

Are endoscopic grading and scoring systems in inflammatory bowel disease the same?

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ABSTRACT

الأهداف: لتقييم نشاط أمراض التنظير في مرض التهاب الأمعاء (IBD). كان الهدف من هذه الدراسة من أجل تقييم العلاقة والفرق لهذه الفئة.

الطريقة: تم تقييم 80 مريضاً يعاني من التهاب القولون المتقترح (UC)، و31 مريضاً يعاني من مرض كرون (CD) بناءً على فئة التنظير المتعددة، خلال الفترة ما بين يونيو 2006م وحتى فبراير 2007م، بمستشفى رينجي - شنغهاي - الصين. تم تقييم نتائج تجرّبي التنظير باستعمال أنظمة مستقلة ومختلفة. تم تحليل البيانات باستعمال درجة كاندليل للانسجام وسبيرمان للصلة.

النتائج: كانت درجة كاندليل للانسجام بالنسبة لأنظمة (UC) و(0.714) ($p < 0.001$)، و(0.342) ($p < 0.001$) على التوالي. لم يكن هنالك فرقاً ملحوظاً بين النظامين (UC) الكل ($p < 0.01$). ولكن لم يتبين وجود انسجام إحصائي بين نظام قياس الدرجات الصيني لمرض كرون (CGSCD) ومدخلات تنظير مرض كرون للشدة ($p = 0.076$)، CDEIS ($rs = 0.323$). تم اكتشاف وجود فروقات ملحوظة بين أنظمة التنظير لالتهاب القولون التقرحي (UC) ($p = 0.001$).

خاتمة: لقد أقتراح في دراستنا أن لدى نظام قياس تنظير الدرجات لمرض التهاب القولون التقرحي انسجام مرضي، وأظهر نظام قياس الدرجات الصيني لمرض كرون مكاناً للتحسن. في الجهة المقابلة كان المقصود من درجات بارون المعدلة من أجل الفئة الشديدة، بينما كان المقصود من تصنيف جيرون الفئة البسيطة.

Objectives: To assess the correlation and difference between various endoscopic grades and indices for assessment of endoscopic disease activity in inflammatory bowel disease (IBD).

Methods: Eighty consecutive patients with ulcerative colitis (UC), and 31 patients with Crohn's disease (CD) were evaluated based on multiple endoscopic criteria between June 2006 and February 2007 at the

Department of Gastroenterology of Renji Hospital, Shanghai, China. Two experienced endoscopists evaluated the endoscopic findings using various systems independently. Data were analyzed using Kendall's coefficient of concordance and Spearman correlations.

Results: For the systems of UC and CD, Kendall's coefficients of concordance were 0.714 ($p < 0.001$) and 0.342 ($p < 0.001$). There was no significant difference between the 2 systems of UC (all $p < 0.01$). However, no statistically significant concordances were found between Chinese Grading System of Crohn's Disease (CGSCD) and Crohn's Disease Endoscopic Index of Severity (CDEIS) ($rs = 0.323$, $p = 0.076$). Significant differences in frequencies were detected among endoscopic systems for UC ($p = 0.001$).

Conclusions: It was suggested in our study that endoscopic grading and scoring systems of UC had satisfactory concordance, and CGSCD showed room for improvement. However, the modified Baron scale was tend to severe category, while Jeroen classification was tend to mild category.

