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Accuracy of the Pancolonic Modified Mayo Score in predicting the long-term outcomes of ulcerative colitis: a promising scoring system

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Abstract

Background: Different endoscopic scoring systems for assessing ulcerative colitis (UC) severity are available. However, most of them are not correlated with disease extent.

Objectives: Our study aimed to compare the predictive value of the PanMay score *versus* the endoscopic Mayo (MES), Ulcerative Colitis Endoscopic Index of Severity (UCEIS), and Dublin score in predicting long-term outcomes of UC.

Design: This retrospective study enrolled consecutive UC patients who underwent colonoscopy before at least a 3-year follow-up.

Methods: The PanMayo, MES, UCEIS, and Dublin scores and the baseline clinical and demographic characteristics of the participants were assessed. Endpoints were disease flare that required novel biological therapy, colectomy, and hospitalization. Patients were stratified using baseline clinical activity.

Results: Approximately 62.8% of the 250 enrolled patients were in clinical remission. In these patients, the PanMayo, MES, and Dublin scores were positively associated with the risk of clinical flare. The MES score increased with clinical flare. The PanMayo score (>12 points), but not the MES score, was associated with the need for novel biological initiation and biological escalation. Furthermore, the Dublin and UCEIS scores of patients in remission who need novel biological treatment had a similar trend. Colectomy risk was associated with PanMayo and Dublin scores.

Conclusion: The combined endoscopic assessment of disease extent and severity can be more accurate in predicting outcomes among patients with UC. PanMayo score can be utilized in addition to the existing scoring systems, thereby leading to a more accurate examination.

Summary: UC endoscopic scores do not assess extension. Our study aimed to analyze the predictive value of the PanMayo score. Based on 250 patients, results showed that the long-term disease outcomes of UC could be predicted with the PanMayo score more accurately.

Keywords: endoscopy, extension, PanMayo, ulcerative colitis

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Introduction

Ulcerative colitis (UC) is a chronic, immune-mediated inflammatory disease that affects the colonic mucosa and extends continuously from the rectum to the proximal colon. The disease course of UC varies widely, from mild to refractory disease that may require colectomy.[1] Approximately 10–15% of patients have an aggressive disease pattern, and the cumulative risk of relapse is 70–80% at 10 years. The overall rate of proximal disease extension ranged from 12% to 30% over the disease course. The 5- and 10-year cumulative risks of colectomy range from 10% to 15%.[2]

To maintain health-related quality of life and prevent disability, patients with UC require life-long follow-up and treatment with well-established and evidence-based monitoring and treatment.[3] In recent years, the therapeutic goals have evolved from symptom-based therapy to the achievement of endoscopic and/or mucosal healing. According to the updated Selecting Therapeutic Targets in Inflammatory Bowel Disease (IBD) II consensus, the long-term goal should be mucosal healing. Thus, endoscopy plays an essential role in disease monitoring and management.[4,5]

Several scoring systems have been developed to objectively measure disease activity and mucosal healing. The easy-to-use Mayo Endoscopic Score (MES) and the validated Ulcerative Colitis Endoscopic Index of Severity (UCEIS) are the most evaluated and used indices for assessing vascular pattern, presence of erythema, friability, erosions, ulcerations, and bleeding.[6,7] In clinical practice, the most important limitation of the MES and UCEIS scoring systems is that they reflect the severity of mucosal inflammation only, not the extension of the disease. Previous data have shown that extensive disease is associated with higher rates of colectomy, hospitalizations, and colorectal cancer.[2,8] The recently developed Dublin score and the modified MES, which is a combination of disease severity and extension, had a good correlation with biochemical activity. However, there are no data on their correlation with long-term disease outcomes.[9,10]

The predictive accuracy of MES, UCEIS, and Dublin scores was investigated by several studies. One-year treatment failure was associated with elevated UCEIS and Dublin scores, while a lower baseline MES score was coupled with a lower risk for relapse. Meta-analyses of real-world and clinical studies of MES proved significantly decreased risk for relapse in the case of baseline MES 0 compared to MES 1 scores.[11–18]

