### REVIEW

**4744** Regulation of transforming growth factor-β signaling as a therapeutic approach to treating colorectal cancer


### MINIREVIEWS

**4762** Immunological mechanisms of fecal microbiota transplantation in recurrent *Clostridioides difficile* infection

_Soveral LF, Korczaguin GG, Schmidt PS, Nunes IS, Fernandes C, Zárate-Blades CR_

**4773** Albumin administration in patients with cirrhosis: Current role and novel perspectives

_de Mattos ÁZ, Simonetto DA, Terra C, Farias AQ, Bittencourt PL, Pase THS, Toazza MR, de Mattos AA, Alliance of Brazilian Centers for Cirrhosis Care – the ABC Group_

### ORIGINAL ARTICLE

#### Basic Study

**4787** Novel therapeutic diiminoquinone exhibits anticancer effects on human colorectal cancer cells in two-dimensional and three-dimensional *in vitro* models


#### Case Control Study

**4812** Previous hepatitis B viral infection–an underestimated cause of pancreatic cancer

_Batskikh S, Morozov S, Dorofeev A, Borunova Z, Kostyushev D, Brezgin S, Kostyusheva A, Chulanov V_

### Retrospective Cohort Study

**4823** Effectiveness, safety, and drug sustainability of biologics in elderly patients with inflammatory bowel disease: A retrospective study


### Retrospective Study

**4834** Prevalence and factors associated with vitamin C deficiency in inflammatory bowel disease


**4846** Development and validation of a risk prediction score for the severity of acute hypertriglyceridemic pancreatitis in Chinese patients

_Liu ZY, Tian L, Sun XY, Liu ZS, Hao LJ, Shen WW, Gao YQ, Zhai HH_
## Contents

**Observational Study**
4861 Are bowel symptoms and psychosocial features different in irritable bowel syndrome patients with abdominal discomfort compared to abdominal pain?
_Fang XC, Fan WJ, Drossman DD, Han SM, Ke MY_

**Randomized Clinical Trial**
4875 Peroral endoscopic myotomy vs laparoscopic myotomy and partial fundoplication for esophageal achalasia: A single-center randomized controlled trial
_de Moura ETH, Jukemura J, Ribeiro IB, Farias GFA, de Almeida Delgado AA, Coutinho LMA, de Moura DTH, Aissar Sallum RA, Nasi A, Sánchez-Luna SA, Sakai P, de Moura EGH_

**SYSTEMATIC REVIEWS**
4890 Chinese herbal formula shen-ling-bai-zhu-san to treat chronic gastritis: Clinical evidence and potential mechanisms
_Jin W, Zhong J, Song Y, Li MF, Song SY, Li CR, Hou WW, Li QJ_

**SCIENTOMETRICS**
4909 Global research trends in the field of liver cirrhosis from 2011 to 2020: A visualised and bibliometric study

**CASE REPORT**
4920 Ectopic bronchogenic cyst of liver misdiagnosed as gallbladder diverticulum: A case report
_Dong CJ, Yang RM, Wang QL, Wu QY, Yang DJ, Kong DC, Zhang P_

**LETTER TO THE EDITOR**
4926 Prediction of moderately severe and severe acute pancreatitis in pregnancy: Several issues
_Yang QY, Hu JW_
ABOUT COVER
Editorial Board Member of World Journal of Gastroenterology, Osamu Toyoshima, MD, PhD, Director, Department of Gastroenterology, Toyoshima Endoscopy Clinic, Tokyo 157-0066, Japan. t@ichou.com

AIMS AND SCOPE
The primary aim of World Journal of Gastroenterology (WJG, World J Gastroenterol) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. WJG mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING
The WJG is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports, Index Medicus, MEDLINE, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 impact factor (IF) for WJG as 5.374; IF without journal self cites: 5.187; 5-year IF: 5.715; Journal Citation Indicator: 0.84; Ranking: 31 among 93 journals in gastroenterology and hepatology; and Quartile category: Q2. The WJG's CiteScore for 2021 is 8.1 and Scopus CiteScore rank 2021: Gastroenterology is 18/149.

RESPONSIBLE EDITORS FOR THIS ISSUE
Production Editor: Ying-Yi Yuan; Production Department Director: Xiang Li; Editorial Office Director: Jia-Ru Fan.

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

EDITORS-IN-CHIEF
Andrzej S Tarnawski

EDITORIAL BOARD MEMBERS
http://www.wjgnet.com/1007-9327/editorialboard.htm

PUBLICATION DATE
September 7, 2022

_COPYRIGHT_
© 2022 Baishideng Publishing Group Inc
Observational Study

Are bowel symptoms and psychosocial features different in irritable bowel syndrome patients with abdominal discomfort compared to abdominal pain?

Xiu-Cai Fang, Wen-Juan Fan, Douglas D Drossman, Shao-Mei Han, Mei-Yun Ke

Abstract

BACKGROUND
The Rome IV criteria eliminated abdominal discomfort for irritable bowel syndrome (IBS), which was previously included in Rome III. There are questions as to whether IBS patients with abdominal discomfort (seen in Rome III but not Rome IV) are different from those with abdominal pain (Rome IV).

AIM
To compare bowel symptoms and psychosocial features in IBS patients diagnosed with Rome III criteria with abdominal discomfort, abdominal pain, and pain & discomfort.

METHODS
We studied IBS patients meeting Rome III criteria. We administered the IBS symptom questionnaire, psychological status, and IBS quality of life. Patients were classified according to the predominant abdominal symptom associated with defecation into an only pain group, only discomfort group, and pain & discomfort group. We compared bowel symptoms, extraintestinal symptoms, IBS quality of life, psychological status and healthcare-seeking behaviors, and efficacy among the three groups. Finally, we tested risk factors for symptom reporting in IBS patients.

