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Editorial

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Histological Scores in Inflammatory Bowel Disease: A New Kid in the Block

Mathurin Fumery,[a] Denis Chatelain[b]

[a]Department of Gastroenterology, Amiens University Medical Center and Jules Verne University of Picardie, Amiens, France [b]Department of Pathology Unit, Amiens University Medical Center and Jules Verne University of Picardie, Amiens, France

Corresponding author: Mathurin Fumery, MD, PhD, Service Hépato-Gastroentérologie, CHU Amiens Picardie, Université de Picardie Jules Verne Site Sud—D408, F-80054 Amiens, France. Tel.: +33-322-088-840; email: fumery.mathurin@chu-amiens.fr

The treatment of inflammatory bowel diseases [IBD] has profoundly changed during recent decades with the availability of more effective therapies targeting different immunological pathways. In parallel, the treatment target has also evolved, from symptom resolution to endoscopic healing.[1] This was supported by evidence of improved long-term outcomes in those who achieve endoscopic remission. However, several patients with endoscopic healing still have histological activity. In ulcerative colitis [UC], a growing body of literature has demonstrated that this persistent histological activity may be associated with higher rates of relapse, need for surgery or hospitalization, and development of dysplasia and adenocarcinoma.[2,3] In Crohn's disease [CD], histological healing was associated with decreased risk of clinical relapse, medication escalation, and corticosteroid use; but in contrast to UC, the relevance of histology in CD outcomes is less clear, because inflammation is discontinuous, transmural, and can exist beyond the reach of the endoscope.[3] Nevertheless, all these observations support the role of histology as a potential new therapeutic target. Recent international guidelines stated that histological measurements are important to determine therapeutic efficacy in UC, and histological remission, as well change in histology score, were recognised as an appropriate and realistic histological endpoint in clinical trial.[4] Both guidelines and regulatory agencies recently defined mucosal healing as the combination of endoscopic improvement and histological remission.

However, there is still a need for reliable histological scores able to assess the microscopic mucosal response to treatment as well as to define a 'histologicaj healing' in both clinical trial and clinical practice. More than 40 histological scoring systems in IBD have emerged over the past seven decades, varying considerably in the type and number of histological features that they include. Most of them do not fulfill the currently accepted standards for index development and very few of these indices has been fully validated to date. Finally, few of them are currently used and none is worldwide applied in clinical practice and is mainly reserved for investigational settings. The Simplified Geboes score [SGS], the Robarts Histopathology Index [RHI], and the Nancy Histological Index [NHI] were currently considered as appropriate instruments for assessing disease activity in UC and have been the most thoroughly evaluated tools in the literature.[4–6] There are strengths and limitations to each scoring system and direct comparisons are limited because criteria for inflammation and activity are inconsistent and study designs are different. However, only the RHI and the NHI are fully validated.

Both the NHI and the RHI include inflammatory features only, as architectural features were thought unlikely to be responsive to change following therapy. However, even findings associated with chronic inactive inflammatory changes have been associated with an increased risk of clinical relapse. In a recently published systematic review and meta-analysis including 28 studies with 2806 patients with IBD, crypt architectural irregularities were also one of the individual features that predicted relapse, as were basal plasmacytosis, neutrophilic infiltrations, and mucin depletion.[7]

Therefore, the ideal histological score should be able to assess not only disease activity but also restoration of a normal mucosal architecture for both UC and CD. It should be reproducible among pathologists and easily implemented into routine daily practice. Given the urgent clinical need, an international consortium aimed to develop and validate, in a large group of IBD specialists, a simple histological activity scoring index: the Inflammatory Bowel Disease—Distribution, Chronicity, Activity [IBD-DCA] score. In this work, reported in the current issue of the *Journal of Crohn's and Colitis*, the authors aimed to propose a score easy to calculate for both clinical trials and routine daily pathology practice, to assess the amount and severity of active and chronic changes in IBD.[8] The score consists of three main parameters which also constitute the name of the new index: [D] for assessment of the distribution of overall active or chronic changes in the IBD colon biopsy, regardless of whether they are epithelial, architectural, or inflammatory; [C] for assessment of features of chronic injury [architectural distortion or chronic inflammation]; and [A] for assessment of activity features [neutrophils].

D0 refers to normal mucosa assessed in scanning magnification [2.5-4x]. D1 and D2 refer to overall active or chronic histological changes from normal, irrespective whether they are architectural, epithelial, or inflammatory in nature [D1 when modifications are seen in less than 50% of the tissue area on one slide, and D2 when present in more than 50%]. In the second step, parameter C [features of chronic injury] should be assessed, which includes: C0 defined as absence of chronic features; C1 as the presence of crypt architectural distortion alone [may include crypt branching, loss of parallelism, tortuosity, and crypt dilation or variation in shape or size], or a mild lymphoplasmacytosis; and C2 that corresponds to the presence of marked lymphoplasmacytosis in the lamina propria, regardless of whether there is architectural distortion or not. In the last step, active inflammatory features are evaluated. A0 is defined by the absence of active inflammation. Mild active inflammation with two or more neutrophilic granulocytes in one high-power field in the lamina propria or any neutrophils in the epithelium should be scored A1. A2 denotes the presence of crypt abscesses or erosion or ulceration. Inter-rater reliability was moderate to good for the UC cohort and at best moderate for the CD cohort. Intra-rater agreement ranged from good to excellent in both cohorts. Correlation with the NHI was moderate and strong with the SGS. In internal responsiveness analysis all three histological parameters showed a large magnitude of change, correlated to NHI and SGS changes.

Despite these potential benefits, substantial barriers still exist to the use of the IBD-DCA as an outcome measure in clinical trials and practice. First, further prospective validation would be necessary. Second, to date there are no widely accepted endpoint definitions for histological response and remission according to IBD-DCA. It is uncertain how many biopsies are required or where biopsies should be taken to obtain optimal results, especially in CD for which further prospective validation on larger cohorts for both the upper and lower gastrointestinal tract would be necessary. Its prognostic and therapeutic value has also to be confirmed on larger series of UC and CD patients, by evaluating in particular the relevance of the different elements of the score, specially distribution and chronic lesions.

The major advantage of the IBD-DCA is its relative simplicity. The score is composed of three items, including features of chronic injury as well as active inflammatory findings, which are—apart from normal—only divided into two levels of severity. Another strength of the IBD-DCA score relies in its good inter- and intra-rater reliability, which was assessed in a large group of pathologists expert in gastrointestinal pathology. This score seems easily accessible to non-expert pathologists. So could these many advantages allow this newcomer to shine among the best histological scores in IBD and contribute to change the way histology is used in the management of these diseases?

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Conflict of Interest

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