Recently, the Pancolonic Modified Mayo Score (PanMayo), a new disease extent endoscopic score, has been found to have a strong association with MES and UCEIS, biomarker levels, and histological activity in UC.[19] Although the PanMayo score is a potentially promising scoring system, its accuracy, and ability to predict long-term clinical outcomes should be validated. Nevertheless, data comparing the accuracy of the PanMayo score, MES, UCEIS, and Dublin score in predicting the long-term disease outcomes of UC are limited.

This study aimed to compare the performance and accuracy of the PanMayo score *versus* the MES, UCEIS, and Dublin scores for predicting long-term disease outcomes in patients with UC.

Materials and methods

Study design and participants

This retrospective study was conducted at two referral IBD centers, including the IBD Center at Montreal General Hospital, McGill University Health Center, Montreal, Canada, and the Department of Medicine at Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary. Consecutive adult patients (aged ⩾18 years) diagnosed with UC, who underwent colonoscopy to assess disease activity between 1 January 2016 and 31 December 2019, were eligible to enroll in this research. The baseline was defined as the time of the index colonoscopy examination upon study admission. Patients were followed up for at least 3 years. Patients with incomplete colonoscopy, those with a follow-up duration of <3 years, and those with indeterminate colitis (IBD-U), previous colectomy, and *Clostridioides difficile* infection at the time of index colonoscopy were excluded from the analysis. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology statement.[20]

Data collection

Data on the demographic characteristics of the patients (including age at inclusion, sex), disease phenotype, and treatment history (previous and

concomitant medications) were collected from the electronic medical records upon study inclusion. Baseline disease characteristics, including date of diagnosis, disease duration, presence of extraintestinal manifestation, and history of intestinal surgery, were obtained. Disease extent and severity were classified using the Montreal classification.[21] Clinical activity was assessed using the partial Mayo (pMayo) score. All laboratory and biochemical parameters, including C-reactive protein, and fecal calprotectin upon study admission and during follow-up, were assessed.

Colonoscopy procedures were performed with high-definition optical colonoscopes (Olympus© CF Q165I; Olympus© CF-Q185H; or Olympus© CF-H190L) by trained gastroenterologists with 15–25 years of experience in endoscopy. Endoscopic scoring was based on written reports of colonoscopies, which always contained segmental MES scores. If segmental MES or UCEIS scores were not available on medical records, visual re-evaluation of images/videos was made by experienced gastroenterologists. PanMayo score, MES, UCEIS, and Dublin scores were recorded. The PanMayo score was calculated as the sum of the MES scores of the five colorectal segments and was multiplied by an inflammatory constant of 3 if the MES is >1 in at least one segment. Supplemental Table 1 shows the details of the PanMayo score calculation. Supplemental Tables 2–4 depict the calculation of the Dublin score, MES, and UCEIS.

At least 3 years after the index colonoscopy, information was collected from patients with disease flare, which required therapy modification, including the need for biological treatment, biologic-dose escalation, systemic corticosteroids, hospitalizations, and colectomy.

Outcome measurements

The co-primary outcomes were the rate of clinical flare in patients with clinical remission at baseline and the rate of colectomy in patients with clinical activity at baseline. The secondary outcomes were endoscopic remission and disease complication rates (IBD-related hospitalization and need for new systemic corticosteroid and novel biologic treatment or biologic-dose escalation).

Clinical activity, clinical remission, and flare were dichotomous variables. Clinical activity was defined as a pMayo score of $\geqslant 2$. Clinical remission was defined as a pMayo score of <2 and the absence of rectal bleeding. Clinical flare was defined as a pMayo score of $\geqslant 2$ and/or the presence of rectal bleeding in patients who were previously in clinical remission. Endoscopic activity in any segment was defined as an endoscopic Mayo score of $\geqslant 1$. Meanwhile, endoscopic remission in all segments was defined as an endoscopic Mayo of $\leqslant 1$.

