**Mayo Endoscopic Score and Ulcerative Colitis Endoscopic Index Are Equally Effective for Endoscopic Activity Evaluation in Ulcerative Colitis Patients in a Real Life Setting**

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**Abstract:** The role of endoscopic evaluation in ulcerative colitis (UC) is well recognized, but a universally accepted gold standard for endoscopic activity evaluation is still lacking, and many scores have been proposed to this purpose. Among these, the Mayo Endoscopic Score (MES) and the Ulcerative Colitis Endoscopic Index (UCEIS) are currently the most used in trials and clinical practice. The aim of the study is to evaluate feasibility and performance of MES and UCEIS among expert endoscopists with no specific expertise in inflammatory bowel diseases (IBD), in a single hospital center. Two minutes video recordings, from colonoscopy of 12 UC patients, were observed and scored, according to MES and UCEIS, by seven hospital gastroenterologists with experience in digestive endoscopy and no particular expertise in IBD. Knowledge and utilization of the two scores were investigated. Inter-observer agreement and agreement with an IBD-expert gastroenterologist of the same center (central reader), and correlation between the two scores, was calculated. Among the endoscopists, MES was much more known and currently used than UCEIS. Both the scores displayed a similar good performance. Agreement with central reader was moderate for MES and UCEIS, and interobserver agreement was good, for both MES and UCEIS. Correlation between the two scores was very good both for central reader and for the hospital endoscopists. This single center study confirmed potential feasibility and usefulness of MES and UCEIS for assessment of endoscopic activity in UC patients in a real-life setting.

**Keywords:** ulcerative colitis; endoscopy; endoscopic scores; Mayo Endoscopic Score; Ulcerative Colitis Endoscopic Index of Severity; interobserver agreement; central reader

1. **Introduction**

Ulcerative colitis (UC) is a chronic inflammatory disease that affects the colonic mucosa, involving the rectum and proximally extending throughout the colon to a variable degree. It is clinically characterized by a relapsing and remitting course with symptoms like bloody diarrhea, abdominal pain and loss of weight during flare periods [1]. The annual incidence of UC in Europe is about 24.3 per 100,000 per person years, and the prevalence is about 322 per 100,000 per person years, with highest occurrence between the second and fourth decade of life with a relatively equal gender distribution. Recent findings in geographic trends seem to question the previously observed north–south gradient, for
UC incidence is rising in countries such as Asia and North Africa, in parallel with the industrialization and “westernization” of these areas [2].

Since the etiology of the disease is still unknown, no curative therapy exists. Current approved treatments, such as mesalamine, corticosteroids, immunomodulatory drugs (immunosuppressant, biologic drugs, small molecules), are directed to control the inflammatory burden, with the final goal of inducing and maintaining remission. Moreover, the definition of “disease remission” has consistently changed throughout the years. In fact, until the end of the 1990’s, the primary therapeutic goal has been symptom control, with corticosteroids being the most effective therapy for disease flares control [3]. At the turn of the century, from the advent of biologic drugs, the consideration of the therapeutic target has dramatically changed. The profound effect of such drugs at the mucosal level has pushed forward the concept that the healing of the colonic mucosa, confirmed by endoscopic examination, should represent a more solid end-point to achieve in UC patients. The importance of mucosal healing (MH) was recognized as early as 1966, when Wright and Truelove performed serial biopsies on UC patients and concluded that patients with MH after cortisone treatment were more frequently in clinical remission after 1 year (40% vs. 18%) [4]. More recently, consistent literature data confirmed that MH is associated not only with short term symptoms improvement, but even with long-term complications prevention, such as steroid use, hospitalization, uncontrolled bleeding, colorectal cancer and colectomy [5–7]. In accordance with that, the importance of a correct and objective reporting of endoscopic activity of UC patients has been clearly addressed and underlined. In fact, inaccuracy and misinterpretation of endoscopic pictures may lead to results variation in clinical trials and erroneous management in clinical practice. In a randomized, double-blind, placebo-controlled, multicenter study investigating the safety and efficacy of a delayed-released mesalamine formulation in UC patients, final results profoundly changed after endoscopic reports’ revision by expert central readers [8].

