



ORIGINAL ARTICLE

# Ulcerative Colitis Endoscopic Index of Severity (UCEIS) versus Mayo Endoscopic Score (MES) in guiding the need for colectomy in patients with acute severe colitis

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## Abstract

**Background:** The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) and the Mayo Endoscopic Score (MES) were developed as an objective method of the endoscopic severity in ulcerative colitis (UC); however, it was still unclear whether UCEIS vs MES could guide the need for colectomy in acute severe colitis (ASC).

**Methods:** Consecutive ASC patients between January 2012 and May 2016 were retrospectively evaluated. Demographic data, previous therapy, clinical observations, laboratory parameters, medical therapy and endoscopic assessments were documented. The primary outcome was the need for colectomy during admission and follow-up.

**Results:** Ninety-two patients were enrolled. 37 (40.2%) needed colectomy. UCEIS score is a predictor of requirement for colectomy in multivariate analysis (OR, 3.25; 95% CI, 1.77–5.97;  $P < 0.001$ ). Receiver-operator characteristic (ROC) area of UCEIS is 0.85, with a sensitivity of 60.3% and specificity of 85.5% using cut-off value of 7, which outperforms MES with the ROC area of 0.65; When UCEIS score  $\geq 7$ , 80% of patients eventually need colectomy.

**Conclusion:** UCEIS outperformed MES as a predictor for need for colectomy in ASC patients. The high probability of medical treatment failure and benefits of early colectomy should be discussed in patients with baseline UCEIS  $\geq 7$ .

Acute severe colitis; colectomy; Ulcerative Colitis Endoscopic Index of Severity; Mayo Endoscopic Score

## Introduction

Ulcerative colitis (UC) is a chronic inflammatory disorder involving exclusively the colonic mucosa. Overall, 24.8% had at least one admission for acute severe colitis (ASC) [1]. When ASC arises, the cornerstone of management remains intravenous (IV) corticosteroids, with a response rate between 57 and 70%

[2,3]. The introduction of rescue therapy with cyclosporine A (CsA) and infliximab (IFX) has provided an effective alternative to early colectomy. However, the failure rate of rescue therapy is about 54–60% [1,4]. Therefore, a substantial number of patients will eventually need colectomy, and 19.9% of ASC patients required colectomy at first admission. As prolonged

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medical therapy is associated with increased health care expenditures and probably a delay to subsequent restorative procedures and post-colectomy complications, it is important to identify patients who will not respond to corticosteroid therapy and necessitate prompt rescue therapy or colectomy.

Traditionally, outcomes following IV corticosteroid therapy in ASC were predicted by clinical or laboratory parameters, such as stool frequency, C-reactive protein (CRP) and serum albumin levels. Prognostic models such as Ho-index, Travis and Lindgren criteria have also been used [5,6], but these indices are somewhat subjective and inconsistently used in clinical practice. As mucosal healing is increasingly emerging as a specific treatment goal in UC, the importance of endoscopic evaluation in predicting outcomes is being increasingly recognized.

Currently, there are mainly two endoscopic score systems of mucosal inflammation in clinical practice. The sigmoidoscopic component of the Mayo Endoscopic Score (MES) and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) show the most promise as reliable evaluative instruments of endoscopic disease activity. The MES has been widely used since 1987, and a score of 0 and 1 is used as a definition of mucosal healing in clinical studies and trials [7]. The UCEIS was developed by Travis *et al.* in 2012 as a tool to accurately predict the overall assessment of the endoscopic severity of UC [8]. It was found that UCEIS scoring is minimally affected by clinical information of disease activity and strongly correlated with patient-reported symptoms. Ikeya *et al.* suggest that the UCEIS is more responsive to change following tacrolimus remission induction therapy for active UC than the MES [9]. Also, Ikeya *et al.* found that endoscopic severity is associated with the outcome in ASC and when the UCEIS is  $\geq 7$ , almost all patients need salvage therapy [10]. However, there is a lack of studies comparing the predictive value of the need for colectomy by the two scoring systems in ASC. The aim of the current study is to compare the predictive value of need for colectomy with two endoscopic score systems in our cohort of ASC patients.

## Patients and methods

### Patients

The Ethics Committee of Jinling Hospital approved the study protocol. Consecutive patients diagnosed as ASC from the inflammatory bowel disease (IBD) centre of the hospital between January 2012 and May 2016 were retrospectively reviewed through the medical records. Inclusion criteria were as follows: (i) age 18 or over, (ii) a confirmed diagnosis of ASC, (iii) available data on the in-hospital clinical course, (iv) availability of a flexible sigmoidoscopy within 1 week before start of treatment. Patients with toxic megacolon, emergency situations needing urgent surgery (massive bleeding, perforation), Crohn's colitis or indeterminate colitis were excluded.

The diagnosis of UC was based on clinical, radiological and pathological criteria. The definition of ASC was made using Truelove & Witt's criteria [11], defined as six or more bloody stools per day with one or more additional criteria (pulse  $> 90$  bpm; temperature  $> 37.8^\circ\text{C}$ ; haemoglobin  $< 105$  g/L; erythrocyte sedimentation rate (ESR)  $> 30$  mm/h; or CRP  $> 30$  mg/dL). The extent of colon involvement was determined by abdominal CT scan.