The association between the different endoscopic scoring systems (PanMayo, MES, UCEIS, and Dublin) and long-term outcomes, including clinical flare and need for colectomy, novel biological therapy or biologic-dose escalation, and IBD-related hospitalization during the 3-year follow-up period after index colonoscopy was analyzed. The association between the endoscopic stores and long-term outcomes was assessed.

Statistical analysis

Descriptive statistics were expressed as mean and standard deviation or median and interquartile range (IQR) for continuous variables and numbers and percentages for categorical variables. Normality was tested using histograms and quantile–quantile plots. After checking assumptions, the groups with categorical variables were compared using the chi-square test or Fisher's exact test. The Kaplan–Meier survival curves with the log-rank test were used to determine the predictive ability of the PanMayo score, Dublin score, MES, and UCEIS score to predict long-term outcomes including clinical remission, disease flare, and need for colectomy, novel biological therapy, and hospitalization.

Based on the involvement of at least two segments and at least one that is affected by severe inflammation, the PanMayo score was categorized into three groups: 0, 1–12, and >12. The prediction of non-time-dependent categorical variables was analyzed using the logistic regression models. A p value of <0.05 indicated a statistically significant difference. Statistical analysis was performed using the Statistical Package for the Social Sciences software (IBM SPSS Statistics for Windows, version 20.0; IBM Corp., Armonk, NY, USA).

Ethical consideration

The present study was approved by the Regional and Institutional Human Medical Biological

Research Ethics Committee, University of Szeged (approval no.: 38/2022-SZTE), and by the Research Ethics Board, McGill University Health Centre (approval no.: 2023-8849) and carried out according to the guidelines stipulated in the declaration of Helsinki (1975 Declaration of Helsinki, 6th revision, 2008). Patients included in the retrospective study have given written informed consent for regular healthcare.

Results

Baseline characteristics of the patients

The data of patients with UC ($n=250$) were analyzed, and the median age at inclusion was 45 (IQR: 35.0–57.3) years. Furthermore, 46.8% of the patients were men. The median follow-up duration was 50 (IQR: 39.0–65.3) months. Approximately half (43.6%) of the patients had pancolitis, and almost two-thirds (63.2%) of the patients had an MES score of >0 at baseline, while the UCEIS and DUBLIN scores showed remission to mild disease in most of the patients [1 (IQR: 0–3) and 1 (IQR: 0–3)]. Of 250 patients, 93 (37.2%) had clinical activity (pMayo score of >1), while biochemical activity was characterized by a median of 3 (IQR: 1.7–7.0) mg/L of C-reactive protein and a median of 152 (IQR: 59–464) μg/g of fecal calprotectin at baseline. Approximately 34.7%, 17.6%, and 13.6% of patients received biological therapy, azathioprine, and systemic corticosteroids at the time of index colonoscopy, respectively. Table 1 shows data on the baseline demographic and clinical characteristics of the participants.

Prediction of long-term outcomes in patients in clinical remission at baseline

In total, 157 (62.8%) patients had clinical remission at baseline, while 45.2% of patients had nonzero MES at inclusion. The distribution of baseline MES scores were MES0 = 86 (55%), MES1 = 48 (31%), MES2 = 20 (13%), and MES3 = 3 (2%), while USEIS and DUBLIN scores were 0 (IQR: 0–0) and 0 (IQR: 0–2). A higher baseline PanMayo score (>0, any mucosal inflammation at any segment, $p=0.001$; >12, at least two segments involved and severe inflammation in at least one segment, $p=0.003$; Figure 1) was associated with the risk of clinical flares. A high baseline MES score (>0, $p=0.006$; Figure 2) and Dublin score (>0; $p=0.005$), but not UCEIS score was associated with an increased risk of clinical flare.