In order to unify endoscopic reports and decrease interpretation variations, endoscopic scores for UC activity evaluation have been proposed. To date, while 31 different scores have been described so far in literature, very few are currently used, and the way to improve the objectivity of endoscopic reports in UC patients is still matter of debate [9]. Among endoscopic scores, Mayo Endoscopic Score (MES) and Ulcerative Colitis Endoscopic Index of Severity (UCEIS), are those that are more often used in clinical trials. Both the scores consider the more affected bowel segment and give a numeric score with the higher points indicating more severe disease. The first one was first described in 1987, as a part of a composite score including both endoscopic and clinical items, in a clinical trial comparing oral 5-aminosalicylic acid therapy vs. placebo [10]. It is characterized by four classes of severity ranging from 0 to 3, with 0 indicating inactive disease with normal mucosa; 1 mild disease (erythema and mild friability); 2 moderate disease (marked erythema, friability, absent vascular pattern and erosions); and 3 severe disease (spontaneous bleeding and diffuse ulceration). The UCEIS has been recently developed and has demonstrated a strong prognostic value [11,12]. This score provides a continuous 0 to 8 scale, resulting from the sum of separate scores for the vascular pattern, the presence of bleeding and of mucosal lesions (erosions or ulcers). Summary of the characteristics of the two scores are presented in Table 1.

The aim of the present study is to evaluate feasibility and performance of MES and UCEIS in real-life settings in a single center observational study, including expert hospital endoscopists with no specific expertise in IBD.
Table 1. Summary of the characteristics of MES and UCEIS.

| Characteristics             | Mayo Endoscopic Score (MS) | Ulcerative Colitis Endoscopic Index of Severity (UCEIS) |
|-----------------------------|----------------------------|--------------------------------------------------------|
| Type                        | Discrete (4 classes)       | Continuous                                             |
| Variables                   | Mucosal lesions, bleeding and hyperaemia | Mucosal lesions, vasculature, bleeding |
| Range                       | 0–4                        | 0–8                                                    |
| Mucosal healing Score       | Score 0–1                  | Not specified                                          |
| Severe disease              | Score 3                    | Score ≥ 7                                              |
| Statistical validation      | Partial                    | Partial                                                |
| Used in trials              | Yes                        | Scant                                                  |
| Diffuse in clinical practice| Yes                        | No                                                     |
| Strength                    | Simple, diffuse            | Objective, prognostic value                             |
| Limitation                  | Subjective, imperfect agreement | More complex                                          |

2. Materials and Methods

2.1. Videos

Colonoscopy of 12 consecutive UC outpatients at S. Andrea Hospital in Rome, Italy, were performed by Olympus colonoscopes and recorded by ENDOBASE software (Olympus Group Company, Hamburg, Germany). Inclusion criteria were: certain diagnosis of UC (by consistent clinical, biochemical, endoscopic and histologic features), complete routine colonoscopy (emergency examinations were excluded), consent to the recording of the examination. From the full videos, two-minutes recordings, representing all the colonic segments, were extracted by Magix Video Deluxe software (MAGIX Software GmbH, Berlin, Germany). The videos were anonymized from anagraphic data, and they present a superscript indicating every bowel segment. The videos have already been previously utilized in another published study [13].

2.2. Evaluation

The videos were observed and scored, according to MES and UCEIS, by seven hospital gastroenterologists with at least 5 years of experience in digestive endoscopy, with no particular expertise in IBD, at S. Giovanni Addolorata Hospital in Rome, Italy. The two scores were compared in a total of 84 reads, from 12 patients. A gastroenterologist with more than 15 years of endoscopic experience and a particular expertise in IBD was considered as central reader. Before the observation of the videos, the gastroenterologists were asked whether they knew and currently used the two scores. After that, a brief summary of the two scores was presented, and a resuming chart of the two scores was given to the gastroenterologists. Then, every single gastroenterologist, in an isolated room, watched the videos and, after the indication of the most affected colonic segment in every video, scored it according to the two scoring systems. All the operators were unaware of the clinical data of the patients and of the colleagues’ evaluation.