### Management

Inpatient management followed the standard protocol. *Clostridium difficile* and cytomegalovirus infection were excluded. IV steroids were started with methylprednisolone 60 mg/d or

hydrocortisone 400 mg/d. Malnourished patients received nutritional support, and enteral nutrition was preferred over parenteral nutrition. For patients with hypoalbuminemia ( $< 25$  g/L), IV albumin was given. Subcutaneous low-molecular heparin as thromboembolic prophylaxis was used.

The response to IV steroid therapy was assessed at days 3 to 5. The decision and timing of colectomy were made by the joint discussion of the gastroenterologists and colorectal surgeons. Patients with deterioration in general condition or adverse prognostic characteristics underwent emergency colectomy in 24–48 hours. Those who were refractory or had incomplete response to steroid were colectomized, switched to rescue therapy with IV infliximab 5 mg/kg/d or cyclosporine 2 mg/kg/d, or maintained under IV corticosteroids for a few additional days (7–10 days maximum). Those who had complete response were switched to oral prednisolone. Data on duration of IV steroid therapy and response were recorded, as well as rescue therapy. All patients were followed up until May 2016.

### Data collection

For each patient, clinical data recorded during hospital admission were retrieved, which included: (i) demographics, age, sex, duration of disease, previous maintenance therapy, maximum extent of macroscopic disease on CT scan, baseline sigmoidoscopy appearances; (ii) clinical observation—daily stool frequency, pulse rate and temperature; and (iii) laboratory parameters.

### Image analysis

Sigmoidoscopy images within 1 week before initiation of treatment were obtained from the PACS system of the hospital and endoscopy was performed using an Olympus-CF-H260 endoscopy (9.8-mm diameter; Tokyo, Japan) without fluoroscopic guidance. Two gastrointestinal endoscopic physicians majored in IBD who were unaware of the outcome were involved in image analysis, with disagreement being resolved by a senior physician. All cases were evaluated using the UCEIS and the MES. The UCEIS consists of the following three descriptors and was calculated as a simple sum: vascular pattern (scored 0–2), bleeding (scored 0–3), and erosions and ulcers (scored 0–3). Since this was a pragmatic study, vascular pattern (scored 0–2), erosions and ulcers (scored 0–3) were analysed according to colonoscopic images, and bleeding (scored 0–3) was analysed according to colonoscopic reports that contained the colonoscopy performer's description at the time of the bleeding situation. The range in the UCEIS scores is 0 to 8 (Table 1), which was stratified into four grades: remission (0–1); mild (2–4); moderate (5–6); and severe (7–8).

The MES was classified into the following four categories: 0, normal or inactive disease; 1, mild disease with erythema, decreased vascular patterns and mild friability; 2, moderate disease with marked erythema, absence of vascular patterns, friability and erosions; 3, severe disease with spontaneous bleeding and ulceration.

### Outcome assessments

The main objective was to compare the predictive value of two widely used scoring systems (the UCEIS and the MES) in ASC, and the primary outcome was the need for colectomy during admission or on follow-up. Corticosteroid non-responders during admission, including patients who needed rescue therapy,

**Table 1.** UCEIS (Ulcerative Colitis Endoscopic Index of Severity) descriptors and definitions

Descriptor	Likert scale (anchor points)	Definition
Vascular pattern	Normal (0)	Normal vascular pattern with arborization of capillaries clearly defined, or with blurring or patchy loss of capillary margins
	Patchy obliteration (1)	Patchy obliteration of vascular pattern
	Obliterated (2)	Complete obliteration of vascular pattern
Bleeding	None (0)	No visible blood
	Mucosal (1)	Some spots or streaks of coagulated blood on the surface of the mucosa ahead of the scope, which can be washed away
	Luminal mild (2)	Some free liquid blood in the lumen
	Luminal moderator severe (3)	Frank blood in the lumen ahead of endoscope or visible oozing from mucosa after washing intraluminal blood or visible oozing from a haemorrhagic mucosa
Erosions and ulcers	None (0)	Normal mucosa, no visible erosions or ulcers
	Erosions (1)	Tiny ( $\leq 5$ mm) defects in the mucosa, of a white or yellow colour with a flat edge
	Superficial ulcer (2)	Larger ( $> 5$ mm) defects in the mucosa, which are discrete fibrin-covered ulcers in comparison with erosions, but remain superficial
	Deep ulcer (3)	Deeper excavated defects in the mucosa, with a slightly raised edge

colectomy or died, were documented. The overall costs of patients during admission were also recorded.

