ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2022 January 14; 10(2): 397-752

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

Contents

Thrice Monthly Volume 10 Number 2 January 14, 2022

EDITORIAL

397 New trends in treatment of muscle fatigue throughout rehabilitation of elderlies with motor neuron diseases

Mohamed A

MINIREVIEWS

401 What emotion dimensions can affect working memory performance in healthy adults? A review

Hou TY, Cai WP

412 Quadrilateral plate fractures of the acetabulum: Classification, approach, implant therapy and related research progress

Zhou XF, Gu SC, Zhu WB, Yang JZ, Xu L, Fang SY

ORIGINAL ARTICLE

Case Control Study

426 Methylprednisolone accelerate chest computed tomography absorption in COVID-19: A three-centered retrospective case control study from China

Lin L, Xue D, Chen JH, Wei QY, Huang ZH

Retrospective Study

437 Analysis of photostimulable phosphor image plate artifacts and their prevalence

Elkhateeb SM, Aloyouny AY, Omer MMS, Mansour SM

448 N6-methyladenine-modified DNA was decreased in Alzheimer's disease patients

Lv S, Zhou X, Li YM, Yang T, Zhang SJ, Wang Y, Jia SH, Peng DT

458 Inflammation-related indicators to distinguish between gastric stromal tumors and leiomyomas: A retrospective study

Zhai YH, Zheng Z, Deng W, Yin J, Bai ZG, Liu XY, Zhang J, Zhang ZT

469 Relationship between Ki-67 and CD44 expression and microvascular formation in gastric stromal tumor tissues

Ma B, Huang XT, Zou GJ, Hou WY, Du XH

477 Modified surgical method of supra- and infratentorial epidural hematoma and the related anatomical study of the squamous part of the occipital bone

Li RC, Guo SW, Liang C

485 Combined molybdenum target X-ray and magnetic resonance imaging examinations improve breast cancer diagnostic efficacy

Gu WQ, Cai SM, Liu WD, Zhang Q, Shi Y, Du LJ

World Journal of Clinical Cases

Thrice Monthly Volume 10 Number 2 January 14, 2022

Contents

492 Value of thyroglobulin combined with ultrasound-guided fine-needle aspiration cytology for diagnosis of lymph node metastasis of thyroid carcinoma

Zhang LY, Chen Y, Ao YZ

502 Locking compression plate + T-type steel plate for postoperative weight bearing and functional recovery in complex tibial plateau fractures

Li HF, Yu T, Zhu XF, Wang H, Zhang YQ

511 Effect of Mirena placement on reproductive hormone levels at different time intervals after artificial abortion

Jin XX, Sun L, Lai XL, Li J, Liang ML, Ma X

518 Diagnostic value of artificial intelligence automatic detection systems for breast BI-RADS 4 nodules

Lyu SY, Zhang Y, Zhang MW, Zhang BS, Gao LB, Bai LT, Wang J

Clinical Trials Study

528 Analysis of 20 patients with laparoscopic extended right colectomy

Zheng HD, Xu JH, Liu YR, Sun YF

Observational Study

538 Knowledge, attitude, practice and factors that influence the awareness of college students with regards to breast cancer

Zhang QN, Lu HX

547 Diagnosing early scar pregnancy in the lower uterine segment after cesarean section by intracavitary ultrasound

Cheng XL, Cao XY, Wang XQ, Lin HL, Fang JC, Wang L

554 Impact of failure mode and effects analysis-based emergency management on the effectiveness of craniocerebral injury treatment

Shao XL, Wang YZ, Chen XH, Ding WJ

563 Predictive value of alarm symptoms in Rome IV irritable bowel syndrome: A multicenter cross-sectional study

Yang Q, Wei ZC, Liu N, Pan YL, Jiang XS, Tantai XX, Yang Q, Yang J, Wang JJ, Shang L, Lin Q, Xiao CL, Wang JH

Prospective Study

576 5-min mindfulness audio induction alleviates psychological distress and sleep disorders in patients with COVID-19

Li J, Zhang YY, Cong XY, Ren SR, Tu XM, Wu JF

META-ANALYSIS

585 Efficacy and safety of argatroban in treatment of acute ischemic stroke: A meta-analysis

Lv B, Guo FF, Lin JC, Jing F

World Journal of Clinical Cases

Thrice Monthly Volume 10 Number 2 January 14, 2022

Contents

SCIENTOMETRICS

594 Biologic therapy for Crohn's disease over the last 3 decades

Shen JL, Zhou Z, Cao JS, Zhang B, Hu JH, Li JY, Liu XM, Juengpanich S, Li MS, Feng X

CASE REPORT

607 Novel compound heterozygous *GPR56* gene mutation in a twin with lissencephaly: A case report

Lin WX, Chai YY, Huang TT, Zhang X, Zheng G, Zhang G, Peng F, Huang YJ

618 Patients with SERPINC1 rs2227589 polymorphism found to have multiple cerebral venous sinus thromboses despite a normal antithrombin level: A case report

Liao F, Zeng JL, Pan JG, Ma J, Zhang ZJ, Lin ZJ, Lin LF, Chen YS, Ma XT

625 Successful management of delirium with dexmedetomidine in a patient with haloperidol-induced neuroleptic malignant syndrome: A case report

Yang CJ, Chiu CT, Yeh YC, Chao A

631 Malignant solitary fibrous tumor in the central nervous system treated with surgery, radiotherapy and anlotinib: A case report

Zhang DY, Su L, Wang YW

643 Anesthesia and perioperative management for giant adrenal Ewing's sarcoma with inferior vena cava and right atrium tumor thrombus: A case report

Wang JL, Xu CY, Geng CJ, Liu L, Zhang MZ, Wang H, Xiao RT, Liu L, Zhang G, Ni C, Guo XY

656 Full-endoscopic spine surgery treatment of lumbar foraminal stenosis after osteoporotic vertebral compression fractures: A case report

Zhao QL, Hou KP, Wu ZX, Xiao L, Xu HG

663 Ethambutol-induced optic neuropathy with rare bilateral asymmetry onset: A case report

Sheng WY, Wu SQ, Su LY, Zhu LW

671 Vitrectomy with residual internal limiting membrane covering and autologous blood for a secondary macular hole: A case report

Ying HF, Wu SQ, Hu WP, Ni LY, Zhang ZL, Xu YG

677 Intervertebral bridging ossification after kyphoplasty in a Parkinson's patient with Kummell's disease: A case report

Li J, Liu Y, Peng L, Liu J, Cao ZD, He M

685 Synovial chondromatosis of the hip joint in a 6 year-old child: A case report

Yi RB, Gong HL, Arthur DT, Wen J, Xiao S, Tang ZW, Xiang F, Wang KJ, Song ZQ

691 Orthodontic retreatment of an adult woman with mandibular backward positioning and temporomandibular joint disorder: A case report

