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Original Article

ORIGINAL ARTICLE

Time-adjusted average Mayo endoscopic score predicts the risk of disease extent progression in distal ulcerative colitis patients

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Abstract

Background: Ulcerative colitis (UC) is a chronic lifelong disease. The disease extent of UC can progress over time. This study aimed to assess whether cumulative inflammatory burden (CIB) is associated with disease extension in distal UC (proctitis [E1] and left-sided colitis [E2]) patients, and to develop a quantified indicator of CIB.

Methods: In this retrospective study based on a prospective registry, distal UC patients receiving colonoscopies in Xijing Hospital (Xi'an, China) from January 2000 to May 2019 were studied. We developed a new score, namely the time-adjusted average Mayo endoscopic score (TA-MES), calculated as dividing the sum of the cumulative average MES over a period of surveillance time by the length of the endoscopic examination interval, to quantify the CIB. Cox regression was used to identify other potential risk factors.

Results: A total of 295 UC patients were followed for 1,487.02 patient-years. Among them, 140 patients (47.5%) experienced disease extension. Multivariate analysis showed that the TA-MES was significantly associated with disease extension in E1 (hazard ratio [HR], 2.90; 95% confidence interval [CI], 1.58–5.33, $P = 0.001$) and E2 (HR, 1.89; 95% CI, 1.16–3.09, $P = 0.011$) patients. Other risk factors included hemoglobin of <90 g/L and appendiceal skip inflammation; the protective factors included age, E2 at diagnosis, former smoking, and 5-aminosalicylic acid dose. Otherwise, MES at diagnosis, maximal MES, and mean MES failed to estimate the risk of disease extension.

Conclusion: TA-MES is a good quantified indicator of CIB and is independently associated with increased disease extension in distal UC patients. Whether the dynamic multiple scoring system could be used as a risk factor in other chronic relapsing–remitting diseases is a direction for future research.

Key words: Mayo endoscopic score; disease extension; ulcerative colitis; distal

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Introduction

Ulcerative colitis (UC), a subtype of inflammatory bowel disease (IBD), is a chronic inflammatory disease affecting the colorectum [1]. UC is characterized by starting from the rectum and extending back towards the cecum proximally [1]. UC phenotypes include proctitis (E1), left-sided colitis (E2), and extensive colitis (E3) according to the Montreal classification [2]. About 30% of patients with UC had E1 when they were diagnosed. The proportions of patients with E2 and E3 at diagnosis were 16%–45% and 14%–35%, respectively, based on some population-based studies [3].

Most likely, UC might extend from E1 to E3 over time. About 10%–19% of UC patients with initial E1 would progress in 5 years and the progression rate would increase to 28% in 10 years [4, 5]. With disease extension, UC patients will suffer more serious symptoms and even have a higher incidence of UC-associated colorectal cancer [5–7]; these patients usually require more aggressive and surgical therapies [8, 9]. Therefore, identification of the risk factors for disease extent progression is of great significance. Previous studies reported that several factors might be associated with the disease extension, such as younger age, non-smoking, extra-intestinal manifestations (EIMs), refractory disease at diagnosis, and the occurrence of one or more flares after the first year of diagnosis [5, 10–13]. However, these factors have not been widely accepted as accurate factors.

A previous study demonstrated that continuous active disease itself was an independent risk factor for disease extension [14], which suggested that cumulative inflammatory burden (CIB) might play an important role in disease extension. The Mayo endoscopic score (MES) is an important and widely used tool to assess the inflammatory activity of UC during clinical practice. However, MES is a static score for measuring inflammation at a single point of time. It cannot provide a reliable estimate of the dynamic changes of the inflammation. Hence, we proposed a novel calculation named time-adjusted average MES (TA-MES) as an alternative to a single MES to quantify the CIB. The TA-MES was calculated by dividing the sum of the cumulative average MES over a period of surveillance time by the length of the endoscopic examination intervals. The TA-MES might be more representative of CIB than the MES. We hypothesized that the TA-MES over a period of time could be a more precise parameter that provided a warning of the possibility of disease extension. This study also aimed to explore other relevant risk factors for the disease extension to provide evidence for optimizing the individualized management of patients with UC.