RESULTS
Of the 367 Rome III IBS patients enrolled, 33.8% (124 cases) failed to meet Rome IV criteria for an IBS diagnosis. There were no meaningful differences between the pain group ($n = 233$) and the discomfort group ($n = 83$) for the following: (1) Frequency of defecatory abdominal pain or discomfort; (2) Bowel habits; (3) Coexisting extraintestinal pain; (4) Comorbid anxiety and depression; and (5) IBS quality of life scores except more patients in the discomfort group reported mild symptom than the pain group (22.9% vs 9.0%). There is a significant tendency for patients to report their defecatory and non-defecatory abdominal symptom as pain alone, or discomfort alone, or pain & discomfort (all $P < 0.001$).

CONCLUSION
IBS patients with abdominal discomfort have similar bowel symptoms and psychosocial features to those with abdominal pain. IBS symptoms manifesting abdominal pain or discomfort may primarily be due to different sensation and reporting experience.

Key Words: Irritable bowel syndrome; Abdominal pain; Abdominal discomfort; Diagnosis; Psychosocial distress; Quality of life

Core Tip: It is generally accepted that abdominal pain is the most predominant symptom of irritable bowel syndrome (IBS), and Rome IV eliminated abdominal discomfort as diagnostic criteria for IBS. Asian studies showed about one-third of IBS patients diagnosed using Rome III criteria had abdominal discomfort alone. In this study, we compared bowel symptoms, extraintestinal symptoms, IBS-quality of life, psychological status and healthcare-seeking behaviors, and efficacy between the abdominal pain and abdominal discomfort groups expecting to find a difference between the two groups but did not. We also assessed risk factors for symptom reporting for IBS patients.

INTRODUCTION
Irritable bowel syndrome (IBS) is a common functional bowel disorder with a global prevalence of 4.1% according to the Rome IV criteria and 10.1% with Rome III criteria[1]. Using the Rome III definition, IBS is characterized by recurrent abdominal pain or discomfort associated with altered bowel frequency or stool form[2]. However, the term “discomfort” was deleted from the 2016 Rome IV diagnostic criteria because some languages do not have a word for discomfort or it has different meanings in different languages or cultures[3,4]. Possibly abdominal discomfort has qualitative and quantitative levels of distinction with abdominal pain[5]. The data from a population-based survey of adults in the United States, Canada, and the United Kingdom showed that eliminating “discomfort” from the criteria for IBS affected diagnostic rates only slightly[6], and only 10% of Rome III-IBS patients among the Swedish cohort did not fulfill Rome-IV IBS diagnosis due to reporting only abdominal discomfort and not pain [7]. However, clinical studies from Thailand and central China revealed that about one-third of patients with IBS diagnosed using Rome III criteria had abdominal discomfort alone[8,9]. This rate is as high as 84.2% from another clinical retrospective report from Tianjin, China[10]. Evidence regarding pathophysiological differences between abdominal pain and abdominal discomfort such as whether these symptoms are categorically different or exist on a continuum of severity is lacking[11,12]. It is also unclear whether there are clinical or phenotypical distinctions with IBS presenting with abdominal pain...
This study aimed to: (1) Compare the bowel and extraintestinal symptoms of patients with IBS presenting with abdominal discomfort alone to those with pain alone as well as with pain & discomfort; (2) Evaluate the anxiety, depression, quality of life (QOL), and symptom reporting tendency for patients with pain and discomfort; and (3) Validate whether the discomfort is milder than pain on a continuum of severity for Chinese patients. The clinical data were drawn from the IBS database of Peking Union Medical College Hospital.

**MATERIALS AND METHODS**

**Subjects**
Consecutive patients with IBS aged 18-65 years from Peking Union Medical College Hospital gastroenterology clinics were enrolled in this study from June 2009 to February 2016. All patients met Rome III diagnostic and subtype criteria[2], including IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), and mixed IBS. Patients with organic gastrointestinal diseases and metabolic diseases were excluded based on the results of routine tests for blood, urine, stool; liver, kidney, and thyroid function, measurements of carcinoembryonic antigen, erythrocyte sedimentation rate, and C-reactive protein, and abdominal ultrasound and colonoscopy/barium enema in the past year. The participating patients provided oral or written consent to participate before study enrollment. This study was approved by the Peking Union Medical College Hospital Ethics Committee (S-234).

**IBS symptom questionnaire**
The IBS symptom questionnaire was administered by well-trained investigators in face-to-face interviews. The questionnaire was adapted from a previous symptom-related questionnaire for adult functional gastrointestinal disorders in Beijing[13], the Rome III diagnostic questionnaire for adult functional gastrointestinal disorders, and the Rome III psychosocial alarm questionnaire for functional gastrointestinal disorders[2]. Information collected included demographic data, IBS disease course, frequency and severity of IBS symptoms, defecation-related symptoms, extraintestinal symptoms, physical examination and supplementary examination results, and IBS treatments in the whole disease course and the last year.

Patients were evaluated according to abdominal pain, abdominal discomfort, or both abdominal pain & discomfort just before defecation (pre-defecatory), at IBS onset, and between IBS symptom episodes without association to defecation (ordinary). Patients with the presence or worsening of pre-defecatory abdominal pain and without pre-defecatory abdominal discomfort were categorized as the pain group regardless of whether they had abdominal pain or discomfort during the ordinary period. Similarly, patients with pre-defecatory abdominal discomfort and without pre-defecatory abdominal pain were categorized as the discomfort group, and patients with pre-defecatory abdominal pain and discomfort were categorized as the pain & discomfort group.

The main intestinal symptom score for IBS-D was calculated according to the report by Zhu et al[14]. Diagnosis of gastroesophageal reflux disease and functional dyspepsia were made according to the Montreal consensus[15] and Rome III diagnostic and subtype criteria[2], respectively. Patients who did not meet Rome IV diagnostic criteria for IBS (including patients with pre-defecatory abdominal discomfort alone or symptom frequency < 1 d/wk) were evaluated for possible diagnoses of other functional bowel disorders using Rome IV criteria, including functional diarrhea, functional constipation, functional abdominal bloating/distension, and unspecified functional bowel disorder[3].

**QOL evaluation**
The simplified Chinese version of the IBS-QOL instrument was used to evaluate patient QOL[16], which was translated from IBS-QOL[17] and well validated. This instrument was completed by patients according to the instructions provided; the total score and eight domain scores were calculated as in a previous publication[14].

