ADVANCES IN IBS

Current Developments in the Treatment of Irritable Bowel Syndrome

Section Editor: William D. Chey, MD

Improving the Treatment of Irritable Bowel Syndrome With the Rome IV Multidimensional Clinical Profile

Douglas A. Drossman, MD
President, Rome Foundation
Professor Emeritus of Medicine and Psychiatry
UNC Center for Functional GI and Motility Disorders
University of North Carolina
Chapel Hill, North Carolina

G&H How do the Rome IV criteria differ from the Rome III criteria?

DD One of the biggest changes with the Rome IV criteria is the removal of the term functional from certain diagnoses (eg, centrally mediated abdominal pain syndrome, esophageal disorders, fecal incontinence) in order to eliminate the stigma surrounding such disorders. These conditions have been redefined as disorders of the gut-brain interaction. The terminology is currently interchangeable, but the hope is that over time, the use of the latter term will become more widespread.

Another change is the addition of new diagnoses such as reflux hypersensitivity, cannabinoid hyperemesis syndrome, opioid-induced constipation, and narcotic bowel syndrome. Reflux hypersensitivity refers to patients who have hypersensitivity to normal levels of acid reflux, resulting in heartburn. This condition is separate from functional heartburn, in which patients have heartburn without any sensitivity to normal physiologic reflux. Cannabinoid hyperemesis syndrome relates to an increased sensitivity to this agent causing nausea and vomiting, and is relieved by discontinuation of cannabis. Recognizing the epidemic of opioid use, Rome IV includes criteria and guidelines for the management of opioid-induced constipation. This is an update from Rome III, which identified only functional constipation; other constipation-causing drugs had to be eliminated for a diagnosis. Narcotic bowel syndrome, a central hyperalgesia, is a new entity that was first identified in 2007. This condition involves an upregulation of nerves in the central nervous system that causes paradoxically increased pain in a subset of patients on opioids, and these patients experience worsening abdominal pain when given opioids. Thus, narcotic bowel syndrome has to be identified in order to prescribe proper treatment that excludes opioids.

A third major change is the modification of sphincter of Oddi dysfunction from 3 types to 1. Originally, sphincter of Oddi dysfunction type I was defined as biliary pain associated with increased enzymes in patients who had their gallbladder removed. This classification was considered more of a structural abnormality, and, therefore, was removed. Type III, defined as just biliary pain, was also eliminated due to evidence demonstrating that it is not related to the bile duct and aligns with

> ... when clinicians treat patients in real life, they consider more than just the diagnosis to create a treatment plan.

functional abdominal pain. What remains is sphincter of Oddi dysfunction type II (now just sphincter of Oddi dysfunction), which is diagnosed in a patient who has either dilatation or increased enzymes.

G&H What changes were made to the Rome IV criteria concerning irritable bowel syndrome?

DD The primary change relating to irritable bowel syndrome (IBS) in the Rome IV updates is the recognition that functional bowel disorders (eg, IBS, functional constipation, functional diarrhea, bloating) are not categorical diagnoses. These disorders exist on a continuum rather than as discrete entities, meaning that the patient can start with one condition and switch to another condition 6 months later. For example, a patient with functional constipation may experience more pain and be diagnosed with constipation-predominant IBS (IBS-C), or can present with IBS-C and later convert to a more diarrhea-predominant pattern. This is important to recognize in terms of treatment because medication intended to manage constipation may result in diarrhea-predominant IBS (IBS-D).

Another change includes the removal of the term discomfort; what was previously termed abdominal pain or discomfort is now referred to as abdominal pain. Additionally, pain can be related to a bowel movement rather than be relieved by it, meaning that in some patients, the pain could worsen. Lastly, the frequency with which patients need to exhibit symptoms of IBS has changed from 3 times per month to 1 time per week in order to meet criteria.

G&H What is the Multidimensional Clinical Profile, and why was it developed?

DD Approximately 4 years ago, the Rome board realized that much of what was taught concerning IBS treatment was presented in a categorical sense, that is, a patient diagnosed with IBS should be followed up with a specific treatment. However, when clinicians treat patients in real life, they consider more than just the diagnosis to create a treatment plan. For example, a patient with IBS-D can show evidence of a physiologic disturbance (eg, fecal incontinence), an impaired quality of life (eg, the symptoms are so severe that the patient cannot function), or associated distress (eg, anxiety or depression) as a result of his or her symptoms. Thus, the Multidimensional Clinical Profile (MDCP) was developed to gain an understanding of the patient in the context of all the factors that play a role in the severity of the illness, and to allow clinicians to better specify the treatment. The MDCP is made up of 5 categories that break down the clinical profile of the patient's condition. The first category is the predominant diagnosis as outlined in the Rome criteria. The clinician should take into account the second category relating to any subsets, such as IBS-C; IBS-D; mixed IBS; postinfection IBS; or sensitivity to fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (ie, FODMAPs). The third category is the impact of the disorder, or the quality of life. The clinician should ask the patient how much the disorder has affected his or her work, school, or social activities on a scale of none, mild, moderate, or severe. The fourth category is psychologic comorbidities; the clinician should ask whether the patient has anxiety, depression, or a history of abuse or trauma. The fifth category is physiologic disturbance, such as associated gastroparesis or incontinence, or biomarkers. With regard to biomarkers, looking ahead, calprotectin or another serologic finding might tailor treatment to the patient.

