The Degree of Ulcerative Colitis Burden of Luminal Inflammation score is superior to predicting medium- to long-term prognosis in patients with active ulcerative colitis

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Abstract

Aims: The endoscopic evaluation is crucial for the management and treatment of ulcerative colitis (UC). Currently, the Mayo Endoscopic Score (MES) and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) are two major endoscopic score systems to evaluate the status of mucosal inflammation and disease activity. However, in both MES and UCEIS systems, the disease extent is not included. The Degree of Ulcerative Colitis Burden of Luminal Inflammation (DUBLIN) score is a simple clinical score which is calculated as a product of the MES (0–3) and the extent of disease (E1–E3). The objective of this study was to compare the correlation among DUBLIN, UCEIS and MES, and also investigate the clinical characteristics for predicting treatment failure in patients with active UC.

Methods: Between March 2015 and April 2019, 172 patients who were previously diagnosed with UC and had undergone colonoscopy were recruited in this study. We retrospectively reviewed the endoscopic scores and clinical characteristics at the time of the colonoscopy and assessed the prognosis of the patients. Endoscopic response was defined as the decrease in MES \geq 1 grade.

Results: DUBLIN showed significant correlation with MES (r=0.748) and partial Mayo score (pMayo) (r=0.707), and moderately correlated with CRP (r=0.590). UCEIS also showed strong correlation with MES (r=0.712) but moderate correlation with pMayo (r=0.609) and CRP (r=0.588). Compared with the UCEIS (cut-off value: 4; sensitivity: 75.73%), DUBLIN score (cut-off value: 4; sensitivity: 86.41%) showed higher diagnostic sensitivity than UCEIS score (McNemar test, p < 0.05). Furthermore, a multivariate analysis also revealed that DUBLIN \geq 4 was the independent factor for predicting treatment failure for UC (p < 0.001, odds ratio: 1.547; 95% confidence interval: 1.32–1.88).

Conclusion: The DUBLIN score shows superior diagnostic performances in terms of sensitivity value compared with the UCEIS. Moreover, multivariate analysis indicates that DUBLIN \geq 4 is an independent factor for predicting medium- to long-term treatment failure in active UC patients.

Keywords: DUBLIN, endoscopic response, treatment failure, UCEIS, ulcerative colitis

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Introduction

Ulcerative colitis (UC) is a chronic relapsing immune-mediated inflammatory disease affecting rectal and colonic mucosa; the rectum is usually involved, and the inflammation extends proximally in a variable but contiguous manner.¹ During the past three decades, studies from countries of Europe and North America have shown Ther Adv Gastroenterol

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the prevalence of UC is 505/100,000 and 286/100,000, respectively.² Furthermore, since 1990, the annual percentage change of UC has been rising in newly industrialized countries like South America and Asia, which include Brazil (14.9/100,000) and South Korea (4.2/100,000), respectively.² These data highlight the urgent need for research into the prevention of UC and effective treatment in health systems to manage this complex and costly immune-mediated intestinal disease.

More recently, the evaluation of therapeutic effects for UC has been changing from assessing clinical response to endoscopic mucosal improvement.³ The endoscopic evaluation is crucial for the treatment and management of UC because endoscopic remission or mucosal healing contributes to an favorable prognosis in UC patient which includes the increased rates of steroid-free remission, reduced need for colectomy and decreased rates of hospitalization.^{4–7} These data suggest that endoscopic evaluation plays a critical role in assessing the severity of intestinal inflammation and may predict the prognosis of patients with UC following the initiation endoscopic score.

Currently, the Mayo Endoscopic Score (MES) and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) are two major endoscopic score systems to evaluate the status of mucosal inflammation and disease activity. The MES, which was presented by Schroeder et al. in 1987, has been the most commonly used endoscopic evaluation scale until now.8,9 Recent studies have demonstrated that a MES of 0 was associated with less colectomy than a MES of 1.10 In 2012, Travis et al.11 proposed the UCEIS score system, with a greater number of stratifications (0-8) than those of MES (0-3), which thus could distinguish mucosal inflammation and disease activity in greater detail. Also, it has been demonstrated that UCEIS outperforms MES in predicting the medium- to long-term prognosis for UC with clinical remission and the need for escalation treatment.^{12,13} UCEIS was also reported to predict corticosteroid treatment failure in acute severe colitis and assess the long-term response to anti-TNFa therapy.14,15 Furthermore, UCEIS was also proved to be strongly correlated with patient-reported symptoms and minimally affected by clinical information.¹⁶ However, for both MES and UCEIS, only the most severely

affected tract of the intestine is evaluated, suggesting that the disease extent is not included in these two systems. Importantly, the IBSEN study demonstrated that disease extension is a crucial independent factor for colectomy in patients with UC.¹⁷ Qiu and coworkers further proved that proximal disease extension increases the risk of recurrence and treatment intensification.¹⁸ Furthermore, Ekbom *et al.*¹⁹ and Lutgens MW *et al.*²⁰ also reported the close relationship between colorectal cancer and disease extension.

