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Do the Symptom-Based, Rome Criteria of Irritable Bowel Syndrome Lead to Better Diagnosis and Treatment Outcomes? The Con Argument

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Abstract

Some claim that symptom-based Rome criteria are diagnostic and enhance clinical practice and choice of therapy for patients presenting with gastrointestinal symptoms. This overview focuses on lower gastrointestinal symptoms: constipation, diarrhea, pain and bloating. The main con arguments for using such criteria for diagnosis are: insufficient specificity, overlap of symptom-based categories or disorders, insufficient and therefore non-specific characterization of pain in the criteria, inability to differentiate the “mimics” of IBS-C and IBS-D, and inability to optimize treatment for IBS-M or bloating in the absence of objective measurements. While doctors may not land in trouble using “symptom diagnosis” of IBS, this should not deter them from optimizing diagnosis and treatment of diseases associated with gastrointestinal dysfunction.

Introduction

A fundamental credo of symptom-based criteria, enshrined in the Rome documents, is that they are diagnostic and enhance clinical practice and choice of therapy for patients presenting with gastrointestinal symptoms such as constipation, diarrhea, pain and bloating. While “symptom diagnosis” of functional gastrointestinal disorders (FGID) is generally “safe”, this should not deter doctors from optimizing diagnosis and individualizing treatment of the diseases that result in disorders of function. Quigley's con arguments are summarized in Table I (1).

For the Rome criteria to have clinical utility, they would be expected to help identify symptoms with greater precision, confirm the clinician's diagnosis, differentiate clinically similar syndromes that have clearly different mechanisms, identify treatments or strategies that are individualized according to the etiologic mechanism, and exclude organic disease or prevent the need for further tests to identify the cause of symptoms.

Rome criteria fall short on all these expectations.

Limitations of the Symptom Phenotype in Irritable Bowel Syndrome (IBS)

The Rome III “diagnostic” criteria for IBS are listed in Table II.

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Community-based questionnaire studies show that the sub-phenotypes of the FGIDs are not so distinct, with significant transition probability in patients classified with one condition identified at one point in time (2,3).

Data from large clinical samples question whether some entities are indeed different. Wong et al. (4) mailed two questionnaires 12 months apart to 1615 patients: 12.4% met Rome III criteria for IBS-C and 14.5% for functional constipation (FC). At enrollment, 97.5% of IBS-C patients met the criteria for FC and, if the criteria allowed overlap, 45.9% of FC patients would fulfill criteria for IBS. They documented alternation between diagnoses over 12 months, suggesting that Rome III FC and IBS-C may not be etiologically distinct groups of patients. Distinguishing IBS-C from FC may be clinically irrelevant, since prokinetic and secretagogue treatments of constipation are also effective for IBS-C (5-11).

Rome III criteria for FC identified only 20% of patients with constipation diagnosed in a clinical practice of 550 cases (12). Eliminating Rome criteria “constraints” such as absence of loose stools and exclusion of IBS led to 33.5% and 75.8% concordance with the clinical diagnosis of constipation. Moreover, patients with Rome-negative, clinically positive “constipation” were clinically indistinguishable from Rome-positive FC on several *a priori* criteria (12).

Pain and IBS Rome Criteria

Apart from the confusing “lumping” of pain and discomfort in the Rome criteria, there is not one stereotypic pain quality or location in IBS. Rome criteria do not identify these differences nor reflect the fact that the pain may be secondary to bowel dysfunction.

A common complaint is chronic dull discomfort located in several regions overlying the colon during periods of constipation and relief of pain with bowel movements (BM) with different forms of constipation: IBS-C, FC, and functional defecatory disorders. Patients with painful constipation more closely resemble those with IBS-C than painless constipation (13).

A qualitatively different pain in IBS is left-sided cramp or colic before loose or urgent bowel movements, and relief with defecation. Don't all diarrhea diseases cause this symptom? Does it justify separating IBS-D from functional diarrhea?

The location of the pain may not differentiate FGID phenotypes. Is central or upper abdominal pain aggravated by meal ingestion due to functional dyspepsia or to the gastrocolonic reflex in IBS?