Patients with a PanMayo score of more than 12 points at baseline were more likely to require new biological therapies and biological dose escalation (Figure 3, $p=0.001$ and $p=0.031$), while a higher Dublin score ⩾4 (Figure 4, $p=0.003$) and UCEIS ⩾2 ($p=0.04$) were only associated with the need for new biological initiation.

In addition, a baseline PanMayo score of >12 ($p=0.002$) and a Dublin score of >3 ($p=0.002$) were associated with the need for IBD-related hospitalization. Similarly, a baseline PanMayo score of >0 ($p=0.002$), MES score of >0 ($p=0.002$), and Dublin score of >0 ($p=0.017$) were significantly associated with the need for systemic corticosteroids. In this cohort, 3/157 colectomies were performed during follow-up.

Prediction of long-term outcomes in patients with clinical activity at baseline

In total, 93 (37.6%) patients had clinically active UC at baseline while 93.5% of patients had nonzero MES at inclusion. The distribution of baseline MES scores were MES0 = 6 (6%), MES1 = 13 (14%), MES2 = 40 (43%), and MES3 = 34 (37%), while UCEIS and DUBLIN scores were 4 (IQR: 3–5) and 3 (IQR: 2–6). Furthermore, 15 (16.1%) of 95 patients required colectomy. The risk of colectomy was associated with a higher baseline PanMayo score (>12, $p=0.016$) (Figure 5) and Dublin score (⩾4, $p<0.001$) (Figure 6).

The Dublin score was associated with the risk of IBD-related hospitalization ($p=0.026$). Meanwhile, the PanMayo ($p=0.028$) and UCEIS ($p=0.019$) scores were associated with the need for novel biological therapy. Further connections were not identified between PanMayo, Dublin, MES, and UCEIS scores and secondary outcomes.

Supplemental Table 5 shows the predictive value of the PanMayo, MES, UCEIS, and Dublin scores for long-term endoscopic remission. Based on the logistic regression models, lower baseline endoscopic scores were associated with long-term endoscopic remission ($p<0.001$). These correlations were found in all endoscopic scoring systems. The odd ratios of the PanMayo, Dublin, UCEIS, and MES scores were 0.954, 0.762, 0.687, and 0.506, respectively.

Table 1. Baseline demographic and clinical characteristics of UC patients.

Variables	Total cohort ($n = 250$)	Clinical remission (pMayo < 2) at baseline ($n = 157$)	Clinical activity (pMayo > 1) at baseline ($n = 93$)
Follow-up duration, months, median (IQR)	50 (39.0–65.3)	51 (40.5–67.0)	50 (26.0)
Sex, male (%)	117 (46.8)	77 (49.0)	40 (43.0)
Age at inclusion, years, median (IQR)	45.0 (35.0–57.3)	46.0 (37.5–58.0)	42 (29.0-54.0)
Disease duration at inclusion, years, median (IQR)	10.0 (15.0–18.0)	11.0 (6.0–19.0)	8.0 (5.0–14.0)
Disease extent, *n* (%)			
Proctitis	43 (17.2)	26 (16.6)	17 (18.3)
Left-sided	93 (37.2)	57 (36.3)	37 (39.8)
Pancolitis	113 (45.2)	74 (47.1)	39 (41.9)
Disease activity			
pMayo median (IQR)	1 (0–2)	0 (0–0)	4 (3–6)
MES median (IQR)	1 (0–2)	0 (0–1)	2 (2–3)
MES > 0, *n* (%)	158 (63.2)	71 (45.2)	87 (93.5)
UCEIS median (IQR)	1 (0–3)	0 (0–0)	4 (3–5)
DUBLIN median (IQR)	1 (0–3)	0 (0–2)	3 (2–6)
PanMayo median (IQR)	2 (0–18)	0 (0–3)	18 (9–30)
CRP, mg/L median (IQR)	3 (1.7–7.0)	3 (1.1–5.25)	6 (2.8–11.9)
FC, μg/g median (IQR)	152 (59–464)	97 (51.5–206)	277 (159.5–925.5)
Extraintestinal manifestations, *n* (%)			
Arthritis	35 (14.0)	25 (15.9)	10 (10.8)
Spondylitis	10 (4.0)	5 (3.2)	5 (5.4)
Skin disease	7 (2.8)	5 (3.2)	2 (2.2)
Primary sclerosing cholangitis	11 (4.4)	9 (5.7)	2 (2.2)
Treatment at baseline, *n* (%)			
Oral 5-ASA	181 (72.4)	113 (72.0)	68 (73.1)
Topical 5-ASA	34 (13.6)	20 (12.7)	14 (15.1)
Oral budesonide	22 (8.8)	5 (3.2)	17 (18.3)
Topical budesonide	10 (4.0)	1 (0.6)	9 (9.7)
Azathioprine	44 (17.6)	28 (17.8)	16 (17.2)
Systemic corticosteroid	34 (13.6)	9 (5.7)	25 (26.9)
Biologics	90 (36.0)	50 (31.8)	40 (43.0)