Considering the potential importance of disease extent in evaluating the severity of UC, recent data proposed the Degree of Ulcerative Colitis Burden of Luminal Inflammation (DUBLIN) score, which is calculated as a product of the MES (0–3) and the extent of disease (E1–E3).²¹ Compared with the Modified Mayo Endoscopic Score (MMES)²² and Ulcerative Colitis Colonoscopic Index of Severity (UCCIS),²³ the DUBLIN score is easier to calculate and more suitable for clinical decisionmaking. Moreover, it also shows a significant correlation with inflammatory markers such as fecal calprotectin²¹ and demonstrates a favorable association with MES and histological activity as well.²⁴

Currently, to our knowledge, there are no other evidences to evaluate the predictive value of the prognosis for active UC patients using DUBLIN and UCEIS score. Hence, in this retrospective clinical study, we aimed to compare the correlation between DUBLIN and UCEIS, a well-evidenced endoscopic score system, and also to investigate the clinical factors for predicting treatment failure in patients with active UC.

Materials and methods

Patients

Between March 2015 and April 2019, 654 patients with UC in the Shanghai Tenth People's Hospital of Tongji University were reviewed. All of the UC patients were diagnosed according to the established standard for clinical, radiological, pathological and endoscopic criteria. Inclusion criteria of this study were as follows: (1) adult patients ($18 \le age \le 65$); (2) confirmed diagnosis of UC at least 3 months before screening; (3) active UC, defined as Mayo score ≥ 3 and a subscore of MES ≥ 1 ; (4) flexible endoscopy and reexamination data and in-hospital clinical course data were available. Exclusion criteria included: (1) Crohn's

disease, intestinal Bechet's disease, intestinal tuberculosis, toxic megacolon and inflammatory bowel disease unclassified; (2) history of colon surgery; (3) lack of endoscopy procedures, laboratory parameters and clinical information; (4) disease extent could not be evaluated. Finally, 172 patients with active UC were included in this study. All of the 172 patients had regular visits and received regular colonoscopy and reexamination. This study was approved by the Institutional Review Boards of the Shanghai Tenth People's Hospital (SHSY-IEC-4.1/20-182/01) and got exemption from informed consent because of the retrospective study design. The endoscopic severities were evaluated at the original time of the endoscopy. The clinical indices including partial Mayo score (sum of individual scores for physician global assessment, rectal bleeding and stool frequency), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), hemoglobin, platelets and albumin (ALB) were collected during regular follow-up visits.

Endoscopic scoring for UC: MES, DUBLIN and UCEIS

All of the UC patients were required to drink polvethylene glycol electrolytes powder prior to the procedures. During endoscopy, a group of endoscopists (<4), who, unaware of the outcome, assessed and scored the visualized colon for the severity under endoscopic examination using the MES and recorded the extent of disease according to the Montreal classification (E1 = proctosigmoid; E2 = distal to splenic flexure; E3 = proximal to splenic flexure).²⁵ Photographs were scored again by two experienced assessors (L.C. and M.S.) and UCEIS (Supplemental Table 1),¹¹ MES and DUBLIN scores were calculated. DUBLIN was calculated as a result of the MES and proximal disease extent (Supplemental Table 2).²¹ The disease extent (E1, E2, E3) was confirmed by using computed tomography or magnetic resonance imaging if the disease extent was not clear. The disagreements were solved by negotiating with a senior author (Z.L.). The typical endoscopic images of UCEIS, MES and DUBLIN are shown in Figure 1.

Assessment of the outcome

The primary endpoint of this retrospective study was to evaluate the predictive value of two endoscopic scoring systems including UCEIS and DUBLIN. The primary outcome was treatment failure (i.e. no endoscopic response) during the follow-up. According to the international consensus, the endoscopic response was defined as the decrease in MES ≥ 1 grade.³ The secondary endpoint of this study was to investigate the independent clinical factors for predicting treatment failure for UC.