**Psychological evaluation**
The Hamilton Anxiety (HAMA) and Hamilton Depression (HAMD) scales were used to evaluate patient psychological status by specially trained professionals through conversation and observation. A HAMA score ≥ 14 was judged as anxiety and ≥ 21 as moderate-to-severe anxiety. A HAMD score ≥ 17 was judged as depression and ≥ 24 as moderate-to-severe depression[18,19].

**Statistical analysis**
All analyses were performed using SPSS version 19.0 (IBM Corporation, Somers, NY, United States). Parametric distribution was evaluated by Kolmogorov-Smirnov test. Parametric and categorical data are presented as mean ± SD or rate, respectively. Nonparametric data were presented as median and interquartile range. Comparisons among the three groups were made by one-way analysis of variance.
There were no significant differences in the prevalence of gastroesophageal reflux disease or functional extraintestinal symptoms (all bloating, abdominal distension, and anorectal pain was significantly higher than that in the pain group (all P < 0.05)). Incomplete evacuation, and passing mucus were high overall for all 3 groups. More patients in the discomfort group reported having urgency, sensation of incomplete evacuation, and passing mucus than those in the pain group (all P < 0.05). In the pain & discomfort group, the prevalence of abdominal bloating, abdominal distension, and anorectal pain was significantly higher than that in the pain group (all P < 0.05) (Table 2).

**Abdominal pain and/or discomfort improvement after defecation**
Abdominal pain and/or discomfort improved after defecation except for 1 patient in the pain group. There was no significant difference in the waiting time and degree for improvement among the three groups (Figures 2C and D).

In IBS-D patients, the main intestinal symptom score was 9.3 ± 1.6 in the pain group, 9.4 ± 1.5 in the discomfort group, and 9.6 ± 1.3 in the pain & discomfort group (P > 0.05).

**Defecation-related symptoms**
The prevalence of defecation related symptoms such as abdominal bloating, urgency, sensation of incomplete evacuation, and passing mucus were high overall for all 3 groups. More patients in the discomfort group reported having urgency, sensation of incomplete evacuation, and passing mucus than those in the pain group (all P < 0.05). In the pain & discomfort group, the prevalence of abdominal bloating, abdominal distension, and anorectal pain was significantly higher than that in the pain group (all P < 0.05) (Table 2).

**Extraintestinal symptoms**
There were no significant differences in the prevalence of gastroesophageal reflux disease or functional...
Table 1 Demographic data for irritable bowel syndrome patients with abdominal pain alone, abdominal discomfort alone, and abdominal pain & discomfort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pain group (n = 233)</th>
<th>Discomfort group (n = 83)</th>
<th>Pain &amp; discomfort group (n = 51)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>117 (50.2)</td>
<td>56 (67.5)</td>
<td>32 (62.7)</td>
<td>0.012</td>
</tr>
<tr>
<td>Age in yr</td>
<td>43.7 ± 11.7</td>
<td>42.3 ± 10.6</td>
<td>40.8 ± 11.0</td>
<td>0.23</td>
</tr>
<tr>
<td>BMI in kg/m²</td>
<td>23.0 ± 4.0</td>
<td>22.8 ± 4.0</td>
<td>22.3 ± 3.8</td>
<td>0.56</td>
</tr>
<tr>
<td>Education level, college and above, %</td>
<td>71 (30.5)</td>
<td>29 (34.9)</td>
<td>13 (25.5)</td>
<td>0.51</td>
</tr>
<tr>
<td>Physical labor, %</td>
<td>135 (57.9)</td>
<td>42 (50.6)</td>
<td>34 (66.7)</td>
<td>0.18</td>
</tr>
<tr>
<td>Family economic status, well-off &amp; above, %</td>
<td>105 (45.1)</td>
<td>44 (53.0)</td>
<td>18 (35.3)</td>
<td>0.13</td>
</tr>
<tr>
<td>Marriage status, married, %</td>
<td>201 (86.3)</td>
<td>71 (85.5)</td>
<td>41 (80.4)</td>
<td>0.56</td>
</tr>
<tr>
<td>IBS disease course in yr¹</td>
<td>6.0 (7.5)</td>
<td>5.3 (7.0)</td>
<td>6.0 (7.0)</td>
<td>0.38</td>
</tr>
<tr>
<td>IBS type</td>
<td></td>
<td></td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>IBS-D, %</td>
<td>95.7</td>
<td>96.4</td>
<td>86.3</td>
<td></td>
</tr>
<tr>
<td>IBS-C, %</td>
<td>3.0</td>
<td>2.4</td>
<td>7.8</td>
<td></td>
</tr>
<tr>
<td>IBS-M, %</td>
<td>1.3</td>
<td>1.2</td>
<td>5.9</td>
<td></td>
</tr>
</tbody>
</table>

¹Data presented as median (interquartile range), Kruskal-Wallis test. Note: P value is the difference among pain group, discomfort group, and pain & discomfort group, superscript letter is significantly different at a P < 0.05.
²The difference is between the pain group and discomfort group.

Data presented as number (%) or mean ± SD. Analysis of variance and χ² tests. IBS-D: Irritable bowel syndrome with diarrhea; BMI: Body mass index; IBS-C: Irritable bowel syndrome with constipation; IBS-M: Mixed irritable bowel syndrome.

Figure 1 Constitution diagram of irritable bowel syndrome patients diagnosed with Rome III and Rome IV criteria. About one-third of irritable bowel syndrome patients (parts dragged out of ring) diagnosed with Rome III criteria failed in irritable bowel syndrome diagnosis with Rome IV criteria because of only having abdominal discomfort before defecation (in green, 22.6%) or frequency of abdominal pain less than 1 d/wk (in light colors, 14.2%), which 3% of patients among them have discomfort alone with less frequency (in light green). IBS: Irritable bowel syndrome.

dyspepsia between the pain group and the discomfort group (P > 0.05), but the prevalence of epigastric pain syndrome, mainly epigastric pain was higher in the pain group than the discomfort group (21.0% vs 7.2%, 18.5% vs 6.0%, P < 0.05). More patients in the pain & discomfort group reported early satiation, dyspareunia, and menstrual pain for women than in the pain group (all P < 0.05). The prevalence of dyspareunia in the pain & discomfort group was also higher than in the discomfort group (P < 0.001) (Table 3).

