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Importance of Early Diagnosis in Patients with Irritable Bowel Syndrome

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Abstract: Patients with irritable bowel syndrome (IBS) account for > $20 billion in direct and indirect costs annually, a large portion of which relates to making the diagnosis. The diagnosis of IBS is challenging because symptoms can vary between patients and overlap with those of other disorders. This review examines the current diagnostic approach in IBS and discusses new tools that may improve diagnostic confidence earlier in the process. The prevalence of organic disease among patients who meet symptom-based criteria for IBS (eg, Rome III) is generally low; therefore, in the absence of "alarm features," the probability for organic disease is very low. Increased public awareness of IBS symptoms and physician awareness of symptom-based criteria for IBS are needed to facilitate earlier diagnosis. Accumulating evidence suggests that fecal and/or serum biomarkers may be helpful in differentiating IBS from non-IBS disorders. These tools may help minimize unnecessary testing and diagnostic delays. As biomarkers are further studied and developed, they are likely to become an integral part of the diagnosis of IBS and reduce the potential for incorrect diagnosis and treatment delays.

Keywords: irritable bowel syndrome; functional gastrointestinal disorders; biomarkers; diagnostic tests; quality of life; early diagnosis

Introduction

Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by chronically recurring abdominal pain or discomfort associated with a change in bowel habit.[1] A highly prevalent disorder, IBS affects an estimated 10% to 15% of the US population (ie, 30–45 million adults).[2] The disorder is diagnosed more commonly in patients aged < 50 years[2–4] and approximately twice as often in women than in men.[2] The clinical presentation of IBS is variable, with a range of predominant symptoms that may include abdominal pain or discomfort, bloating, urgency, constipation, and/or diarrhea.[5] The clinical course of IBS tends to be dynamic; most patients experience intermittent, mild-to-moderate symptoms that wax and wane, and most move between subtypes (with predominant constipation, diarrhea [IBS-D], or alternating patterns of both) over time.[5–8]

A number of pathophysiologic pathways have been identified in patients with IBS. In addition to the well-recognized alterations in gut motility,[9,10] visceral hypersensitivity,[11] and brain-gut dysregulation, increasing evidence points to a role for immune dysregulation in the gastrointestinal (GI) tract,[10,12] altered gut microbiota,[3,13–15] and complex interactions between neuronal and hormonal factors.[16]

Although only a minority of patients with IBS seek medical care for their symptoms,[17] they consume a disproportionately high amount of health care resources. More than $20 billion in annual direct and indirect costs have been attributed to IBS.[18,19] Direct costs result from an estimated 3.6 million annual physician visits for symptoms of IBS.[18] Further contributing to direct costs are high rates of abdominal

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and pelvic surgeries in IBS patients,[20] with more than one-third of patients who are admitted to surgical services with nonspecific abdominal pain eventually receiving a diagnosis of IBS.[21] Questionnaire data from approximately 89 000 health-maintenance organization members indicate that patients with physician-diagnosed IBS have triple the cholecystectomy rates, double the appendectomy and hysterectomy rates, and 50% higher back surgery rates than those without IBS.[22] This suggests that preoperative diagnostic error is an important reason for these findings.[22] The indirect costs attributed to IBS are also significant, with losses in work productivity among employees with the disorder estimated to be as high as 21% per week.[23] The US Householder survey examined illness-related work and school absenteeism over the preceding year among patients with functional GI symptoms and those with no bowel symptoms.[24] Respondents with IBS symptoms had almost 3 times more absences (13.4 vs 4.9 days; $P < 0.0001$), and 11.3% of patients with IBS, but only 4.2% of patients with no bowel symptoms, reported that they had been too sick to work or attend school during the year.[24]

Irritable bowel syndrome is also associated with significant human cost in terms of impaired health-related quality of life (HRQoL). Patients with IBS experience an average of > 200 episodes per year,[25] spend nearly 10 days in a 3-month period in bed due to illness,[26] and report having to restrict their activities an average of 73 days annually.[27] Patients with IBS also may experience social isolation when planned activities do not lend themselves to the easy availability of bathroom facilities. The embarrassing nature of the symptoms, the lack of understanding and empathy from others, and the need for frequent trips to the bathroom may all contribute to social isolation.[28] Studies examining the impact of IBS on HRQoL have demonstrated that IBS patients have similar or worse HRQoL than those with other chronic disorders, such as depression, gastroesophageal reflux disease, diabetes, and organic GI disorders (eg, inflammatory bowel disease [IBD], liver disease, pancreatic/biliary disease).[26,29,30] In one study of the effect of IBS on HRQoL, IBS patients reported worse bodily pain, energy/fatigue, and social functioning than patients with dialysis-dependent end-stage renal disease—a striking observation given the disabling nature of renal disease.[30]

The purpose of this review is to examine how the diagnosis of IBS is currently made and how emerging practices can be leveraged to make a confident diagnosis of IBS in a more timely manner, which may in turn lower the substantial economic burden and human cost of the disorder.