### Statistics

Statistical analysis was performed using SPSS 20.0 (SPSS, Inc., IBM Company, Chicago, IL). Categorical variables were compared using the  $\chi^2$  test or Fisher's exact test. Correlations were tested using Spearman's test. Parametric variables were analysed using t-tests and non-parametric variables were compared using the Mann-Whitney *U* test. Kaplan-Meier survival analysis was performed to examine the development of endpoints by UCEIS at admission over time, with significance determined using a log rank test. Univariate analysis was performed and factors with a significant univariate probability ( $p < 0.1$ ) were included in the multivariate logistic regression analysis to examine the binary outcomes and hypothesized predictors. The receiver-operating characteristic (ROC) curve analysis was also performed. A two-tailed  $p < 0.05$  was considered statistically significant.

## Results

### Patients

Of the 764 UC patients screened, 92 met the criteria of modified Truelove & Witts criteria for ASC. Among them, 50 (54.3%) were male. The mean age was  $42.1 \pm 14.8$  years. The median disease duration was 23 (range 1-296) months. For previous medical history in the past 1 year of admission, 6 (6.5%) patients had no treatment, 31 (33.70%) had 5-ASA, 10 (10.9%) with sulfasalazine, 16 (17.4%) with azathioprine, 29 (31.5%) had steroid therapy for  $\geq 3$  months and 7 (7.6%) had previous rescue therapy with infliximab or cyclosporine. Other baseline characteristics (significant comorbid diseases, active smokers, location and extent of disease, nutritional support during admission) are included in [Table 2](#).

### Clinical course

Among the 92 patients, 41 succeeded with IV steroid therapy and switched to oral steroid and maintenance therapy. Of the remaining 51 patients, 23 had deterioration of the situation and need emergency colectomy and 28 patients had incomplete respond to IV steroid therapy by day 5. Among the 28 patients with incomplete response, 13 had prolonged IV steroid therapy and 15 (39.4%) received rescue therapy with IFX ( $n = 14$ ) and CsA ( $n = 1$ ),

among whom 6 patients (5 with IFX and 1 with CsA rescue therapy) did not achieve clinical remission and underwent colectomy during the hospital stay. Of the 63 patients who were discharged after medical therapy, 50 were maintained at remission and 13 were re-admitted, among whom 8 patients underwent colectomy during a median follow-up of 73.7 (range 40.1-123.1) weeks. Thus, a total of 37 patients (40.2%) underwent colectomy during hospital admission and follow-up. Surgical procedures performed were subtotal colectomy ( $n = 2$ ), proctocolectomy with ileal pouch anal anastomosis ( $n = 31$ ) and proctocolectomy with permanent ileostomy ( $n = 4$ ). There was one death after colectomy due to multiple organ dysfunction syndrome (MODS).

### Univariate and multivariate analysis of factors related to need for colectomy

The UCEIS and the MES score were significantly higher in colectomized patients compared to non-colectomized patients (UCEIS:  $6.24 \pm 1.21$  vs  $4.49 \pm 1.15$ ,  $p < 0.001$ ; MES:  $2.89 \pm 0.32$  vs  $2.56 \pm 0.50$ ;  $p = 0.010$ ). Other factors found to be significantly associated with the need for colectomy in the univariate analysis included baseline CRP level ( $31.8 \pm 23.6$  vs  $42.4 \pm 26.0$ ;  $p = 0.042$ ) and albumin level ( $35.3 \pm 7.3$  vs  $31.1 \pm 5.8$ ;  $p = 0.004$ ). These factors were then analysed using a multivariate analysis model to determine the risk factors independently associated with the need for colectomy. Age, stool frequency and platelet were also included in the multivariate model (all  $p < 0.10$ ). In the multivariate analysis, only the UCEIS was found to be an independent risk factor for colectomy ( $p < 0.001$ ; odds ratio [OR]: 3.25, 95% confidence interval [CI]: 1.77-5.97). Details of colectomy and non-colectomy groups are listed in [Table 3](#).

The colectomy rate was 0% when the UCEIS = 3, 17.4% when the UCEIS = 4 and 80.0% when the UCEIS = 7-8, with an OR of colectomy from 1 to 4.37 (95% CI: 1.17-9.05;  $p < 0.001$ ) when the UCEIS increased from 3 to 8, as shown in [Figure 1A](#). The colectomy rate was 13.8% when the MES = 2 and 60.0% when the MES = 3, with an OR of colectomy from 1 to 3.42 (95%CI: 1.35-8.74;  $p < 0.001$ ) when the UCEIS increased from 2 to 3, as [Figure 1B](#) shows.

### Prognostic accuracy of the UCEIS vs the MES for the need for colectomy

The ROC curve analysis was performed to evaluate the performance of the UCEIS vs the MES to predict the need for colectomy.

The UCEIS score has a good predictive value with an area under the ROC curve (AUC) of 0.85 (sensitivity 60.3%, specificity 85.5%, cut-off value 7 points). The predictive value of the MES was lower, with an AUC of 0.65 (sensitivity 89.2%, specificity 43.6%, cut-off value 3 points), as shown in **Figure 2**.

A significant association between the UCEIS and the MES was noted (Spearman's rho = 0.704,  $p < 0.001$ ). We also tested the correlation between the UCEIS score and Mayo Clinic score, and there was significant correlation (Spearman's rho = 0.762,  $p < 0.001$ ).