Materials and methods

Study design and research population

This was a retrospective study based on a prospective registry of consecutive patients with UC in the IBD clinic in Xijing Hospital (Xi'an, China) from January 2000 to May 2019. The diagnosis and management of UC were based on the European Crohn's and Colitis Organization (ECCO) consensus [8, 15–17]. Study inclusion criteria were as follows: (i) patients with distal UC (E1 or E2) according to Montreal classification [2] when diagnosed with UC; and (ii) age at diagnosis of ≥18 years old. The exclusion criteria were as follows: (i) patients who received fewer than three colonoscopies before the study endpoint, (ii) patients with Crohn's disease or indeterminate colitis, and (iii) patients with incomplete clinical data.

The endpoint of the study

Disease extent progression was defined as the disease extent change from E1 to E2/E3 or the change from E2 to E3. The endpoint of the study was defined as the time at which disease extension was first detected by colonoscopy or surgery after the diagnosis of UC during surveillance. If the patient had no disease extension, they were censored at the date of intestinal surgery or the latest available colonoscopy up to May 2019.

Clinical data collection and definition

Medical records of the study patients were reviewed. Collected clinical data included age, age at onset, gender, body mass index (BMI), disease duration, family history of IBD, appendicectomy history, tobacco use, EIM, the extent of disease when diagnosed, each endoscopy result, the lowest hemoglobin concentration, and treatments. Among all the clinical data, BMI measurements at least 6 months apart were included and then the mean BMI was calculated. For the BMI, EIM, appendicectomy, hemoglobin, MES, appendiceal skip inflammation, and post-inflammation polyps, only the values obtained from the time of diagnosis to the last follow-up before the study endpoint were included. Smoking status was recorded at the time of diagnosis. The 5-aminosalicylic acid (5-ASA) dose was defined as the average daily dose used within 1 year before the endpoint of the study. Ever use of corticosteroids, immunosuppressants, and biologics before the endpoint of the study was analysed. All colonoscopies were performed by experienced endoscopists who had extensive experience in evaluating the disease status of patients with UC. The endoscopic severity was evaluated by using the MES, which was taken from the worst inflammation of the colorectum.

Calculation of TA-MES and mean MES

The total Mayo endoscopic score (TMES) was calculated for each endoscopic examination interval by multiplying the average MES between a pair of endoscopic examination episodes by the length of endoscopic examination interval in months. The TA-MES was calculated by dividing the sum of the TMES by the length of the endoscopic examination interval between the time of the first endoscopy and the endpoint of the study in months. (An example is shown in Figure 1.)

The mean MES (MMES) was calculated by dividing the sum of all the MESs from all the colonoscopies before the endpoint of the study by the total number of colonoscopy procedures.

The MES at the time of endpoint of the study was not included in the calculation of the TA-MES and MMES.

Ethical considerations

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki (revised in 2008). The study was approved by the ethical committee of Xijing Hospital affiliated to the Fourth Military Medical University (KY20203298). All of the patients or their legal representatives signed the informed consent form.

Statistical methods

The data were analysed using the SPSS 19.0 (IBM, Armonk, NY, USA) computer software for Windows. Quantitative variables are presented as the median and interquartile range (IQR), and Student's *t*-test or Wilcoxon rank-sum test were used to compare them, as appropriate. Categorical variables are expressed

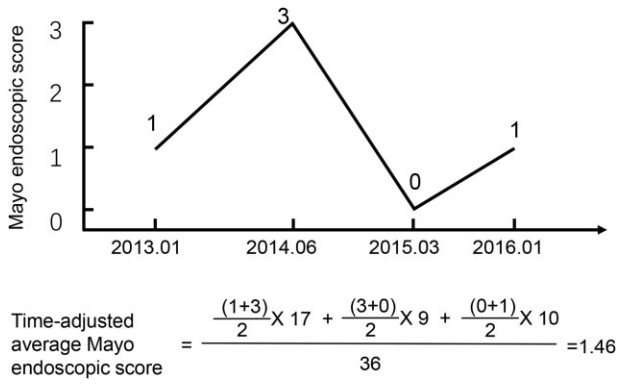

Figure 1. An example of the calculation method of time-adjusted average Mayo endoscopic score (TA-MES). The total MES for the first surveillance interval (from January 2013 to June 2014) would be an average MES between the two surveillance endoscopies ([1 + 3]/2 = 2) multiplied by the length of surveillance interval (17 months), which was 34. The TA-MES was calculated by dividing the sum of the total MES from all surveillance intervals by the length of the endoscopic examination intervals (36 months).

as frequency and percentage, and χ^2 test or Fisher's exact test was used to compare them when appropriate. All the *P*-values were two-sided and $P < 0.05$ was considered statistically significant. Cox regression was used to select risk factors associated with the occurrence of progression of disease extent. The significant factors ($P < 0.10$) in the univariate analysis were included in the final Cox proportional hazards model. We used hazard ratios (HRs) with 95% confidence intervals (CIs) to quantify the association of the factors with the progression of disease extent.