Yu LY, Xia K, Sun WT, Huang XQ, Chi JY, Wang LJ, Zhao ZH, Liu J

World Journal of Clinical Cases

Thrice Monthly Volume 10 Number 2 January 14, 2022

Contents

703 Autosomal recessive spinocerebellar ataxia type 4 with a *VPS13D* mutation: A case report

Huang X, Fan DS

709 Primary adrenal diffuse large B-cell lymphoma with normal adrenal cortex function: A case report

Fan ZN, Shi HJ, Xiong BB, Zhang JS, Wang HF, Wang JS

717 Varicella-zoster virus-associated meningitis, encephalitis, and myelitis with sporadic skin blisters: A case report

Takami K, Kenzaka T, Kumabe A, Fukuzawa M, Eto Y, Nakata S, Shinohara K, Endo K

725 Tension pneumocephalus following endoscopic resection of a mediastinal thoracic spinal tumor: A case report

Chang CY, Hung CC, Liu JM, Chiu CD

733 Accelerated Infliximab Induction for Severe Lower Gastrointestinal Bleeding in a Young Patient with Crohn's Disease: A Case Report

Zeng J, Shen F, Fan JG, Ge WS

741 Occupational fibrotic hypersensitivity pneumonia in a halogen dishes manufacturer: A case report

Wang M, Fang HH, Jiang ZF, Ye W, Liu RY

747 Using a fretsaw in treating chronic penial incarceration: A case report

Zhao Y, Xue XQ, Huang HF, Xie Y, Ji ZG, Fan XR

World Journal of Clinical Cases

Thrice Monthly Volume 10 Number 2 January 14, 2022

Contents

ABOUT COVER

Associate Editor of *World Journal of Clinical Cases*, Bruno Ramos Chrcanovic, DDS, MSc, PhD, Associate Professor, Department of Prosthodontics, Malmö University, Malmö 241 21, Sweden. bruno.chrcanovic@mau.se

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for *WJCC* as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The *WJCC*'s CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Jia-Hui Li*; **Production Department Director:** *Xu Guo*; **Editorial Office Director:** *Jin-Lei Wang*.

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

EDITORS-IN-CHIEF
Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2307-8960/editorialboard.htm

PUBLICATION DATE
January 14, 2022

COPYRIGHT
© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

© 2022 Baishideng Publishing Group Inc. All rights reserved. 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

E-mail: bpgoffice@wjgnet.com https://www.wjgnet.com

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2022 January 14; 10(2): 563-575

DOI: 10.12998/wjcc.v10.i2.563

ISSN 2307-8960 (online)

ORIGINAL ARTICLE

Observational Study

Predictive value of alarm symptoms in Rome IV irritable bowel syndrome: A multicenter cross-sectional study

Qian Yang, Zhong-Cao Wei, Na Liu, Yang-Lin Pan, Xiao-Sa Jiang, Xin-Xing Tantai, Qi Yang, Juan Yang, Jing-Jie Wang, Lei Shang, Qiang Lin, Cai-Lan Xiao, Jin-Hai Wang

ORCID number: Qian Yang 0000-0002-6563-7876; Zhong-Cao Wei 0000-0001-8931-680X; Na Liu 0000-0003-3246-9674; Yang-Lin Pan 0000-0002-7183-6716; Xiao-Sa Jiang 0000-0002-7121-8520; Xin-Xing Tantai 0000-0002-4105-6890; Qi Yang 0000-0001-5573-3031; Juan Yang 0000-0002-3193-5082; Jing-Jie Wang 0000-0001-7770-8232; Lei Shang 0000-0003-0470-0066; Qiang Lin 0000-0002-1105-3074; Cai-Lan Xiao 0000-0001-8476-5008; Jin-Hai Wang 0000-0003-1365-4727.

Author contributions: Yang Q, Wang JH and Liu N concepted and designed the study; Yang Q, Wei ZC, Yang Q, Yang J, Wang JJ, Lin Q, Jiang XS and Xiao CL responsible for the acquisition of the data; Yang Q, Wei ZC, Shang L and Tantai XX involved in analysis and interpretation of data; Yang Q, Wang JH, Pan YL and Liu N drafted the manuscript and revised the article critically for important intellectual content; all authors have read and approved the final version of manuscript.

Institutional review board statement: The study was reviewed and approved by the Ethics Committee of the Second Affiliated Hospital of Xi'an Jiaotong University.

Qian Yang, Zhong-Cao Wei, Na Liu, Xiao-Sa Jiang, Xin-Xing Tantai, Cai-Lan Xiao, Jin-Hai Wang, Department of Gastroenterology, The Second Affiliated Hospital, Xi'an Jiaotong University, Xi'an 710004, Shaanxi Province, China

Yang-Lin Pan, State Key Laboratory of Cancer Biology, National Clinical Research Center for Digestive Diseases and Xijing Hospital of Digestive Diseases, Air Force Medical University, Xi'an 710032, Shaanxi Province, China

Qi Yang, Juan Yang, Department of Gastroenterology, Xi'an No. 3 Hospital, The Affiliated Hospital of Northwest University, Xi'an 710018, Shaanxi Province, China

Jing-Jie Wang, Qiang Lin, Department of Gastroenterology, Tangdu Hospital, Air Force Medical University, Xi'an 710038, Shaanxi Province, China

Lei Shang, Department of Health Statistics, Air Force Medical University, Xi'an 710032, Shaanxi Province, China

Corresponding author: Jin-hai Wang, MD, Professor, Department of Gastroenterology, The Second Affiliated Hospital, Xi'an Jiaotong University, No. 157 Xiwu Road, Xi'an 710004, Shaanxi Province, China. jinhaiwang@hotmail.com

Abstract

BACKGROUND

Irritable bowel syndrome (IBS) is a common functional bowel disease that shares features with many organic diseases and cannot be accurately diagnosed by symptom-based criteria. Alarm symptoms have long been applied in the clinical diagnosis of IBS. However, no study has explored the predictive value of alarm symptoms in suspected IBS patients based on the latest Rome IV criteria.

AIM

To investigate the predictive value of alarm symptoms in suspected IBS patients based on the Rome IV criteria.

METHODS

In this multicenter cross-sectional study, we collected data from 730 suspected IBS patients evaluated at 3 tertiary care centers from August 2018 to August 2019. Patients with IBS-like symptoms who completed colonoscopy during the study

Informed consent statement: The patient's personal information will be treated in a cryptic manner and given a code that distinguishes it from other individuals to mark the patient. No personal information will be disclosed in any report or publication related to the study, and therefore no harm will be caused to the patient mentally or physically. In view of the above, we apply for exemption of subject's informed consent.

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.

Supported by the Key Research and Development Program of Shaanxi Province, No. 2017ZDXM-SF-046.

Country/Territory of origin: China

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

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,

period were initially identified by investigators through medical records. Eligible patients completed questionnaires, underwent laboratory tests, and were assigned to the IBS or organic disease group according to colonoscopy findings and pathology results (if a biopsy was taken). Independent risk factors for organic disease were explored by logistic regression analysis, and the positive predictive value (PPV) and missed diagnosis rate were calculated.