Comorbid anxiety and depression

There were no significant differences in HAMA score, HAMD score, or the prevalence and severity of anxiety and depression among the three groups (Table 4).

IBS-QOL

The QOL of patients with IBS showed an obvious decrease with an IBS-QOL score of 72.2 ± 17.9 in the
Table 2 Characteristics of bowel symptoms in irritable bowel syndrome patients with abdominal pain alone, abdominal discomfort alone, and abdominal pain & discomfort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pain group (n = 233)</th>
<th>Discomfort group (n = 83)</th>
<th>Pain &amp; discomfort group (n = 51)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location1, %</td>
<td></td>
<td></td>
<td></td>
<td>0.213</td>
</tr>
<tr>
<td>Left lower quadrant</td>
<td>67 (28.8)</td>
<td>14 (16.9)</td>
<td>12 (23.5)</td>
<td></td>
</tr>
<tr>
<td>Umbilical</td>
<td>79 (33.9)</td>
<td>27 (32.5)</td>
<td>20 (39.2)</td>
<td></td>
</tr>
<tr>
<td>Lower abdomen</td>
<td>65 (27.9)</td>
<td>23 (27.7)</td>
<td>15 (29.4)</td>
<td></td>
</tr>
<tr>
<td>Epigastric</td>
<td>11 (4.7)</td>
<td>2 (2.4)</td>
<td>2 (3.9)</td>
<td></td>
</tr>
<tr>
<td>Whole abdomen</td>
<td>12 (4.0)</td>
<td>8 (9.6)</td>
<td>5 (9.8)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>24 (10.3)</td>
<td>18 (21.7)</td>
<td>7 (13.7)</td>
<td></td>
</tr>
<tr>
<td>Severity, %</td>
<td></td>
<td></td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>Mild</td>
<td>21 (9.0)</td>
<td>19 (22.9)</td>
<td>6 (11.7)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>160 (68.7)</td>
<td>55 (66.3)</td>
<td>37 (72.6)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>52 (22.3)</td>
<td>9 (10.8)</td>
<td>8 (15.7)</td>
<td></td>
</tr>
<tr>
<td>Frequency, %</td>
<td></td>
<td></td>
<td></td>
<td>0.290</td>
</tr>
<tr>
<td>3 d/mo</td>
<td>37 (15.9)</td>
<td>11 (13.3)</td>
<td>4 (7.84)</td>
<td></td>
</tr>
<tr>
<td>1 d/wk</td>
<td>25 (10.7)</td>
<td>5 (6.0)</td>
<td>2 (3.9)</td>
<td></td>
</tr>
<tr>
<td>&gt;1 d/wk</td>
<td>108 (46.4)</td>
<td>38 (45.8)</td>
<td>27 (52.94)</td>
<td></td>
</tr>
<tr>
<td>Every day</td>
<td>63 (27.0)</td>
<td>29 (34.9)</td>
<td>18 (35.5)</td>
<td></td>
</tr>
<tr>
<td>Ordinary pain/discomfort, %</td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pain alone</td>
<td>84 (36.1)</td>
<td>6 (7.2)</td>
<td>6 (11.8)</td>
<td></td>
</tr>
<tr>
<td>Discomfort alone</td>
<td>21 (9.0)</td>
<td>43 (51.8)</td>
<td>3 (5.9)</td>
<td></td>
</tr>
<tr>
<td>Pain &amp; discomfort</td>
<td>7 (3.0)</td>
<td>2 (2.4)</td>
<td>28 (54.9)</td>
<td></td>
</tr>
<tr>
<td>No pain or discomfort</td>
<td>121 (51.9)</td>
<td>32 (38.6)</td>
<td>14 (27.4)</td>
<td></td>
</tr>
<tr>
<td>Defecation-related symptoms, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal bloating</td>
<td>93 (39.9)</td>
<td>43 (51.8)</td>
<td>35 (68.6)</td>
<td>0.001²</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>21 (9.0)</td>
<td>13 (15.7)</td>
<td>12 (23.5)</td>
<td>0.01³</td>
</tr>
<tr>
<td>Urgency</td>
<td>197 (84.6)</td>
<td>80 (96.4)</td>
<td>42 (82.4)</td>
<td>0.01²⁴</td>
</tr>
<tr>
<td>Defecation straining</td>
<td>70 (30.0)</td>
<td>25 (30.1)</td>
<td>23 (45.1)</td>
<td>0.10</td>
</tr>
<tr>
<td>Sensation of anorectal obstruction</td>
<td>62 (26.6)</td>
<td>30 (36.1)</td>
<td>19 (37.3)</td>
<td>0.13</td>
</tr>
<tr>
<td>Anorectal pain</td>
<td>28 (12.0)</td>
<td>15 (18.1)</td>
<td>17 (33.3)</td>
<td>0.001²</td>
</tr>
<tr>
<td>Sensation of incomplete evacuation</td>
<td>164 (70.4)</td>
<td>74 (89.2)</td>
<td>39 (76.5)</td>
<td>0.005²</td>
</tr>
<tr>
<td>Passing mucus</td>
<td>141 (60.5)</td>
<td>66 (79.5)</td>
<td>39 (76.5)</td>
<td>0.002²</td>
</tr>
</tbody>
</table>

⁵Some patients reported more than one location. χ² test, data presented as number (%).
⁶The difference is between pain group and discomfort group.
⁷The difference is between pain group and pain & discomfort group.
⁸The difference is between discomfort group and pain & discomfort group.