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Endoscopy is useful for the assessment of inflammatory bowel disease (IBD).^{1,2} It is necessary to establish a differential diagnosis, to determine the extent of inflammatory activity, preoperatively to guide the surgeon, and to predict clinical outcome by endoscopic grades and indices in patients with IBD. Therefore, colonoscopy and mucosal biopsy have been considered the "gold standard" investigation for the evaluation of disease activity and disease extent in IBD. Furthermore, endoscopy plays a key role in the surveillance of patients with long-standing colitis who are at increased risk for dysplasia and the development of colorectal cancer.³ Although there are new endoscopic techniques under evaluation in IBD, such as wireless capsule endoscopy or double balloon enteroscopy for the imaging of small bowel, and endoscopic ultrasound for evaluation of strictures or of perianal disease, colonoscopy performed by an expert endoscopist allows accurate diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) in up to almost 90% of cases.⁴ Clinical trails often use various disease activity indices as there was no clear standard. However, patients with IBD were subjected to multiple endoscopies for evaluation of disease activity because endoscopy was still part of the most standard indices.⁵⁻⁹ Multiple endoscopic grades and indices for IBD have been devised for assessment of endoscopic disease activity, but none have been rigorously validated. The best evaluating strategy of endoscopy has still to be identified. Without a validated endoscopic standard for disease activity, clinical and endoscopic experts have advocated different endoscopic grading and scoring systems, which probably indicate some potential difference for evaluation of endoscopic disease activity. Accordingly, in this study, we aimed to measure the endoscopic disease activity of the patients with IBD using 6 endoscopic grading or scoring systems of UC, and 3 of CD, and assessed the concordance, and difference of these endoscopic grading and scoring systems.

Methods. The bibliographic searches for endoscopic grading and scoring systems of colonoscopy were performed using Medline and Chinese Biomedical Database. A standardized sheet of each system was prepared before colonoscopy. Between June 2006 and February 2007, 80 consecutive patients with UC, and 31 patients with CD underwent colonoscopy in the Department of Gastroenterology of Renji Hospital, Shanghai, China using Olympus CF240 endoscopes (Olympus Optical Co., Tokyo, Japan). The study inclusion criteria were as follows: (i) the diagnoses were proven by at least 3 doctors based on clinical, endoscopic, histopathologic, and serologic evaluation; (ii) the need for endoscopic diagnosis, colonic activity

assessment, or colonic disease extent assessment; and (iii) signed informed consent was obtained from all patients. The study exclusion criteria were as follows: (i) inability to give signed, informed consent; (ii) pregnancy; (ii) previous colonic resection or formation of an ileoanal pouch anastomosis; (iv) grade 3 bowel preparation (<90% mucosal visualization);¹⁰ (v) CD patients without colorectal evolved; and (vi) previous or current intraepithelial neoplasia or colorectal cancer. Ethical approval for the study was obtained from the Research Ethics Committee of Shanghai Jiao Tong University. Six endoscopic grading or scoring systems of UC, and 3 of CD were included for evaluation. The endoscopic grading and scoring systems of UC were as follows: (i) Chinese Grading System of Ulcerative Colitis (CGSUC);¹¹ (ii) Truelove classification;¹² (ii) Baron classification;¹³ (iv) modified Baron scale;⁵ (v) Jeroen classification;¹⁴ and (vi) Azzolini classification.¹⁵ The endoscopic grading and scoring systems of CD were as follows: (i) Chinese Grading System of Crohn's disease (CGSCD);¹¹ (ii) Crohn's Disease Endoscopic Index of Severity (CDEIS);¹⁶ and (iii) Simple Endoscopic Score for Crohn's Disease (SESCD).¹⁷ Two experienced endoscopists, who were blinded regarding the histopathology and clinical presentation of the cases, evaluated the endoscopic findings using various systems independently. Disagreements were resolved by consulting a third reviewer. Data extracted from the medical records included age, gender, duration of disease, extent of disease, number of patients hospitalized, and endoscopic findings. Descriptive statistics were used to report the demographics and characteristics of patients. For the overall systems of UC and CD, Kendall's coefficient of concordance (W) was performed to determine the correlations. Comparison of the systems was performed by Spearman's correlation coefficient (rs). Kruskal-Willis analysis of frequency was used to test the correlations of endoscopic criteria for different endoscopic severity. A p-value of less than 0.05 was considered to be statistically significant. Statistical uncertainty was quantified by calculating 95% confidence interval (CI) using the exact binomial method. Calculations were made using the Microsoft SPSS statistical package 13.0 (SPSS Institute, Chicago, IL).