RESULTS

The incidence of alarm symptoms in suspected IBS patients was 75.34%. Anemia [odds ratio (OR) = 2.825, 95% confidence interval (CI): 1.273-6.267, P = 0.011], fecal occult blood [OR = 1.940 (95%CI: 1.041-3.613), P = 0.037], unintended weight loss (P = 0.009), female sex [OR = 0.560 (95%CI: 0.330-0.949), P = 0.031] and marital status (P = 0.030) were independently correlated with organic disease. The prevalence of organic disease was 10.41% in suspected IBS patients. The PPV of alarm symptoms for organic disease was highest for anemia (22.92%), fecal occult blood (19.35%) and unintended weight loss (16.48%), and it was 100% when these three factors were combined. The PPV and missed diagnosis rate for diagnosing IBS were 91.67% and 74.77% when all alarm symptoms were combined with Rome IV and 92.09% and 34.10% when only fecal occult blood, unintended weight loss and anemia were combined with Rome IV, respectively.

CONCLUSION

Anemia, fecal occult blood and unintended weight loss have high predictive value for organic disease in suspected IBS patients and can help identify patients requiring further examination but are not recommended as exclusion criteria for IBS.

Key Words: Alarm symptom; Irritable bowel syndrome; Predictive value; Rome IV; Organic disease

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: The diagnosis of irritable bowel syndrome (IBS) depends on symptom-based criteria, but the accuracy of these criteria is poor. For suspected IBS patients meeting the Rome IV criteria, considering alarm symptoms does not significantly improve the positive predictive value for diagnosing IBS. However, alarm symptoms can help identify patients with organic disease; in particular, fecal occult blood, unintended weight loss and anemia have a high predictive value for organic disease. The presence of those alarm symptoms suggests that further examination may be needed, but they are not recommended as exclusion criteria for IBS.

Citation: Yang Q, Wei ZC, Liu N, Pan YL, Jiang XS, Tantai XX, Yang Q, Yang J, Wang JJ, Shang L, Lin Q, Xiao CL, Wang JH. Predictive value of alarm symptoms in Rome IV irritable bowel syndrome: A multicenter cross-sectional study. *World J Clin Cases* 2022; 10(2): 563-575
URL: https://www.wjgnet.com/2307-8960/full/v10/i2/563.htm
DOI: https://dx.doi.org/10.12998/wjcc.v10.i2.563

INTRODUCTION

As a functional bowel disease (FBD), irritable bowel syndrome (IBS) is characterized by recurrent abdominal pain with changes in bowel habits[1]. The most recent study showed that the prevalence of IBS is 4.6%[2] and ranges from 6.8% to 33.3% in Asia[3]. Although IBS does not directly increase mortality, it significantly affects patients' quality of life, the results in the waste of medical resources and increases social burden [4,5].

The diagnosis of IBS depends on symptom-based criteria. Due to a lack of reliable diagnostic tests and specific biomarkers and overlap between symptoms of IBS and those of multiple organic diseases, the accuracy of symptom-based criteria is poor in practical applications[6,7]. Guidelines and consensus[8-10] advocate positive diagno-

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/

Received: July 31, 2021
Peer-review started: July 31, 2021
First decision: October 22, 2021
Revised: November 8, 2021
Accepted: December 10, 2021
Article in press: December 10, 2021
Published online: January 14, 2022

P-Reviewer: Caballero-Mateos AM, Gravina AG
S-Editor: Gong ZM
L-Editor: A
P-Editor: Gong ZM

stic strategies and recommend further examinations for patients with alarm symptoms. Previous studies[6,11] have suggested that IBS symptoms combined with alarm symptoms are helpful in detecting organic disease. However, alarm symptoms are very common, and excluding alarm symptoms may not significantly improve diagnostic accuracy[12,13]. In addition, as an alarm symptom, onset age guides the application of colonoscopy. The Rome IV criteria[1] and Asian consensus[10] recommend colonoscopy for patients aged over 50 years, while the Chinese consensus recommends the procedure for those aged over 40 years[9]. However, the Asian consensus and Chinese consensus[9,10] are dependent on population-based colorectal cancer (CRC) screening data rather than findings in IBS patients. No relevant study has explored the predictive value of alarm symptoms in suspected IBS patients based on the Rome IV criteria, and this knowledge gap motivated the design of this study.

MATERIALS AND METHODS

Study population

This multicenter cross-sectional study was conducted at three academic urban tertiary care centers from August 2018 to August 2019. These included the Second Affiliated Hospital of Xi'an Jiaotong University, Tangdu Hospital of Air Force Medical University and the Affiliated Hospital of Northwest University (Xi'an No. 3 Hospital). Patients came to the centers with gastrointestinal symptoms, and they were initially evaluated and managed by gastroenterologists. Those with IBS-like symptoms who completed colonoscopy during the study period were identified by investigators through medical records. Then, investigators further called eligible patients to confirm whether they met the inclusion and exclusion criteria and whether they had completed a routine fecal exam, routine blood exam and fecal occult blood test. Patients who had undergone blood and stool tests within 6 mo were not re-examined. Otherwise, eligible patients were required to finish these tests. Detailed information on qualified candidates was obtained *via* telephone and a questionnaire (paper questionnaires were handed out face-to-face or sent as an electronic version *via* WeChat). Oral informed consent was acquired from all included patients. This study was approved by the ethics committee of the Second Affiliated Hospital of Xi'an Jiaotong University and registered at Clinical Trials.gov (NCT 03620994).

Inclusion and exclusion criteria

Inclusion criteria: (1) The presence of IBS symptoms that met the Rome IV criteria; (2) Age 18 years old or older; (3) Visited the gastroenterology clinics and completed colonoscopy; and (4) A routine blood examination, routine fecal examination, and fecal occult blood test were performed within the last 6 mo (otherwise, eligible patients were required to finish these tests).

Exclusion criteria: (1) Other diagnosed diseases that can explain patients' IBS symptoms; (2) Metabolic diseases (uncontrolled thyroid diseases and diabetes); (3) Severe neurological and psychiatric disorders; (4) Severe and unstable extraintestinal conditions; (5) History of major abdominal surgery; (6) Pregnancy, possible pregnancy or lactation; (7) Colonoscopy was performed in the past 6 mo; (8) Currently taking large doses of anti-anxiety/anti-depressant drugs or enteric sensitive antibiotics; (9) Malignancy diagnosed to be in an active state within the last year of enrollment (excluding completely resected localized basal cell or squamous cell carcinoma of the skin); or (10) Refusal to take part in the study (see Supplementary material for details).