CRP, C-reactive protein; FC, fecal calprotectin; IQR, inter-quartile range; MES, Mayo Endoscopic Score; *n*, number of patients; pMayo, partial Mayo score; UC, ulcerative colitis; UCEIS, Ulcerative Colitis Endoscopic Index of Severity; 5-ASA, 5-aminosalicylic acid.

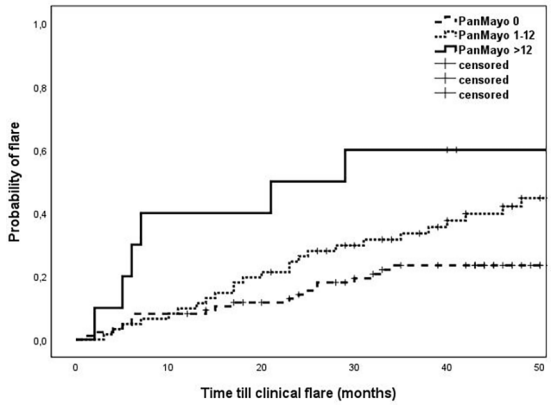

Figure 1. Survival analysis of the remission cohort showed an increased risk of flare parallel with a higher baseline PanMayo score (non-zero score, $p = 0.001$; a score of >12 points, $p = 0.003$).

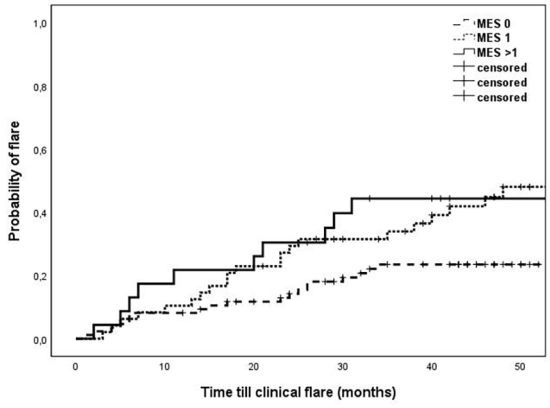

Figure 2. Survival analysis of the remission cohort showed an increased risk of flare parallel with a higher baseline MES score ($p = 0.006$).
MES, Mayo Endoscopic Score.

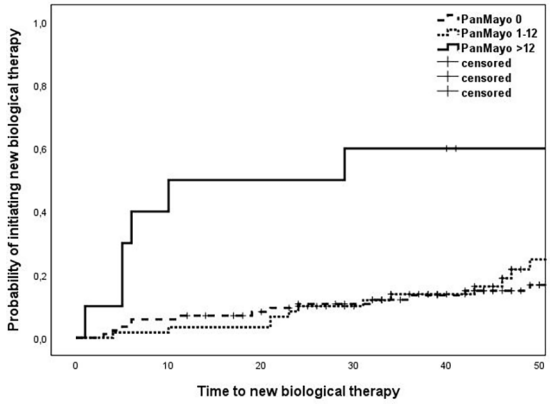

Figure 3. Survival analysis of the remission cohort showed an increased risk of novel biological treatment initiation parallel with a higher baseline PanMayo score (score of >12, $p < 0.001$).

