ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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Measuring Structural Damage in Crohn's Disease

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G&H Can you briefly describe the natural course of Crohn's disease?

JC Early-stage Crohn's disease is characterized by a relapsing and remitting inflammatory process. Symptoms usually consist of intermittent diarrhea and abdominal pain, but damage and symptoms then progress to chronic disease that ultimately lead to irreversible damage to the bowel. From the description of the postoperative recurrence model, it has been learned that anatomic lesions of Crohn's disease progress from aphthous ulcers to deep ulcers then to strictures and/or fistulae. A stricture may be associated with a fistula that develops above it, or a fistula may develop within the most severely inflammatory area. Once developed, strictures and fistulae are, as a rule, not reversible and result in the need for surgery sooner or later. Crohn's disease is a lifelong disease, and after 25 years of progression, a stricture or fistula requiring surgery will have developed in approximately 70–80% of patients.

G&H What modalities are currently used to assess bowel damage? What are their limitations in relation to advancing care of patients with Crohn's disease?

JC Bowel damage can be assessed from endoscopy and cross-sectional imaging, magnetic resonance imaging (MRI), and computed tomography (CT) scans. Endoscopy and cross-sectional imaging give complementary information. They should be used concomitantly.

The limitations are that endoscopy is invasive and cannot be repeated several times per year, a CT scan irradiates, and intestinal MRI is not very comfortable. Thus, repeat assessment of bowel damage cannot be performed every 3–6 months—although this is the correct interval, particularly in the first few years following diagnosis, for evaluating which diseases are the most destructive and for determining an appropriate treatment.

G&H Can you provide background about the International Program to Develop New Indexes in Crohn's Disease?

JC The International Program to Develop New Indexes in Crohn's Disease (IPNIC) formed in 2007, but my colleagues and I started the process of developing the Lémann score in 2006. IPNIC is an international working group that operates under the auspices of the French association INTESTINFO (http://www.intestinfo.com[in French]). It includes 28 gastroenterologists, 2 radiologists, a surgeon, and a radiologist. The team hails from 15 countries. One of the group's main objectives is to develop a tool that can measure cumulative bowel damage in Crohn's disease. That tool is the Lémann score, named after my colleague Marc Lémann, a professor in the Department of Hepatogastroenterology at Hôpital Saint-Louis in Paris, France.

G&H In having a standardized protocol for measuring the structural damage that occurs in Crohn's disease over time, what aspects about the disease process would you and colleagues in the IPNIC most like to gain a deeper understanding of?

JC Predictors have been established to identify disabling disease, the development of a stricture or fistula, and the need for surgery, in this order, but all these events have not been pooled into an overall entity. The global assessment of digestive damage using the score being developed (ie, the Lémann score) is unique in that it takes into account both the extent and depth of damage throughout the digestive tract. By measuring the damage score at dif-

ferent time points in an individual, it will be possible to identify different phenotypes of the disease according to the speed of damage progression. What is important for the long term is not control of symptoms but control of anatomic lesions.

G&H What advantages—in terms of prognosis and, ultimately, clinical care—are inherent in being able to measure structural damage in Crohn's disease?

JC The most important point is to identify patients who progress rapidly to significant damage in the short term. If these patients can be identified during the first few months following diagnosis, they can be treated aggressively with more potent drugs (ie, biologic agents) with the objective of delaying or avoiding surgery. Conversely, patients in whom notable damage does not develop or who do not progress may be treated with standard drugs.

G&H What are the ideal imaging technologies for measuring structural damage over time? What are the advantages of one modality over another?

JC At the present time, MRI is clearly the ideal technique. Minimal preparation and no radiation are involved. The modality has good acceptance, and, in general, the quality of images is excellent. However, some progress is needed regarding the standardization of the technique and the preparation—for the colonic examination in particular. The objective is not to visualize aphthous ulcers or minor lesions that will heal without sequelae, but to assess the severity of transmural damage. If the quality of MRI could be improved—and I think this will be achieved in the near future—it could be possible to obtain a correct assessment of a patient's digestive damage without performing an endoscopy.

G&H How will the ability to measure structural damage over time impact pharmaceutical development of maintenance/antisymptomatic and disease-modifying agents for treatment of Crohn's disease?

JC For the present time, I think the Lémann score will be reserved for use in clinical trials. This score will be an important component for measuring the efficacy of a treatment, specifically for measuring the achievement of clinical remission or mucosal healing. It should be noted that the notion of damage is different from that of mucosal healing. Damage assessment considers not only the mucosal surface but also the depth and extent of the lesions. Again, the targets of therapy are changing. In addition to alleviating symptoms, the goals of therapy include minimizing or perhaps reversing digestive damage to achieve better control of the disease in the long term.

G&H Would you briefly explain the steps taken to develop the Lémann score and how it will be validated?

JC Development of the score involved many meetings, letters, conference calls, and financial support from Abbott Laboratories. Briefly, approximately 150 patients from the different units that participated were included in the construction set. These patients underwent concomitant upper endoscopy, colonoscopy, and abdominal and pelvic MRI. The results of these examinations were analyzed and scored by the investigators. The severity of the damage was scored for each segment, then for each organ, and then for the entire digestive tract. These different scores were used to build a score for each pathologic situation and to give a weight coefficient for the damage of each organ. The results are, in part, validated by an independent Delphi method, which scored theoretical damage. Moreover, the final Lémann score will be validated in a second set of approximately 100–150 patients, whose examinations already have been performed. My colleagues and I plan to reinvestigate our patient data to assess the Lémann score's sensitivity to change.

G&H How is this instrument expected to be an improvement over, say, the Montreal classification for Crohn's disease?

JC The Montreal classification for Crohn's disease is cumulative and is a limited descriptor of the extent and severity of disease at any given time. For example, 2 patients may be classified as L1B2 (ie, ileal location plus stricturing behavior). One patient might have a very short stricture localized to 5 cm of the distal ileum and the other patient might have multiple strictures extended on 50–100 cm of the small bowel and associated severe perianal disease. Of course, these patients are different and need different therapeutic strategies. These patients would be classified very differently according to the Lémann score. In addition to being more precise and quantitative, the Lémann score provides a photographic record of the damage of the entire digestive tract at any given time. Although Crohn's disease progresses over time, this progression can hopefully be stopped through diagnostic and therapeutic innovations, such as the Lémann score.

Suggested Reading

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