Current Standard of IBS Diagnosis

Irritable bowel syndrome is identified based on clinical symptoms[1] and occurs in the absence of physical, radiologic, or laboratory abnormalities indicative of organic disease.[19] Ideally, little formal testing will be necessary to diagnose patients who fulfill symptom-based criteria (Table 1) and do not have features suggestive of organic disease (ie, alarm features) (Table 2).[3] Although the American College of Gastroenterology (ACG) Task Force on IBS does not recommend routine diagnostic testing (ie, complete blood count, thyroid function studies, serum chemistries, stool evaluation for ova and parasites, and abdominal imaging) in patients with typical IBS symptoms in the absence of alarm features,[3,17,31] such additional tests are often performed to exclude organic disease despite a low diagnostic yield and a low prevalence of organic disease in this patient population.[3,17,19] Moreover, when the diagnosis of IBS is symptom based and does not include alarm features, the likelihood of an incorrect IBS diagnosis is also very low and does not change over time.[32] Despite formal diagnostic criteria[1,33] and published guidelines from the ACG[3] and the American Gastroenterological Association (AGA),[17] establishing a prompt diagnosis of IBS remains a challenging problem for both clinicians and patients owing to several barriers.

Barriers to Achieving Early Diagnosis in IBS

Symptomatology and Comorbidities

The symptoms of IBS are heterogeneous and can be difficult to objectively quantify.[34] The wide variety of symptoms reported by IBS patients may lead to uncertainty during the diagnostic process. Irritable bowl syndrome is often comorbid with other functional GI conditions (eg, chronic constipation, functional dyspepsia, gastroesophageal reflux disease) and other nonfunctional GI disorders (eg, celiac disease, lactose maldigestion),[35,36] which can present with symptoms similar to those of IBS. Celiac disease and lactose intolerance can

Table 1. Rome III IBS Diagnostic Criteria[a]

Recurrent abdominal pain or discomfort[b] 3 d/mo in the last 3 mo associated with ≥ 2 of the following:

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form of stool

[a]Criteria fulfilled for the last 3 mo with symptom onset at least 6 mo prior to diagnosis; [b]Discomfort is defined as an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, it is a pain/discomfort occurring ≥ 2 d/wk during screening evaluation for subject eligibility.

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Table 2. Alarm Features for Organic Disease in Patients Being Evaluated for IBS

Age > 50 years
Unexplained weight loss
Iron-deficiency anemia
Rectal bleeding
Nocturnal symptoms/pain
Family history of:
Colorectal cancer
Celiac sprue
Inflammatory bowel disease

Abbreviation: IBS, irritable bowel syndrome.

be identified using simple tests.[37,38] The prevalence of celiac sprue in the IBS population is higher than in the general population (3.6% vs 0.7%).[39] As a result, the ACG Task Force on IBS recommends that patients with suspected IBS, particularly mixed and diarrhea-predominant subtypes, undergo serological screening for celiac sprue.[3] The role of lactose maldigestion and small bowel bacterial overgrowth in IBS is still not well defined.

Testing for lactose maldigestion or using breath testing for small bowel bacterial overgrowth can be performed based on the clinical presentation, but routine use of these tests in IBS is not currently recommended. Routine colonic imaging is not recommended in patients aged < 50 years who have typical IBS symptoms and no alarm features. Colonoscopy should be performed in IBS patients with alarm features to rule out organic diseases and in those aged > 50 years for the purpose of colorectal cancer screening. When colonoscopy is performed in patients with IBS-D, obtaining random biopsies should be considered to rule out microscopic colitis. Somatic comorbidities that occur in IBS patients, including such conditions as fibromyalgia, chronic fatigue syndrome, temporomandibular joint disorder, and chronic pelvic pain, may further complicate the clinical picture.[36,40] In addition, IBS patients frequently have psychological comorbidities, including anxiety, depression, and somatization.[17,36,41] Thus, the differential diagnosis in patients presenting with IBS symptoms is quite broad.[19]