Results

A total of 436 patients with distal UC were admitted to our clinic between January 2000 and May 2019. Among them, 141 patients were excluded from our study due to incomplete data ($n = 10$) and lack of enough colonoscopies ($n = 131$). Finally, 295 patients were included for further study. Of these patients, 127 (43.1%) were E1 when diagnosed with UC and 168 (56.9%) were E2. The cumulative follow-up time from the first colonoscopy to the study endpoint was 1,487.02 patient-years. The median number of endoscopies before the study endpoint of each patient was three (range, 3–9). The characteristics of the patients are shown in Table 1.

Progression of disease extent

A total of 140 (140/295, 47.5%) distal UC patients experienced disease extension (E1, 53.5% [68/127]; E2, 42.9% [72/168]) (Figure 2). Among the 68 E1 patients, 35 (51.5%) progressed to E2 and the other 33 (48.5%) progressed to E3. The median time of progression of disease extent was 2.0 years (IQR, 1.3–4.3 years) for E1 to E2 and 3.1 years (IQR, 1.3–5.3 years) for E1 to E3 ($P = 0.177$). The median time of progression of disease extent was 3.6 years (IQR, 1.7–4.2 years) for E2 to E3.

Factors for disease extent progression in distal UC patients

The final result of the multivariate Cox regression model is shown in Table 2. The TA-MES was significantly associated with the progression of disease extent (HR, 2.28; 95% CI, 1.61–3.22, $P < 0.001$). Hemoglobin of <90 g/L (HR, 2.18; 95% CI, 1.40–3.38, $P = 0.001$) and appendiceal skip inflammation (HR, 1.69; 95% CI, 1.11–2.56, $P = 0.014$) were also significant contributory factors for disease extension. The protective factor included age (HR, 0.98 per 1-year increase; 95% CI, 0.97–1.00, $P = 0.044$), E2 at diagnosis (HR, 0.48; 95% CI, 0.32–0.73, $P = 0.001$) (Figure 3), former smoking (vs never smoking; HR, 0.48; 95% CI, 0.24–0.95, $P = 0.035$), and 5-ASA dose (HR, 0.84 per 1-g/d increase; 95% CI, 0.74–0.95, $P = 0.008$).

Subgroup analysis of E1 patients and E2 patients

The cumulative rates of disease extension at 1, 3, 5 and 10 years were 8%, 30%, 48%, and 70% for E1 patients, respectively, and 4%, 16%, 27%, and 44% for E2 patients, respectively (Figure 3). The univariate analyses of risk factors associated with disease extension for E1 and E2 patients are shown in Supplementary Tables 1 and 2, respectively. The final results of the multivariate Cox regression model for E1 patients and E2 patients are shown in Table 3. For E1 patients, hemoglobin of <90 g/L (HR, 2.65; 95% CI, 1.26–5.56, $P = 0.010$) and the TA-MES (HR, 2.90; 95% CI, 1.58–5.33, $P = 0.001$) were significantly associated with disease extension. For E2 patients, age (HR, 0.98 per 1-year increase; 95% CI, 0.95–1.00, $P = 0.036$), 5-ASA dose (HR, 0.83 per 1-g/d increase; 95% CI, 0.70–0.98, $P = 0.031$), and the TA-MES (HR, 1.89; 95% CI, 1.16–3.09, $P = 0.011$) were significantly associated with the progression of disease extent.