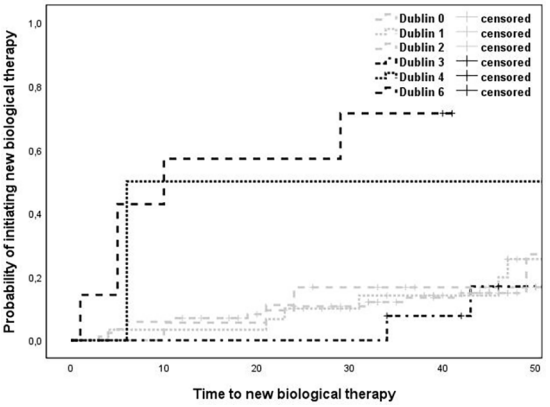

Figure 4. Survival analysis of the remission cohort showed that an increased risk of novel biological treatment initiation was coupled with severe pancolitis assessed based on a baseline Dublin score of >4 ($p = 0.003$).

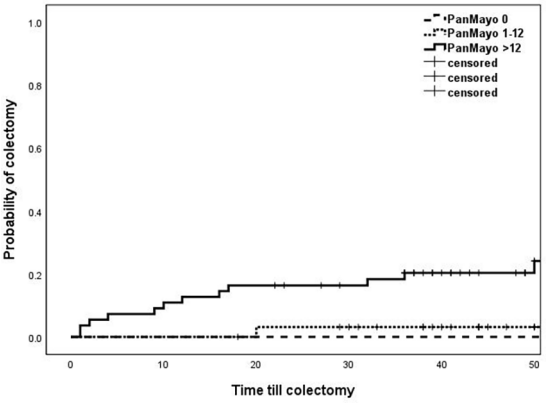

Figure 5. Survival analysis of the flare cohort showed that the increased risk of colectomy was coupled with a baseline PanMayo score of >12 ($p = 0.016$).

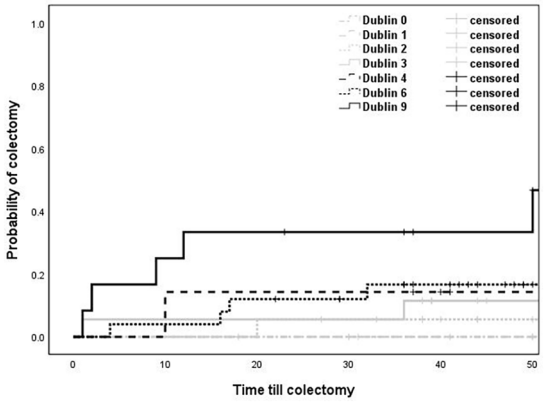

Figure 6. Survival analysis of the flare cohort showed an increased risk of colectomy parallel with a higher baseline Dublin score ($p < 0.001$).

Discussion

In this current study, the predictive ability of the endoscopic scoring systems (MES, UCEIS, PanMayo, and Dublin score) was compared to predict the long-term outcomes of UC. Clinical flare was more accurately predicted using scores combining disease extent and severity of mucosal inflammation (PanMayo and Dublin score compared with UCEIS score). In patients with clinical remission, a high PanMayo score (>12) or Dublin score (⩾4) was associated with the need for novel biologic therapy and hospitalizations. The PanMayo and Dublin scores were associated with an increased risk of colectomy in patients with clinical activity. However, the absolute number of colectomies was low (16.1%) in patients with clinical activity. Lower endoscopic scores at baseline were correlated with long-term endoscopic remission across all examined scoring systems.