Data collection

In this study, data were collected by designated researchers according to a specifically designed questionnaire. The main points included basic demographic characteristics, gastrointestinal symptoms, alarm symptoms, lifestyle habits, personal history, family history, medical expenses, psychological self-rating scale (self-rating anxiety scale, self-rating depression scale), laboratory results (routine fecal exam, routine blood exam and fecal occult blood test), colonoscopy findings and pathological results (if a biopsy was taken). Alarm symptoms included rectal bleeding, fecal occult blood [using the Fecal Occult Blood Test Kit (Colloidal Gold)], anemia, fever, nocturnal symptoms, unintended weight loss (in the last 3 mo), onset age > 50 years, and family history (CRC, inflammatory bowel disease (IBD) and celiac disease)[1,13-15]. With regard to organic diseases, we only included lesions that may explain IBS symptoms, and the results of colonoscopy and pathology were the gold standard. If not obstructive, colorectal polyps, melanosis coli, colonic diverticulum without inflammation, rectal

varices, colic cyst, colonic leiomyoma, lipoma and neuroendocrine tumor, hemorrhoids, and anal fissures were identified as nonorganic diseases.

Rome IV criteria for IBS

Suspected IBS patients were those with IBS-like symptoms according to the Rome IV criteria, *i.e.*, recurrent abdominal pain occurring, on average, at least 1 d a week in the last 3 mo and associated with 2 or more of the following criteria: defecation, a change in stool frequency, or a change in the form (appearance) of the stool. Criteria fulfilled for the last 3 mo with symptom onset at least 6 mo before diagnosis. In this study, patients with IBS-like symptoms and no organic diseases found by colonoscopy were defined as the IBS group.

Colonoscopy and pathology examination

In this study, all subjects signed an informed consent form for colonoscopy. Before undergoing colonoscopy, the patients were required to take 3000 mL of pegylated electrolyte powder in batches for bowel preparation. Colonoscopy was performed independently by experienced endoscopy operators who remained blinded to other patient information. The operators took biopsies when necessary according to endoscopic findings. When colorectal mucosa appeared normal, random biopsy was generally not performed. The pathologists also evaluated the specimens and made a pathological diagnosis without knowing other information about each patient.

Statistical analysis

In this study, quantitative variables are presented as the mean ± SD, and qualitative variables are expressed as percentages. Univariate analysis was performed using the chi-square test or Fisher's exact test when appropriate. Multivariate logistic regression analysis (forward stepwise) was used to explore the independent risk factors for organic diseases, and the results are presented as odds ratios (ORs) and 95% confidence intervals (CIs). The positive predictive value (PPV) and missed diagnosis rate were calculated to evaluate the predictive value of alarm symptoms. Statistical analyses were performed using SPSS 18.0 (SPSS Inc. Chicago, IL, United States) software. Double-tailed $P<0.05$ values were considered statistically significant.

RESULTS

Subject characteristics

In this study, 945 patients were identified in the initial screening; of these, 89 were not successfully contacted, and 126 did not meet the eligibility criteria. Finally, a total of 730 patients were enrolled (Figure 1). With the exception of the psychological self-rating scale, which was completed by only 328 patients, all other data for the 730 patients were obtained and included in the data analysis. According to the colonoscopy and pathology results, suspected IBS patients were divided into the IBS group ($n = 654$) and the organic disease group ($n = 76$).

Univariate analysis showed that marital status ($P = 0.014$) was significantly different between the two groups. However, there were no significant differences in gender, body mass index, educational level, alcohol use, tobacco use, exercise time, history of gastrointestinal infection, sleep quality, dietary factors, psychological self-rating scale or medical expenses ($P > 0.05$) (Table 1).

Predictive value of alarm symptoms

The incidence of alarm symptoms in suspected IBS patients was as high as 75.34%. Univariate analysis indicated that fecal occult blood ($P = 0.003$), anemia ($P = 0.007$) and unintended weight loss ($P = 0.003$) were associated with significant differences (**T**able 1). All factors in Table 1**,** except the psychological self-rating scale (which only 328 patients completed), were included in the logistic regression analysis. The results showed that female sex [OR = 0.560 (95%CI: 0.330-0.949), $P = 0.031$], marital status ($P = 0.030$), anemia [OR = 2.825 (95%CI: 1.273-6.267), $P = 0.011$], fecal occult blood [OR = 1.940 (95%CI: 1.041-3.613), $P = 0.037$] and unintended weight loss ($P = 0.009$) were independently associated with organic diseases (Table 2). In addition, there was a significant difference in the prevalence of organic disease when the number of alarm symptoms varied ($P = 0.013$) (Table 3).

In this study, colonoscopy was used as the gold standard, and patients with a normal colonoscopy were identified as having IBS. Patients with one or more alarm

Table 1 Prevalence of organic disease according to clinical factors and alarm symptoms (*n* = 730), *n* (%)

Characteristics	IBS (*n* = 654)	Organic disease (*n* = 76)	*P* value
Female	307 (46.94)	27 (35.53)	0.059
Onset age (yr)[1]			0.682
> 50	268 (40.98)	33 (43.42)	
≤ 50	386 (59.02)	43 (56.58)	
BMI (kg/m^2)			0.360
< 18.5	37 (5.66)	1 (1.32)	
18.5-23.9	357 (54.59)	45 (59.21)	
24.0-27.9	212 (32.42)	26 (34.21)	
≥ 28	48 (7.34)	4 (5.26)	
Marital status			0.014
Married	592 (90.52)	60 (78.95)	
Never married	46 (7.03)	11 (14.47)	
Divorced	3 (0.46)	1 (1.32)	
Widowed	13 (1.99)	4 (5.26)	
Educational level			0.446
Elementary	88 (13.46)	13 (17.11)	
Junior high school	176 (26.91)	14 (18.42)	
High school	153 (23.39)	19 (25.00)	
University or technical college	218 (33.33)	29 (30.86)	
Postgraduate	19 (2.91)	1 (1.32)	
Alcohol use			0.394
Almost not	488 (74.62)	52 (68.42)	
Previous	45 (6.88)	5 (6.58)	
At present	121 (18.50)	19 (25.00)	
Tobacco use			0.102
Almost not	456 (69.72)	44 (57.89)	
Previous	49 (7.49)	7 (9.21)	
At present	149 (22.78)	25 (32.89)	
Exercise time			0.406
< 0.5 h/d	154 (23.55)	24 (31.58)	
≥ 0.5 h/d	183 (27.98)	21 (27.63)	
≥ 1 h/d	139 (21.25)	12 (17.11)	
≥ 2 h/d	178 (27.22)	19 (25.00)	
History of GI infection	72 (11.01)	6 (7.89)	0.405
Poor sleep quality	236 (36.09)	26 (34.21)	0.747
Dietary factor			0.900
Raw or cold food	131 (20.03)	17 (22.37)	
Spicy food	258 (39.45)	37 (48.68)	
Lipid food	119 (18.20)	18 (23.68)	
Milk and dairy products	95 (14.53)	9 (11.84)	
Animal protein	32 (4.89)	4 (5.26)	