P value is the difference among pain group, discomfort group, and pain & discomfort group, and superscript letters are significantly different at a P < 0.05.

pain group, 72.0 ± 20.0 in the discomfort group, and 70.4 ± 15.0 in the pain & discomfort group while comparing to the mean overall score in healthy Chinese subjects (95.50 ± 6.73 with the scores on each of the eight domains being ≥ 90.00)⁶. The most meaningful impairment for all 3 groups was food avoidance, following by dysphoria, interference with activity, and health worry. There were no significant differences in the eight domain scores between the pain group and discomfort group (Figure 3), while patients in the pain & discomfort group had lower QOL than patients having discomfort alone (P = 0.03).
Table 3 Coexisting extraintestinal symptoms of irritable bowel syndrome patients with abdominal pain alone, abdominal discomfort alone, and abdominal pain & discomfort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pain group (n = 233)</th>
<th>Discomfort group (n = 83)</th>
<th>Pain &amp; discomfort group (n = 51)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GERD, %</td>
<td>60 (25.8)</td>
<td>14 (16.9)</td>
<td>10 (19.6)</td>
<td>0.20</td>
</tr>
<tr>
<td>Heartburn</td>
<td>35 (15.0)</td>
<td>6 (7.2)</td>
<td>6 (11.8)</td>
<td>0.18</td>
</tr>
<tr>
<td>Acid reflux</td>
<td>44 (18.9)</td>
<td>10 (12.1)</td>
<td>5 (9.8)</td>
<td>0.15</td>
</tr>
<tr>
<td>Food regurgitation</td>
<td>14 (6.0)</td>
<td>4 (4.8)</td>
<td>3 (5.9)</td>
<td>0.92</td>
</tr>
<tr>
<td>Retrosternal chest pain</td>
<td>10 (4.3)</td>
<td>3 (3.6)</td>
<td>2 (3.9)</td>
<td>0.96</td>
</tr>
<tr>
<td>Functional dyspepsia, %</td>
<td>86 (36.9)</td>
<td>23 (27.7)</td>
<td>18 (35.3)</td>
<td>0.32</td>
</tr>
<tr>
<td>Epigastric pain syndrome</td>
<td>49 (21.0)</td>
<td>6 (7.2)</td>
<td>7 (13.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>43 (18.5)</td>
<td>5 (6.0)</td>
<td>7 (13.7)</td>
<td>0.02</td>
</tr>
<tr>
<td>Epigastric burning</td>
<td>12 (5.2)</td>
<td>2 (2.4)</td>
<td>3 (5.9)</td>
<td>0.54</td>
</tr>
<tr>
<td>Postprandial distress syndrome</td>
<td>64 (27.5)</td>
<td>22 (26.5)</td>
<td>15 (29.4)</td>
<td>0.94</td>
</tr>
<tr>
<td>Postprandial fullness</td>
<td>57 (24.5)</td>
<td>20 (24.1)</td>
<td>9 (17.7)</td>
<td>0.57</td>
</tr>
<tr>
<td>Early satiation</td>
<td>14 (6.0)</td>
<td>6 (7.2)</td>
<td>9 (17.7)</td>
<td>0.02</td>
</tr>
<tr>
<td>Somatic pain, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>17 (45.9)</td>
<td>37 (44.6)</td>
<td>26 (51.0)</td>
<td>0.76</td>
</tr>
<tr>
<td>Neck pain</td>
<td>21 (9.0)</td>
<td>7 (8.4)</td>
<td>3 (5.9)</td>
<td>0.77</td>
</tr>
<tr>
<td>Backache</td>
<td>41 (17.6)</td>
<td>8 (9.6)</td>
<td>7 (13.7)</td>
<td>0.21</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>12 (5.2)</td>
<td>6 (7.2)</td>
<td>11 (21.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Menstrual pain1</td>
<td>30 (25.9)</td>
<td>10 (37.0)</td>
<td>11 (57.9)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

The number of female patients in the abdominal pain, abdominal discomfort, and pain & discomfort groups was 116, 27, and 19, respectively. χ² test. Data presented as number (%).

1 P value is difference between the pain group and the discomfort group.
2 The difference is between the discomfort group and the pain & discomfort group.
3 P value is the difference among the pain group, discomfort group, and pain & discomfort group, and superscript letters are significantly different at P < 0.05. GERD: Gastroesophageal reflux disease.

Healthcare-seeking behaviors and efficacy

There were no significant differences among the three groups in the average number of consultations and colonoscopies in the whole disease course and the average consultations and intermittent and long-term medication use in the last year (all P > 0.05). More patients in discomfort group used antispasmodics (muscarinic cholinergic receptor antagonists and selective intestinal calcium channel blockers), and all patients who used the antispasmodics had a reasonably good response (response rate over 50%). The overall satisfaction rate (including complete satisfaction and satisfaction) with medical care showed no significant difference among the three groups (P > 0.05) (Table 5).

Risk factors for IBS patients describing pre-defecatory symptoms as abdominal pain alone, discomfort alone, and pain & discomfort