Efficacy of different MES calculation methods in disease extent progression

Neither the MES at diagnosis (HR, 1.31; 95% CI, 0.99–1.74, $P = 0.057$) nor the max MES (HR, 0.91; 95% CI, 0.67–1.23, $P = 0.501$) was significantly associated with the disease extension in distal UC patients in the multivariate analysis (Table 4). No significance was found in the subgroup analysis of E1 and E2 patients. The MMES was significantly associated with disease extension in distal UC patients in the multivariate analysis (HR, 1.71; 95% CI, 1.12–2.67, $P = 0.021$). But in the subgroup analysis, the MMES was not significantly associated with disease extension in both E1 patients (HR, 1.46; 95% CI, 0.82–2.58, $P = 0.199$) and E2 patients (HR, 1.53; 95% CI, 0.91–2.57, $P = 0.098$).

Discussion

This is the first study to assess the association between CIB and disease extent progression in distal UC patients. The study showed that the higher the CIB, the more likely the disease extent is to progress. Other risk factors for disease extension included hemoglobin concentration of <90 g/L and appendiceal skip inflammation; the protective factors included age, E2 at diagnosis, former smoking, and 5-ASA dose. The TA-MES is proved to be a good quantified indicator of CIB and can be easily used in clinical work.

The rates of disease extension in UC patients varied a lot in many previous studies. A meta-analysis demonstrated that the overall pooled frequency of UC extent progression was 17.8% at 5 years and 31% at 10 years [18]. A Danish population-based inception cohort reported that 33% of limited colitis patients experienced disease extension after 7 years of follow-up [19]. The European population-based study showed that during a 5-year follow-up, 21% (90 of 435) of the limited colitis patients experienced a progression in extent and, among them, 15% (67 of 435) progressed to extensive colitis [20]. In our study, the rate of extent progression in distal UC was 47.5% (140/295) followed by a total of 1,487.02 patient-years, which seemed to be higher than

Table 1. Characteristics of 295 patients with distal ulcerative colitis enrolled in the study

Variable	Total ($n = 295$)	E1 ($n = 127$)	E2 ($n = 168$)	P
Age, years, median (IQR)	44 (34–54)	44 (33–54)	44 (34–54)	0.937
Female, *n* (%)	139 (47.1)	71 (55.9)	68 (40.5)	0.009
Age at onset, years, median (IQR)	38 (28–48)	38 (29–49)	36 (27–48)	0.388
Disease duration, years, median (IQR)	3.9 (2.0–7.2)	3.0 (1.8–6.0)	4.5 (2.3–8.6)	0.011
Body mass index, median (IQR)	21.9 (19.6–23.8)	21.8 (19.7–23.7)	22.0 (19.6–23.9)	0.909
Smoking, *n* (%)				0.046
Never	238 (80.7)	107 (84.3)	131 (78.0)	
Former	31 (10.5)	12 (9.4)	19 (11.3)	
Current	26 (8.8)	8 (6.3)	18 (10.7)	
Extra-intestinal manifestations, *n* (%)	16 (5.4)	8 (6.3)	8 (4.8)	0.564
Appendicectomy history, *n* (%)	5 (1.7)	2 (1.6)	3 (1.8)	0.889
Family history of IBD, *n* (%)	1 (0.3)	1 (0.8)	0 (0)	0.431
Hemoglobin <90 g/L, *n* (%)	43 (14.6)	11 (8.7)	32 (19.0)	0.050
Number of colonoscopies, median (range)	3 (3–9)	3 (3–8)	3 (3–9)	0.191
TA-MES, median (IQR)	2.0 (1.5–2.5)	2.0 (1.5–2.5)	2.1 (1.6–2.5)	0.026
Appendiceal skip inflammation, *n* (%)	130 (44.1)	69 (54.3)	61 (36.3)	0.002
Post-inflammatory polyps, *n* (%)	63 (21.4)	21 (16.5)	42 (25.0)	0.079
5-ASA dose, g/d, median (IQR)	2.17 (0.75–3.33)	1.50 (0.50–2.94)	2.67 (1.00–3.82)	0.000
Corticosteroid, *n* (%)	90 (30.5)	25 (19.7)	65 (38.7)	0.001
Immunosuppressant, *n* (%)	28 (9.5)	8 (6.3)	20 (11.9)	0.104
Biologics, *n* (%)	13 (4.4)	2 (1.6)	11 (6.5)	0.039

E1, proctitis; E2, left-sided colitis; IQR, interquartile range; IBD, inflammatory bowel disease; TA-MES, time-adjusted average Mayo endoscopic score; 5-ASA, 5-aminosalicylic acid.