FODMAP diet	103 (15.75)	12 (15.79)	
Psychological self-rating scale[2]			
Anxiety			0.507
No	207 (71.13)	26 (70.27)	
Mild	52 (17.87)	5 (13.51)	
Moderate	27 (9.28)	6 (16.22)	
Severe	5 (1.72)	0 (0)	
Depression			0.672
No	184 (63.23)	26 (70.27)	
Mild	53 (18.21)	4 (10.81)	
Moderate	43 (14.78)	5 (13.51)	
Severe	11 (3.78)	2 (5.41)	
Medical expenses (RMB)			0.197
< 500 yuan	120 (18.35)	17 (22.37)	
500-1000 yuan	174 (26.61)	13 (17.11)	
1000-3000 yuan	138 (21.10)	16 (21.05)	
3000-5000 yuan	74 (11.31)	6 (7.89)	
≥ 5000 yuan	148 (22.63)	24 (31.58)	
Rectal bleeding[1]	115 (17.58)	20 (26.32)	0.063
Fecal occult blood[1]	75 (11.47)	18 (23.68)	0.003
Unintended weight loss (kg)[1,3]			0.003
Without	507 (77.52)	47 (61.84)	
< 2.5	68 (10.40)	16 (21.05)	
2.5-5.0	40 (6.12)	7 (9.21)	
5.0-7.5	35 (5.35)	3 (3.95)	
≥ 7.5	4 (0.61)	3 (3.95)	
Anemia[1]	37 (5.66)	11 (14.47)	0.007
Fever[1]	17 (2.60)	1 (1.32)	0.770
Nocturnal symptoms[1]	164 (25.08)	17 (22.37)	0.605
Family history of IBD, CRC or celiac disease[1]	55 (8.41)	5 (6.58)	0.582

[1]Referred to alarm symptom.
[2]Only data of 328 patients were available.
[3]Referred to weight loss in the last 3 mo. BMI: Body mass index; CRC: Colorectal cancer; FODMAP: Fermentable Oligo-, Di-, Mono-saccharides And Polyols; GI: Gastrointestinal; IBD: Inflammatory bowel disease; IBS: Irritable bowel syndrome.

symptoms were predicted to have organic disease, and those without alarm symptoms were predicted to have IBS. As shown in Table 4, the PPV for organic disease in suspected IBS patients with alarm symptoms was calculated. The PPVs of individual alarm symptoms for organic disease ranged from 5% to 30% and decreased from high to low as follows: anemia (22.92%), fecal occult blood (19.35%), unintended weight loss (16.48%), rectal bleeding (14.81%), onset age > 50 years (10.96%), nocturnal symptoms (9.39%), family history of CRC, IBD or celiac disease (8.33%) and fever (5.56%). The PPVs of anemia combined with fecal occult blood, anemia combined with unintended weight loss, and fecal occult blood combined with unintended weight loss were 69.23%, 38.89% and 30.00%, respectively. The PPV was 100% when anemia, fecal occult blood and unintended weight loss were combined. As shown in Table 5, the PPV of symptom-based criteria (Rome IV) in diagnosing IBS was calculated with and without considering alarm symptoms. The PPV of Rome IV for diagnosing IBS was 89.59% without considering alarm symptoms; the PPV and missed diagnosis rate were 91.67%

Table 2 Multivariate analysis for clinical factors and alarm symptoms[1]

Characteristics	OR (95%CI)	*P* value	Partial regression coefficient
Female (ref male)	0.560 (0.330, 0.949)	0.031	-0.580
Marital status		0.030	
Married	–	–	–
Never married	2.499 (1.199, 5.209)	0.015	0.916
Divorced	1.184 (0.088,15.956)	0.899	0.169
Widowed	3.260 (0.964,11.029)	0.057	1.182
Anemia (ref absence)	2.825 (1.273, 6.267)	0.011	1.038
Fecal occult blood (ref absence)	1.940 (1.041, 3.613)	0.037	0.663
Unintended weight loss (kg)[2]		0.009	
Without	–	–	–
< 2.5	2.389 (1.255, 4.548)	0.008	0.871
2.5-5.0	1.868 (0.751, 4.642)	0.179	0.625
5.0-7.5	0.904 (0.263, 3.110)	0.872	-0.101
≥ 7.5	8.027 (1.638,39.335)	0.010	2.083

[1]All factors in Table 1, except the psychological self-rating scale were included in the logistic regression analysis.
[2]Referred to weight loss in the last 3 mo. CI: Confidence interval; OR: Odds ratio.

Table 3 Prevalence of organic disease according to number of alarm symptoms

Number of alarm symptoms	Number of patients (*n* = 730)	Patients with organic disease, *n* (%)	*P* value
0	180	15 (8.33)	0.013
1	250	21 (8.40)	
2	180	20 (11.11)	
3	91	12 (13.19)	
4	19	2 (10.53)	
5	7	3 (42.86)	
6	3	2 (66.67)	

and 74.77% when all alarm symptoms were combined with Rome IV and 92.09% and 34.10% when only fecal occult blood, unintended weight loss and anemia were combined with Rome IV.

Organic diseases

The prevalence of organic disease was 10.41% in suspected IBS patients. The most common lesion was non-IBD and noninfectious colitis (a significant colonoscopic finding indicative of inflammation, differentiated from IBD and infectious colitis[16]) (*n* = 42, 5.75%), followed by terminal ileitis (*n* = 18, 2.47%), CRC (*n* = 11, 1.51%), and ulcerative colitis (*n* = 8, 1.10%) (Table 6). We also randomly collected colonoscopy findings of 725 healthy examiners who went to the physical examination centers in the same period. The prevalence of terminal ileitis, CRC, ulcerative colitis and total organic disease were higher in suspected IBS patients than in healthy examiners ($P < 0.05$) (Supplementary Table 1).

DISCUSSION

Alarm symptoms are common in IBS patients, but not all alarm symptoms have good predictive value for organic disease[13]. Hammer *et al*[6] suggested that onset age > 50

Table 4 Utility of alarm symptoms for identifying organic disease

Alarm symptoms	PPV (%)
Onset age > 50 yr	10.96
Rectal bleeding	14.81
Fecal occult blood	19.35
Unintended weight loss[1]	16.48
Anemia	22.92
Fever	5.56
Nocturnal symptoms	9.39
Family history of IBD, CRC or celiac disease	8.33
Anemia + fecal occult blood	69.23
Anemia + unintended weight loss	38.89
Fecal occult blood + unintended weight loss	30.00
Anemia + fecal occult blood + unintended weight loss	100.00

[1]Referred to weight loss in the last 3 mo. CRC: Colorectal cancer; IBD: Inflammatory bowel disease; PPV: Positive predictive value.

Table 5 The accuracy of alarm symptoms in diagnosing irritable bowel syndrome

	Colonoscopy findings		PPV (%)	Missed diagnosis (%)
	IBS	Organic disease		
Without considering alarm symptoms	654	76	89.59	–
All alarm symptoms considered				
Absence (predicted IBS)	165	15	91.67	74.77
Presence (predicted organic disease)	489	61		
Certain alarm symptoms considered[1]				
Absence (predicted IBS)	431	37	92.09	34.10
Presence (predicted organic disease)	223	39		

[1]Referred to anemia, fecal occult blood and unintended weight loss. IBS: Irritable bowel syndrome; PPV: Positive predictive value.