Perception of IBS Diagnosis as a "Diagnosis of Exclusion"

Recent data indicate that identifying the minority of patients with organic disease remains an overriding concern among physicians who manage IBS. In a survey of 472 physicians (gastroenterologists, family practitioners, and internists), most respondents indicated that their primary concern was to exclude organic disease.[42] This focus, in conjunction with medicolegal concerns stemming from misdiagnosis, is thought to contribute to a widely held perception that IBS is a diagnosis of exclusion rather than a primary diagnosis.[3,34] This view is common among patients as well, with many considering IBS to be a "catch-all" diagnosis[43] requiring further testing to rule out more serious disease.[44] Approaching IBS as a diagnosis of exclusion is inherently problematic however, as it may contribute to treatment delays and promote unnecessary and costly diagnostic investigation. Spiegel[34] conducted a national vignette survey among 45 experts in IBS and a group of randomly selected community physicians. When questioned about their beliefs regarding IBS diagnosis, 8% of the IBS experts compared with 72% of the community physicians approached IBS as a diagnosis of exclusion. Those physicians who viewed IBS as a diagnosis of exclusion ordered 1.6 more tests and spent $364 more per patient on tests than those who did not.[34]

Diagnostic Guideline Utility and Application

Another potential barrier to effective IBS diagnosis is the relative lack of practical utility of symptom-based diagnostic criteria in primary care settings.[45,46] Although useful in research settings,[19] symptom-based criteria may be too restrictive when used in routine clinical practice (ie, physician-made diagnosis is more liberal). The most recent symptom-based diagnostic criteria for IBS are the Rome criteria, now in a third iteration (Rome III) after having been revised in 2006 (Table 1).[1,47] Although the original Rome diagnostic criteria were validated,[31] neither the subsequently developed Rome II nor Rome III IBS diagnostic criteria have reached this level of scientific vigor.[3] The diagnostic accuracy of the Rome criteria is enhanced in the absence of alarm features and should reassure the clinician that the diagnosis of IBS is correct.[3]

Alarm features include rectal bleeding, weight loss, iron-deficiency anemia, nocturnal symptoms, age > 50 years at onset, and family history of colorectal cancer, IBD, or celiac disease. Rectal bleeding and nocturnal abdominal pain offer little value in distinguishing patients with IBS from those with organic diseases.[3] Anemia and weight loss show very good specificity for organic disease and, when seen in a patient with IBS symptoms, should prompt further investigation, including colonic imaging.[3] Other alarm symptoms that should prompt investigation in this population include a family history of colorectal cancer, celiac sprue, or IBD.[3] When colonoscopy is performed in patients with IBS-D, obtaining random biopsy samples should be considered

to rule out microscopic colitis. In patients who meet the symptom-based criteria for IBS, the absence of selected alarm features, including anemia, weight loss, and a family history of colorectal cancer, IBD, or celiac sprue, should reassure the clinician that the diagnosis of IBS is correct.

More important than the practical utility of the Rome criteria, the general lack of physician knowledge regarding symptom-based criteria for IBS is a barrier to early and accurate diagnosis. In a 2003 study, 35 US family practitioners were surveyed on 2 occasions, and only 35% indicated that they knew the Manning, Rome I, and Rome II criteria were used for diagnosing IBS.[48] In another study, IBS diagnostic criteria used in the primary care practice setting, as defined by 10 European family practitioners, differed substantially from the established Rome III criteria.[46]

Lack of Physician Confidence

Lack of physician confidence in diagnosing IBS may also contribute to delays in diagnosis. Physicians may feel uncomfortable about diagnosing a functional disorder and feel compelled to coordinate an exhaustive diagnostic workup to reassure "demanding patients" or themselves.[42,49] When the 35 US family physicians were asked to rank IBS among 5 chronic, painful syndromes, they ranked it fourth in diagnostic confidence and tied it with headache for causing the most difficulty in practice strategy decisions.[48] In this study, fewer than half of surveyed physicians were able to identify a group of typical IBS symptoms.[48] In another survey, physicians managing IBS patients felt comfortable diagnosing IBS at the patient's first visit only 40% of the time.[42]