Twelve variables differing between the pain group and the discomfort group at a P value with significant difference in Tables 1-3 were utilized for a multiple logistic regression analysis. We found that male patients [odds ratio (OR) = 1.955, 95% confidence interval (CI): 1.104-3.462, P = 0.021] and patients with mild defecatory abdominal pain or discomfort (OR = 4.020, 95%CI: 1.436-11.253, P = 0.008) were the predictors for patients to describe their pre-defecatory symptoms as abdominal discomfort alone rather than abdominal pain alone (Table 6). Similar analyses were performed between the pain group and the pain & discomfort group (11 variables) and the discomfort group and the pain & discomfort group (10 variables). We found that abdominal bloating (OR = 2.238, 95%CI: 1.080-4.638, P = 0.030) and anorectal pain (OR = 2.979, 95%CI: 1.347-6.585, P = 0.007) were the predictors for patients to describe their symptom as pain & discomfort rather than pain alone (Table 6), and no predictors were found for patients to describe their symptom as discomfort alone or pain & discomfort.
Table 4 Comorbid anxiety and depression among irritable bowel syndrome patients with abdominal pain alone, abdominal discomfort alone, and abdominal pain & discomfort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pain group (n = 233)</th>
<th>Discomfort group (n = 83)</th>
<th>Pain &amp; discomfort group (n = 51)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAMA score</td>
<td>16.1 ± 7.3</td>
<td>15.5 ± 7.3</td>
<td>17.3 ± 7.4</td>
<td>0.36</td>
</tr>
<tr>
<td>Comorbid anxiety, %</td>
<td>141 (60.5)</td>
<td>49 (59.0)</td>
<td>38 (74.5)</td>
<td>0.14</td>
</tr>
<tr>
<td>Mild</td>
<td>69 (29.6)</td>
<td>25 (30.1)</td>
<td>21 (41.2)</td>
<td>0.26</td>
</tr>
<tr>
<td>Moderate-severe</td>
<td>72 (30.9)</td>
<td>24 (28.9)</td>
<td>17 (33.3)</td>
<td>0.86</td>
</tr>
<tr>
<td>HAMD score</td>
<td>13.2 ± 6.2</td>
<td>12.3 ± 6.1</td>
<td>14.3 ± 5.5</td>
<td>0.18</td>
</tr>
<tr>
<td>Comorbid depression, %</td>
<td>66 (28.3)</td>
<td>22 (26.5)</td>
<td>18 (35.3)</td>
<td>0.53</td>
</tr>
<tr>
<td>Mild</td>
<td>54 (23.2)</td>
<td>20 (24.1)</td>
<td>17 (33.3)</td>
<td>0.31</td>
</tr>
<tr>
<td>Moderate-severe</td>
<td>12 (5.2)</td>
<td>2 (2.4)</td>
<td>1 (2.0)</td>
<td>0.40</td>
</tr>
<tr>
<td>Comorbid anxiety &amp; depression, %</td>
<td>62 (26.6)</td>
<td>20 (24.1)</td>
<td>18 (35.3)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD or number (%). Student’s t test and χ² tests. P value is difference among the pain group, discomfort group, and pain & discomfort group. HAMA: Hamilton Anxiety Scale; HAMD: Hamilton Depression Scale.

Table 5 Consultations and medications of irritable bowel syndrome patients with abdominal pain alone, abdominal discomfort alone, and abdominal pain & discomfort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pain group (n = 233)</th>
<th>Discomfort group (n = 83)</th>
<th>Pain &amp; discomfort group (n = 51)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the whole disease course</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consultation times per year¹</td>
<td>4.6 ± 6.7</td>
<td>5.7 ± 6.2</td>
<td>4.2 ± 4.1</td>
<td>0.54</td>
</tr>
<tr>
<td>Colonoscopies²</td>
<td>1.9 ± 1.4</td>
<td>1.5 ± 0.8</td>
<td>1.6 ± 0.9</td>
<td>0.22</td>
</tr>
<tr>
<td>In the last year</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consultation times¹</td>
<td>4.0 ± 5.7</td>
<td>4.5 ± 4.5</td>
<td>4.9 ± 4.7</td>
<td>0.54</td>
</tr>
<tr>
<td>Medications, intermittent and long-term use, %</td>
<td>164 (70.4)</td>
<td>56 (67.5)</td>
<td>43 (84.3)</td>
<td>0.09</td>
</tr>
<tr>
<td>Antispasmodics use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use rate</td>
<td>29 (12.4)</td>
<td>24 (28.9)</td>
<td>12 (23.5)</td>
<td>0.002³</td>
</tr>
<tr>
<td>Response rate</td>
<td>22 (75.9)</td>
<td>13 (54.2)</td>
<td>10 (83.3)</td>
<td>0.12</td>
</tr>
<tr>
<td>Overall satisfaction to medical care, %</td>
<td>125 (53.7)</td>
<td>39 (47.0)</td>
<td>21 (41.2)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

¹Consultation times were average consultation times of consulters.
²Colonoscopies were average colonoscopies of patients who performed colonoscopies.
³The difference is between the pain group and the discomfort group.

Data presented as mean ± SD or number (%). Analysis of variance and χ² test. P value is difference among pain group, discomfort group, and pain & discomfort group, and superscript letter is significantly different at a P < 0.05.

**Diagnosis of patients with abdominal discomfort alone according to Rome IV criteria**

Among 83 patients having pre-defecatory abdominal discomfort alone and not meeting Rome IV criteria for IBS, 48 patients (57.8%) met the diagnosis for functional diarrhea, 28 patients (33.7%) for functional abdominal bloating/distension, 2 patients (2.4%) for functional constipation, and 5 patients (6.0%) were classified as unspecified functional bowel disorder.

**DISCUSSION**

The present study comprehensively compared the bowel symptoms and psychosocial features of IBS
Table 6 Risk factors for irritable bowel syndrome patients describing symptoms as abdominal pain alone, abdominal discomfort alone, and abdominal pain & discomfort

<table>
<thead>
<tr>
<th>Partial regression coefficient</th>
<th>Standard error</th>
<th>Wald $\chi^2$</th>
<th>95%CI</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal discomfort alone vs abdominal pain alone</td>
<td>Male sex</td>
<td>0.671</td>
<td>0.291</td>
<td>5.293</td>
</tr>
<tr>
<td></td>
<td>Severity (mild defecatory pain or discomfort)</td>
<td>1.391</td>
<td>0.525</td>
<td>7.018</td>
</tr>
<tr>
<td>Abdominal pain alone vs abdominal pain &amp; discomfort</td>
<td>Abdominal bloating</td>
<td>0.805</td>
<td>0.372</td>
<td>4.692</td>
</tr>
<tr>
<td></td>
<td>Anorectal pain</td>
<td>1.091</td>
<td>0.405</td>
<td>7.272</td>
</tr>
</tbody>
</table>

*P < 0.05. Multiple logistic regression analysis. Superscript letter is significantly different at a $P < 0.05$.

CI: Confidence interval.