Results. A total of 80 consecutive patients (53 men, 27 women, mean age 46.14 years, 95% CI 42.80-49.48 years) with UC, and 31 consecutive patients (15 men, 16 women, mean age 37.87 years, 95% CI 31.47-44.27 years) with CD who underwent colonoscopy were evaluated based on the systems by 2 endoscopists independently. Fifteen inpatients with UC and 15 with CD were enrolled. The mean duration of UC was 12.84

months (95% CI 0.00-84.47), and CD was 8.56 months (95% CI 0.02-36.90). The distributions of endoscopic disease activity values of UC are presented in **Figure 1**. The rank of CGSUC was 2.09, of Truelove classification was 1.97, of Baron classification was 3.71, of modified Baron scale was 2.79, of Jeroen classification was 5.11, and of Azzolini classification was 5.33. Endoscopic grading and scoring systems of UC showed significant concordance ($W=0.714$, $p<0.001$). The distributions of endoscopic disease activity values of CD are presented in **Figure 2**. The rank of CGSCD was 1.61, of CDEIS was 2.66, and of SESCD was 1.73. Endoscopic grading and scoring systems of CD showed significant concordance ($W=0.342$, $p<0.001$). Our data suggested positive correlations of endoscopic grading and scoring systems for UC and CD. To show the coherence of systems in detail, it is necessary to determine the correlations of all systems. The 6 endoscopic grading and scoring systems of UC were presented as a matrix scatter plot (**Figure 3**). The Spearman correlation coefficients of each system ranged from 0.685-0.828 ($p<0.001$), which indicated satisfactory correlations between each system for UC (**Table 1**). The 3 endoscopic grading and scoring systems of CD are as a scatter plot (**Figure 4**). However, no significant concordance was indicated between CGSCD and CDEIS ($r_s=0.323$, $p=0.076$) (**Table 2**). The patients with UC had a full range of endoscopic severity. Therefore, it is important to demonstrate if the of endoscopic grading and scoring systems are valid for different endoscopic severities. Patients were divided into inactive, mild, moderate, and severe categories as defined by system. The frequency of each endoscopic grade is presented in **Figure 5**. Kruskal-Wallis test, based

on the frequency of each system showed significant difference among each system ($p=0.001$). The rank of CGSUC was 238.13, of Truelove classification was 228.85, of Baron classification was 239.64, of modified Baron scale was 0.54, Jeroen classification 192.56, and Azzolini classification was 262.28, which indicated that modified Baron scale was tend to severe category, while Jeroen classification was tend to mild. However, it was impossible to perform Kruskal-Wallis test to of CD, as the not clearly defined in CDEIS or SESCD.

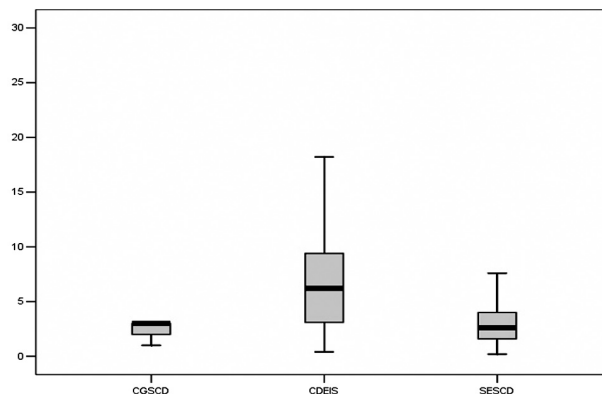


Figure 2 - The distributions of endoscopic disease activity values of Crohn's disease. The ranks of Chinese Grading System of Crohn's disease (CGSCD)¹¹ was 1.61, Crohn's Disease Endoscopic Index of Severity (CDEIS)¹⁶ 2.66 and Simple Endoscopic Score for Crohn's Disease (SESCD)¹⁷ 1.73, with an overall Kendall's Coefficient of Concordance of 0.342 ($p<0.001$).