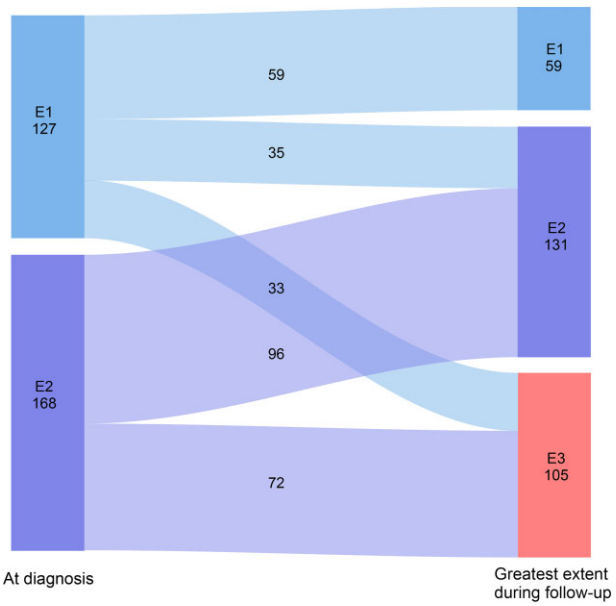

Figure 2. Change of disease extent in patients with ulcerative colitis. E1, proctitis; E2, left-sided colitis; E3, extensive colitis.

those in the previous studies. But it was similar to a recent Spanish retrospective study [13] which demonstrated that extent progression occurred in 41.6% (32 of 77) of E1 patients during a median follow-up period of 5 years. We thought this might be due to our cohort being a tertiary hospital cohort, probably made up of patients with more severe diseases.

The disease extent was a determining factor in the long-term progression of UC patients [13]. The prognosis of UC patients usually deteriorated with the progression of disease extent [21]. In patients with distal UC, disease extension was associated with a higher prevalence of EIM, steroid-refractory course, the requirement for thiopurines and infliximab, and surgery [10]. What is more, patients with extensive colitis had a higher risk of UC-associated colorectal cancer [7] and mortality [22]. Therefore, it is of great significance to identify patients at high risk of disease extension.

UC is a lifelong disease that is often presented with a relapsing and remitting form [1]. CIB might explain the increased disease extension than transient inflammatory status more powerfully. The MES is a widely used clinical tool to assess the inflammation activity of UC. However, a single MES, including the MES at diagnosis and the maximal MES, may overlook some severe inflammations during the disease course and thus could not reflect CIB. Previous studies demonstrated that the MES at diagnosis was not significantly associated with disease extension [13, 23], which was consistent with our result. An evaluation of the cumulative effect caused by the disease through assessing the multiple colonoscopies over many preceding years was required. In our study, we hypothesized that the MMES and TA-MES might be two indicators to quantify CIB. Finally, we found that the MMES was significantly associated with disease extension in all patients, but the significance was lost in the subgroup analysis. A time-adjusted calculation method of the MES seemed to be a more convincing tool to reflect the inflammation over time and relate to disease extent progression. The TA-MES was independently associated with disease extension in distal UC patients and the subgroup analysis reached the same conclusion. This suggested that chronic inflammation may have a causative role in disease extension in distal UC patients. Patients with more persistent active colitis were at risk of disease extension irrespective of inflammation severity. Colonoscopy is widely used to monitor the disease activity and colorectal cancer in UC patients [24]; the calculation of the TA-MES from the previously available MES might be useful for risk stratification of disease extent progression. We believe this is an important implication for clinical practice. It is important to give rigorous treatment to

Table 2. Factors associated with the progression of distal ulcerative colitis ($n = 295$)