Patient Reluctance to Seek Medical Care

Finally, reluctance of IBS patients to seek medical care may delay diagnosis. Up to 70% of patients with IBS in the US do not seek medical attention,[17,50] which may be related to cultural factors, degree and severity of pain, psychological factors, and access to health care.[17,24,51–57] Patient barriers to seeking medical attention may include the embarrassing nature of symptoms,[28] a tendency for patients to trivialize their symptoms,[51] or a feeling that symptoms may not be viewed seriously by their physicians.[58] Physician attitudes may contribute to patient reluctance in seeking care. Studies have found physicians to have a negative view of IBS patients, with some patients perceiving their physicians as unsympathetic, not wanting to care for them, trivializing their symptoms, and/or labeling them as neurotic.[28,49]

Consequences of Delayed Diagnosis in IBS

Considering the numerous challenges encountered in diagnosing IBS, it is not surprising that the diagnosis is frequently missed or delayed. Indeed, > 40% of patients report experiencing symptoms for at least 5 years before receiving an IBS diagnosis,[25] while others report visiting their physician 5 times or more before a diagnosis is established.[4] Such delays in diagnosis can lead to anxiety, unnecessary testing, and increased costs.[59]

Patients generally find the diagnostic process confusing, and those who are worried about more serious illness are often relieved by receiving an established diagnosis of IBS.[44] Moreover, given the well-recognized negative impact of the disease on patients' HRQoL[26,27,29,30] and the corresponding improvement observed in those responding to therapeutic intervention,[29,60,61] delayed diagnosis and inappropriate therapy likely prolongs patients' pain and suffering. This is especially important in light of the disruptive and embarrassing nature of the symptoms, which can lead to frustration, social isolation,[28] and loss of productivity.

Emerging IBS Biomarkers

The challenges inherent in diagnosing IBS and the potential consequences of delayed diagnosis underscore the need for new and improved diagnostic approaches. Ideally, such approaches would be noninvasive, simple to use, reproducible, transferable between centers, and have a reasonable effect size. Additionally, the test would have sufficient sensitivity and specificity in the detection of IBS and also be cost effective.

Detection of IBS-specific biomarkers will likely reduce the need for further testing[59] and will yield more timely diagnoses. With this goal in mind, attempts to develop biomarkers have targeted multiple pathophysiologic mechanisms: motility/transit time (eg, whole-gut transit scintigraphy), visceral hypersensitivity (eg, rectal barostat), mucosal inflammation (eg, colonic biopsies, fecal proteases), immune markers (eg, increased peripheral cytokines), microbiota (eg, fecal cultures), and genetic factors (eg, serotonin reuptake gene polymorphisms). Most IBS biomarkers have clinical limitations, given that IBS is likely a heterogeneous disorder with different pathophysiologic mechanisms predominating in various IBS subtypes. The most clinically relevant of these emerging diagnostic approaches include measurement of fecal markers,[62–65] examination of stool forms,[59] and analysis of patterns of serum biomarker expression.[16,38]

Fecal Markers

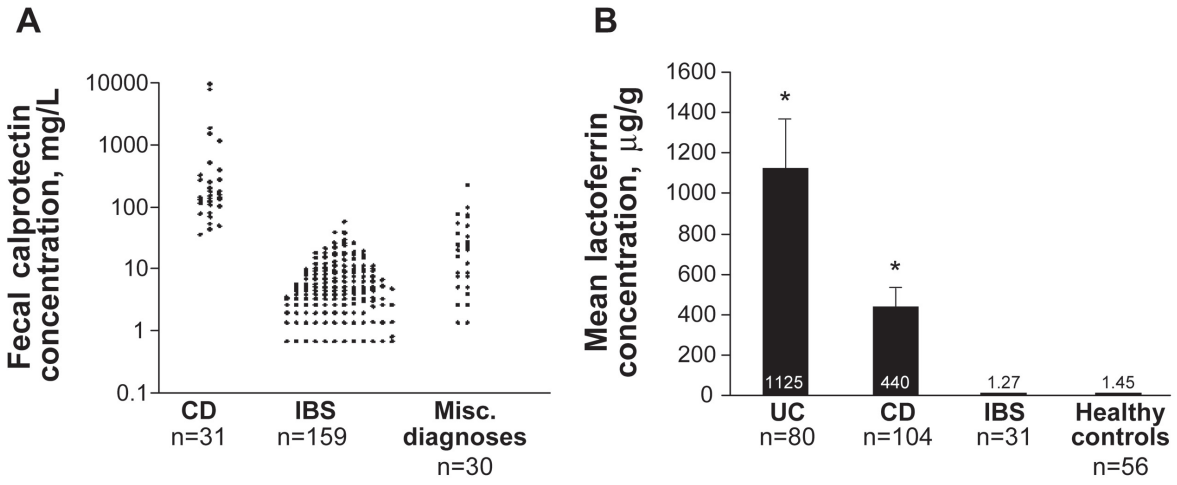
Distinguishing between IBS and IBD, especially IBD that is mild in severity, can be challenging.[38] Several investigators have focused on differentiating the 2 disorders by detection of the active intestinal inflammation found in IBD through measurement of fecal lactoferrin and calprotectin.[38,63–67] Lactoferrin and calprotectin are neutrophil-derived proteins and efficient markers of inflammation. Lactoferrin is an iron-binding protein and a major component of the secondary granules of polymorphonuclear neutrophils, which are key to the acute inflammatory response. Calprotectin is a calcium- and zinc-binding protein released most likely as a result of cell disruption and death.[38,63–67] In a prospective study of patients newly referred to a gastroenterology clinic, fecal calprotectin measurements were significantly higher in patients with Crohn's disease compared with patients with IBS ($P < 0.0001$) (Figure 1A). Overall, fecal calprotectin in this group demonstrated an 89% sensitivity and 79% specificity for organic disease, with an odds ratio for disease of 27.8 (95% confidence interval, 17.6–43.7; $P < 0.0001$).[62] Similarly, fecal lactoferrin measurements were significantly greater among patients with active IBD than patients with IBS ($P < 0.05$) (Figure 1B).[65]