Table 6 Colonoscopy findings in suspected irritable bowel syndrome patients

Colonoscopy findings	Number	Percentage (%)
Ulcerative colitis	8	1.10
Non-IBD and noninfectious colitis	42	5.75
CRC	11	1.51
Terminal ileitis	18	2.47
Total organic diseases	76	10.41

CRC: Colorectal cancer; IBD: Inflammatory bowel disease.

years and blood stains on toilet paper had good predictive value for organic disease. In China, one study[17] showed that onset age > 40 years, hemafecia, melena and anemia helped distinguish organic disease from functional disease, while another study[18] found that hematochezia, emaciation and anemia helped distinguish the two. However, both of these studies focused on patients with lower gastrointestinal

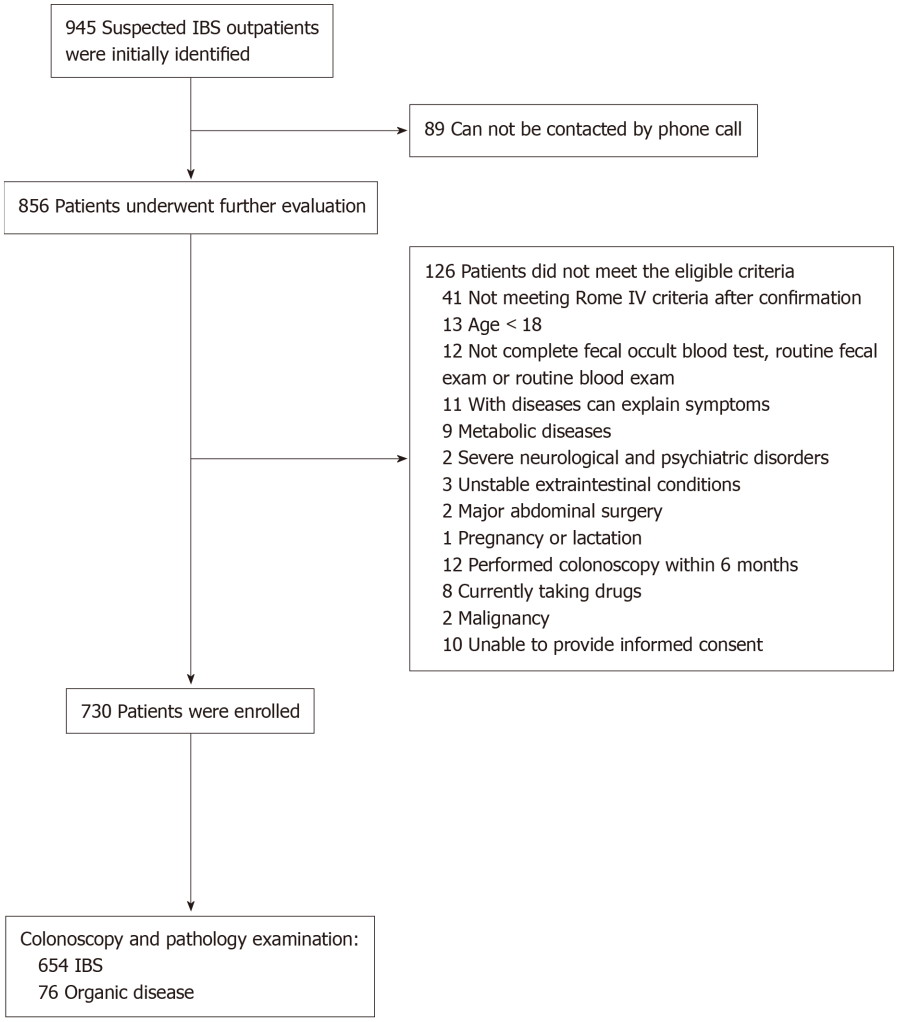

Figure 1 Flow chart of the study. IBS: Irritable bowel syndrome.

symptoms rather than suspected IBS patients. Based on the Rome IV criteria, we found that fecal occult blood, unintended weight loss and anemia had high predictive value for organic disease. Hemorrhoids were not regarded as organic disease, considering that their prevalence rate is as high as 50.28% in Chinese adults[19], which could affect the judgment of the value of rectal bleeding. In addition, the proportion of patients with organic disease increased as the number of alarm symptoms increased, consistent with previous studies[15].

Some studies[6,11,12] have shown that symptom-based criteria combined with alarm symptoms have high predictive value for diagnosing IBS. Vanner *et al*[11] found that the PPVs in prospective and retrospective studies were 98% and 100%, respectively. Whitehead *et al*[12] showed that the PPV was 47.9% without considering alarm symptoms and increased to 52.1% when considering alarm symptoms, with a missed diagnosis rate of 84%, and the PPV of individual alarm symptoms for identifying organic disease was 7%-9%. In this study, the PPV of Rome IV for diagnosing IBS was 89.59% when ignoring alarm symptoms and increased to 91.67% when all alarm symptoms were considered, with a missed diagnosis rate of 74.77%. When only fecal occult blood, unintended weight loss and anemia were considered, the PPV was 92.09%, but the missed diagnosis rate decreased to 34.10%. Furthermore, anemia, fecal occult blood and unintended weight loss alone had a higher PPV for organic disease, and the PPV for organic disease was 100% when anemia, fecal occult blood and unintended weight loss were combined.

These results indicate that for suspected IBS patients, considering alarm symptoms does not significantly improve PPV for diagnosing IBS. However, alarm symptoms can help identify patients with organic disease; in particular, fecal occult blood, unintended weight loss and anemia have a high value in predicting organic disease. The presence of those factors suggests that further examination may be needed, but they are not recommended as exclusion criteria for diagnosing IBS, consistent with the

findings of Whitehead *et al*[12], for several reasons. First, the prevalence of organic disease is relatively low, making the PPV of Rome IV criteria for diagnosing IBS high. As the incidence of alarm symptoms is high, the PPV is not significantly improved when considering all alarm symptoms, and the missed diagnosis rate is high. When only fecal occult blood, unintended weight loss and anemia are considered, the PPV remains high and almost unchanged, while the missed diagnosis rate decreases significantly. Second, a missed diagnosis of organic disease, such as IBD or CRC, has serious consequences[1]. However, a comprehensive diagnostic examination of all suspected IBS patients to exclude organic disease would place a huge burden on patients and society, especially given the expensive and invasive nature of colonoscopy[20]. Alarm symptoms have certain predictive value for organic disease. Evaluating the risk of organic disease individually by collecting alarm symptoms and other risk factors is an important part of the correct diagnosis of IBS and ensuring that high-risk patients (such as those with anemia, fecal occult blood and unintended weight loss) receive necessary tests and greater attention.