Extensive disease is associated with a worse disease course and an increased risk of colectomy and colorectal cancer.[22,23] Of note, the Selecting Therapeutic Targets in IBD II consensus aims for endoscopic mucosal healing in UC.[5] Despite the correlations between histological scores and clinical and biochemical disease activities, the most commonly used MES and UCIES scores do not include disease extent.[24] Furthermore, the comparability of these endoscopic scores is also subject to inter-observer variation.[25,26]

The Dublin scoring system and the modified MES were established to simply measure endoscopic inflammation, with consideration of extension and severity.[9,10] Dublin score provides an easy-to-use tool to assess disease extension and severity of three colorectal segments based on the overall MES score; however, the scale is relatively short (0–9). A retrospective study revealed that a Dublin score of >2 points predicted a 50% probability of treatment failure (defined as therapeutic escalation, hospitalization, and/or colectomy) at 24 months. Meanwhile, a Dublin score of <3 predicted a 10.4% probability of treatment failure.[13] Modified Mayo Endoscopic Score (MMES) combines the simplicity of MES and the relatively high-resolution capacity to describe colonic activity with a decimeter measurement; however, the calculation procedure limits usability in daily care. A prospective study analyzed the MMES including 150 UC patients during a 5-year follow-up and demonstrated the additional value of the MMES over MES in predicting clinical outcomes in UC.[14] According to our analysis, the PanMayo, Dublin, and MES scores, but not the UCEIS score, were associated with an increased risk of clinical flare in patients with clinical remission.

In the current cohort, the need for novel biological treatment initiation was associated with high baseline PanMayo and UCEIS scores in patients with baseline clinical activity. Meanwhile, patients with increased baseline Dublin scores had higher IBD-related hospitalization rates. PanMayo scores of >12 and Dublin scores of ⩾4 indicated a high risk of disease flare and colectomy. However, there were no associations between MES and long-term outcomes in patients with clinically active UC.

A retrospective study of patients with UC ($n = 87$) revealed an association between Dublin score and clinical and biochemical activity. The significant discriminative power of UCEIS (>5) scores could predict 1-year treatment failure. However, a higher Dublin score (>3) was not associated with the probability of remaining in clinical remission.[15] Chen *et al.*[11] investigated the predictive value of the Dublin score in contrast to UCEIS and proved superiority regarding mid- and long-term outcomes of UC patients in a retrospective trial. In the analysis, a Dublin score of ⩾4 was associated with an increased risk of colectomy, the need for infliximab, and the need for cyclosporine therapy. In the current study, higher PanMayo, MES, and Dublin scores, but not UCEIS scores, were associated with an increased risk of clinical flare. Furthermore, lower baseline PanMayo, Dublin, MES, and UCEIS scores were associated with higher rates of endoscopic remission. In our analysis, a PanMayo cutoff score of 12 and a Dublin cutoff score of 4 were associated with a higher disease burden (increased risk of flare, colectomy, hospitalizations, and treatment escalations).

Most clinical trials on UC defined an MES score of ⩽1 as the target for mucosal healing. However, in recent years, there has been accumulating evidence from real-world studies and meta-analyses that complete mucosal healing (an MES score of 0 compared with an MES score of 1) is associated with a 52% lower risk of clinical relapse.[16–18] Based on the result, an MES or UCEIS score of 0 may be recommended as an endoscopic target in UC treatment in the near future.[27] The study result also supports the notion that an MES score

of 1 was associated with a higher risk of flare compared with an MES score of 0. Of note, the incremental benefit of achieving endoscopic remission is associated with a lower risk of clinical relapse (relative risk: 0.37; 95% confidence interval: 0.24–0.56).[16–18] It is notable that approximately half of the enrolled patients with clinical remission at baseline had non-zero MES scores which highlights the further need to achieve strong therapeutic targets and continuous disease monitoring defined by STRIDE-II. The discrepancy between clinical symptoms and endoscopic activity described by MES enhances the importance of the combined endoscopic assessment of disease extent and severity.