Statistical analysis

Continuous variables were presented using standard descriptive statistics such as mean \pm standard deviation or median with an interguartile range. The Chi-square test was performed to compare categorical data including patient sex and other clinical features. The Mann-Whitney U test was performed to compare non-parametric variables. The correlations between the DUBLIN and the MES, partial Mayo (pMayo) score (clinical severities), and serum CRP were tested using Spearman's rank correlation coefficient. Receiver operating characteristic (ROC) curve analysis was performed to identify the cut-off value with the optimal specificity and sensitivity of the DUBLIN and UCEIS. The sensitivity and specificity between DUBLIN and UCEIS were compared by McNemar test. Binary logistic regression analvsis was used to identify predictive factors for the prognosis among the items of the DUBLIN. The statistical significance was defined as a p value less than 0.05. All statistical analyses were accomplished using the Statistical Package for the Social Sciences 22.0 software (SPSS Inc.).

Results

Clinical characteristics at the baseline

The clinical characteristics of patients recruited in this study are shown in Table 1. A total of 172 patients with active UC were finally included. All of the 172 patients were followed up for 18.24 ± 5.05 months. The mean follow-up time for colonoscopy was 6 months (4–7 months). Patients had mean baseline age of 44 years (30–58 years). Mean course duration was 24 months (8–68 months). Of these patients, 165 (95.83%), 103 (59.88%) and 78 (45.35%) were taking oral 5-aminosalicylates, corticosteroids and azathioprine, respectively. Five patients (2.91%) were treated with anti-tumor necrosis factor agent (i.e. infliximab) at the baseline. Serum CRP levels ranged from 7.39 to 46.45 mg/

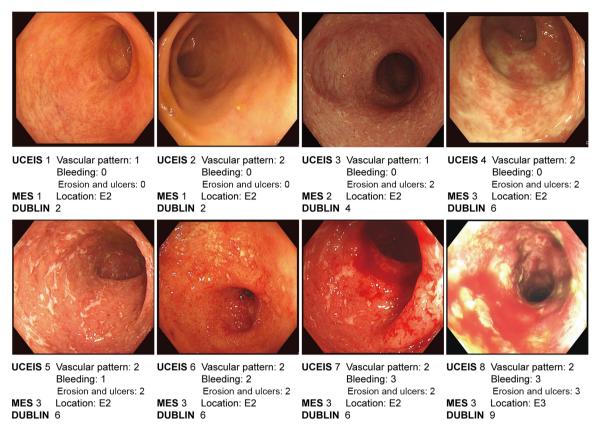


Figure 1. Typical endoscopic images demonstrating the scores of UCEIS, MES and DUBLIN. DUBLIN, Degree of Ulcerative Colitis Burden of Luminal Inflammation; MES, Mayo Endoscopic Score; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.

dl (normal change: < 8.2 mg/l in our institution). The levels of ALB ranged from 33 to 43 g/l. The vast majority of the patients exhibited a moderate active disease with a mean total MES of 2. The distribution of the disease extent was E1 (*n*=41, 23.84%), E2 (*n*=62, 36.05%) and E3 (*n*=69, 40.12%), respectively.

Correlations among DUBLIN, MES, UCEIS and laboratory parameters

The correlation among the DUBLIN, MES and UCEIS was tested. DUBLIN score showed significant correlation with MES (r=0.748) (Figure 2A), followed by obvious correlation with pMayo (r=0.707, Figure 2B). In contrast, CRP was moderately correlated with the DUBLIN, as revealed in Figure 2C (r=0.590). UCEIS also showed strong correlation with MES (r=0.712, Figure 2D), but mild correlation with pMayo (r=0.609, Figure 2E). Additionally, CRP was found to be mildly correlated with UCEIS

(r=0.588, Figure 2F). The distribution of DUBLIN, UCEIS and MES is shown in Table 2.

The cut-off value and diagnostic performances of the DUBLIN score and UCEIS

We considered treatment failure (i.e. no endoscopic response) as the primary outcome. According to the recent international consensus, the endoscopic response was defined as the decrease in MES ≥ 1 grade.³ ROC curves were conducted to determine the optimal cut-off values of DUBLIN and UCEIS to predict treatment failure. A DUBLIN score of 5 showed the best sensitivity and specificity in predicting treatment failure [sensitivity 68.0%; specificity 73.9%; area under the curve (AUC) = 0.752] (Figure 3A). When considering CRP as an outcome (cut-off value 3.5, sensitivity 87.9%; specificity 72.9%; AUC = 0.871), a DUBLIN score of 4 had the best clinically useful cut-off value to predict the long-term prognosis of patients with active UC.

