Functional Bowel Disease

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KEYWORDS

• Functional gastrointestinal disorders • Functional bowel disorders
• Irritable bowel syndrome

KEY POINTS

- Irritable bowel syndrome (IBS) is a common functional bowel disorder that affects individuals regardless of age and gender and can result in impaired quality of life and significant health care resource utilization.
- The diagnosis of IBS is based on clinical symptoms using the Rome IV criteria; laboratory or radiographic abnormalities suggest an alternate diagnosis.
- IBS is categorized into 4 subtypes based on the predominant bowel habit: constipation, diarrhea, mixed, or unclassified.
- The treatment of IBS is individually tailored based on subtype, predominant symptoms, symptom severity, age, and comorbidities.
- Therapeutic options for IBS include dietary and lifestyle modifications, pharmacotherapy that alter gut function, neuromodulators, and psychotherapy.

INTRODUCTION

Functional gastrointestinal disorders (FGIDs), also referred to as disorders of gut-brain interaction, are among the most commonly encountered diagnoses in gastroenterology.[1] Although these disorders can affect individuals regardless of age, gender, and race, they are more commonly diagnosed in women and at age 50 years or younger.[1–3] The symptoms range in severity and can result in impaired quality of life, absenteeism, and significant health care resource utilization.[4–6]

FGIDs exist in a separate clinical domain from organic or motility disorders and relate to an "illness experience."[1] The biopsychosocial conceptual model has been used to explain the gut-brain relationship in FGIDs, in which physiologic symptoms result from the connection between the central and enteric nervous systems.[1] Proposed alterations in the function and communication of the 2 nervous systems that result in the patient's symptom presentation include motility disturbance, visceral hypersensitivity, altered mucosal and immune function, altered gut microbiota, and/or altered central nervous system processing.[1]

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The Rome IV (2016) is the current diagnostic standard for FGIDs.[1] It categorizes the disorders based on anatomic region and symptoms. It identifies 6 functional bowel disorders with symptoms attributable to the small and large intestine: irritable bowel syndrome (IBS), functional constipation, functional diarrhea, functional abdominal bloating/distention, unspecified functional bowel disorder, and opioid-induced constipation.[7,8] This article provides a framework for managing a patient with IBS, the most common of the functional bowel disorders, with special consideration to the management of the geriatric patient in whom IBS is suspected.

EPIDEMIOLOGY

The prevalence of IBS in the United States ranges between 8% and 17%.[9,10] A limited number of population studies have compared prevalence based on age, but most found that rate of IBS decreased with increased age without statistical significance.[2] Nonetheless, IBS was prevalent in up to 7.3% of individuals older than 60 years.[2]

Associated Conditions

Patients with IBS can be diagnosed with additional FGIDs, most commonly functional dyspepsia.[11] Significantly higher levels of anxiety and depression have been found in patients with IBS compared with healthy controls.[12,13] Associated extraintestinal conditions include fibromyalgia, chronic fatigue syndrome, chronic pelvic pain, and sleep disturbances.[13]

DEFINITION

The Rome IV diagnostic criteria for IBS is the presence of recurrent abdominal pain, on average, at least 1 day per week in the last 3 months, associated with 2 or more of the following criteria:

- Related to defecation
- Associated with a change in frequency of stool
- Associated with a change in form (appearance) of stool

Criteria must be fulfilled for the previous 3 months with symptom onset at least 6 months before diagnosis.[1]

Classification

IBS can be categorized into 4 subtypes based on the predominant bowel habit, using the Bristol Stool Form Scale (**Fig. 1**).[14] The scale, which has been validated for use in adults, ranges from 1 to 7 based on stool consistency: 1 and 2 correspond to hardened stools that may be difficult to pass (constipation), 3 to 5 correspond to normal consistency, and 6 to 7 to softer consistencies (diarrhea).[15] The current threshold for the predominant bowel type is 25% of bowel movements.

- IBS with constipation (IBS-C): greater than 25% of bowel movements are type 1 or 2 and less than 25% are type 6 or 7.
- IBS with diarrhea (IBS-D): greater than 25% of bowel movements are type 6 or 7 and less than 25% are type 1 or 2.
- IBS with mixed symptoms (IBS-M): greater than 25% of bowel movements are type 1 or 2 and greater than 25% are type 6 or 7.
- Unclassified IBS (IBS-U): meets the criteria for IBS as mentioned earlier, but the bowel habits are not accurately described by any of the aforementioned subtypes.