Some results of this study differ from those presented in previous studies. Reasons for these discrepancies include the following: (1) Hammer *et al*[6] evaluated all presenting patients and performed a full diagnostic workup for patients; Vanner *et al*[11] included only patients without alarm symptoms; Whitehead *et al*[12] conducted systematic chart reviews of patients with clinical diagnoses of IBS. In the above studies, the physician's final diagnosis was the gold standard; (2) The diagnostic criteria for IBS and definitions of alarm symptoms vary among studies. We used the Rome IV criteria, while other studies used the Manning criteria and Rome I or Rome II criteria; and (3) The prevalence of organic disease, which could affect the assessment of predictive value, was 10.41% in this study, compared with 10.3% and 30.3% in previous studies[21,22]. Currently, there is no standard definition of organic disease that distinguishes it from IBS. The organic diseases in this study included ulcerative colitis, CRC, terminal ileitis, non-IBD and noninfectious colitis, which could explain IBS symptoms.

It has been suggested that not all symptoms should be attributed to IBS, which would delay colonoscopy[16,22]. Studies have also shown that a negative colonoscopy does not provide protection for IBS patients[23]. In this study, the prevalence of terminal ileitis, CRC and ulcerative colitis was significantly higher in suspected IBS patients than in healthy examiners. Although the prevalence of organic diseases is low, they incur a great deal of harm. Thus, a necessary colonoscopy should not be delayed in suspected IBS patients. The Chinese consensus recommends colonoscopy for patients aged over 40 years[9]. However, our results suggest that the predictive value of onset age is poor in suspected IBS patients. It is necessary to conduct more research based on IBS patients.

We also found that male sex (reference female) and never-married status were risk factors for organic disease. Studies have shown that females are more likely to have IBS[2]. The relationship between marital status and FBD may be related to differences in lifestyle and stress according to marital status[24].

One of the major advantages of this study is its large sample size. A total of 730 subjects were enrolled. Patients were evaluated independently by the receiving doctors. Colonoscopy and pathology were performed independently by operators without knowledge of other patient information, ensuring that the results were more consistent with the clinical reality. This is also the first study to explore the predictive value of alarm symptoms in suspected IBS patients based on the Rome IV criteria.

There were some limitations in this study. First, older patients are more likely to undergo colonoscopy, which may lead to a high incidence of alarm symptoms. However, the incidence of alarm symptoms in previous studies is similar to that in our study (70%-84%)[12,13,15]. Second, this study was mainly conducted in the form of questionnaires, which may have caused information bias. Third, due to the normal appearance of microscopic colitis under colonoscopy and because tests related to celiac disease, lactose malabsorption and bacterial overgrowth were not widely evaluated, we could not exclude the above diseases. However, the prevalence of these diseases is low in China. Finally, this study was conducted in 3 tertiary centers and limited to a northwest Chinese population. The findings deserve further validation in primary care units in gastrointestinal clinics and in national multicenters.

CONCLUSION

In conclusion, based on the Rome IV criteria, anemia, fecal occult blood and unin-

tended weight loss have high predictive value for organic disease in suspected IBS patients and can help identify patients who need further examination, but they are not recommended as exclusion criteria for diagnosing IBS. Moreover, a necessary colonoscopy should not be delayed.

ARTICLE HIGHLIGHTS

Research background

The diagnosis of irritable bowel syndrome (IBS) depends on symptoms, while the accuracy of symptom-based criteria is poor. Alarm symptoms have long been applied in the diagnosis of IBS. However, no study has explored the predictive value of alarm symptoms in suspected IBS patients based on the latest Rome IV criteria.

Research motivation

The symptoms of IBS overlap with those of many organic diseases, and IBS lacks specific diagnostic tests and biomarkers. There are differences in previous research results on the predictive value of alarm symptoms in IBS, and there is no relevant study based on Rome IV. Evaluating the value of alarm symptoms provides guidance for clinical evaluation of the risk of organic diseases in suspected IBS patients, giving necessary auxiliary examination and correct diagnosis of IBS.

Research objectives

The objective was to investigate the predictive value of alarm symptoms in suspected IBS patients based on Rome IV. Furthermore, an IBS prediction model was established to guide the clinical and scientific work of IBS.

Research methods

This cross-sectional study was conducted at three academic urban tertiary care centers to ensure the sample size, sample representativeness and reliability of the results. Eligible patients completed questionnaires (paper version or electronic version), underwent laboratory tests, and were assigned to the IBS or organic disease group according to colonoscopy findings and pathology results. Investigators did not give any intervention to the patients and inspectors, and the results were more in line with clinical practice.

Research results

Anemia, fecal occult blood, unintended weight loss, female sex and marital status were independently correlated with organic disease. The positive predictive value (PPV) of alarm symptoms for organic disease was highest for anemia, fecal occult blood and unintended weight loss, and it was 100% when these three factors were combined. The PPV and missed diagnosis rate for diagnosing IBS were 91.67% and 74.77% when all alarm symptoms were combined with Rome IV and 92.09% and 34.10% when only fecal occult blood, unintended weight loss and anemia were combined with Rome IV, respectively.

Research conclusions

Alarm symptoms, especially fecal occult blood, unintended weight loss and anemia, have a high predictive value for organic disease in suspected IBS patients based on Rome IV. The presence of those alarm symptoms suggests that further examination may be needed, but they are not recommended as exclusion criteria for diagnosing IBS.

Research perspectives

By collecting large-scale, high-quality and national multicenter data, a simple, practical and efficient IBS diagnosis model can be further constructed. Of course, we should continue to deepen the research on the etiology and mechanism of IBS, actively look for specific biomarkers and/or diagnostic tests and achieve a more accurate diagnosis of IBS.

REFERENCES

1 **Mearin F**, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel Disorders. *Gastroenterology* 2016 [PMID: 27144627 DOI: 10.1053/j.gastro.2016.02.031]

2 **Palsson OS**, Whitehead W, Törnblom H, Sperber AD, Simren M. Prevalence of Rome IV Functional Bowel Disorders Among Adults in the United States, Canada, and the United Kingdom. *Gastroenterology* 2020; **158**: 1262-1273.e3 [PMID: 31917991 DOI: 10.1053/j.gastro.2019.12.021]

3 **Gwee KA**, Ghoshal UC, Chen M. Irritable bowel syndrome in Asia: Pathogenesis, natural history, epidemiology, and management. *J Gastroenterol Hepatol* 2018; **33**: 99-110 [PMID: 28901578 DOI: 10.1111/jgh.13987]

4 **Canavan C**, West J, Card T. Review article: the economic impact of the irritable bowel syndrome. *Aliment Pharmacol Ther* 2014; **40**: 1023-1034 [PMID: 25199904 DOI: 10.1111/apt.12938]

5 **Tack J**, Stanghellini V, Mearin F, Yiannakou Y, Layer P, Coffin B, Simren M, Mackinnon J, Wiseman G, Marciniak A; IBIS-C Study group. Economic burden of moderate to severe irritable bowel syndrome with constipation in six European countries. *BMC Gastroenterol* 2019; **19**: 69 [PMID: 31064345 DOI: 10.1186/s12876-019-0985-1]