Sense of Incomplete Evacuation in the Definition of IBS-C

The Rome III definition of IBS includes “features of disordered defecation”. This may include a sense of incomplete evacuation and overlap with Rome III's “functional defecation disorders (FDD)”. FDD result in symptoms that overlap with IBS-C: constipation, straining, sense of incomplete evacuation, bloating, left-sided abdominal pain that is relieved by BM. The Rome III definition of FDD requires at least 2 or more symptoms of impaired evacuation, inappropriate contraction of the pelvic floor muscles, and inadequate propulsive forces. Therefore, symptoms alone are insufficient, and rectal examination and physiological tests are essential to positively identify FDD.

In a community-based survey of 278 women, the need to strain to begin or to end BMs can differentiate normal from constipation (14); however, it is unclear whether these symptoms differentiate IBS-C, FC or FDD. In 59 tertiary referral patients with persistent constipation, 29% with, and 24% without puborectalis dyssynergia were diagnosed with IBS prior to defecography (15). Biofeedback retraining resulted in significant relief of abdominal pain and

bloating scores in patients with pelvic floor disorders (16), suggesting the overlap of syndromes may originate from the pelvic floor disorder. The latter requires very different therapy from that typically used in IBS-C or FC. In FDD, fiber is ineffective (17), whereas biofeedback is effective (18-20).

Diagnosis of FDD is essential in any suspected lower FGID through history and examination, assessment of perineal descent, anorectal manometry and balloon expulsion test (21,22). Differentiation between spastic disorders (puborectalis spasm, or anismus) from flaccid disorder [descending perineum syndrome (23)] facilitate choice of appropriate physical medicine retraining.

Conditions Mimicking IBS-D

In 94 patients with Rome III IBS-D, patient-defined diarrhea occurred in one-fifth of the days and of the BMs. Diarrhea BMs were generally accompanied by urgency, pain or discomfort, increase in other IBS symptoms and stress (24). Several disorders or diseases mimic IBS-D (Table III). Symptom criteria cannot identify those conditions; yet this is essential for optimal management (Table III). A few specific comments are pertinent.

First, *bile acid malabsorption* [BAM (25)] may affect 30-50% of patients with chronic diarrhea than previously recognized (26-29), and was documented in patients with IBS-D (30). Bile acid binding in patients with BAM results in reduced stool frequency (31). Simple screening for BAM is available [e.g., serum 7αC4 (32,33)] and would indicate more specific treatment of the chronic diarrhea.

Second, despite low overall prevalence of positive tissue transglutaminase serology in IBS or dyspepsia (34), a cost-utility study suggested that *testing for celiac disease* became the dominant strategy when its prevalence was >8%, specificity of celiac test was >98%, or the cost of IBS treatment was >$130/month (35). The prevalence of biopsy-proved celiac disease in cases meeting diagnostic criteria for IBS was more than 4-fold that in controls without IBS (36).

Third, *gluten intolerance without celiac disease* may cause chronic diarrhea (37). There may be a genetic predisposition to response of the diarrhea to gluten free diet; HLA DQ_2 +ve 62%; DQ_2 −ve 12% (38). The bowel dysfunction (39) appears to result from low grade inflammation, barrier dysfunction, and enhanced motor responses.

Fourth, there is considerable symptomatic overlap between IBS-D and *microscopic colitis*; in a population based study of 131 patients with microscopic colitis, 33% had previously been diagnosed with IBS (40). Positively identifying microscopic colitis is relevant since anti-inflammatory therapy [e.g. with budesonide (41)] is effective.

Objective Measurements Are Available to Supplement the History

In my clinical practice, physiologic tests [e.g. radiopaque markers or scintigraphy for transit (42-46)] rather than symptoms alone guide selection of therapy for patients. For example, prokinetic or secretagogue therapy is used in patients with slow transit constipation, and fiber and osmotic laxative in normal transit FC. Similarly, clonidine and octreotide are reserved for rapid transit diarrhea.

What Is the Treatment Target in Functional Bloating?