### Patient outcomes according to the UCEIS or MES risk stratifications

According to the day 3 risk criteria of IV steroid therapy, patients categorized as high-risk (UCEIS 7–8 and MES 3) were more likely to

**Table 2.** Demographics and management of patients with acute severe colitis

Characteristics	Values (n=92)
Mean age, years	42.1±14.8
Male, n (%)	50 (54.3)
Significant comorbid diseases, n (%)	16 (17.4)
Median course of disease, months	23 (1–296)
Active smokers, n (%)	12 (13.04)
<b>Location and extent of disease, n (%)</b>	
E2, left-sided colitis	31 (33.70)
E3, extensive colitis	61 (66.30)
<b>Therapy before admission, n (%)</b>	
5-aminosalicylic acid	31 (33.7)
Sulfasalazine	8 (8.7)
Preoperative steroids for ≥3 months	29 (31.5)
Immunosuppressant	16 (17.4)
Infliximab	7 (7.6)
No treatment	6 (6.5)
<b>Nutritional support during admission, n (%)</b>	
Enteral nutrition	42 (45.7)
Parenteral nutrition	24 (26.1)

be refractory to IV steroids than low-risk patients: 84.0% for UCEIS 7–8 vs 57.6% for UCEIS 5–6 vs 11.8% for UCEIS 2–4 ( $p < 0.001$ ) and 62.1% for MES 3 vs 11.5% for MES 2 ( $p < 0.001$ ). Patients classified as high-risk according to UCEIS criteria were also more likely to be refractory to salvage therapy: 87.5% for UCEIS 7–8 vs 14.3% for UCEIS 5–6 vs 0.0% for UCEIS 2–4 ( $p = 0.003$ ). The MES high-risk group did not demonstrate an increased failure rate of salvage therapy compared to the low-risk group (53.8% vs 50.0%,  $p = 1.000$ ). The UCEIS and MES classifications identified a population that was at higher risk of colectomy. Overall colectomy rates were 80.0% for UCEIS 7–8 vs 39.4% for UCEIS 5–6 vs 11.8% for UCEIS 2–4 ( $p < 0.001$ ) and 51.5% for MES 3 vs 11.5% for MES 2 ( $p < 0.001$ ). Details are explained in **Table 4**.

A Kaplan–Meier survival analysis was performed in patients with UCEIS ≥ 7 vs UCEIS < 7, and in patients with MES = 3 vs MES = 2, as shown in **Figure 3**. The overall colectomy-free survival rate at week 100 in patients with UCEIS 7–8 was significantly lower compared to those with UCEIS < 7 ( $p < 0.001$ ). When MES = 3, the overall colectomy-free survival rate at 100 was significantly lower compared to MES = 2 ( $p < 0.001$ ).

### Cost-effectiveness of early colectomy vs late or no colectomy in patients with UCEIS ≥ 7

Early colectomy was defined as colectomy without rescue therapy. Late colectomy was defined as colectomy after rescue therapy on admission or during follow-up. Among the 25 patents with UCEIS ≥ 7, 11 (44%) underwent early colectomy, 9 (36%) underwent late colectomy and 5 (20%) were maintained on medical therapy without surgery.

**Figure 4** depicts the mean hospitalization cost of different treatment strategies in ACS patients with UCEIS ≥ 7. The mean hospitalization costs of patients with non-colectomy, early colectomy and late colectomy were CNY 120 082.2±11 029.2, 115 255.5±35 532.1 and 183 550.2±33 054.5, respectively. Costs of late-colectomy patients were significantly higher compared with others ( $p < 0.001$ ); costs between the early-colectomy group and the non-colectomy group were comparable ( $p = 0.221$ ) (**Table 5**).

**Table 3.** Univariate and multivariate analyses of possible risk factors associated with the need for colectomy

	Univariate analysis			Multivariate analysis	
	Colectomy (n=55)	Non-colectomy (n=37)	p-value	Odds ratio (95% confidence interval)	p-value
Mean age, years	44.3±14.3	38.8±15.1	0.076	1.01 (0.96–1.05)	0.768
Male, n (%)	29 (52.7)	21 (56.76)	0.704		
Comorbidity, n (%)	9 (16.4)	7 (18.9)	0.751		
Median course of disease, months	22 (1–296.00)	24 (1–276)	0.428		
<b>Location and extend of disease, n (%)</b>					
E2, left-sided colitis	21 (38.2)	10 (27.0)	0.267		
E3, extensive colitis	34 (61.8)	27 (83.0)	0.267		
Mean temperature, °C	36.9±0.7	37.1±0.6	0.422		
Mean pulse rate, per minute	81.6±16.5	83.0±10.7	0.601		
Mean stool frequency, per day	8.32±2.63	9.72±4.48	0.062	1.00 (0.85–1.19)	0.960
Mean UCEIS score	4.49±1.15	6.24±1.21	<0.001	3.25 (1.77–5.97)	<0.001
Mean MES score	2.58±0.49	2.89±0.31	0.010	0.45 (0.08–2.59)	0.372
Mean leukocytes, ×10 <sup>9</sup> /L	8.94±6.05	10.51±7.37	0.264		
Mean C-reactive protein, mg/L	31.8±23.6	42.4±26.0	0.042	1.00 (0.98–1.03)	0.726
Mean ESR, mm/h	33.4±20.4	32.3±20.9	0.854		
Mean haemoglobin, g/L	106.4±24.5	98.0±21.4	0.166		
Mean platelet, /mm <sup>3</sup>	301.7±133.1	362.9±153.9	0.085	1.01 (0.99–1.01)	0.114
Mean albumin, g/L	35.3±7.3	31.1±5.8	0.004	0.96 (0.88–1.05)	0.419