Schoepfer et al[38] prospectively compared the diagnostic efficacy of these fecal markers with that of C-reactive protein (CRP), blood leukocyte panels, and anti-*Saccharomyces cerevisiae* (ASCA) and perinuclear antineutrophil cytoplasmic antibodies (pANCA) in differentiating IBD from IBS in 30 patients with IBS, 64 patients with IBD, and 42 healthy controls.[38] As expected, IBS patients and healthy controls had comparable levels of fecal markers, CRP, blood leukocytes, and ASCA/pANCA profiles, whereas IBD patients had significantly elevated levels of calprotectin and lactoferrin compared with IBS patients and healthy controls ($P < 0.0001$).[38] These markers provide utility in identifying inflammation associated with active IBD and may have use as a surrogate marker for mucosal healing during anti-tumor necrosis factor-α therapy.[65,68] However, current testing for fecal markers is largely relegated to research settings and is not routinely available for use in clinical practice. Other gut inflammatory processes, such as nonsteroidal anti-inflammatory drug enteropathy[69] and microscopic colitis,[70] have been associated with elevations of calprotectin, while both calprotectin and lactoferrin have been found to be elevated in radiation proctitis[71]; thus, elevated fecal marker levels do not provide a definitive diagnosis for the inflammatory process that is ongoing. Although fecal markers have been shown to discriminate IBD from IBS, they were not able to discriminate IBS patients from healthy controls without GI disease.[38] Therefore, a "normal" level of these fecal markers does not "rule in" IBS.

Stool Form Examination

Pimentel et al[59] prospectively evaluated the utility of examining fluctuations in bowel pattern and stool form to distinguish IBS-D from other causes of diarrhea. Ninety-nine patients with diarrhea as their primary symptom completed a questionnaire regarding their bowel habits and stool forms over the previous week. Sixty-two patients met the Rome I criteria and had symptoms consistent with IBS-D, whereas 37

Figure 1. A) Fecal calprotectin concentrations (logarithmic scale) in patients with Crohn's disease (CD), irritable bowel syndrome (IBS), and miscellaneous diagnoses. The upper limit of normal (+2 SD) for calprotectin is 10 mg/L. Reprinted with permission from *Gut*.[67] **B)** Mean fecal lactoferrin concentrations among patient groups. Reprinted with permission from *Am J Gastroenterol*.[65]



*$P < 0.05$ for CD vs IBS and healthy controls and for UC vs IBS and healthy controls.

patients had non-IBS causes of diarrhea (eg, ulcerative colitis [UC], Crohn's disease, celiac disease). Comparisons between patient groups showed more daily variation in stool form and frequency in the preceding week among IBS patients than non-IBS patients (79% vs 35%; $P < 0.00001$).[59] The majority (81%) of IBS patients reported having ≥ 3 stool forms per week compared with those without IBS (41%), translating to a clinical threshold of 3 differing stool forms per week denoting a sensitivity of 68% and specificity of 84% in discriminating IBS from non-IBS.[59] The authors suggested that in distinguishing between IBS and non-IBS diarrheal disease, this simple tool may help prevent the need for unnecessary diagnostic testing in both the research and clinical practice environments.[59] However, because of the small sample size of the study and the potential for patient recall reporting bias, this tool should be validated in large-scale prospective studies in a more heterogeneous patient population before routine use in clinical practice can be recommended.

