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Recent advances in the endoscopic assessment of ulcerative colitis

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ABSTRACT

Endoscopic assessment of the severity and extent of inflammation as well as the presence of neoplastic lesions is integral to the management of ulcerative colitis (UC). Numerous scoring systems to assess endoscopic severity indicate that a perfect scoring system is still lacking. Many of the scoring systems were designed in the era of standard-definition white-light endoscopy. The resolution and details provided by the new-generation endoscopes and high-definition equipment of both mucosal pattern and vascular pattern mandates a fresh look at endoscopic scoring in UC. In this context, we describe some of the scoring systems recently designed using novel endoscopic techniques. Current definitions of mucosal healing do not completely reflect histologic healing but this gap is being closed rapidly by novel endoscopic techniques with high-definition images that can be optically and digitally enhanced. The best technique to detect dysplasia in UC is still widely debated. New endoscopic resection techniques may now be able to limit the number of colectomies that need to be performed in the presence of dysplasia owing to improvement in performing local resection.

Introduction

The disease-activity assessment for ulcerative colitis (UC) is evolving—after nearly 2 decades of having a multitude of clinical disease-activity indices, some incorporating endoscopic assessment (eg, Mayo score) and some without endoscopy component (eg, Simple Clinical Colitis Activity Index), the regulatory agencies are simplifying the indices to make them more robust, objective, reproducible, and less prone to subjective bias. It is proposed that in UC, diarrhea and rectal bleeding are combined with endoscopic appearance to represent patient-reported outcomes [1]. This is likely to become a standard tool in clinical trials. On the contrary, in clinical practice, tools to assess disease burden and disability are becoming more widely used.

Endoscopy remains a pivotal tool to assess disease severity, extent, and complications such as dysplasia in clinical practice [2,3]. In addition, central readout of the endoscopic mucosal appearance in clinical trials has resulted in more reproducible efficacy end points for assessing response to therapy. Endoscopic remission is now the target of therapy as recommended by the Selecting Therapeutic Targets in Inflammatory Bowel Disease group and is associated with better clinical outcomes, less disease flares, less hospitalizations, and less surgery in the short-, medium-, and long-term studies [4,5].

Although in clinical trials, using formal scoring of endoscopy is standard; there is an evolution in clinical practice to use scoring systems at endoscopy to follow-up patients objectively and to optimize therapeutic management. This has increased the need for educational platforms and endoscopic training for UC assessment [6-8].

The relationship between endoscopic appearance and outcomes

Mucosal healing (MH) is an important therapeutic goal to achieve in UC to prevent complications, hospitalization, and colectomy. Endoscopic MH is becoming established as the target in a treat-to-target strategy in UC [9-11]. However, the term endoscopic healing has not yet had a clear commonly accepted definition. Currently, endoscopic MH in inflammatory bowel disease (IBD) is defined by resolution of visible mucosal inflammation and ulceration. In clinical trials, Mayo endoscopic subscores of 0 or 1 are considered MH but this clearly allows for some endoscopic activity [12].

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After the introduction of the biological therapies, endoscopic MH has become an important measure for treatment efficacy. Froslie et al [13] demonstrated that endoscopic MH achieved after 1 year of treatment is a clinical indicator and predictive factor for favorable outcome with a lower risk of colectomy in the long term. In UC, 2 large studies—Active Ulcerative Colitis (ACT) I and II—demonstrated that remission rates were significantly better with infliximab than with placebo and such remission was maintained with infliximab. In ACT I, clinical remission rates at week 8 for placebo, 5 mg/kg infliximab, and 10 mg/kg infliximab were 15%, 39%, and 32%, respectively, whereas MH was 34%, 62%, and 59%, respectively. Similar results were found in ACT II [14]. In the ACT studies if only an endoscopic subscore of 0 was considered, the results were comparable to clinical remission rates, both in the short and long term. After start of therapy, MH at week 8 (Mayo endoscopic score of 0 or 1) predicted a significantly lower colectomy rate at week 52 compared with those who had Mayo endoscopy subscore of 2 or 3. Subsequent studies with adalimumab, golimumab, vedolizumab, and tofacitinib have all provided robust evidence of the association between MH and clinical response and remission.

Existing UC endoscopy scoring systems

Numerous scores have been used for the assessment of endoscopic activity in UC, and a recent systematic review of the measurement of endoscopic healing identified 31 scoring systems [15]. The Table shows the most important endoscopic scoring systems in use in UC.