2.3. Statistics

Knowledge and utilization of the two scores among the seven hospital endoscopists were investigated and expressed as proportion (%) of endoscopists who declared to know and/or currently use the two scores. Inter-observer agreement and agreement with central reader were calculated and expressed as $k \pm$ standard deviation. Agreement grade was defined minimal ($k \leq 0.2$), poor ($k = 0.21–0.40$), moderate ($k = 0.41–0.60$), good ($k = 0.61–0.80$), and excellent ($k \geq 0.81$). Considering the different ranges of the two scores, the data were weighted as previously described in literature [14]. Spearman’s rank correlation ($r$) between the two scores has been calculated, both for hospital gastroenterologists and for the central reader, as an indirect measure of validity of the two scores. MedCalc software (version 12.5) has been used for statistical analysis of the data.
3. Results

Among the hospital gastroenterologists, MES was known by 7/7 (100%), and currently used by 5/7 (71%), while UCEIS was known by 2/7 (29%) and currently used by none (Figure 1).

Both the scores displayed similar satisfactory results. The identification of the most affected segment showed good agreement between the operators (k = 0.79 ± 0.41) and moderate agreement between operators and central reader (k = 0.54 ± 0.50). Inter-observer agreement was good, both for MES (k = 0.68 ± 0.2) and UCEIS (k = 0.64 ± 0.17) (Figure 2A). Agreement with central reader was moderate for MES (k = 0.52 ± 0.29) and UCEIS (k = 0.59 ± 0.22) (Figure 2B). Correlation between the two scores was excellent, both for the hospital gastroenterologists (r = 0.82, p < 0.0001) and for the central reader (r = 0.90, p = 0.0001) (Figure 3A,B).

Figure 1. Knowledge and utilization of MES and UCEIS among hospital endoscopists. Percent and absolute numbers of yes/no answers of the seven operators to the questions about the knowledge and their current use of the two score are represented.
be extensively validated, diffuse and user-friendly, with consistent inter-rater agreement between different operators (not necessarily IBD experts), and eventually correlated with gold standards for endoscopic evaluation of UC is still lacking, and current scores are either rarely used or have suboptimal validity. In the present study we focused on the potential application of two of the most known and used UC endoscopic scores, namely the MES and UCEIS, in a real-life setting. In fact, besides the relevance in clinical trials, the implementation of utilizing valid endoscopic scores among clinical gastroenterologists may provide consistent advantages for the correct management of UC patients. First, endoscopic scores may help the clinician to better evaluate response to therapy and guide a possible reduction or increment of medical treatment. Moreover, the higher objectivity of endoscopic reports may facilitate the interpretation of colonoscopic findings among different physicians/centers, considering that often IBD specialists are called to evaluate their UC patients’ colonoscopy reports performed by non-IBD dedicated endoscopists. Finally, a score with a consistent prognostic value may help the clinician to discriminate between patients to refer to intensive care or to a tight follow-up from those in which frequent visits are unnecessary, with evident resource optimization.