Variable	Univariate		Multivariate	
	P-value	HR (95% CI)	P-value	HR (95% CI)
Age, per 1-year increase	0.002	0.98 (0.96–0.99)	**0.044**	**0.98 (0.97–1.00)**
Gender (female vs male)	0.858	1.03 (0.74–1.44)	NS	
Age at onset, per 1-year increase	0.259	1.01 (0.99–1.02)	NS	
Left-sided colitis vs proctitis	0.003	0.60 (0.43–0.84)	**0.001**	**0.48 (0.32–0.73)**
Body mass index, per 1-unit increase	0.109	0.96 (0.91–1.01)	NS	
Smoking				
Current vs never	0.456	0.81 (0.47–1.41)	0.079	0.55 (0.28–1.07)
Former vs never	0.008	0.43 (0.23–0.80)	**0.035**	**0.48 (0.24–0.95)**
Extra-intestinal manifestations	0.845	0.93 (0.48–1.84)	NS	
Appendicectomy history	0.202	1.92 (0.71–5.22)	NS	
Family history of IBD	0.400	2.33 (0.33–16.74)	NS	
Hemoglobin <90 g/L	< 0.001	2.14 (1.42–3.22)	**0.001**	**2.18 (1.40–3.38)**
Number of colonoscopies	0.082	1.10 (0.99–1.23)	0.323	1.07 (0.94–1.22)
TA-MES	< 0.001	2.08 (1.58–2.74)	**< 0.001**	**2.28 (1.61–3.22)**
Appendiceal skip inflammation	< 0.001	1.86 (1.32–2.60)	**0.014**	**1.69 (1.11–2.56)**
Post-inflammatory polyps	0.017	1.54 (1.08–2.19)	0.260	1.27 (0.84–1.91)
5-ASA dose, per 1-g/d increase	0.001	0.83 (0.74–0.93)	**0.008**	**0.84 (0.74–0.95)**
Corticosteroid	0.007	1.59 (1.13–2.22)	0.125	1.41 (0.91–2.19)
Immunosuppressant	0.069	1.55 (0.97–2.50)	0.895	1.04 (0.58–1.86)
Biologics	0.936	1.03 (0.54–1.96)	NS	

IBD, inflammatory bowel disease; TA-MES, time-adjusted average Mayo endoscopic score; 5-ASA, 5-aminosalicylic acid; HR, hazard ratio; CI, confidence interval; NS, no significant in the univariate analysis ($P > 0.10$).

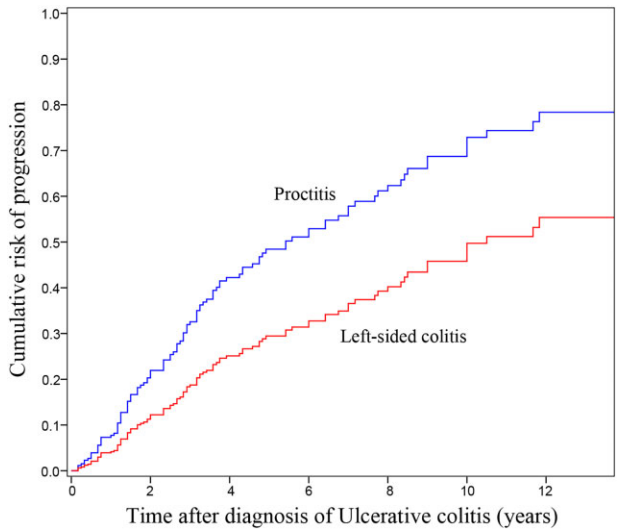

Figure 3. The cumulative risk of progression of patients with proctitis and left-sided colitis at diagnosis

patients with active disease to achieve persistent endoscopic healing, thereby preventing disease extension in UC. Future research needs to identify the cut-off value of the TA-MES to help determine the timing of step-up therapy including biologic and/or immunomodulator or even surgery. As we know, many immune diseases such as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, and Crohn's disease are characterized by alternations in relapse and remission. Whether such a dynamic multiple scoring system could also predict the disease progression and assess the disease condition of these immune diseases is a future research direction.

Table 3. Multivariate analysis of factors on the disease extension of E1 and E2 patients

Variable	P-value	HR (95% CI)
E1		
Hemoglobin <90 g/L	0.010	2.65 (1.26–5.56)
TA-MES	0.001	2.90 (1.58–5.33)
E2		
Age, per 1-year increase	0.036	0.98 (0.95–1.00)
TA-MES	0.011	1.89 (1.16–3.09)
5-ASA dose, per 1-g/d increase	0.031	0.83 (0.70–0.98)

E1, proctitis; E2, left-sided colitis; TA-MES, time-adjusted average Mayo endoscopic score; 5-ASA, 5-aminosalicylic acid; HR, hazard ratio; CI, confidence interval.

