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EDITORIAL

Defining the irritable bowel

Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders (FGIDs) encountered in the community, primary care, and specialist clinics.[1–3] It is recognized to have a complex multifactorial pathophysiology, including psychological and cultural factors, previous gut infections, visceral hypersensitivity, increased permeability, and bile acid malabsorption.[4] IBS does not cause mortality but results in an increased healthcare burden and impaired quality of life due to its poor response to standard medical therapy.[5] To date, there are no specific endoscopic/imaging features, or biomarkers, to diagnose the condition. In clinical practice, the diagnosis of IBS is largely based on the presence of chronic lower gastrointestinal (GI) symptoms with negative investigations for organic diseases such as inflammatory bowel disease, GI malignancy, metabolic diseases, or atypical GI infections. However, for the purposes of standardization and research, a group of experts have attempted to define IBS according to certain symptom clusters, which have now been internationally accepted as the Rome Foundation diagnostic criteria. Since their initial iteration, the Rome criteria have been updated every 10 years, with the latest Rome IV criteria developed in 2016.[6]

Despite attempting to standardize the diagnosis of IBS, the latest Rome criteria have unfortunately been criticized for their lack of sensitivity. A systemic review of population-based studies has shown that the global prevalence of IBS decreased from 9.2% based on the previous Rome III criteria to 3.8% based on the latest Rome IV criteria.[7] The frequency of IBS in a primary care study similarly decreased from 4% (Rome III) to 0.8% (Rome IV). Most of those who did not fulfill the Rome IV IBS criteria were reclassified into other FGIDs, including functional constipation and functional diarrhea.[3] The main reason for the reduced sensitivity of the Rome IV criteria lies in their requirement for the presence of "abdominal pain" to make a diagnosis of IBS. In contrast, the earlier Rome III criteria defined IBS with "the presence of abdominal discomfort with or without pain that is relieved by defecation (Table 1)."[6,8] The difference in perception of "abdominal pain" *versus* "abdominal discomfort" is believed to have resulted in an under-diagnosis of IBS, particularly among Asian patients.[9]

Although less sensitive in diagnosing IBS, the latest Rome IV criteria appear to be more specific in the classification of IBS subtypes. The IBS subtypes of predominant-diarrhea (IBS-D), constipation (IBS-C), mixed (IBS-M), or unclassified (IBS-U) are based on the predominant stool morphology on the day of abnormal bowel movements (Table 1).[6] A multinational, population-based study has shown that the frequency of IBS-M significantly decreased and that of IBS-U remained low when the diagnostic criteria were changed from Rome III to Rome IV.[10] Although the increased specificity for IBS subtypes could potentially facilitate appropriate pharmacological therapy, this approach has not been proven to date. More importantly, the less sensitive Rome IV criteria may misclassify less clearly defined IBS with other FGID diagnoses such as functional diarrhea or bloating.[3] These less common FGID conditions are less likely to get effective treatment because of the lack of established treatment guidelines, compared with IBS.

Another issue with the Rome criteria for FGID diagnosis was that they are categorized according to anatomical divisions of the gastrointestinal tract (GI), that is, esophageal, gastroduodenal, bowel, biliary tract, and anorectal regions. Owing to the nature of FGIDs, including IBS, considerable overlap of FGID symptoms are frequent and there is a lack of symptom stability over time.[11] In contrast, Siah *et al.* identified nine dominant symptom clusters among Asian patients with FGIDs in a multicenter study. Three bowel clusters with IBS-like symptomatology that differed from the Rome criteria were reported, in particular "meal-related bowel symptoms" and "upper abdominal pain that was associated with constipation (Table 2)."[12] The different clusters may be better explained by the putative pathophysiological mechanism, with little or no overlap between the clusters. With

Table 1 Rome III *versus* Rome IV irritable bowel syndrome diagnostic criteria

Rome III[8]	Rome IV[6]	Main differences
Recurrent abdominal pain or discomfort at least 3 days per month in the last 3 months associated with two or more of the following: 1. Improvement with defecation 2. Onset associated with a change in frequency of stool 3. 3. Onset associated with a change in form (appearance) of stool	Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months, associated with two or more of the following criteria: 1. Related to defecation 2. Associated with a change in frequency of stool 3. Associated with a change in form (appearance) of stool	1. Abdominal discomfort is removed from the diagnostic criteria in Rome IV. 2. Frequency of abdominal pain was changed. 3. Rome IV requires the abdominal pain to be related to defecation, instead of improved with defecation 4. To be categorized into a subtype in Rome IV, only the predominant bowel habits of patients on the days of abnormal bowel movements should be taken into consideration.

Table 2 . Novel classifications for irritable bowel syndrome (IBS)

Asian functional gastrointestinal disorder symptom clusters: Clusters with IBS-like symptomatology[12]	Subgroup of patients with IBS based on gastrointestinal symptoms and psychological profiles[13]
F2: Abdominal pain or discomfort starting with more frequent or looser stools with improvement of symptom after bowel movement, and.	Cluster 1: Diarrhea and urgency with low psychological burden
F3: Epigastric pain or burning affected by eating, which gets better after bowel movement or passing gas and preceded by a change in the number of bowel movements	Cluster 2: Low overall GI symptom severity with high psychological burden
F7: Upper abdominal pain or discomfort associated with passing less frequent or passing harder stools	Cluster 3: Low overall GI symptom severity with low psychological burden
	Cluster 4: Diarrhea, abdominal pain, and urgency with high psychological burden
	Cluster 5: Constipation, abdominal pain, and bloating with high psychological burden
	Cluster 6: High overall GI symptom severity with high psychological burden
	Cluster 7: Constipation and bloating with low psychological burden

this unique classification, more effective therapeutic target could potentially be identified.

Recently, with the recognition of a strong association between psychological morbidity and IBS, a new subtype classification has been proposed by a group of researchers from the United Kingdom. Seven distinct IBS subgroups, based on a combination of GI symptoms, extra-intestinal symptoms, and psychological comorbidity, were identified (Table 2).[13] In a longitudinal study of these seven IBS subgroups, most (84%) of the patients stratified according to high psychological burden remained in the same cluster after 1 year. In contrast, only 70% of IBS patients still met the Rome IV criteria on follow-up. In addition, patients in the subgroups with high psychological comorbidity were also found to be associated with more severe symptoms and had greater healthcare utilization.[14] Therefore, this novel classification for IBS may have prognostic value and the treatment based on these subgroups may potentially achieve a better therapeutic response: for example, early introduction of neuromodulators or psychotherapy in subgroups with high psychological comorbidity rather than using the traditional step-up approach.

In conclusion, the latest Rome IV diagnostic criteria for IBS appear to be less sensitive and have limitations for epidemiological surveys. The newer concepts of reclassifying IBS beyond bowel symptoms by taking into consideration meal-related symptoms, extraintestinal symptoms, and psychological comorbidity may be useful to direct therapy and could potentially improve clinical outcome.

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