Figure 2 Comparison of bowel movements and stool forms in irritable bowel syndrome with diarrhea patients and improvement of abdominal pain or discomfort after defecation in irritable bowel syndrome patients among the abdominal pain alone, abdominal discomfort alone, and abdominal pain & discomfort groups. A: Bowel movements during irritable bowel syndrome with diarrhea non-onset and onset status; B: Stool forms based on Bristol Stool Form Scale during irritable bowel syndrome with diarrhea non-onset and onset status; C: Degree of improvement of abdominal pain and discomfort with defecation; D: Waiting time for improvement of abdominal pain and discomfort with defecation in irritable bowel syndrome patients. Numbers in the column are percentages. *P < 0.01. BM: Bowel movement.

patients with pre-defecatory abdominal pain alone to pre-defecatory abdominal discomfort alone, and abdominal pain & discomfort. We found that patients with abdominal discomfort had similar bowel and extraintestinal symptoms, comorbid anxiety and depression, QOL, and healthcare-seeking behaviors to those with abdominal pain.

It is generally accepted that abdominal pain is the most predominant symptom of IBS[3]; however, a previous clinical study from the United States found only 21% of IBS patients with moderate to severe symptoms reported their predominant symptom in terms of abdominal pain[11]. Another study conducted by Lembo et al[12] showed that the proportions of IBS patients who reported pain or gas
Figure 3 Comparison of irritable bowel syndrome-quality of life. There were no significant differences in the total score and eight domain scores among the three groups. Numbers in the column are percentages. IBS-QOL: Irritable bowel syndrome-quality of life.

(bloating-type discomfort) as one of their viscerosensory symptoms were similar (60% vs 66%). Currently, several studies compared the diagnostic rate between Rome III and IV criteria for IBS in the general population and consulting cohorts. The proportions of having abdominal discomfort varied among the western countries (2.4%-9.9%)\(^{[6,7,20,21]}\) and the eastern countries (29.8%-84.2%)\(^{[8-10]}\). In this study, IBS patients with abdominal discomfort accounted for 22.6%. The elimination of abdominal discomfort from the diagnostic criteria had little effect on the diagnosis of IBS for the western countries\(^{[3]}\), while a significant proportion of IBS patients were no longer IBS in Asian, including in China\(^{[8-10]}\).

The significant difference between the western and eastern countries indicates there may be cultural factors that affect the experience and reporting of abdominal symptoms. The definition of abdominal pain is more uniformly accepted, while the definition for abdominal discomfort is ambiguous; “discomfort means an uncomfortable sensation not described as pain” according to the Rome III criteria\(^{[2]}\). Further, there are no comparison studies concerning abdominal discomfort descriptions in cross-cultural cohorts. In this study, Chinese patients with IBS accurately reported abdominal discomfort, including the location and association with defecation (both in pre-defecatory and non-defecatory periods), as well as other defecation related symptoms (i.e. urgency and so on). Symptom characteristics were similar with abdominal pain, which indicated that abdominal discomfort was a relatively explicit symptom for Chinese patients, unlike the impression from a cognitive study from American IBS patients\(^{[6]}\) in which abdominal discomfort might encompass a wide range of symptoms such as bloating, gas, fullness, flatulence, sensation of incomplete evacuation, and urgency.

Abdominal pain and discomfort are both visceral perceptions of abnormality on the same continuum with pain appearing at the more severe end of the spectrum\(^{[11]}\). In this study, there were no meaningful differences between the pain alone group and discomfort alone group in frequencies as well as the main intestinal symptom score for IBS-D patients except more patients in the discomfort group reported mild symptoms than the pain group. In addition, we found patients with mild defecatory abdominal pain or discomfort were predisposed to describe their pre-defecatory symptoms as abdominal discomfort alone rather than abdominal pain alone, which indicated abdominal discomfort may appear as the milder form of pain. However, it was reported that more IBS patients rank abdominal discomfort as their most bothersome symptom than abdominal pain (60% vs 29% in America\(^{[12]}\), 15.3% vs 4.5% of IBS-C in Japan\(^{[22]}\)), and the severity of abdominal discomfort had the strongest independent relationship with QOL impairment\(^{[10]}\). Patients in the three groups had similar healthcare-seeking behavior and satisfaction to medical care in this study. We speculated in terms of the symptom itself, the overall severity of IBS, and occupation of medical resources that abdominal discomfort is as important as abdominal pain.

Nevertheless, more patients in the discomfort group reported accompanying urgency, sensation of incomplete evacuation, and passing mucus than the pain group. Patients with abdominal pain & discomfort had a higher prevalence of abdominal bloating/distension and anorectal pain than patients with abdominal pain alone, and a lower score of QOL than patients with abdominal discomfort alone. In addition, we found that abdominal bloating and anorectal pain were the predictors for patients to describe their symptom as pain & discomfort rather than pain alone, suggesting coexisting symptoms played important roles in the generation of discomfort feeling.

We noticed that the previous studies seldom paid attention to the abdominal symptoms of IBS patients during non-defecatory period. An interesting finding in this study is more patients having pre-defecatory abdominal discomfort alone also reported non-defecatory abdominal discomfort than the other two groups, and a similar report tendency for patients with pain alone and pain & discomfort
during defecatory period and non-defecatory period. In terms of extraintestinal symptoms, more patients in the pain group reported coexisting epigastric pain. The possible explanation for this reporting tendency is individual sensation and reporting experience to the similar stimulations and pathophysiological changes[11].

The relationships between diary stress, psychological distress, and severity of abdominal discomfort symptoms in women with IBS have been noted[23]. In this study, the scores of HAMA and HAMD and comorbid anxiety and depression were comparable between the pain group and the discomfort group. The impact of mental status to the symptom sensation and reporting could be ignored.

To date, studies on the pathophysiology of IBS mainly focused on abdominal pain[12,24-27]. As far as we know, there was no direct evidence focused on mechanism of abdominal discomfort or comparison of the difference of pathogenesis between abdominal pain and discomfort. Abdominal discomfort could simultaneously improve with abdominal pain and/or bloating to antispasmodics tiropramide and octylonium, secretagogue linaclotide, or simethicone and *Bacillus* coagulans for IBS or IBS-C patients[28-31]. It is unclear whether the treatments focused on bloating, diarrhea, or constipation could relieve the abdominal discomfort for those patients having defecatory abdominal discomfort alone while they are diagnosed as other bowel disorders according to Rome IV criteria (as shown in the results). Therefore, we realized that it may be more beneficial to classify patients with bowel-related abdominal discomfort into IBS from a therapeutic consideration.