Functional bloating is typically diagnosed after constipation and sugar maldigestion are excluded. Bloating alone (not bloating with distension) is associated with rectal hypersensitivity, whereas bloating with distension (but not bloating alone) is associated with

prolonged colonic transit [relative to patients with bloating alone (47,48)]. In addition, reduction in abdominal girth overnight (49), as well as difficulties with rectal gas expulsion (50) in patients with bloating suggest there may be a significant contribution of rectal evacuation to bloating. Selection of therapy may be enhanced by physiological measurements.

Is Symptom Criteria-Based "Diagnosis" Safe in IBS and Is There an Opportunity Cost?

The risk of significant organic disease is low, given the high prevalence of FGID. This suggests that symptom-based, *provisional* diagnosis based on such criteria is reasonable in primary care. However, this approach may miss significant disease such as celiac sprue, colon cancer, carcinoid diarrhea. Among 112 Olmsted County, Minnesota residents followed for a median of 15 years after diagnosis of IBS, organic gastrointestinal disease occurred in 10 patients [2 chronic pancreatitis, 4 GI cancer, 2 subacute obstruction and 2 gastric ulcers (51)], based on practice several decades ago! Though symptom criteria-based diagnosis may be "safe", it is not necessarily the best practice; individualizing therapy requires accurate diagnosis of the dysfunction.

Conclusions

"IBS" is a constellation of symptoms, a phenotype that may reflect a spectrum of underlying diseases/disorders. Symptom-based criteria lack the specificity that the clinician can obtain with a thorough history. Optimal management requires identification of the cause of symptoms.

In my practice, I optimize diagnosis through validated function tests (e.g. spastic from flaccid FDD, slow transit constipation, rapid transit diarrhea, BAM, gluten or disaccharide intolerance) and select therapy accordingly. Symptom-based criteria do not help me diagnose or treat FGIDs.

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Abbreviations

BAM	bile acid malabsorption
C	constipation
D	diarrhea
FC	functional constipation
FD	functional diarrhea
FDD	functional defecatory disorders
FGID	functional gastrointestinal disorders
IBS	irritable bowel syndrome

Table I
Quigley's Arguments against Rome Criteria

1	It is fallacious to make a syndrome out of every symptom or to create new entities and therapeutic targets; Rome criteria created disorders for which there is no independent confirmation (demographic, epidemiology, pathophysiology or response to treatment) of their existence.
2	Symptoms non-specific and following the symptoms can lead the clinician into an ambush by disregarding distinct pathologies (especially in diarrheal disorders).
3	“Real diarrhea” should never be accepted as IBS, unless it has been thoroughly evaluated.
4	Different generations of Rome criteria result in very different study populations (e.g. Rome II being too pain focused.
5	Attempts to further subtype Rome diagnoses have exposed the limitations of symptom-based definitions and led to diagnostic confusion and therapeutic dead ends.
6	Simple and inexpensive tests (blood count, ESR, CRP, and fecal blood and calprotectin) are used by most clinicians to exclude organic disease; the symptoms alone are not diagnostic.
7	Failure of Rome-based studies to presage therapeutic advances
8	Clinically unwieldy nature of the criteria

Table II

Rome III Criteria for IBS

Recurrent abdominal pain or discomfort for at least 3 days per month in the last 3 months associated with *2 or more* 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 (appearance) of stool

Table III

Mimics of IBS-D

Disorder/Disease	Management
Food allergy/intolerance	Dietary exclusion
Sugar maldigestion	Sugar-breath H_2 test; exclusion diet
Celiac disease	prevalence ~1:80; TTG serology; GFD
Gluten intolerance, not CD	HLA-DQ_2 +ve, 5:1 respond to GFD
Microscopic colitis	Colon bx; bismuth, budesonide
Idiopathic bile acid malabsorption	^{75}Se methionine retention; serum 7-αHCO; fecal bile acids, bile acid binding therapeutic trial
Bacterial overgrowth	unclear prevalence; find the underlying cause

TTG tissue transglutaminase

GFD gluten free diet

7-αHCO 7alpha-hydroxy-4-cholesten-3-one