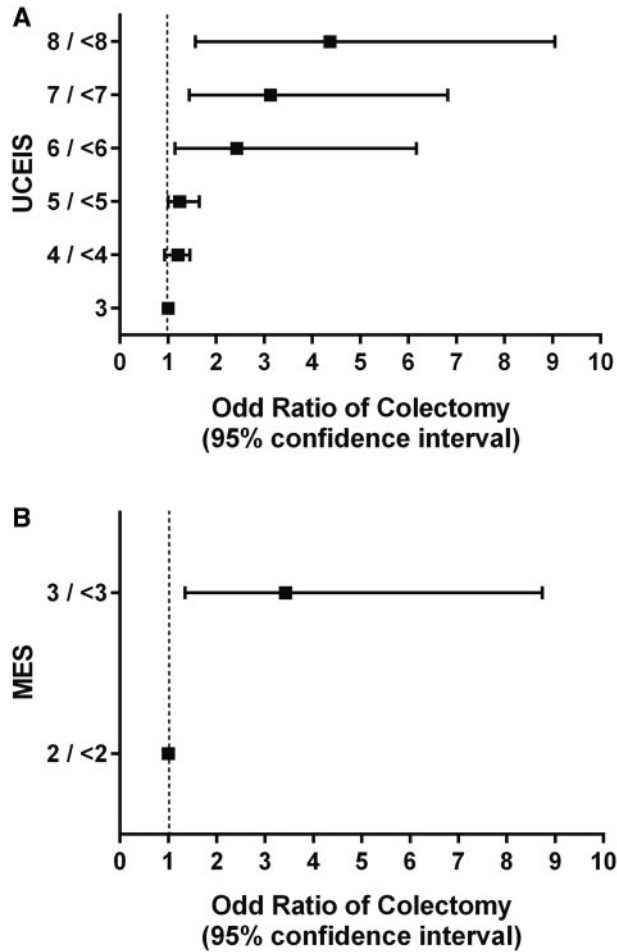


Figure 1. Relationship between the different UCEIS score and colectomy during admission or follow-up expressed as odds ratio of colectomy. Bars represent 95% confidence interval.

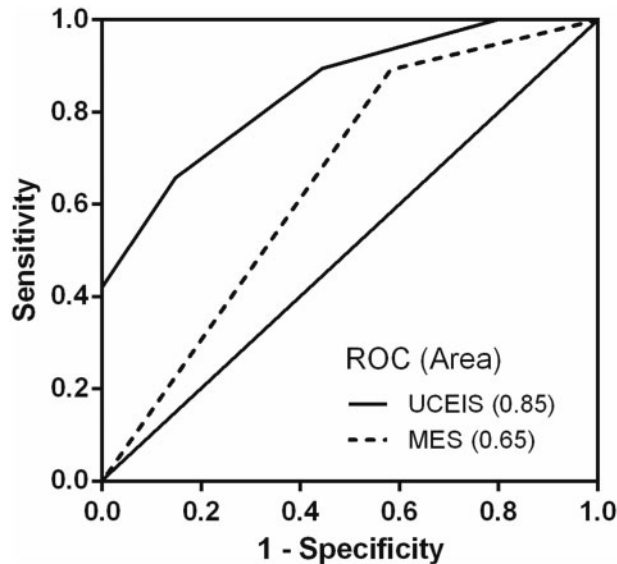


Figure 2. ROC curves of UCEIS vs MES in predicting colectomy. UCEIS (area under the curve [AUC] = 0.85, cut-off value: 7) had a sensitivity of 60.3% and specificity of 85.5%, and MES (AUC=0.65, cut-off value: 2.5) had a sensitivity of 89.2% and specificity of 43.6%.

## Discussion

Despite improvements in medical care and the introduction of biologics therapy, a substantial number of patients with ASC require subsequent colectomy. The present study was to examine the role of the UCEIS vs the MES as a predictive measure to translate endoscopic disease appearance into a prediction of the clinical course of ASC. In our study, the UCEIS had a better predictive value for colectomy than the MES in ASC patients; when the UCEIS is  $\geq 7$ , 80% of the patients will require colectomy during admission and follow-up, whether or not the patients received rescue therapy, and the clear economic advantages of early colectomy in patients with UCEIS 7–8 are also worth mentioning.