Serum Biomarkers

Based on the pathophysiologic differences between IBS and non-IBS patients, Lembo et al[16] reported on a panel of 10 serum biomarkers that can be used to distinguish IBS from non-IBS patients. The 10 biomarkers were identified in a multistep process beginning with the identification of pathophysiologic processes in GI disorders. Biomarkers that were common across multiple pathways were identified and narrowed to those that could differentiate IBS from non-IBS. The biomarkers were then further filtered for their presence in serum and measurability by commercially available assays. The biomarkers derived were measured to find those that had significant differences in levels of expression between IBS patients and controls. Ultimately, 16 biomarkers were identified, and all possible combinations of these were used to determine the biomarker set that best differentiated between IBS and non-IBS, with 10 biomarkers finally selected.[16] Six of the biomarkers included in the panel are associated with metabolic pathways that, when dysregulated, contribute to IBS pathophysiology.

Clinical use of the test involves obtaining a serum sample, measuring the levels of the 10 individual biomarkers, and then evaluating the information in a smart diagnostic algorithm (patent pending) that identifies subtle differences in biomarker expression patterns to differentiate IBS patients from those with non-IBS GI disease and from healthy controls. This algorithm was originally created in a study of 1721 samples taken from patients with IBS (n = 876), IBD (n = 398), non-IBS functional GI disorders (n = 155), and celiac disease (n = 57) and from healthy controls (n = 235). Diagnoses of IBS and other functional GI disorders were based on fulfillment of Rome II or Rome III criteria for at least 6 months before entry into the study and no evidence of other causes of disease. Inflammatory bowel disease diagnoses were confirmed either by endoscopy or histopathology.

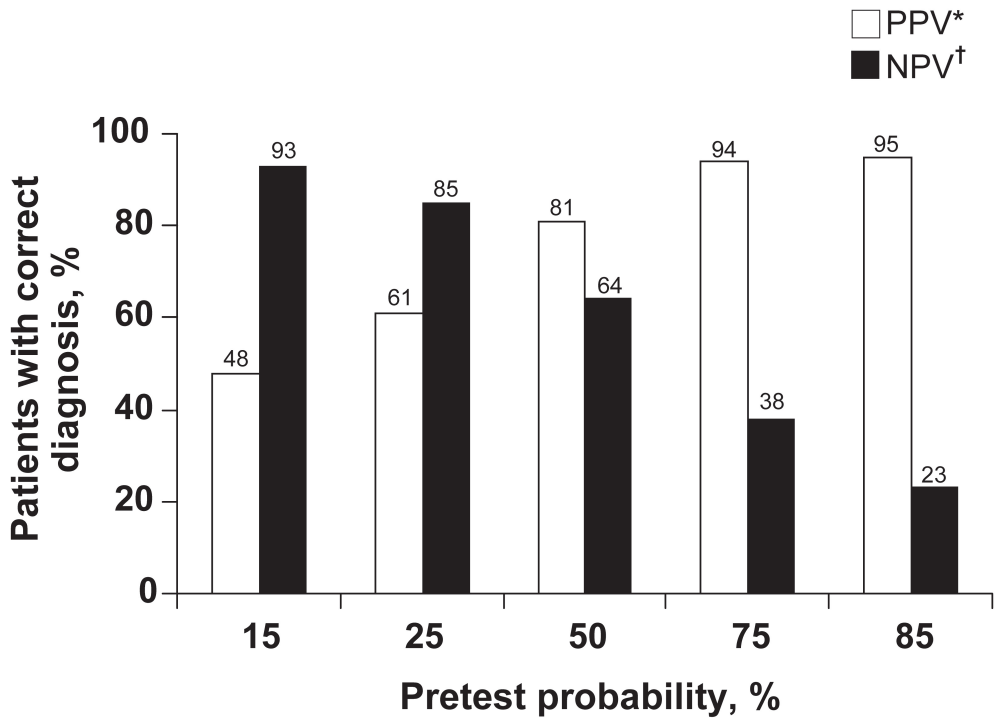
Diagnoses of celiac disease were based on biopsy results. Healthy controls had no history of GI disturbance and no significant GI symptoms. Of the 1721 samples, a training cohort (n = 1205) was used to teach the algorithm to recognize biomarker pattern differences between known IBS and non-IBS samples. A naïve validation cohort (n = 516) was then used to test the algorithm's ability to differentiate IBS from non-IBS samples after the algorithm training phase. In the validation cohort, the 10-biomarker panel showed an overall diagnostic accuracy of 70%, a sensitivity of 50%, and a specificity of 88% for differentiating IBS from non-IBS.[16]