The risk of colectomy has been associated with male sex, younger age at diagnosis, chronic continuous disease activity, and severe and extensive disease.[2,8,28–30] However, parallel endoscopic evaluation of disease extent and severity has never been observed in a real-world setting as assessed using the MES or UCEIS score. This current study showed an association between the novel endoscopic scores assessing both disease extent and severity and the risk of colectomy in parallel with the study of Chen *et al*.

The current study had several strengths. That is, it first showed the use of the new scoring system, which is a combination of endoscopic disease extent and severity of mucosal inflammation, in predicting UC outcomes. This is a relatively large cohort with a long follow-up duration, thereby allowing us to assess long-term outcomes including clinical flare, need for biological therapy, hospitalizations, and colectomy. However, our study also had some limitations. First, the retrospective design did not allow to calculate exact predictive values, while the overall low absolute number of colectomies may be regarded as a possible confounder bias. Second, inter-observer bias may have existed regarding the endoscopic evaluation among different interpreters (PLL and TM); however, endoscopies were done by experienced gastroenterologists with special interest in treating IBD patients. Of note, a central reading of endoscopy was not performed in our study. Despite these limitations, our study can provide additional evidence supporting the use of extent-adjusted endoscopic severity in UC. The PanMayo score was better in predicting long-term disease outcomes. The PanMayo score is simple and can be calculated using the MES scoring system and the disease extent (active segments). Therefore, it can be implemented in daily clinical practice.

In conclusion, an endoscopic scoring system with combined disease extent and severity is more specific in predicting long-term disease outcomes in UC and can be useful in identifying patients with a more aggressive disease course. The PanMayo score can be an additional tool to the existing scoring systems, thereby providing a more accurate assessment in predicting disease outcomes.

Declarations

Author's note

TM and PLL are the guarantors of the article. All authors have read and agreed to the submitted version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Regional and Institutional Human Medical Biological Research Ethics Committee, University of Szeged (approval no.: 38/2022-SZTE), and by the Research Ethics Board, McGill University Health Centre (approval no.: 2023-8849) and carried out according to the guidelines stipulated in the declaration of Helsinki (1975 Declaration of Helsinki, 6th revision, 2008). Patients included in the retrospective study have given written informed consent for regular healthcare.

Consent for publication

Not applicable.

Author contributions

Péter Bacsur: Conceptualization; Data curation; Formal analysis; Investigation; Writing – original draft.

Panu Wetwittayakhlang: Conceptualization; Data curation; Formal analysis; Investigation; Writing – review & editing.

Tamás Resál: Data curation; Formal analysis; Investigation; Writing – original draft.

Emese Földi: Data curation; Writing – original draft.

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Bernadett Farkas: Data curation; Writing – review & editing.

Mariann Rutka: Data curation; Writing – review & editing.

Talat Bessissow: Data curation; Writing – review & editing.

Waqqas Afif: Data curation; Writing – review & editing.

Anita Bálint: Data curation; Writing – review & editing.

Anna Fábián: Data curation; Writing – review & editing.

Renáta Bor: Data curation; Writing – review & editing.

Zoltán Szepes: Data curation; Writing – review & editing.

Klaudia Farkas: Data curation; Writing – review & editing.

Peter L. Lakatos: Conceptualization; Formal analysis; Investigation; Methodology; Resources; Writing – review & editing.

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Availability of data and materials

TM and PLL are the guarantors of the article. All authors have read and agreed to the submitted version of the manuscript. Data are available on request. The data cannot be shared publicly for the privacy of individuals that participated in the study. The data underlying this article will be shared on reasonable request to the corresponding author. The current manuscript, including related data and figures, has not been previously published and is not under consideration elsewhere.

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Supplemental material

Supplemental material for this article is available online.

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