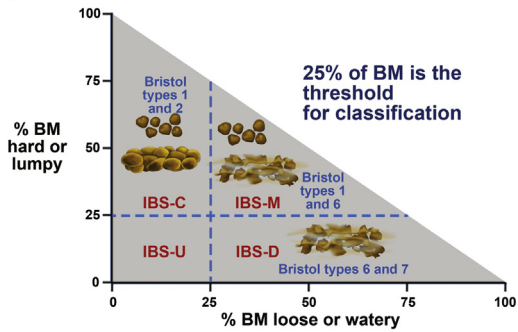

Fig. 1. IBS subtypes using 25% of bowel movement consistency for classification. (*From* Mearin F, Lacy BE, Chang L, et al. Bowel disorders. Gastroenterology 2016;150(6):1396; with permission.)

It is important to recognize that IBS subtype assigned to an individual patient may change over time.

Symptom Severity

In addition to classification by stool morphology, IBS can be categorized based on severity of symptoms into mild, moderate, and severe disease.[1] The severity is determined by psychosocial difficulties, number of additional symptoms, health care use, and activity or work restriction.[1] More severe symptoms tend to occur in women compared with men and in younger patients compared with elderly.[1] As detailed later in the Management section, severity can be used to guide treatment.

POSTINFECTIOUS IRRITABLE BOWEL SYNDROME

Postinfectious IBS (PI-IBS) refers to the development of new IBS symptoms after an acute gastrointestinal illness in a patient who did not previously meet criteria for IBS.[16,17] The incidence of PI-IBS ranges from 3.7% to 36%.[17] Proposed mechanisms to explain the pathophysiology of PI-IBS include mucosal injury and inflammation, mast cell hyperplasia, changes in enteric neuromodulation, and changes in the gut microbiome.[16,17] It tends to occur more frequently following bacterial infections associated with mucosal ulceration, for example, *Campylobacter jejuni* and *Escherichia coli* O157:H7.[17,18] Additional risk factors for developing PI-IBS include prolonged duration of initial illness, female gender, age younger than 60 years, and psychological stressors such as anxiety, depression, or an adverse life event preceding illness.[17,19,20] Management is similar to the treatment of IBS as detailed later. Most patients can expect their symptoms to gradually improve over time, whereas others will continue to experience persistent symptoms for years after diagnosis.[21]

DIAGNOSIS

Clinical Evaluation

A thorough history of a patient's presenting symptoms is integral to the diagnosis of IBS (**Table 1**). The goal is to understand the characteristics of the patient's abdominal pain and bowel habits, at baseline and when symptoms are active. The presence of alarm signs and symptoms should be part of the history, as their absence supports a diagnosis of IBS.[3,22]

Table 1
Evaluation of a patient with suspected irritable bowel syndrome

A Guided Approach to Interviewing the Patient with Suspected IBS
- Describe bowel habits (eg, frequency, consistency of stool, duration of bowel movements, degree of evacuation)
- Is abdominal pain associated with a change in bowel habits? If so, describe the pain
- How often do these symptoms occur?
- When did the symptoms start?
- Is there a previous diagnosis of IBS? If so, are these symptoms similar or different?
- Are there any associated symptoms (gastrointestinal and extraintestinal)?
- Are there any triggers or patterns to shift (eg, medications, foods, travel, mood)?
- List of current medications
- Was there a recent infection?
- Is there a family history of gastrointestinal disorders or diseases?

Alarm Signs and Symptoms*
- Onset of symptoms after 50 years or age
- Unintentional weight loss
- Family history of gastrointestinal malignancy in first-degree relative
- Gastrointestinal bleeding
- Iron-deficiency anemia
- Progressively worsening symptoms
- Nocturnal diarrhea

*The presence of any of these symptoms should warrant further evaluation.