The authors suggest that early clinical use of this 10-biomarker panel may help avoid more costly invasive procedures and surgeries, as well as reduce delays in treatment. In a patient with a pretest IBS probability of 50%, the positive predictive value (PPV) was found to be 81% and the negative predictive value (NPV) was 64%.[16] The PPV increases with increasing pretest probability (Figure 2). In a patient with a high pretest probability for IBS (eg, 75%), the IBS diagnostic test has a PPV of 94% and an NPV of 38%, indicating that a positive result warrants a high level of confidence and a negative result does not reliably exclude IBS. If the pretest probability of IBS is low (eg, 15%), the PPV is 48% and the NPV is 93%, making a diagnosis of IBS less secure with a positive result, while a negative result suggests the absence of IBS.[16] Like many other tests, the serum biomarker panel is envisioned to be used adjunctively in combination with symptom-based criteria rather than alone, where it may add confidence in and support for making a diagnosis of IBS. Further characterization of the relative diagnostic accuracy and cost-effectiveness of this diagnostic panel versus other diagnostic approaches is needed, as well as validation of its utility when used earlier in the diagnostic work-up of suspected IBS. Improved sensitivity and specificity of this panel is expected as additional IBS-specific biomarkers are discovered.[16]

Early Diagnosis of IBS: Physician and Patient Benefits

The ability to discriminate IBS from organic disease using biomarkers may help reverse the view of IBS as a diagnosis of exclusion and reduce unnecessary, invasive, and costly

Figure 2. Positive predictive value (PPV) and negative predictive value (NPV) of serum biomarkers based on pretest probability of IBS.[16]



*PPV, proportion of patients with positive test results who were diagnosed correctly. †NPV, proportion of patients with negative test results who were diagnosed correctly. Adapted from *Ailment Pharmacol Ther*.[16]

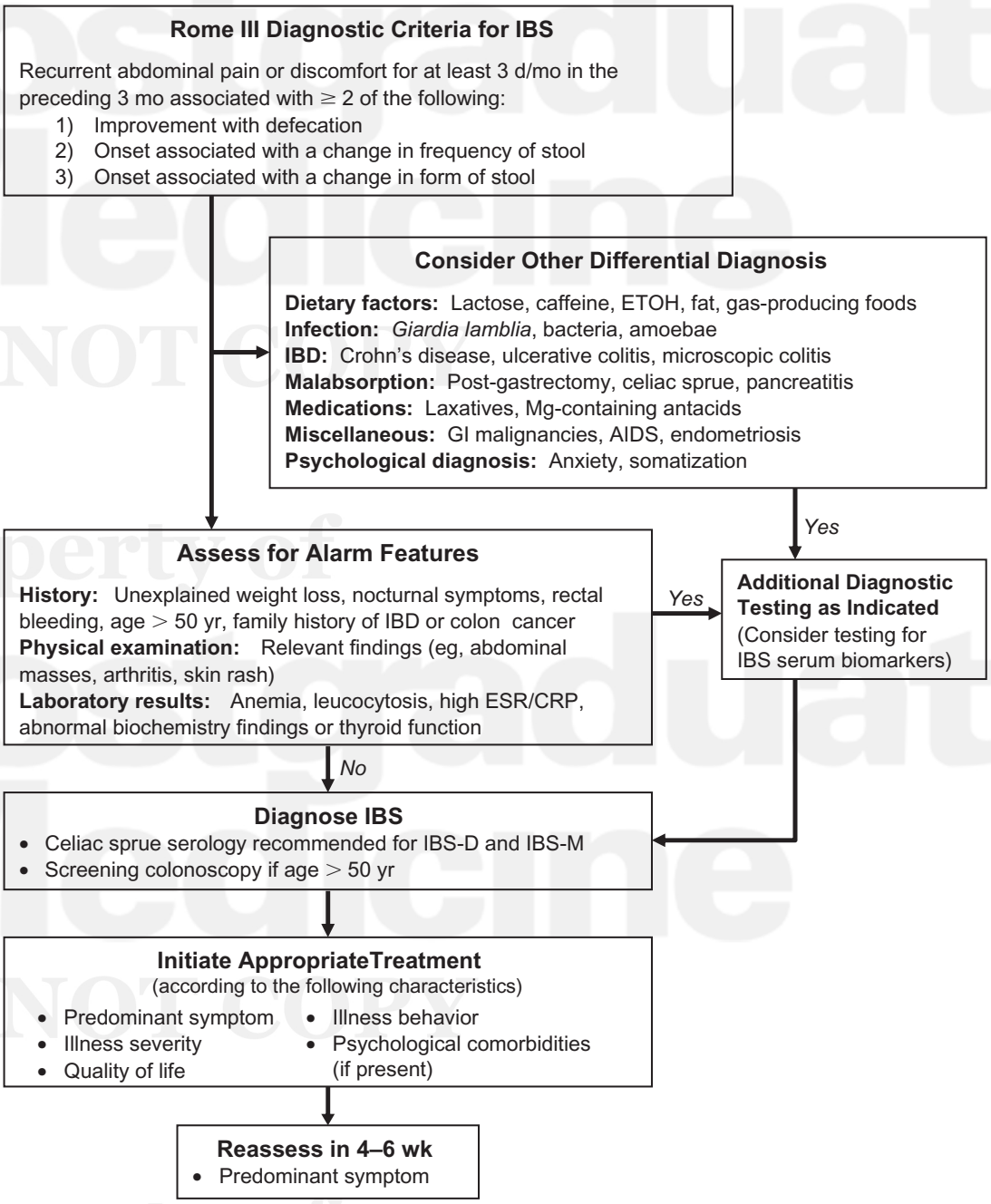
testing, particularly in the early stages of evaluation.[59] For patients, receiving a definitive diagnosis of IBS may be reassuring that a more malignant process is not ongoing and may even promote a willingness to begin treatment. Diagnosing IBS early in the course of the evaluation may also increase patients' confidence in the diagnosis, thereby strengthening the therapeutic alliance, which has been found to be an important predictor of outcomes.[34] A diagnostic algorithm for the evaluation of a typical patient presenting with IBS symptoms is provided in Figure 3.