Table 1. Clinical characteristics at the baseline

Baseline characteristics	
Female/male	74/98
Age	44 (30–58)
Duration, months	24 (8–68)
Background treatment	
5-ASA (%)	165 (95.93)
Steroids (%)	103 (59.88)
Immunosuppressant (%)	78 (45.35)
MTX (%)	3 (1.74)
AZA (%)	78 (45.34)
Anti-TNF (%)	5 (2.91)
C-reactive protein	24.06 (7.39–46.45)
Erythrocyte sedimentation rate	22 (14–35)
Albumin	38.5 (33–43)
Location	
E1 (%)	41 (23.84)
E2 (%)	62 (36.05)
E3 (%)	69 (40.12)
Extraintestinal manifestations	
Oral ulcer (%)	3 (1.74)
Arthropathy (%)	2 (1.16)
Skin lesion (%)	1 (0.58)
Current smoker/non-smoker	41/131
Modified Mayo score	8 (7–10)
Mild (%)	80 (46.51)
Moderate (%)	82 (47.67)
Severe (%)	10 (5.81)
MES	2 (2-3)
DUBLIN	6 (3-6)
UCEIS	4 (3–6)

5-ASA, 5-aminosalicylate; AZA, azathioprine; DUBLIN, Degree of Ulcerative Colitis Burden of Luminal Inflammation; MES, Mayo Endoscopic Score; MTX, methotrexate; TNF, tumor necrosis factor; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.

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Similarly, given the endoscopic response (cut-off value 4.5; sensitivity 59.2%; specificity 72.5%; AUC = 0.705) (Figure 3B), CRP value (cut-off value 4.5; sensitivity 62.9%; specificity 95.8%; AUC = 0.873) and the diagnostic value of out-come, UCEIS of 4 showed the best cut-off point in predicting treatment failure.

We further investigated the diagnostic performances of the DUBLIN score and UCEIS using the best cut-off value. As shown in Table 3, compared with the UCEIS (cut-off value: 4), DUBLIN score (cut-off value: 4) showed higher diagnostic sensitivity, (75.73%, 86.41%, respectively; McNemar test, p < 0.001), but no significant difference in specificity (52.17%, 49.28%, respectively; McNemar test, p=0.774) was observed.

The DUBLIN score \geq 4 is an independent factor for predicting treatment failure

We subsequently investigated the clinical factors for predicting treatment failure. A multivariate analysis indicated that DUBLIN score ≥ 4 was the independent factor for predicting treatment failure for UC (p < 0.001, odds ratio: 1.547; 95% confidence interval: 1.32–1.88). Other factors, such as the disease extent, course of disease, concomitant use of corticosteroids and thiopurine, were not correlated with the longterm prognosis.

We further investigated the differences between DUBLIN score \geq 4 and DUBLIN score <4. The biochemical data and demographics for each DUBLIN score category are described in Table 4. There were significant differences in disease duration, CRP, ALB and ESR measurements between patients with high (\geq 4) and low DUBLIN scores (<4).

At the end of the study, seven patients (4.07%) required the salvage therapy using cyclosporine. DUBLIN scores were higher in patients who received cyclosporine therapy (p=0.017; Mann– Whitney U test) (Figure 4A). Compared with the DUBLIN score <4, eight patients (4.65%) whose initial DUBLIN scores were \geq 4 were prescribed infliximab treatment during the follow-up (p=0.0158; Mann–Whitney U test) (Figure 4B). Furthermore, DUBLIN score <4 had a greater possibility of remaining colectomy-free at the end of the follow-up visit compared with patients with

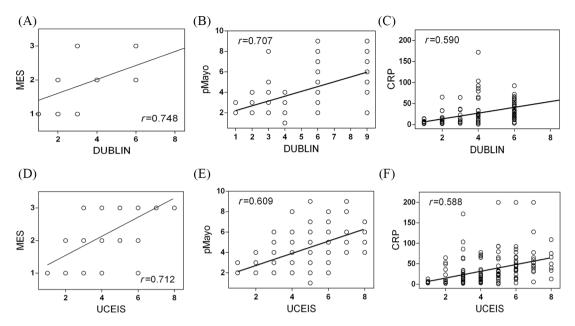


Figure 2. Correlations between the DUBLIN and (A) the MES, (B) pMayo and (C) serum CRP. Correlations between UCEIS and (D) the MES, (E) pMayo and (F) serum CRP (Spearman's rank correlation coefficient). CRP, C-reactive protein; DUBLIN, Degree of Ulcerative Colitis Burden of Luminal Inflammation; MES, Mayo Endoscopic Score; pMayo, partial Mayo; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.