Diagnostic Testing
- All patients should receive standard laboratory evaluation including complete blood count, basic metabolic panel, liver function testing, and age-appropriate colorectal cancer and gynecologic cancer screening. Additional testing can be tailored based on specific IBS subtype suspected

IBS-Constipation	IBS-Diarrhea/IBS-Mixed
• Thyroid function testing	• C-reactive protein
• Stool guaiac	• Thyroid function testing
• Colonoscopy	• Inflammatory markers (ESR, CRP)
• Motility testing	• Celiac serologies
• Anorectal manometry	• Fecal calprotectin or lactoferrin
	• Stool culture, ova and parasites
	• Breath Tests
	• Stool guaiac
	• Colonoscopy with biopsy

Data from Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: a clinical review. JAMA. 2015;313(9):949–58; and Moayyedi P, Mearin F, Azpiroz F, et al. Irritable bowel syndrome diagnosis and management: A simplified algorithm for clinical practice. United European Gastroenterol J. 2017;5(6):773–88.

Physical Examination

The physical examination in patients with IBS is often unremarkable, although patients may report nonspecific tenderness on abdominal examination.[7] The presence of significant physical examination findings suggests alternative cause of the patient's symptoms.[8]

Laboratory Evaluation

The diagnosis of IBS is not made based on the presence of biomarkers. The decision to check certain laboratories and stool tests should be based on the predominant bowel pattern the patient reports at the time of evaluation and suspicion for alternative causes (see **Table 1**).[3,8,22] The presence of laboratory abnormalities in a patient with symptoms that suggest IBS should warrant further evaluation.

Imaging/Procedures

No radiographic abnormalities should be identified in a patient with IBS. Luminal evaluation (upper endoscopy, flexible sigmoidoscopy, colonoscopy) may be performed in selected cases.[8] Indications include age-appropriate screening, alarming signs or symptoms, positive family history of colorectal cancer or inflammatory bowel disease, and/or persistent diarrhea despite empirical treatment of IBS-D.[3,8,22] If a colonoscopy is pursued for evaluation of diarrhea, random biopsies should be taken to evaluate for microscopic colitis.[23] Testing for other suspected diagnoses, for example, hydrogen or urea breath test, can be considered based on clinical suspicion.[8]

Differential Diagnosis

The differential diagnosis for IBS includes organic causes (infection, inflammatory, autoimmune, structural, and malignancies) as well as motility disorders. Inflammatory bowel disease, celiac disease, lactose and fructose intolerances, microscopic colitis, and laxative abuse are examples of causes that can mimic IBS.[3,22] It is possible to have an overlap of both IBS and organic or motility disorders, and clinical judgment must be used to determine if further evaluation is warranted.

MANAGEMENT

The treatment of IBS is tailored on an individual basis based on IBS-subtype, predominant symptoms (eg, diarrhea, constipation, abdominal pain), symptom severity, age, and comorbidities. Therapeutic options range from dietary and lifestyle modifications, to over-the-counter and prescription pharmacotherapy to alter gut function, to neuromodulators and psychotherapy.[6,22] These agents target the proposed pathophysiology, including visceral hypersensitivity, motility, secretion, and the microbiome.[1]

When symptom severity is used as a framework for treatment, patients with mild symptoms can often be managed with diet, medication modifications, and over-the-counter options. As the symptoms progress from mild to moderate, additional prescription therapies can be used including neuromodulators. Patients with severe symptoms require the most intensive care and benefit from a multidisciplinary approach, including a psychiatrist. Psychotherapy that focuses on the brain-gut interaction (eg, cognitive behavioral therapy, hypnotherapy, mindfulness) can be beneficial at any symptom level but most often is introduced at the moderate level.[24]

The treatment options are divided into IBS-C and IBS-D. Because of their mixed bowel pattern, patients with IBS-M especially require a personalized approach and can include recommendations from both categories.

Management of Irritable Bowel Syndrome with Constipation

The initial management of IBS-C should begin with soluble fiber supplementation and over-the-counter laxatives. It is important to discuss and monitor adverse symptoms, including the potential to exacerbate bloating, flatulence, and abdominal discomfort.[3,12] Fiber may not be a good first-line option for a patient with IBS who reports bloating as a predominant symptom. Osmotic laxatives (polyethylene glycol and magnesium) have been shown to offer patients relief with their constipation but do not significantly affect abdominal pain and/or bloating.[25] Stimulant laxatives such as senna and bisacodyl are also available over the counter for constipation, but they can worsen abdominal cramping.

The next step in management of constipation in IBS-C includes Food and Drug Administration–approved pharmacologic options: prosecretory agents (intestinal secretagogues) and prokinetics (serotonin agonists).