Early Diagnosis of IBS: Next Steps

Several factors may help facilitate the earlier definitive diagnosis of IBS in clinical practice. Health care professionals need to approach the diagnosis of IBS as a positive diagnosis made based on symptom criteria and appropriate supportive investigations and not as a diagnosis of exclusion. Greater medical community awareness and use of formal diagnostic criteria for IBS (ie, Rome III) might reduce the time required to diagnose IBS but, to date, these criteria are underused and may be too restrictive in the clinical practice setting. Perhaps the next iteration of these criteria will gain more widespread clinical use. Clinician acceptance that classic symptoms in the absence of alarm features require little formal testing for IBS to be diagnosed may lead to an earlier IBS diagnosis as well as avoidance of unnecessary, invasive, and expensive diagnostic workups. Greater public awareness of IBS is needed to help patients overcome the stigma of their symptoms and seek medical attention sooner so that a diagnosis can be established and effective treatment initiated.

Through research efforts, the IBS diagnostic armamentarium has added a variety of new tools that include the examination of fecal forms, evaluation for fecal markers, and the measurement of serum biomarkers. While further clinical experience is needed, it is expected that identification of reliable biomarkers for IBS will reduce both time to definitive diagnosis and diagnostic costs, complementing the symptom-based criteria.[72] As our understanding of the pathophysiology of the disorder progresses, it is likely that new diagnostic tools and IBS disease markers will be identified, facilitating early and accurate diagnosis in IBS.

Figure 3. IBS diagnosis flow diagram.



Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IBS-D, diarrhea-predominant irritable bowel syndrome; IBS-M, mixed-type irritable bowel syndrome.

Conclusion

Given the significant economic and human costs incurred in IBS, establishing a prompt and accurate diagnosis is essential for managing this chronic, highly prevalent disorder. However, diagnosis of IBS poses a considerable challenge for physicians as well as patients, who frequently suffer for years with the disease before receiving a formal diagnosis. Many physicians continue to view IBS as a diagnosis of exclusion, a perspective that contributes to the extensive and costly diagnostic testing that is frequently performed in attempts to exclude organic disease. Education of both patients and the medical community are essential in changing this paradigm, heightening awareness of the disorder and facilitating its prompt diagnosis.

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Conflict of Interest Statement

Albena D. Halpert, MD, discloses conflicts of interest with Proctor & Gamble, Prometheus, and Takeda Pharmaceuticals North America.

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