G&H Is the MDCP applicable to research, or is it only used in clinical practice?

DD The MDCP is mostly used for defining treatment in clinical practice, but it may have a role in research because of the interest in biomarkers. For example, an antivinculin antibody may potentially affect treatment, which would spur the effort to apply the MDCP to research.

G&H How does this edition of the MDCP compare to its previous version?

DD The previous version of the MDCP was based on the Rome III criteria and contained 32 case examples. The current edition of the MDCP is based on Rome IV criteria and includes 72 case examples.

G&H How might the diagnosis of IBS be improved?

DD The Rome criteria categorize IBS diagnoses, and an accompanying book called *The Diagnostic Algorithms* uses standard algorithmic images to lead clinicians through a diagnostic workup and evaluation. The book starts with common symptoms, including nausea, vomiting, pain, and diarrhea, and recommends endoscopy or imaging as necessary, using the Rome criteria to arrive at the diagnosis. The MDCP then provides a broader perspective on treatment options and lists more specific treatments targeted to the particular patient.

G&H What is the Rome IV Interactive Clinical Toolkit, and how might it help clinicians caring for patients with functional gastrointestinal disorders?

DD The Rome IV Interactive Clinical Toolkit, developed from a partnership between the Rome Foundation and a software company called LogicNets, uses intelligent software to allow clinicians to make real-time diagnostic and treatment decisions. The toolkit's software package comprises the information from the Rome IV *Diagnostic Algorithms* book and the MDCP. For 2 years, the Rome board has worked to modify the information to establish real-time interactive decision-making. Clinicians can go online and indicate their patients' symptoms, and through a series of questions and iterations with the computer, the toolkit will guide clinicians through various diagnostic and treatment options. For example, if a patient with chest pain is managed with a proton pump inhibitor and returns after 3 weeks with no improvement, the treatment can be modified and recorded. The Rome IV Interactive Clinical Toolkit gathers and catalogs information while helping the clinician to make the proper diagnosis (via *The Diagnostic Algorithms*) and treatment decisions (via the MDCP) in real time.

Additionally, the toolkit can perform pathways analysis on the catalogued information, which allows researchers to understand the decisions clinicians make. If it appears that a percentage of clinicians are headed in the wrong direction, the program can be modified to help them in their learning in the future.

G&H Looking ahead, is there a role for combining symptom-based criteria and biomarkers?

DD Biomarkers are not likely to replace the Rome criteria. It remains to be seen how they would help make a more precise diagnosis, but it is understood that biomarkers would play a role in managing treatment. For example, the presence of the antivinculin antibody (which signals a previous gastrointestinal infection) in a particular patient might lead the clinician to choose to use a nonabsorbable antibiotic intended for postinfection IBS.

G&H What are the next steps for advancement in this field?

DD Clinicians in places such as China, Japan, and Latin America assess and treat conditions differently than clinicians do in North America or Western Europe. Therefore, it is imperative to incorporate these changes into a multicultural context, and the Rome board is working on adding more translations to the criteria.

The next major step is to make the Rome Foundation the center point for future research in functional gastrointestinal disorders. The Foundation currently has investigators globally who can perform the research with credibility. Additionally, the Foundation is working to attract funding beyond what is provided by the National Institutes of Health and the European Medicines Agency so that it can award grants to young investigators to perform research in this area. In that context, we are currently conducting a global epidemiology study of 70,000 patients across 35 countries for which we are evaluating health practices, prevalence data, and treatments. Within the next several years, this study will be under analysis, and the results will help us understand how doctors practice around the world and where the differences lie. A Rome Foundation Research Institute is also being created, which will include a biobank and a database of patients and will serve as the center for research for investigators who are conducting pharmaceutical-, federal-, or industry-based investigative studies.

Dr Drossman serves as president of the Rome Foundation.

Suggested Reading

Chang L. Updates to the Rome criteria for irritable bowel syndrome. *Gastroenterol Hepatol (N Y)*. 2017;13(5):304-306.

Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features and Rome IV. *Gastroenterology*. 2016;150(6):1262-1279.e2.

Drossman DA. Functional gastrointestinal disorders: what's new for Rome IV? *Lancet Gastroenterol Hepatol*. 2016;1(1):6-8.

Drossman DA. *Rome IV Diagnostic Algorithms for Common GI Symptoms*. 2nd ed. Raleigh, NC: Rome Foundation, Inc; 2017.

Tack J, Drossman DA. What's new in Rome IV? *Neurogastroenterol Motil*. 2017;29(9):e13053.