MES, n (%)	DUBLIN, n (%)	UCEIS, <i>n</i> (%)
MES 1: 30 (17.44)	DUBLIN 1: 20 (66.67)	UCEIS 1: 10 (33.33)
	DUBLIN 2: 4 (13.33)	UCEIS 2: 9 (30.00)
	DUBLIN 3: 6 (20.00)	UCEIS 3: 8 (26.67)
		UCEIS 4: 3 (10.00)
MES 2: 71 (41.28)	DUBLIN 2: 12 (16.90)	UCEIS 2: 7 (9.86)
	DUBLIN 4: 34 (47.89)	UCEIS 3: 21 (29.58)
	DUBLIN 6: 25 (35.21)	UCEIS 4: 20 (28.17)
		UCEIS 5: 19 (26.76)
		UCEIS 6: 4 (5.63)
MES 3: 71 (41.28)	DUBLIN 3: 9 (12.68)	UCEIS 4: 9 (12.68)
	DUBLIN 6: 24 (33.80)	UCEIS 5: 12 (16.90)
	DUBLIN 9: 38 (53.52)	UCEIS 6: 28 (39.44)
		UCEIS 7: 15 (21.13)
		UCEIS 8: 7 (9.86)

Table 2. Distribution of patients with each MES, DUBLIN and UCEIS score at the baseline.

DUBLIN, Degree of Ulcerative Colitis Burden of Luminal Inflammation; MES, Mayo Endoscopic Score; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.

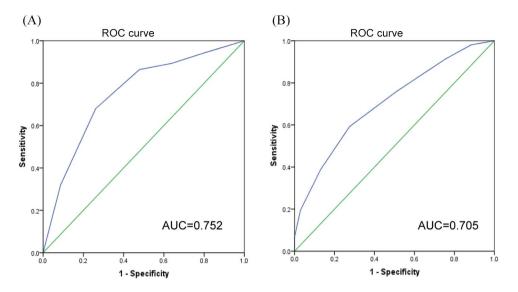


Figure 3. ROC curves of DUBLIN *versus* UCEIS in predicting the prognosis of the patients with active ulcerative colitis. (A) The AUC of DUBLIN score (AUC = 0.752) and (B) the AUC of UCEIS (AUC = 0.705). AUC, area under the curve; DUBLIN, Degree of Ulcerative Colitis Burden of Luminal Inflammation; ROC, receiver operating characteristic; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.

Table 3. Final	performances of th	e DUBLIN and U	CEIS scores for	diagnosis of u	Ilcerative colitis.

Final MES result	DUBLINª		UCEIS⁵	
	Positive result	Negative result	Positive result	Negative result
Non-response	89	33	78	35
Response	14	36	25	34

The endoscopic response was defined as the decrease in MES ≥ 1 grade.³

^aSensitivity, 86.41 (95% CI: 79.68, 93.14); specificity, 52.17 (95% CI: 40.68, 64.26); positive predictive value, 72.95% (95% CI: 64.96, 80.95); negative predictive value, 72% (95% CI: 59.11, 84.89).

^bSensitivity, 75.73 (95% CI: 67.31, 84.15); specificity, 49.28 (95% CI: 31.18, 61.37); positive predictive value, 69.03 (95% CI: 60.37, 77.68); positive predictive value, 75.73 (95% CI: 67.31, 84.15); negative predictive value, 57.63 (95% CI: 44.64, 70.62). CI, confidence interval; DUBLIN, Degree of Ulcerative Colitis Burden of Luminal Inflammation; MES, Mayo Endoscopic Score; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.

DUBLIN score ≥ 4 (*p*=0.0001; Mann–Whitney *U* test) (Figure 4C).