- The prosecretory class includes *lubiprostone, linaclotide, and plecanatide.* These agents increase water secretion into the lumen of the colon to facilitate a decrease in colon transit time.[12] Lubiprostone activates secretion via chloride channels, whereas linaclotide and plecanatide work via stimulation of guanylate cyclase-C.[12,26] In addition to its effects on transit, linaclotide has been shown to improve abdominal pain by its effect on cyclic guanosine monophosphate.[12,27] The main adverse effect of lubiprostone is nausea, whereas diarrhea is the main side effect of linaclotide and plecanatide.
- The prokinetic class includes *prucalopride* and *tegaserod.* These agents activate serotonin 5-HT4 receptors in the gastrointestinal tract and increase colonic transit time.[12,28] Frequent adverse reactions include headache and abdominal pain.[12,28,29] Prucalopride requires altered dosing for renal impairment, and it is important to assess renal function in a geriatric patient before initiation.[28] It is also important to note that tegaserod is only approved for use in female patients younger than 65 years with low risk for cardiovascular ischemia,[29] but prucalopride has no similar restrictions.

Management of Irritable Bowel Syndrome with Diarrhea

The initial management of IBS-D should start with fiber, dietary modification, and over-the-counter antimotility agents such as loperamide. Similar to IBS-C, patients with mild IBS-D can benefit from water-soluble fiber as a bulking agent.[12,30] Loperamide is an μ-opioid receptor agonist that increases colonic transit time and decreases fluid secretion.[31] Although loperamide can improve diarrhea, it may not relieve abdominal pain and bloating.[31] It is important to counsel patients on appropriate use of this medication and set their expectations for symptomatic relief.

The next step in management of diarrhea in IBS-D is pharmaceutical options that include rifaximin, antimotility agents, and bile acid sequestrants.

- *Rifaximin* is a nonsystemic antibiotic whose mechanism of action in IBS-D is not fully understood, but proposed mechanisms include direct antibiotic effects, modulation of host inflammatory response, and modification of gut microbiota and gut motility.[32,33] Studies demonstrate rifaximin can offer short-term symptomatic relief for IBS-D,[34] and it is important to educate the patient on the expected duration of its effects. Patients can be considered for repeat treatment if symptoms recur.[35] It is safe and well tolerated, with no restrictions for use in elderly population.
- The antimotility agents are *eluxadoline* and *alosetron.* Eluxadoline is a mixed μ-opioid and κ-opioid receptor agonist and δ-opioid receptor antagonist in the enteric nervous system.[36] The mechanism of action is complex but includes decreased gastrointestinal motility and secretion and analgesic effects.[36] The most common side effects are nausea, constipation, or abdominal pain.[36] Because of reports of pancreatitis, eluxadoline is contraindicated in patients who had a cholecystectomy, have biliary disease (eg, sphincter of Oddi dysfunction), history of pancreatitis, chronic liver disease, and heavy alcohol use.[12] Alosetron is a selective 5-HT3 antagonist that also results in decreased colonic transit and reduced gastrointestinal secretion.[37,38] A low dose is currently approved only for women with severe IBS-D who have not had a response to conventional therapy.[37] It was previously approved at a higher dose for men and women but was withdrawn due to concerns for ischemic colitis and severe constipation.[39] There is no dose adjustment for age; however, elderly patients may be at greater risk for these complications.[39]

- Bile acid sequestrants include *cholestyramine*, *colestipol*, and *colesevelam.* It has been proposed that bile acid malabsorption may occur in a subset of patients with IBS-D.[22,40] Testing is currently limited in the United States; however, it is a treatment option to consider if other modalities have been unsuccessful.[8,41]

Management of Global Irritable Bowel Syndrome Symptoms

The following treatments can be used for all IBS subtypes to target global symptomatology, including abdominal pain, bloating, and flatulence.