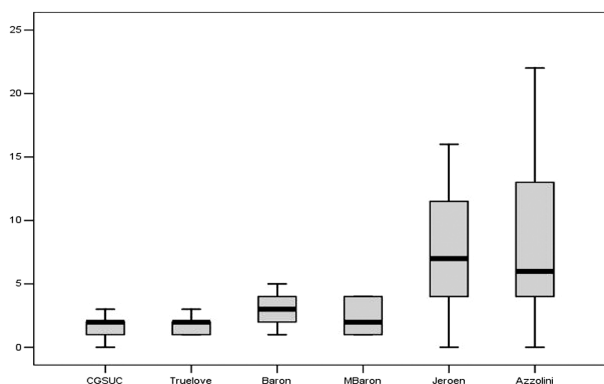


Figure 1 - The distributions of endoscopic disease activity values for each of the indices. The ranks of Chinese Grading System of Ulcerative Colitis (CGSUC)¹¹ was 2.09, Truelove classification (Truelove)¹² 1.97, Baron classification (Baron)¹³ 3.71, modified Baron scale (MBaron)⁵ 2.79, Jeroen classification (Jeroen)¹⁴ 5.11 and Azzolini classification (Azzolini)¹⁵ 5.33, with an overall Kendall's Coefficient of Concordance of 0.714 ($p<0.001$).

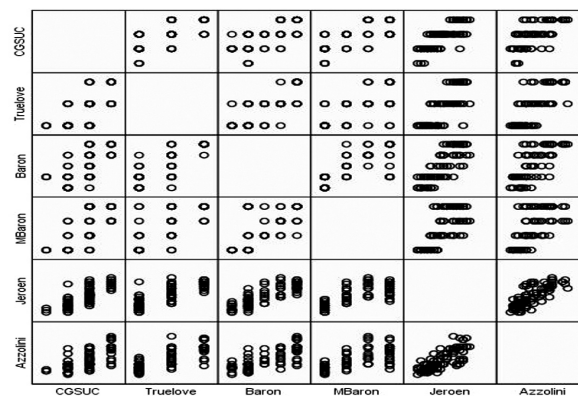


Figure 3 - The matrix of scatter plots indicates that the distribution of the endoscopic index values between every 2 systems of ulcerative colitis (UC) match well. The Spearman correlation coefficients of every 2 systems ranged from 0.69 to 0.83, which indicated satisfactory correlations between every 2 systems for UC. CGSUC¹¹ - Chinese Grading System of Ulcerative Colitis; Truelove¹² - Truelove classification; Baron¹³ - Baron classification; MBaron⁵ - modified Baron scale; Jeroen¹⁴ - Jeroen classification; Azzolini¹⁵ - Azzolini classification.

Table 1 - The Spearman correlation coefficients of indices in ulcerative colitis.

Spearman's correlation coefficient	CGSUC	Truelove classification	Baron classification	Modified Baron scale	Jeroen classification	Azzolini classification
CGSUC ¹¹	1.000	0.750*	0.740*	0.742*	0.799*	0.685*
Truelove classification ¹²	0.750*	1.000	0.814*	0.760*	0.782*	0.756*
Baron classification ¹³	0.740*	0.814*	1.000	0.750*	0.828*	0.732*
Modified Baron scale ⁵	0.742*	0.760*	0.750*	1.000	0.761*	0.693*
Jeroen classification ¹⁴	0.799*	0.782*	0.828*	0.761*	1.000	0.788*
Azzolini classification ¹⁵	0.685*	0.756*	0.732*	0.693*	0.788*	1.000

* $p < 0.001$
CGSUC - Chinese Grading System of Ulcerative Colitis

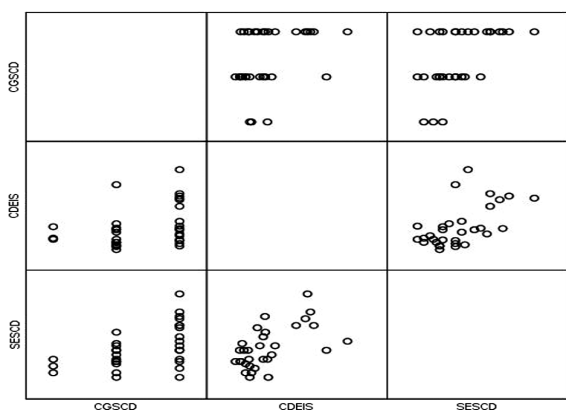


Figure 4 - The distribution of the endoscopic index values between every 2 systems of Crohn's disease (CD) was presented as a matrix of scatter plots. No significant concordance was indicated between Chinese Grading System of Crohn's disease (CGSCD)¹¹ and Crohn's Disease Endoscopic Index of Severity (CDEIS).¹⁶ SESCD¹⁷ - Simple Endoscopic Score for Crohn's Disease.