6 **Hammer J**, Eslick GD, Howell SC, Altiparmak E, Talley NJ. Diagnostic yield of alarm features in irritable bowel syndrome and functional dyspepsia. *Gut* 2004; **53**: 666-672 [PMID: 15082584 DOI: 10.1136/gut.2003.021857]

7 **Chey WD**, Nojkov B, Rubenstein JH, Dobhan RR, Greenson JK, Cash BD. The yield of colonoscopy in patients with non-constipated irritable bowel syndrome: results from a prospective, controlled US trial. *Am J Gastroenterol* 2010; **105**: 859-865 [PMID: 20179696 DOI: 10.1038/ajg.2010.55]

8 **Ford AC**, Lacy BE, Talley NJ. Irritable Bowel Syndrome. *N Engl J Med* 2017; **376**: 2566-2578 [PMID: 28657875 DOI: 10.1056/NEJMra1607547]

9 **Study Group of Functional Gastrointestinal Disorders**; Study Group of Gastrointestinal Motility, Chinese Society of Gastroenterology; Chinese Medical Association. Chinese expert consensus of irritable bowel syndrome in 2020. *Zhonghua Xiaohua Zazhi* 2020; **40**: 803-818 [DOI: 10.3760/cma.j.cn311367-20201116-00660]

10 **Gwee KA**, Gonlachanvit S, Ghoshal UC, Chua ASB, Miwa H, Wu J, Bak YT, Lee OY, Lu CL, Park H, Chen M, Syam AF, Abraham P, Sollano J, Chang CS, Suzuki H, Fang X, Fukudo S, Choi MG, Hou X, Hongo M. Second Asian Consensus on Irritable Bowel Syndrome. *J Neurogastroenterol Motil* 2019; **25**: 343-362 [PMID: 31327218 DOI: 10.5056/jnm19041]

11 **Vanner SJ**, Depew WT, Paterson WG, DaCosta LR, Groll AG, Simon JB, Djurfeldt M. Predictive value of the Rome criteria for diagnosing the irritable bowel syndrome. *Am J Gastroenterol* 1999; **94**: 2912-2917 [PMID: 10520844 DOI: 10.1111/j.1572-0241.1999.01437.x]

12 **Whitehead WE**, Palsson OS, Feld AD, Levy RL, VON Korff M, Turner MJ, Drossman DA. Utility of red flag symptom exclusions in the diagnosis of irritable bowel syndrome. *Aliment Pharmacol Ther* 2006; **24**: 137-146 [PMID: 16803612 DOI: 10.1111/j.1365-2036.2006.02956.x]

13 **Black TP**, Manolakis CS, Di Palma JA. "Red flag" evaluation yield in irritable bowel syndrome. *J Gastrointestin Liver Dis* 2012; **21**: 153-156 [PMID: 22720303]

14 **Quigley EM**, Fried M, Gwee KA, Khalif I, Hungin AP, Lindberg G, Abbas Z, Fernandez LB, Bhatia SJ, Schmulson M, Olano C, LeMair A; Review Team:. World Gastroenterology Organisation Global Guidelines Irritable Bowel Syndrome: A Global Perspective Update September 2015. *J Clin Gastroenterol* 2016; **50**: 704-713 [PMID: 27623513 DOI: 10.1097/MCG.0000000000000653]

15 **Patel P**, Bercik P, Morgan DG, Bolino C, Pintos-Sanchez MI, Moayyedi P, Ford AC. Prevalence of organic disease at colonoscopy in patients with symptoms compatible with irritable bowel syndrome: cross-sectional survey. *Scand J Gastroenterol* 2015; **50**: 816-823 [PMID: 25636675 DOI: 10.3109/00365521.2015.1007079]

16 **Gu HX**, Zhang YL, Zhi FC, Jiang B, Huang Y. Organic colonic lesions in 3,332 patients with suspected irritable bowel syndrome and lacking warning signs, a retrospective case--control study. *Int J Colorectal Dis* 2011; **26**: 935-940 [PMID: 21374060 DOI: 10.1007/s00384-011-1163-2]

17 **Li XB**, Liu WZ, Ge ZZ, Xiao SD. Clinical value of warning symptoms and signs in the diagnosis of gastrointestinal diseases. *Chin J Gastroenterol* 2005; **10**: 198-202

18 **Zhong XF**, Gan AH, Huang RX, Xu AG, Liu YH, Yu ZG. Predictive value of gastrointestinal warning symptoms in the diagnosis of intestinal diseases. *Linchuang Yixue Gongcheng* 2017; **24**: 33-34 [DOI: 10.3969/j.issn.1674-4659.2017.01.0033]

19 **Shi Y**, Yang D, Chen S, Wang S, Li H, Ying J, Zhang M, Li Y, Xing Z, Sun J. Factors influencing patient delay in individuals with haemorrhoids: A study based on theory of planned behavior and common sense model. *J Adv Nurs* 2019; **75**: 1018-1028 [PMID: 30375030 DOI: 10.1111/jan.13900]

20 **Lee V**, Guthrie E, Robinson A, Kennedy A, Tomenson B, Rogers A, Thompson D. Functional bowel disorders in primary care: factors associated with health-related quality of life and doctor consultation. *J Psychosom Res* 2008; **64**: 129-138 [PMID: 18222126 DOI: 10.1016/j.jpsychores.2007.09.004]

21 **Ishihara S**, Yashima K, Kushiyama Y, Izumi A, Kawashima K, Fujishiro H, Kojo H, Komazawa Y, Hamamoto T, Yamamoto T, Sasaki Y, Shimizu T, Okamoto E, Yoshimura T, Furuta K, Noguchi N, Tanaka H, Murawaki Y, Kinoshita Y. Prevalence of organic colonic lesions in patients meeting Rome III criteria for diagnosis of IBS: a prospective multi-center study utilizing colonoscopy. *J Gastroenterol* 2012; **47**: 1084-1090 [PMID: 22460220 DOI: 10.1007/s00535-012-0573-4]

22 **Akhtar AJ**, Shaheen MA, Zha J. Organic colonic lesions in patients with irritable bowel syndrome (IBS). *Med Sci Monit* 2006; **12**: CR363-CR367 [PMID: 16940928]

23 **Begtrup LM**, Engsbro AL, Kjeldsen J, Larsen PV, Schaffalitzky de Muckadell O, Bytzer P, Jarbøl DE. A positive diagnostic strategy is noninferior to a strategy of exclusion for patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol* 2013; **11**: 956-62.e1 [PMID: 23357491 DOI: 10.1016/j.cgh.2012.12.038]

24 **Yao X**, Yang YS, Cui LH, Sun G, Peng LH, Wang WF, Hyder Q, Zhang XL. The overlap of upper functional gastrointestinal disorders with irritable bowel syndrome in Chinese outpatients: A multicenter study. *J Gastroenterol Hepatol* 2016; **31**: 1584-1593 [PMID: 26875585 DOI: 10.1111/jgh.13317]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com

© 2022 Baishideng Publishing Group Inc. All rights reserved.