Benign tumor	11	0.3	8	0.5	0.843	0.359
Interstitialoma	3	0.1	1	0.1		
Air cyst	4	0.1	1	0.1		
Fibroma	1	0.0	1	0.1		
Cyst	2	0.1	2	0.1		
Lipoma	1	0.1	3	0.2		
Melanosis coli	35	1.1	11	0.7	1.486	0.223
Diverticular disease	72	2.2	57	3.6	8.596	0.003
Angiodysplasia	67	2.0	26	1.6		
Rectal varices	5	0.2	1	0.1		
Telangiectasia	12	0.4	10	0.6		
Hemorrhoids	48	1.4	13	0.8		
Ischemic enteritis	2	0.1	1	0.1		
Behcet's disease	0	0.0	1	0.1		

SIBS suspected irritable bowel syndrome, IBD inflammatory bowel disease

^a Chi-square test of fourfold table with continuity correction

The total incidence of neoplastic lesions was 9.7% in suspected IBS patients and 22.3% in controls. These results indicate that compared to normal persons, the suspected IBS patients lacking alarm signs have lower chance to suffer from neoplasm and colonoscopy has minimal value to find tumor in this type of patients.

A population-based study showed that the incidence of colonic diverticular disease in IBS patients was 44.4% and

diarrhea-predominant IBS is associated with colonic diverticular disease [23]. But, the present study showed that the incidence of colonic diverticular disease in patients with suspected IBS (2.2%) was significantly lower than that in controls (3.6%) and cannot show up the association. We think the reason for the contradiction is the different population of the two studies. The population of the previous study was diarrhea-predominant IBS patients and

the mean age was 65 years; however, the population of the present study was based on patients with suspected IBS lacking alarm symptom and the mean age (37.2 years) was obviously younger than the former. In our opinion, small and uncomplicated diverticula are not the corresponding factor to induce IBS-like symptom.

Inflammatory bowel disease is one of the five most common organic diseases both in suspected IBS group and control group. Characteristic colonoscopy and histology change were not always present because about 10% of patients with IBD were defined as ulcer colitis or Crohn's disease. More IBD remained unclassified. Non-IBD and noninfectious colitis was a diagnosis of exclusion and composed of some inflammation in colon different from IBD, infectious colitis, and special gastrointestinal inflammatory such as intestinal tuberculosis and ileo-typhus [24]. Though the prevalence of non-IBD and noninfectious colitis in patients with suspected IBS was significantly higher than that in control, it had limited clinical significance because it is not a specific diagnosis. And, we believe that multiple biopsy specimens from different regions in the colon will help to make more correct diagnosis for the patients with non-IBD and noninfectious colitis.

In this study, the rates of terminal ileitis in suspected IBS patients were significantly higher than that in controls. It indicated that the IBS-like symptoms may be associated with terminal ileitis. Several studies had revealed that increased number of mast cells was found in the terminal ileum in patients with IBS and the increased mast cells may be associated with the altered visceral perception of the gastrointestinal tract [25, 26]. We suggested that for patients with suspected IBS, if small intestinal disorders are indicated, colonoscopy should be performed and the terminal ileum should be intubated.

In summary, this study demonstrates that the sensitivity of symptom criteria without colonoscopy is no more than 69.7% on diagnosis of IBS in patients with suspected IBS lacking warning signs. There were 30.3% of suspected IBS patients lacking warning signs found in organic colonic diseases. Though colonoscopy has low value to find tumor and IBD in this type of patients, it has benefit of finding some other relevant organic lesions such as terminal ileitis. For the patients with suspected diarrhea-predominant IBS, colonoscopy and biopsy should be performed to rule out microscopic colitis.

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Statements The study has been approved by the ethics committee of Southern Medical University and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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