Discussion

In the present study, we identified the role of DUBLIN score *versus* UCEIS in predicting the clinical prognosis of patients with active UC. Compared with UCEIS, DUBLIN score incorporates a user-friendly and validated endoscopic evaluating system weighted for the extent of disease and preferable assessing of the burden of intestinal inflammation. Interestingly, DUBLIN score showed superior diagnostic performances in terms of sensitivity value compared with the UCEIS. Moreover, multivariate analysis indicated that DUBLIN ≥ 4 was an independent factor for predicting medium- to long-term treatment failure in active UC patients. Thus, this cut-off value could be used to assess the disease severity, predict the prognosis and guide the clinical decision-making based on the endoscopic scores.

Recent international consensus in the treatment of inflammatory bowel disease (IBD) has regarded mucosal healing as a desirable therapeutics goal.^{3,6} Several scores have been conducted to depict and calculate endoscopic findings in UC, which

Table 4. Patient demographics and biochemical data based on DUBLIN ≥4 ar	and DUBLIN <4.
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DUBLIN score	≥4	<4	p value
Age	44 (30–58)	46 (30–58)	<i>p</i> =0.398ª
Gender, female/male	49/72	24/26	<i>p</i> = 0.399 ^b
Disease duration, months	30 (10-71.5)	24 (8–55.5)	<i>p</i> =0.045 ^a
CRP	33.48 (20.85–59.18)	16.60 (13.20–23.13)	<i>p</i> =0.0001ª
ESR	24 (15–36.75)	19.5 (9.5–26.5)	<i>p</i> = 0.035ª
ALB	38 (33–42.75)	40.5 (38–44.75)	<i>p</i> = 0.003ª

Data are median and interquartile range.

^aIndependent samples Mann–Whitney U test.

^bPearson's Chi-square.

ALB, albumin; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; DUBLIN, Degree of Ulcerative Colitis Burden of Luminal Inflammation.

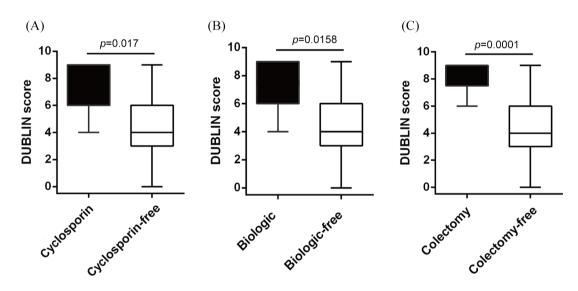


Figure 4. Comparison of DUBLIN score based on outcomes of cyclosporine, infliximab and colectomy. (A) DUBLIN score (median; interquartile range) was significantly higher in the group who received cyclosporine therapy compared with those who remained cyclosporine-free during the follow-up (p = 0.017; Mann–Whitney U test). DUBLIN score was significantly higher in patients requiring the introduction of biologic therapy (B) (p = 0.0158; Mann–Whitney U test) and colectomy (C) (p = 0.0001; Mann–Whitney U test).

include the most commonly used MES⁸ and UCEIS.¹¹ However, the MES and UCEIS do not take into account the endoscopic activity of the disease extent, which may vary during both the natural course and the treatment process in approximately 20–50% of UC cases.^{26–29} In other words, these two scoring systems do not comprehensively reflect the overall inflammatory burden in UC patients. Considering the requirement for a more refined evaluation of endoscopic inflammatory activity in UC, two endoscopic scores,

UCCIS¹³ and MMES, have been developed in the past 7 years. Particularly, UCCIS has been considered as a useful assessment tool for reducing inter-observer variations.^{11,23,30} However, these two scores require the evaluation of five segments of the colon, following by an inconvenient calculation to obtain the final results. Rowan *et al.*²¹ recently proposed the DUBLIN score, which integrates with the extent of disease (E1– E3), is easy to calculate and can be recorded at the moment of endoscopic examination. Meanwhile, it also reported strong correlation with calprotectin level, and clinical outcomes, such as treatment failure.²¹