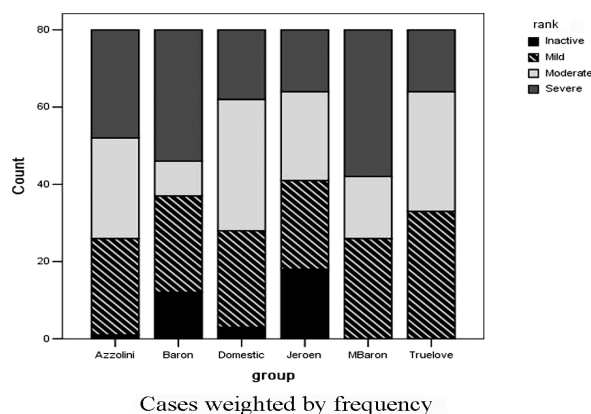


Figure 5 - The frequency correlations of endoscopic criteria of ulcerative colitis (UC), which divided subjects into inactive, mild, moderate and severe categories. Kruskal Wallis Test based on the frequency of every index showed satisfactory concordance ($p=0.001$). CGSUC¹¹ - Chinese Grading System of Ulcerative Colitis; Truelove¹² - Truelove classification; Baron¹³ - Baron classification; MBaron⁵ - modified Baron scale; Jeroen¹⁴ - Jeroen classification; Azzolini¹⁵ - Azzolini classification.

Table 2 - The Spearman correlation coefficients of indices in Crohn's disease.

Spearman's correlation coefficient	CGSCD	CDEIS	SESCD
CGSCD ¹¹	1.000	0.323 ($p=0.076$)	0.500 ($p=0.004$)
CDEIS ¹⁶	0.323 ($p=0.076$)	1.000	0.542 ($p=0.002$)
SESCD ¹⁷	0.500 ($p=0.004$)	0.542 ($p=0.002$)	1.000

CGSCD - Chinese Grading System of Crohn's disease; CDEIS - Crohn's Disease Endoscopic Index of Severity;
SESCD - Simple Endoscopic Score for Crohn's Disease.

Discussion. The 2 major IBDs, CD and UC represent clinical and pathologic entities that traditionally have been diagnosed on the basis of a combination of clinical, radiologic, endoscopic, and histologic features.¹⁸ The presence of an inflammatory syndrome associated with typical clinical manifestations of the intestine should lead to the performance of endoscopic examinations. Magnetic resonance enteroclysis and capsule endoscopy are currently

emerging as new imaging techniques in IBD, particularly for the small bowel in CD.¹⁹ Chromoendoscopy has been studied in patients with long-lasting UC and may be a promising and sensitive technique for the diagnosis of dysplasia.²⁰ However, conventional colonoscopy still plays an integral role in the diagnosis, management, and surveillance of IBD. Colonoscopy helps define the extent and severity of involvement in established IBD, which subsequently influences medical and surgical