The right time for surgery is important for ASC. It is often considered that, in patients with poor prognostic features or fulminant disease, a prolonged preoperative hospitalization correlates with worse outcomes after colectomy [12–14], and the case for early surgery (rather than further medical intervention) may be more compelling in patients with high-risk scores, so an accurate scientific risk-assessing method is of great importance to the clinical pathways. For example, the Ho score and Travis criteria have been widely used to identify patients who are at high risk of failing therapy and needing second-line therapy or colectomy. The value of colonoscopy in predicting the response to medical therapy has been proven in previous studies. Carbonyl et al. found that severe endoscopic lesions with deep extensive ulcerations, well-like ulcerations, large mucosal abrasion or mucosal detachment were associated with an increased risk of failure of intensive intravenous treatment of steroids [15]. According to the study by Cacheux et al., in 118 patients, the presence of severe endoscopic lesions was an independent predictive factor of colectomy in patients undergoing CsA therapy [16]. However, due to the significant inter-observer variation, these evaluations were rather subjective in defining the severity of the endoscopic appearance. The advantage of the UCEIS score is that it is a rather objective method to evaluate the endoscopic severity of UC. According to its developers, Travis et al., the UCEIS and its components show satisfactory intra- and inter-investigator reliability [8]. Among investigators, the UCEIS accounted for a median of 86% of the variability in the evaluation of overall severity on the visual analogue scale (VAS) when assessing the endoscopic severity of UC and was unaffected by knowledge of clinical details [4]. According to the result of Ho et al., 87% of patients with calprotectin greater than 1922.5  $\mu\text{g/g}$  had colectomy at 6 months of follow-up [17]. Theede et al. showed that almost all patients with UCEIS 7–8 had fecal calprotectin  $>1000 \mu\text{g/g}$  [18]. Therefore, correlation of the UCEIS with the need for colectomy seems to be proven indirectly by previous studies.

In our study, the relation between the UCEIS and the MES was evaluated and the result indicated a good correlation. The UCEIS better predicted requirement for colectomy than the MES; this difference is possibly due to the narrow distribution and small range of MES criteria, and UCEIS ranges from 3 to 8 for those patients with MES = 3. Prognostic variables were analysed by ROC curves and the result was consistent with our hypothesis. Despite the MES (cut-off value: 3) having a higher sensitivity (89.2% vs 60.3%) than the UCEIS (cut-off value: 7), the specificity of the MES for colectomy was only 43.6%. Because surgical extirpation was the last effective treatment, the UCEIS might guide a more rational selection.

In the current study, the UCEIS score and the MES score were both based on the examination of sigmoidoscopy, which might underestimate the severity of the disease in some patients,

Table 4. Patient outcomes according to UCEIS or MES risk stratifications

	UCEIS				MES		
	Low, 2-4 (n=34)	Intermediate, 5-6 (n=33)	High, 7-8 (n=25)	p-value	Low, 2 (n=26)	High, 3 (n=66)	p-value
<b>Benefit from corticosteroid therapy (day 3)</b>							
Mean C-reactive protein, mg/L	12.8±11.0	19.9±13.6	35.3±32.3	<0.001	12.8±11.2	24.9±23.7	0.001
Mean stool frequency, per day	3.67±1.22	5.88±1.35	8.93±4.50	0.105	5.32±1.34	8.55±3.58	0.229
Mean haemoglobin, g/L	105.0±18.5	94.6±24.5	93.1±16.5	0.047	105.3±19.1	95.2±20.9	0.034
Mean albumin, g/L	38.5±7.8	32.4±5.8	29.8±5.6	<0.001	37.3±6.4	32.6±7.5	0.005
Mean platelet, /mm <sup>3</sup>	303.3±119.0	305.3±109.8	383.6±126.1	0.019	309.7±124.5	332.2±121.0	0.430
Corticosteroid non-responders, n (%)	4 (11.8)	19 (57.6)	21 (84.0)	<0.001	3 (11.5)	41 (62.1)	<0.001
Rescue therapy non-responders, n (%)	0 (0.0)	1/7 (14.3)	7/8 (87.5)	0.003	1/2 (50.0)	7/13 (53.8)	1.000
Colectomy, n (%)	4 (11.8)	13 (39.4)	20 (80.0)	<0.001	3 (11.5)	34 (51.5)	<0.001
During admission	4 (11.8)	9 (27.3)	16 (64.0)	<0.001	2 (7.7)	27 (40.9)	0.001
During follow-up	0 (0.0)	4 (12.1)	4 (16.0)	0.018	1 (3.8)	7 (10.6)	0.265

UCEIS, Ulcerative Colitis Endoscopic Index of Severity; MES, Mayo Endoscopic Score.