Some researchers had considered the effects of treatment regimens when analysing risk factors for UC extent progression. Unfortunately, few studies could be used to guide clinical work [10, 12, 13, 20, 25, 26]. It has been verified that the exposure to 5-ASA was significantly related to the reduced risk of neoplasia [27]. If UC patients received 5-ASA at doses higher than 1.2 g per day, the reduction in colonic neoplasia risk was more profound [28]. Similarly, we were interested in whether there was also a dose-effect associated with the use of 5-ASA in UC extent progression. We included patients' daily dose of 5-ASA, rather than whether or not they used the medicine in our study. We found that the higher the dose of 5-ASA used, the smaller the risk of disease progression that patients might experience, especially E2 patients. When calculating the dose of 5-ASA, we did not separate oral and topical doses. Many E1 patients were treated with a mesalamine 1-g suppository once daily or once every 2 days. This resulted in the calculation of 5-ASA dose in many patients being <2.4 g/d, which was recommended by ECCO consensus.

Table 4. Efficacy of different MES calculation methods in disease extension

Variable	Univariate		Multivariate	
	P-value	HR (95% CI)	P-value	HR (95% CI)
E1 + E2				
MES at diagnosis	0.302	1.13 (0.90–1.43)	0.057	1.31 (0.99–1.74)
Max MES	0.121	0.82 (0.63–1.06)	0.501	0.91 (0.67–1.23)
MMES	0.001	1.56 (1.19–2.03)	0.021	1.71 (1.12–2.67)
E1				
MES at diagnosis	0.430	1.14 (0.83–1.57)	0.754	0.94 (0.62–1.41)
Max MES	0.327	0.82 (0.55–1.22)	0.133	0.68 (0.41–1.13)
MMES	0.001	1.91 (1.28–2.83)	0.199	1.46 (0.82–2.58)
E2				
MES at diagnosis	0.219	1.25 (0.88–1.79)	0.158	1.38 (0.88–2.16)
Max MES	0.555	0.90 (0.62–1.30)	0.552	0.88 (0.58–1.33)
MMES	0.011	1.68 (1.12–2.50)	0.098	1.53 (0.91–2.57)

All results are per 1-unit increase in each score; E1, proctitis; E2, left-sided colitis; MES, Mayo endoscopic score; MMES, mean MES; HR, hazard ratio; CI, confidence interval.

There were some strengths of the present study. First, we proposed a new quantified indicator, named the TA-MES, to reflect the endoscopic CIB in UC patients. Second, we included a total of four types of MES to test the ability to estimate the risk of disease progression. This made our results more convincing. Third, we found that there was also a dose-effect associated with the use of 5-ASA in disease extent progression in UC patients.

However, there were also some limitations in this study. First, this was a single-center retrospective study of a relatively small population with a long-term follow-up. About 30% of patients were not available for enough colonoscopies or had incomplete data. Second, some potential factors, such as erythrocyte sedimentation rate, C-reactive protein, and histological inflammation score, were not available in all patients in our study due to the limitation of the retrospective study. Third, the MES scores were reported by different endoscopists at the time of examination and were not validated. The possible influence of inter-observer variability on MES grading has not been fully taken into account. Fourth, this study lacks a validation cohort to verify the association between the TA-MES and disease progression. Last but not least, the cohort was enrolled from a single tertiary referral center and referral biases might exist. The patients in our cohort might have had more severe diseases. This could limit the generalizability of our result.

Conclusions

In summary, we developed a quantified indicator, named the TA-MES, to reflect the CIB in distal UC. The TA-MES was independently associated with disease progression in patients with distal UC. The higher the TA-MES, the more likely that the disease extent is going to progress. Therefore, we speculate that patients with active disease should receive rigorous treatment to achieve persistent endoscopic healing, thereby preventing disease extension in UC. The results need to be validated in large-sample prospective studies.

Supplementary Data

Supplementary data is available at Gastroenterology Report online.

Authors' Contributions

K.W., J.L., and J.W. designed the study. J.W., X.W., Y.Z., X.X., and M.W. collected the data. J.W. and X.W. analysed the data. J.L. and K.W. revised the statistical analyses. J.W. and X.W. wrote the paper. X.W., H.J., Y.Z., J.L., and K.W. revised the paper. All the authors have read and approved the final version of the manuscript.

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None.

Conflict of Interest

None declared.

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