decisions, aids in targeting medical therapies, and allows the management of complications. Assessment of the endoscopic appearance is subjective.²¹ To date, a universally accepted classification of endoscopic findings in IBD is still lacking. Truelove and Richards introduced the first qualitative endoscopic grading system evaluating UC activity in 1956.¹² The CGSUC, Baron classification, and modified Baron scale are qualitative endoscopic grading systems, while Jeroen classification and Azzolini classification are not only qualitative but also quantitative. Endoscopic disease activities of the formers were categorized as inactive, mild, moderate, or severe. Therefore, considerable changes could occur without a change in category, which suggested that some endoscopic grading and scoring systems have some degree of bias towards subjective components. To measure the endoscopic activity of CD, the French group of GETAID (Groupe d'Etude Therapeutique des Affections Inflammatoires Digestive) developed the CDEIS in 1989. The CDEIS was used as marker of mucosal healing in a number of therapeutic trials, which almost made it to represent the "gold standard" for evaluation of endoscopic activity.²²⁻²⁴ The SESCD was proposed to simplify endoscopic activity assessment in CD patients.¹⁷ It is easier and faster to score and calculate than CDEIS, and its results are reproducible and reliably correlating with CDEIS.²⁵ In the present study, CGSCD is still a qualitative endoscopic grading system, which may be a possible explanation to the difference between CGSCD and CDEIS. However, CDEIS and SESCD were quantitative, while endoscopic severity was not clearly defined in CDEIS or SESCD, which made it impossible to perform analysis of correlations of frequencies in patients with CD. Three fundamental components in endoscopy including mucosal fragility, presence of lesions, and disease extension should be established together. Indeed, disease extension is a fundamental issue for prognosis and therapeutic choices.^{26,27} The findings of our study suggested that endoscopic grading and scoring systems of UC had satisfactory correlations. Nonetheless, our findings showed that CGSCD was not strongly associated with CDEIS. This might probably be due to the main limitation of CGSCD, that it considers only the grade of mucosal fragility, evaluated by endoscopy, and not the severity of the lesions. Some endoscopic criteria for UC were established on a different basis, where heterogeneity was detected according to endoscopic findings. In the modified Baron scale, severe disease was defined as only "discrete ulceration and spontaneous bleeding" and extension of lesions was not mentioned,⁵ which indicated that the modified Baron scale was not as strict as the other systems and tend to severe category. However, in the Jeroen classification, endoscopic grading

of the most inflamed part involved erythema, vascular pattern, friability, granularity, spontaneous bleeding, occurrence, and severity of ulcers, extent of ulcerated surface, and presence of mucopurulent exudates. All parameters were scored from 0 to 2 points. Severe disease was recognized if the sum of all parameters were over 13.¹⁴ We found that individual patients with UC were seldom accompanied with all those inflamed parts. Therefore, every grading or scoring system is not intended as a substitute for the other system, but would provide another method for endoscopists in evaluations of individual patients. There are still some limits left according to our study. First, most endoscopic grading and scoring systems formerly proposed in the literature predefined another system as the "gold standard".^{5,21} But the "gold standards" were not the same, which indicated that assessing the severity of disease in IBD was still controversial. There was no common agreement on the fundamental question of what parameter(s) should be considered suggestive of disease activity. Second, an ideally endoscopic index of IBD should include features well known to endoscopist and describe the inflammatory state in its mucosal fragility, presence of lesions, and disease extension. Indeed, it should be not only qualitative, but also quantitative that can correlate with the severity of the endoscopic findings, not to discriminate the varied features that can underlie only "severity". Third, clinical test's diagnostic performances are generally estimated by their sensibility, specificity, and positive and negative predictive values.²⁸ The appeal to receiver operating characteristic (ROC) curve appears as a tool of choice for these evaluations.²⁹ The ROC curve is used when the test results are dichotomous.³⁰ For practical uses, we still need to dichotomize the test result so that we can classify subjects as "Yes" or "No". Endoscopic grading systems of IBD were categorized as inactive, mild, moderate, or severe. Furthermore, cutoff points used in every index are arbitrary and different. The difficulty of estimating sensibility and specificity lies in our failure to define and justify a common criterion and statistical model for optimality. Finally, the correlation of endoscopic with clinical activity, however, seemed to be poor.^{31,32} However, endoscopy is necessary to confirm diagnosis, to evaluate disease that is unresponsive to therapy, and to assess complications including stricture, dysplasia, and cancer.

In conclusion, we have found that the endoscopic grading and scoring systems of UC had satisfactory concordance, while CGSCD was not strongly associated with CDEIS. Nevertheless, the modified Baron scale was tended to severe category, while Jeroen classification was tended to mild. An ideal endoscopic index of IBD that can be easily and consistently recognized in clinical practice is necessary. We suggest that multiple

endoscopic grading and scoring systems for UC and CD should be rigorously validated by their sensibility, specificity, and positive and negative predictive values using new models of statistical analysis.

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