In this study, we evaluated the predictive value of prognosis for active UC patients using DUBLIN score and UCEIS. Our work demonstrated that the DUBLIN score (cut-off value: 4) showed preferable diagnostic value in terms of sensitivity value (p < 0.05) compared with the UCEIS (cutoff value: 4) in predicting the long-term prognosis in active UC patients. We further proved that DUBLIN showed significant correlation with MES and correlated well with clinical indices, such as pMayo score, and laboratory parameters, such as CRP. All of these evidences illustrate that the DUBLIN score is capable of the prediction of medium- to long-term prognosis of UC in our study. This difference between the DUBLIN score and UCEIS in our study is possibly due to the inclusion of the disease extent in DUBLIN score. More recently, Silva et al. reported that DUBLIN showed significant correlation with MES and histological activity and allowed to predict treatment failure.24 This study further demonstrated the greater accuracy of DUBLIN score to predict the prognosis of patients with UC. While this study focused on inactive and mildly active UC patients, we mainly targeted patients with mild to moderate diseases, and most patients were treated with immunosuppressants and steroids in our study. Notably, we identified the cutoff value of DUBLIN ≥4 as an independent factor for predicting treatment failure in our work. This cut-off value might introduce a more rational selection for active UC patients receiving escalation therapy.

Our study also has several limitations. Although the MES scores were prospectively assessed during the endoscopy procedure, the UCEIS and DUBLIN scores were retrospectively obtained. However, the detail of clinical activities had been electronically documented at our center. Thus, it was possible to obtain accurate clinical information. Furthermore, a single endoscopist calculated the MES and recorded the disease extent during the colonoscopy procedure. Therefore, the intra-observer and the inter-observer validation was not assessed. Consistent with previous data, in our study, CRP was moderately correlated with the DUBLIN and UCEIS, which implies a weakness in CRP as a biomarker. Although fecal calprotectin has been proved to be

a reliable tool to evaluate and monitor disease activity in IBD patients, there were too few cases in our study to draw any meaningful points (measured in 11 cases, 6.4%), and this was therefore not included in our analysis. Finally, only 172 patients were included in this retrospective, single-center study; a multi-center, prospective cohort study will be warranted to further validate the value of the DUBLIN score in UC evaluation.

In conclusion, the DUBLIN score is a simple index to evaluate endoscopic activity in UC, including both the assessment of mucosal inflammation and disease extent, and exhibited a significant correlation with MES, laboratory parameters and clinical indices.

Further prospective cohort studies are needed to evaluate the clinical value of the DUBLIN score.

Author contributions

Z.L., X.S. and L.C. conceived and designed the study. L.C., J.Y., L.F., M.S. and W.W. recruited subjects, collected the data and worked on its curation and analysis. L.C., X.S., Y.S. and B.F. interpreted the results. L.C. and Z.L. wrote the manuscript. All authors reviewed and approved the manuscript before submission.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Supplemental material

Supplemental material for this article is available online.

References

- Baumgart DC and Carding SR. Inflammatory bowel disease: cause and immunobiology. *Lancet* 2007; 369: 1627–1640.
- Ng SC, Shi HY, Hamidi N, *et al.* Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet* 2018; 390: 2769–2778.
- Vuitton L, Peyrin-Biroulet L, Colombel JF, et al. Defining endoscopic response and remission in ulcerative colitis clinical trials: an international consensus. *Aliment Pharmacol Ther* 2017; 45: 801–813.
- 4. Sandborn WJ, Rutgeerts P, Feagan BG, *et al.* Colectomy rate comparison after treatment of ulcerative colitis with placebo or infliximab. *Gastroenterology* 2009; 137: 1250–1260; quiz 1520.
- Ardizzone S, Cassinotti A, Duca P, *et al.* Mucosal healing predicts late outcomes after the first course of corticosteroids for newly diagnosed ulcerative colitis. *Clin Gastroenterol Hepatol* 2011; 9: 483–489 e483.
- Harbord M, Eliakim R, Bettenworth D, et al. Third European evidence-based consensus on diagnosis and management of ulcerative colitis. part 2: current management. J Crohns Colitis 2017; 11: 769–784.
- Colombel JF, Rutgeerts P, Reinisch W, et al. Early mucosal healing with infliximab is associated with improved long-term clinical outcomes in ulcerative colitis. *Gastroenterology* 2011; 141: 1194–1201.
- Schroeder KW, Tremaine WJ and Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. *N Engl J Med* 1987; 317: 1625–1629.
- Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med 2005; 353: 2462–2476.
- Manginot C, Baumann C and Peyrin-Biroulet L. An endoscopic Mayo score of 0 is associated with a lower risk of colectomy than a score of 1 in ulcerative colitis. *Gut* 2015; 64: 1181–1182.
- Travis SP, Schnell D, Krzeski P, et al. Developing an instrument to assess the endoscopic severity of ulcerative colitis: the Ulcerative Colitis Endoscopic Index of Severity (UCEIS). Gut 2012; 61: 535–542.