Truelove and Witts [16] described the first endoscopic score classifying UC into 1 of 3 categories—mild, moderate, or severe. This score has not been formally validated, is not quantitative, does not include endoscopic criteria, and never included remission or healing criteria. Baron et al [17] developed a score that assessed endoscopic appearance of rectosigmoid mucosa using a rigid proctoscope, and the disease activity was expressed by severity of bleeding and friability without considering ulcerations. The Baron score was modified by Feagan et al [18] with the removal of different levels of bleeding and with the inclusion of ulceration in the evaluation. This endoscopic score has been frequently used in clinical trials.

Schroeder et al [19] described the Mayo score that included both endoscopic and clinical items. The Mayo endoscopy score is now by far the most widely used scoring system, either in conjunction with clinical parameters (score: 0-12) or as a stand-alone tool (score: 0-3). Mayo endoscopy score of 0 and 1 are generally designated as MH in clinical practice and in clinical trials, though some experts advocate aiming for complete MH or Mayo endoscopic score of 0. The Mayo endoscopy score has the distinct advantage of being simple to score and therefore easy to adopt, though training is required to reduce interobserver variability. However, the range of the Mayo endoscopy score is limited to 4 and therefore its operational characteristics are not ideal to detect subtle inflammation at the lower end of the range. Each score grade has multiple features that are unweighted, which may lead to imprecision in assessment, and friability is subjective and detection is not standardized. Moreover, the score has been found to have adequate interobserver and intraobserver agreement from the experts, but markedly lower agreement when the trainees were involved in the scoring [8]. Recently, the interobserver agreement coefficient was higher among nonexperts than expert gastroenterologists ($\kappa = 0.71$ vs 0.53, respectively) [20]. In addition, with the latest generation of high-definition endoscopes, vascular pattern is rarely seen to be obliterated, but more often are distorted and tortuous [21,22]. The need for a better definition of endoscopic activity, the definition of MH and the lack of a fully validated tool have recently led to the proposal of new indices in an attempt to increase interobserver agreement.

New validated UC endoscopy scores

Travis et al [23] proposed the Ulcerative Colitis Endoscopic Index of Severity. The Ulcerative Colitis Endoscopic Index of Severity was developed as reliable and validated score of endoscopic severity of UC. This index takes into account the 3 endoscopic findings such as vascular pattern, bleeding, and erosions and ulcers with the most severely affected mucosa scored. It is a useful tool in clinical practice and is starting to be adopted routinely in the central readout for clinical trial as it is reliable, is easy to reproduce, and it may reduce variations between different observers. However, it also has several limitations. The definition of endoscopic findings of MH remains unclear. In addition, the thresholds for mild-to-moderate and severe disease have not been completely validated. The disease extension is not evaluated and advantage in the interobserver agreement over simpler scores has not yet been demonstrated [24].

The Ulcerative Colitis Colonoscopic Index of Severity was recently proposed to overcome these limitations. The Ulcerative Colitis Colonoscopic Index of Severity includes disease extension [25].

Table
Endoscopic scoring systems in ulcerative colitis.

Endoscopic scores	Technique	Calculation	Validation	Limitations
Mayo subscore [19]	White light	*Four grade scale* Normal (0) Mild (1): erythema Moderate (2): friability, erosions Severe (3): spontaneous bleeding, ulcerations	Partially validated	No endoscopic definition of MH Overlap grade 1-2 Low interobserver agreement
Ulcerative Colitis Endoscopic Index of Severity (UCEIS) [23,24]	White light	Total score (3-11) from the sum of 3 components: *Vascular pattern*: normal (1), patchy obliteration (2), obliterated (3). *Bleeding*: none (1), mucosal (2), luminal mild (3), luminal moderate-severe (4). *Lesions*: none (1), erosions (2), superficial ulcer (3), deep ulcer (4).	Validated	No endoscopic definition of MH No thresholds for mild, moderate, and severe disease No definition of superficial vs deep ulcer
Ulcerative Colitis Colonoscopic Index of Severity (UCCIS) [25]	White light	Total score (0-162) = 3.1 × (sum of A in 5 tracts) + 3.6 × (sum of B) + 3.5 × (sum of C) + 2.5 × (sum of D): vascular pattern, granularity, lesions, friability/bleeding	Partially validated	Requires total colonoscopy No definition of MH No thresholds for mild, moderate, and severe disease