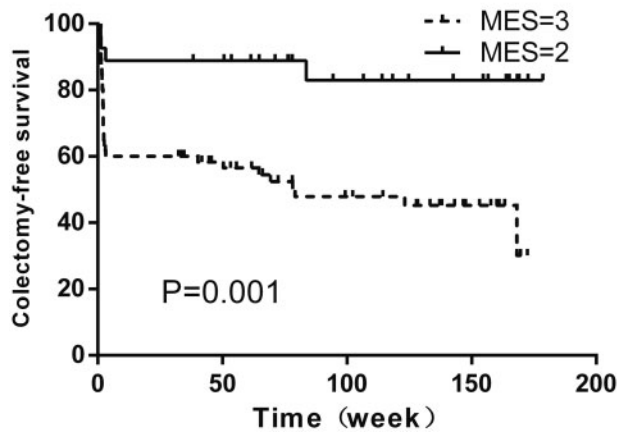
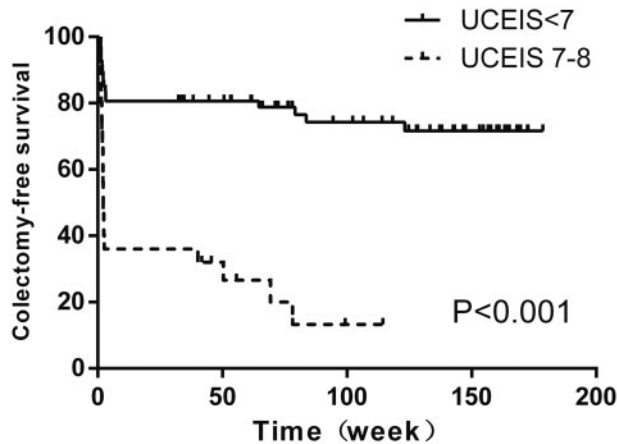


Figure 3. Colectomy-free survival rates in patients with UCEIS  $\geq 7$  vs UCEIS  $< 7$ , and in patients with MES = 3 vs MES = 2.

especially for those with rectum-sparing disease. Menasci *et al.* have shown that the UCEIS calculated as a sum of the single colonic segments performed better than regular UCEIS in UC outpatients [19]. Also, Lobatón *et al.* suggested that the Modified MES, which evaluated all the colon segments, could serve as a new index for the assessment of the extension and severity of endoscopic activity in UC patients [20]. However, full

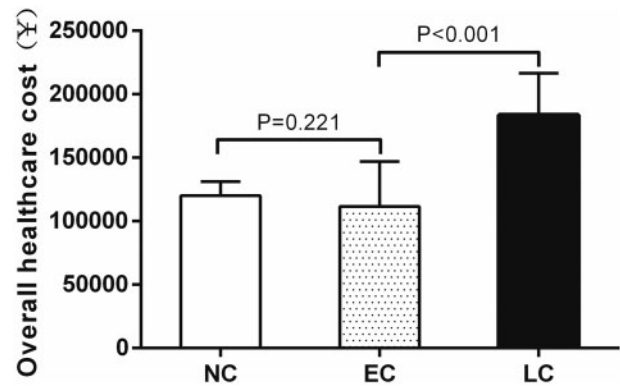


Figure 4. Overall hospitalization expenses of no colectomy (NC) vs early colectomy (EC) vs late colectomy (LC) in patients with UCEIS  $\geq 7$ .

colonoscopy in the presence of ASC is not advisable due to the possibility of toxic megacolon or colonic perforation. Also, according to a recent study by Colombel *et al.*, there is a high degree of correlation in assessments of UC activity made by rectosigmoidoscopy vs colonoscopy in both the UCEIS and the MES scores [21]. In the current study, CT scan was used to evaluate the extent of the disease in ASC patients.

There were three main limitations of our study. First, our study had a retrospective nature and was from a single centre. Thus, treatment was not controlled, which might affect the outcomes. However, a strategy of management was standardized in our centre, including routine use of corticosteroids after admission as well as optimization of patient status with nutritional support and careful timing of surgery. Second, bleeding of the UCEIS (scored 0-3) was analysed according to the report that contains the colonoscopy performer's description at the time of the bleeding situation, and this might decrease the accuracy of estimates to some extent, which should be pointed out as a limitation. Third, some patients who met the conditions of the ASC did not have colonoscopy available for UCEIS analyses after admission and therefore were excluded from the study. Finally, a relatively small sample size, which was not adequate to demonstrate significant correlations between some comparators, makes a valid statistical interpretation of postoperative complications difficult. Further work with larger cohorts is needed to confirm these findings.

**Table 5.** Healthcare costs of early vs late vs no colectomy in patients with UCEIS 7–8

	No colectomy (n=5)	Early colectomy (n=11)	Late colectomy (n=9)	p-value
Medication cost (¥)	84 140.2±6959.1	33 275.0±18 679.5	87 780.4±12 232.2	<0.001
Rescue therapy-related cost	38 645.20±7458.02*	–	41963.33±10 028.79†	0.532
Non-rescue therapy-related cost	45 495.0±4208.8	33 275.0±18 679.5	45 817.1±13 385.6	0.147
Diagnostics procedures (¥)	4902.6±637.2	13 355.5±8736.3	19 306.0±6593.9	0.006
Surgery-related cost (¥)	–	10962.9±2887.7	11 156.2±2212.9	0.611
Hospitalization (¥)	30 240.8±7169.6	50 992.0±14 128.7	73 831.5±21 275.3	<0.001
Nursery care cost (¥)	798.6±131.3	774.6±643.7	1130.66±482.2	0.300
Overall cost (¥)	120 082.2±11 029.2	111 525.5±35 532.1	183 550.2±33 054.5	<0.001

\*Three patients had rescue therapy included; †Five patients had rescue therapy included

In conclusion, the current study revealed that the UCEIS outperformed the MES as a predictor for colectomy in ASC patients. Eighty per cent of ASC patients with UCEIS  $\geq 7$  subsequently needed colectomy, irrespective of medical therapy; also, early colectomy seems to be more cost-effective than late colectomy or prolonged medical therapy. Therefore, for ASC patients with UCEIS  $\geq 7$ , a high probability of medical treatment failure and the benefit of early colectomy should be discussed to avoid treatment delay.