Therefore, an ideal score to evaluate endoscopic activity in real-life settings should be extensively validated, diffuse and user-friendly, with consistent inter-rater agreement
between different operators (not necessarily IBD experts), and eventually correlated with clinical parameters useful for the management of patients. A recent Cochrane meta-analysis evaluated 19 scoring systems for UC previously described in literature. The authors found that none of them has a proper full validation, in terms of validity (evaluation of the components of the score, comparison with other indices of disease activity), reliability (intra- and inter-rater agreement, test-retest reliability, internal consistency), responsiveness (modification after effective treatments) and feasibility (evaluation of the ease of administration and time required). Among those, MES and UCEIS have been evaluated for reliability, construct validity and responsiveness [15]. In an educational program of the Italian Group for Inflammatory Bowel Disease (IG-IBD), the agreement for MES was 0.53 among 14 IBD-expert gastroenterologists and 0.71 among 30 general gastroenterologists [16], and a specific training consistently increased the agreement among 237 physicians (k from 0.51 to 0.76) [17]. Agreement for UCEIS among 25 investigators who scored 28 videos was moderate (k = 0.50) [14]. Few studies directly compared MES and UCEIS performance. A recent study showed a moderate-good interobserver agreement for MES, UCEIS and Ulcerative Colitis Colonoscopy Index of Severity (UCCIS) among three gastroenterologists who scored 67 videos of UC colonoscopies [18]. In another study, MES and UCEIS showed similar good agreement and correlation between two expert endoscopists (k = 0.76 and 0.69, respectively, with r = 0.89) and among trainees, where an image-based training consistently improved performance [13]. In a single center retrospective study including 61 UC patients, UCEIS correlated to no response to biologic therapy and colectomy better than MES [19]. In another single center retrospective study including 92 patients, UCEIS predicted the need for colectomy more accurately than MES (receiver-operator characteristic (ROC) area 0.85 vs. 0.65), and 80% of patients with UCEIS ≥7 underwent colectomy [20]. In a study including 41 UC patients who received colonoscopy before and after tacrolimus remission induction therapy, UCEIS better reflected clinical improvement than MES, and correlated with a better clinical outcome such as reduction of colectomy rate and relapse. Interestingly, the authors explained the difference between the scores for the lower accuracy of MES in the evaluation of ulcer healing, since the score does not discriminate between deep and shallow ulcers, unlike UCEIS [12]. In accordance with previous studies, the present work showed good agreement both for MES and UCEIS, with comparable efficacy in evaluation of UC endoscopic activity. The main limitation of the present investigation is the low number of operators involved, so results of the study should be interpreted with caution. Nonetheless, we intended to evaluated feasibility and efficacy of the scores in a single center, representative of hospital endoscopy, in a real-life scenario, without pre-calculation or selection of sample size.

As further confirmed by our investigation, MES has the advantage of being user-friendly and simple, and more well known and diffuse among general endoscopists in comparison to UCEIS. Limits of MES include imperfect agreement, in particular for intermediate classes (score 1–2), subjectivity, poor definition of severe disease (the aforementioned lack of discrimination between deep and superficial ulcers), and different prognostic values of the scores 0 and 1, that are both generally included in the “mucosal healing” definition. On the other hand, UCEIS has a more rigorous development process, considers objective items, and has a strong prognostic value [20–23]. Nonetheless, UCEIS is slightly more complex than MES and definitely less utilized in clinical practice. For the different characteristics of the two scores, considering the potential advantages of their utilization in a real-life setting, one could speculate that MES should be easily implemented among general and territorial endoscopists, since it is already well known and diffuse, while UCEIS is probably better placed for utilization in IBD centers, where its accurate prognostic relevance could help in refining and tailoring intensity of care for UC patients. A practical model of future application of the scores may be similar to what happen in hepatology for the evaluation of cirrhotic patients, where the Child-Pugh score is more diffuse and used at a basic level and the Model of End-stage Liver Disease (MELD) score the more accurate and relevant prognostic value, is used in the specific setting of liver transplant list building.
In conclusion, the present single center real-life study confirms feasibility and validity of MES and UCEIS for UC endoscopic activity evaluation. Waiting for more relevant and accurate tools to assess disease activity in UC patients, such as histologic activity evaluation, HD endoscopes and chromoendoscopy/magnification, the implementation of the utilization of endoscopic scores represent a practical way to improve reliability and uniformity of endoscopic reports in general gastroenterological hospitals and in referral IBD centers.

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