- Arai M, Naganuma M, Sugimoto S, *et al.* The ulcerative colitis endoscopic index of severity is useful to predict medium- to long-term prognosis in ulcerative colitis patients with clinical remission. *J Crohns Colitis* 2016; 10: 1303–1309.
- de Jong DC, Lowenberg M, Koumoutsos I, et al. Validation and investigation of the operating characteristics of the ulcerative colitis endoscopic index of severity. *Inflamm Bowel Dis* 2019; 25: 937–944.
- Morita Y, Bamba S, Takahashi K, *et al.* Prediction of clinical and endoscopic responses to anti-tumor necrosis factor-alpha antibodies in ulcerative colitis. *Scand J Gastroenterol* 2016; 51: 934–941.
- 15. Saigusa K, Matsuoka K, Sugimoto S, *et al.* Ulcerative colitis endoscopic index of severity is associated with long-term prognosis in ulcerative colitis patients treated with infliximab. *Dig Endosc* 2016; 28: 665–670.
- Ikeya K, Hanai H, Sugimoto K, *et al.* The ulcerative colitis endoscopic index of severity more accurately reflects clinical outcomes and long-term prognosis than the mayo endoscopic score. *J Crohns Colitis* 2016; 10: 286–295.
- Solberg IC, Lygren I, Jahnsen J, et al. Clinical course during the first 10 years of ulcerative colitis: results from a population-based inception cohort (IBSEN Study). Scand J Gastroenterol. 2009; 44: 431–440.
- Qiu Y, Chen B, Li Y, *et al.* Risk factors and long-term outcome of disease extent progression in Asian patients with ulcerative colitis: a retrospective cohort study. *BMC Gastroenterol* 2019; 19: 7.
- Ekbom A, Helmick C, Zack M, et al. Ulcerative colitis and colorectal cancer. A population-based study. N Engl J Med 1990; 323: 1228–1233.
- 20. Lutgens MW, van Oijen MG, van der Heijden GJ, *et al.* Declining risk of colorectal cancer in inflammatory bowel disease: an updated metaanalysis of population-based cohort studies. *Inflamm Bowel Dis* 2013; 19: 789–799.
- Rowan CR, Cullen G, Mulcahy HE, et al. DUBLIN [Degree of Ulcerative colitis Burden of Luminal Inflammation] score, a simple method to quantify inflammatory burden in ulcerative colitis. *J Crohns Colitis* 2019; 13: 1365–1371.
- 22. Lobaton T, Bessissow T, De Hertogh G, *et al.* The Modified Mayo Endoscopic Score (MMES): a new index for the assessment of extension and severity of endoscopic activity in ulcerative colitis patients. *J Crohns Colitis* 2015; 9: 846–852.

- 23. Samuel S, Bruining DH, Loftus EV Jr., *et al.* Validation of the ulcerative colitis colonoscopic index of severity and its correlation with disease activity measures. *Clin Gastroenterol Hepatol* 2013; 11: 49–54.e41.
- Silva JC, Fernandes C, Rodrigues J, et al. Endoscopic and histologic activity assessment considering disease extent and prediction of treatment failure in ulcerative colitis. Scand J Gastroenterol 2020; 55: 1157–1162.
- 25. Satsangi J, Silverberg MS, Vermeire S, *et al.* The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. *Gut* 2006; 55: 749–753.
- Fumery M, Singh S, Dulai PS, et al. Natural history of adult ulcerative colitis in populationbased cohorts: a systematic review. *Clin Gastroenterol Hepatol* 2018; 16: 343–356.e343.

- Meucci G, Vecchi M, Astegiano M, et al. The natural history of ulcerative proctitis: a multicenter, retrospective study. Gruppo di Studio per le Malattie Infiammatorie Intestinali (GSMII). Am J Gastroenterol 2000; 95: 469–473.
- 28. Chatzicostas C, Roussomoustakaki M, Potamianos S, *et al.* Factors associated with disease evolution in Greek patients with inflammatory bowel disease. *BMC Gastroenterol* 2006; 6: 21.
- Chow DK, Leong RW, Tsoi KK, et al. Longterm follow-up of ulcerative colitis in the Chinese population. Am J Gastroenterol 2009; 104: 647–654.
- Travis SP, Schnell D, Krzeski P, et al. Reliability and initial validation of the ulcerative colitis endoscopic index of severity. *Gastroenterology* 2013; 145: 987–995.

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