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## References

- Laharie D, Bourreille A, Branche J et al. Ciclosporin versus infliximab in patients with severe ulcerative colitis refractory to intravenous steroids: a parallel, open-label randomised controlled trial. *Lancet* 2012;**380**:1909–15.
- Bewtra M, Newcomb CW, Wu Q et al. Mortality associated with medical therapy versus elective colectomy in ulcerative colitis: a cohort study. *Ann Intern Med* 2015;**163**:262–70.
- Samaan MA, Mosli MH, Sandborn WJ et al. A systematic review of the measurement of endoscopic healing in ulcerative colitis clinical trials: recommendations and implications for future research. *Inflamm Bowel Dis* 2014;**20**:1465–71.
- Travis SP, Schnell D, Feagan BG et al. The impact of clinical information on the assessment of endoscopic activity: characteristics of the Ulcerative Colitis Endoscopic Index of Severity (UCEIS). *J Crohns Colitis* 2015;**9**:607–16.
- Ho GT, Mowat C, Goddard CJR et al. Predicting the outcome of severe ulcerative colitis: development of a novel risk score to aid early selection of patients for second-line medical therapy or surgery. *Aliment Pharmacol Ther* 2004;**19**:1079–87.
- Lindgren SC, Flood LM, Kilander AF. Early predictors of glucocorticosteroid treatment failure in severe and moderately severe attacks of ulcerative colitis. *Eur J Gastroenterol Hepatol* 1998;**10**:831–5.
- Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis: a randomized study. *N Engl J Med* 1987;**317**:1625–9.
- Travis SP, Schnell D, Krzeski P et al. Reliability and initial validation of the Ulcerative Colitis Endoscopic Index of Severity. *Gastroenterology* 2013;**145**:987–95.
- 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* 2015;**10**:286–95.
- Corte C, Fernandopulle N, Catuneanu AM et al. Association between the ulcerative colitis endoscopic index of severity (UCEIS) and outcomes in acute severe ulcerative colitis. *J Crohns Colitis* 2015;**9**:376–81.
- Dignass A, Eliakim R, Magro F et al. Second European evidence-based Consensus on the diagnosis and management of ulcerative colitis. Part 1: Definitions and diagnosis [in Spanish]. *Rev Gastroenterol Mex* 2014;**79**:263–89.
- Randall J, Singh B, Warren BF. Delayed surgery for acute severe colitis is associated with increased risk of postoperative complications. *Br J Surg* 2010;**97**:404–9.
- Mor IJ, Vogel JD, da Luz Moreira A et al. Infliximab in ulcerative colitis is associated with an increased risk of postoperative complications after restorative proctocolectomy. *Dis Colon Rectum* 2008;**51**:1202–10.
- Schluender SJ, Ippoliti A, Dubinsky M et al. Does infliximab influence surgical morbidity of ileal pouch-anal anastomosis in patients with ulcerative colitis? *Dis Colon Rectum* 2007;**50**:1747–53.
- Carbonnel F, Gargouri D, Lemann M et al. Predictive factors of outcome of intensive intravenous treatment for attacks of ulcerative colitis. *Aliment Pharmacol Ther* 2000;**14**:273–9.
- Cacheux W, Seksik P, Lemann M et al. Predictive factors of response to cyclosporine in steroid-refractory ulcerative colitis. *Am J Gastroenterol* 2008;**103**:637–42.
- Ho GT, Lee HM, Brydon G et al. Fecal calprotectin predicts the clinical course of acute severe ulcerative colitis. *Am J Gastroenterol* 2009;**104**:673–8.
- Theede K, Holck S, Ibsen P. Level of fecal calprotectin correlates with endoscopic and histologic inflammation and identifies patients with mucosal healing in ulcerative colitis. *Clin Gastroenterol Hepatol* 2015;**13**:1929–36.
- Menasci F, Pagnini C, Di Giulio E. Disease extension matters in endoscopic scores: UCEIS calculated as a sum of the single colonic segments performed better than regular UCEIS in outpatients with ulcerative colitis. *J Crohns Colitis* 2015;**9**:692–3.
- Lobatón 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**:846–52.
- Colombel JF, Ordas I, Ullman T et al. Agreement between rectosigmoidoscopy and colonoscopy analyses of disease activity and healing in patients with ulcerative colitis. *Gastroenterology* 2016;**150**:389–95.