- Antispasmodics refer to a group of medications that act as smooth muscle relaxants and can be used to address IBS symptoms.[12,42] In studies, they have been shown to improve stool consistency, stool frequency, and abdominal cramping. Anticholinergics (such as hyoscyamine or dicyclomine) are included in this category. Although generally well tolerated, these agents should be used with caution in elderly patients given their side-effect profiles.
- Peppermint oil, specifically its' L-menthol component, is safe and effective for the relief of abdominal pain and global IBS symptoms compared with placebo.[43] The proposed mechanism of action is antagonism of calcium channel receptors in smooth muscle cells, but it may also have antimicrobial, immunomodulation, and anesthetic properties.[43,44] It can improve pain, bloating, pain with evacuation, and urgency but does not affect bowel habits.[44]
- Probiotics are commonly used by patients with IBS. Multiple studies have had varying results on its efficacy, but probiotics may improve global symptoms, bloating, and flatulence.[12]
- Neuromodulators for use in IBS include tricyclic antidepressants (TCAs), serotonin and norepinephrine reuptake inhibitors (SNRIs), and selective serotonin reuptake inhibitors (SSRIs).[8,45] The decision to use a particular agent is based on IBS subtype and predominant symptoms. TCAs should be considered the first line for treating pain in patients with IBS and IBS-D, whereas SSRIs are favored for IBS-C. SNRIs can be used for both IBS-D and IBS-C.[45]
  - TCAs (*amitriptyline, imipramine, desipramine, nortriptyline)* inhibit the reuptake of serotonin and norepinephrine, which leads to slowed gastrointestinal transit that is advantageous in IBS-D.[45] Their use in the geriatric population is limited by their anticholinergic, antihistamine, and anti-alpha-adrenergic effects. In addition, TCAs are associated with an increased risk of arrhythmias and should be avoided in patients with prolonged QT intervals or bundle branch blocks.[45]
  - SSRIs (*fluoxetine, sertraline, citalopram, and escitalopram)* increase gut motility via their effect on serotonin release in the gastrointestinal tract and can be particularly useful in patients with IBS with anxiety.[45] Their use can be limited by their adverse side effect profile including nausea, insomnia, and sexual dysfunction and the length of time that is required before they have an effect.[3]
  - SNRIs (*duloxetine, venlafaxine*) share similar side-effect profiles with both SSRIs and TCAs; however, they cause less constipation compared with TCAs, thus are an option for patients with pain-predominant IBS-C.

Dietary Modification

Patients with IBS often note their symptoms are sensitive to food and many restrict their diet to modify their symptoms.[3,46] Dietary changes have been shown to provide relief in IBS symptoms, particularly in IBS-D/M, including the low FODMAP (fermentable oligo-di-monosaccharides and polyols) diet.[47,48] FODMAPs are short-chain

carbohydrates commonly found in foods that are poorly absorbed in the gastrointestinal tract.[47] Their impaired digestion can cause abdominal pain, bloating, and alterations in bowel habits.[46] Although the low FODMAP diet (in which foods are restricted, reintroduced, and then personalized to avoid trigger foods) has been shown to effectively reduce symptoms in some patients with IBS, the quality of the evidence remains mixed and the approach may not be sustainable as a long-term therapeutic option.[12,48,49] Patients may benefit from working with a trained dietitian/nutritionist to find individualized dietary modifications based on food-symptom association.[46]

DISCUSSION

IBS is a common functional bowel disorder that requires a strong physician-patient relationship to manage given the complexity of its pathophysiology. It can be particularly challenging to diagnose and manage IBS in the geriatric population, who often have multiple comorbidities, atypical symptom presentations, and higher suspicion to rule out organic pathologies. Multiple targets across the brain-gut interaction are available to address IBS, based on the subtype, predominant symptoms, and severity of symptoms. It is recommended that management start with dietary and lifestyle modifications and over-the-counter modalities before initiation of specialty pharmacotherapy that alter gut function. In a geriatric patient, close attention must be paid to the adverse effects and drug-drug interactions of prescription medication.

CLINICS CARE POINTS

- The diagnosis of IBS is made using the Rome IV diagnostic criteria and is categorized into four subtypes based on the predominant bowel habit.
- Evaluation for the patient with suspected IBS should include a thorough history. Testing (such as labs, breath tests, imaging, endoscopy/colonoscopy) can be obtained to rule out organic etiologies of symptoms based upon history and degree of suspicion for alternate diagnoses.
- The treatment of IBS is tailored on an individual basis based on disease subtype and predominant symptom(s), and includes lifestyle modifications, pharmacotherapy to alter gut function, and psychotherapy.

DISCLOSURE

The authors have nothing to disclose.

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