There are several limitations in this study. We only included the IBS patients with typical changes of bowel habits, i.e. IBS-D and IBS-C. Therefore, some mixed IBS and IBS-unclassified patients might be missed[7,31]. We enrolled patients with Rome III criteria and did not concern the abdominal pain and discomfort during or soon after bowel movement. The proportion of Rome III suspected IBS patients with this kind of pain or discomfort was low (2.9% according to Bai et al[3]). Moreover, we did not ask patients to describe the difference between abdominal pain and discomfort. The data for response to therapies were retrospective recall, including prescription and over-the-counter. In addition, the prevalence of IBS in the general population for males was lower than females (4.1% vs 5.4%)[32], but an equal or higher ratio of male to female consulting patients was reported in clinical studies[9,14]. It is unclear whether male patients have more vigorous healthcare seeking behaviors or priority of medical care than female patients, but more female patients reported frequent consultations and colonoscopies during the whole disease course of IBS than male patients[33]. IBS-D is the predominant subtype, which accounted for 74.1% in the general population of South China[34] and 66.3% in consulting patients[31]. In addition, this was a single-center study.

**CONCLUSION**

Chinese patients with IBS can differentiate and report abdominal pain or/and abdominal discomfort as their key bowel symptom. The patients with abdominal discomfort had similar bowel symptoms and psychosocial features to those with abdominal pain. There is a tendency for IBS patients to report their defecatory and non-defecatory abdominal symptom as pain alone, discomfort alone, or pain and discomfort. Pre-defecatory abdominal discomfort should be considered as an important symptom for IBS patients. Further studies focused on the pathophysiology and therapeutic response (including the cultural influence) of abdominal pain and discomfort are needed.

**ARTICLE HIGHLIGHTS**

**Research background**

The Rome IV criteria eliminated abdominal discomfort for irritable bowel syndrome (IBS), which was previously included in the Rome III criteria. Asian studies showed the rate of IBS patients with abdominal discomfort alone was high.

**Research motivation**

There are questions as to whether IBS patients with abdominal discomfort (seen in Rome III but not Rome IV) are different from those with abdominal pain (Rome IV).

**Research objectives**

To compare the bowel and extraintestinal symptoms of patients with IBS presenting with abdominal discomfort alone to those with pain alone as well as with pain & discomfort and to evaluate the anxiety, depression, quality of life, and symptom reporting tendency for patients with pain and discomfort.

**Research methods**

We enrolled IBS patients and collected their clinical data. Patients were classified to the pain only group,
the discomfort only group, and the pain & discomfort group. We compared bowel symptoms, extraintestinal symptoms, IBS-quality of life, psychological status and healthcare-seeking behaviors, and efficacy among the three groups and tested risk factors for symptom reporting in IBS patients.

**Research results**

About one-third of patients meeting Rome III criteria failed to meet Rome IV criteria for an IBS diagnosis. There were no meaningful differences between the pain group and discomfort group for frequency of defecatory abdominal pain or discomfort, bowel habits, coexisting extragastrointestinal pain, comorbid anxiety and depression, and IBS-quality of life scores.

**Research conclusions**

IBS patients with abdominal discomfort have similar bowel symptoms and psychosocial features to those with abdominal pain.

**Research perspectives**

Further studies focused on the pathophysiology and therapeutic response (including the cultural influence) of abdominal pain and discomfort are needed.

**ACKNOWLEDGEMENTS**

The authors thank their colleagues in the Department of Gastroenterology, Peking Union Medical College Hospital for their contributions to the enrollment of IBS patients.

**FOOTNOTES**

**Author contributions:** Fang XC was responsible for study concept and design, data collection and interpretation, and drafting and revision of the manuscript; Fan WJ participated in data collection, data analysis, and figure drafting; Drossman DD was responsible for critical revision; Han SM participated in data analysis; Ke MY participated in critical revision; all authors approved the final version of the manuscript as submitted.

**Supported by** the Program of International S & T Cooperation, No. 2014DFA31850; the National Natural Science Foundation of China, No. 81870379 and No. 81370488; and the Project of the National Key Technologies R & D Program in the 11th Five Year Plan period, No. 2007BAI04801.

**Institutional review board statement:** This study was reviewed and approved by the Peking Union Medical College Hospital Ethics Committee, No. S-234.

**Informed consent statement:** All study participants provided oral or written consent to participate before study enrollment.

**Conflict-of-interest statement:** There are no conflicts of interest to report.

**Data sharing statement:** No additional data are available.

**STROBE statement:** The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Country/Territory of origin:** China

**ORCID number:** Xiu-Cai Fang 0000-0002-5600-8779; Wen-Juan Fan 0000-0002-2927-9266; Douglas D Drossman 0000-0002-8178-0453; Shao-Mei Han 0000-0003-2081-7969; Mei-Yun Ke 0000-0001-5793-9500.

S-Editor: Chen YL
L-Editor: Filipodia
P-Editor: Yuan YY
hypersensitivity in patients with irritable bowel syndrome. Ludidi S, Hertig VL, Kanazawa M.


A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23: 56-62 [PMID: 14399272 DOI: 10.1136/jnnp.23.1.56]

Individuals with Self-reported Irritable Bowel Syndrome Based on the Rome IV vs Rome III Criteria. Black CJ, Hamilton M, Yiannakou Y, Houghton LA, Ford AC.


Patcharatrakul T, Thanaiprom K, Gonlaanchai V. Application of Rome III vs. Rome IV diagnostic criteria for irritable bowel syndrome (IBS) in clinical practice: is the newer the better? Gastroenterology 2017; 152: S717


Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23: 56-62 [PMID: 14399272 DOI: 10.1136/jnnp.23.1.56]


Features of pain and discomfort IBS


