Clinical and Endoscopic Classification and Activity Indices of Inflammatory Bowel Diseases

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Abstract

Inflammatory bowel diseases (IBD) are chronic inflammatory disorders of the gastrointestinal system (GIS) that have shown increasing incidence and prevalence over the past two decades. Ulcerative colitis and Crohn's disease are the two primary conditions under the IBD umbrella. These diseases are not confined to the gastrointestinal system but can present with extraintestinal manifestations, including locomotor, dermatologic, and ocular symptoms. To simplify complex clinical scenarios, activity indices have been developed. These indices incorporate individual or combined clinical and endoscopic findings to facilitate the rapid and reliable assessment, treatment planning, and monitoring of patients.

Keywords: Activity indices, Crohn's disease, ulcerative colitis

INTRODUCTION

Inflammatory bowel diseases (IBD) present with highly heterogeneous clinical and endoscopic findings. Accurate evaluation of disease behavior, inflammatory activity, and its impact on the intestinal system requires classifications based on objective parameters. Initially, activity indices were developed for clinical trials to assess treatment efficacy and have since been integrated into current clinical practice.

Ideally, classifications and activity indices in clinical practice should be simple (i.e., not cumbersome, easily calculated at the bedside, and containing optimal parameters), objective (free from observer variability), reproducible, and dynamic. However, there are ongoing issues with the validation and objectivity of clinical activity indices, including discrepancies between patient-reported outcomes and clinician assessments, as well as observer variability in endoscopic activity indices. Despite these challenges, the use of classifications and indices in IBD remains prevalent, aiding in prognostic predictions, the selection and adjustment of treatment protocols, and the assessment of treatment success.

CURRENT CLASSIFICATION OF INFLAMMATORY BOWEL DISEASES

Under the IBD category, ulcerative colitis (UC) and Crohn's disease (CD) are the two major disease groups. Additionally, cases of colonic inflammation that cannot be classified into either group are termed unclassified colitis (IBD-U). In the initial evaluation and management of IBD, the Montreal classification is widely used. This system considers anatomical location and severity of activity for ulcerative colitis, as well as age of onset, disease behavior, and anatomical location for Crohn's disease. The Paris classification, a modified version that includes pediatric patients, is also commonly applied.[1,2] Tables 1 and 2 present the Montreal and Paris classifications for UC and CD, respectively.

Table 1. Montreal and Paris Classification Based on the Location and Severity of Inflammation in Ulcerative Colitis Cases

	Montreal Classification	**Paris Classification**
Anatomical Extent (E)	E1 Ulcerative proctitis E2 Left Sided Ulcerative Colitis E3 Extensive / Pancolitis	E1 Ulcerative proctitis E2 Left Sided Ulserative Colitis E3 Extensive E4 Pancolitis
Severity (S)	S0 Klinik remisyonda S1 Mild Ulcerative Colitis S2 Moderate Ulcerative Colitis S3 Severe Ulcerative Colitis	S0 Never Severe* S1 Ever Severe*

* Severe defined by Pediatric Ulcerative Colitis Activity Index (PUCAI) ≥65

ACTIVITY INDICES IN INFLAMMATORY BOWEL DISEASES

Inflammatory activity indices in IBD are developed and updated to provide an objective assessment of inflammation severity, guide treatment planning, and evaluate whether treatment goals have been achieved. This section discusses the most commonly used scoring systems in current clinical practice.

INDICES USED IN ULCERATIVE COLITIS

Indices used to assess inflammatory activity in UC include clinical indices based on clinical findings and simple laboratory parameters (e.g., Truelove and Witts' severity index, Simple Clinical Colitis Activity Index (SCCAI)); endoscopic indices based on colonoscopic findings (e.g., Baron Index, Rachmilewitz Index, Ulcerative Colitis Endoscopic Index of Severity (UCEIS)); and combined indices that incorporate both clinical and endoscopic findings (e.g., Mayo Index, Ulcerative Colitis Activity Index (UCAI)).

Clinical Activity Indices

The Truelove and Witts severity index is the oldest and still widely used bedside tool for assessing UC severity.[3] This index classifies disease severity into three categories: mild, moderate, and severe (Table 3). However, it is considered somewhat crude, insufficiently dynamic, and inadequate for quantitative assessment. Clinical remission is characterized by 1–2 bowel movements per day without blood, absence of fever and tachycardia, normalization or near-normalization of hemoglobin and erythrocyte sedimentation rate (ESR), and weight gain. Clinical non-response and deterioration are subjectively determined, while all intermediate cases are categorized as improvements.

Walmsley and colleagues modified the Powel-Tuck index to develop the Simple Clinical Colitis Activity Index (SCCAI), which emphasizes parameters affecting patients' quality of life.[4] The SCCAI provides a numerical score ranging from 0 to 19, with scores below 2 indicating

MAIN POINTS

- Inflammatory bowel disease activity indices should be simple (e.g., easily calculated at the bedside with optimal parameters), objective (e.g., free from inter-observer variability), reproducible, and dynamic.
- For ulcerative colitis, UC-PRO2 serves as a bedside index, the Ulcerative Colitis Endoscopic Index of Severity is used for endoscopic evaluation, and the total Mayo score functions as a combined index for global assessment.
- The Pouchitis Disease Activity Index is utilized to evaluate disease activity in patients with pouchitis.
- In Crohn's disease, bedside indices such as CD-PRO2 and the Harvey-Bradshaw Index, along with the Simple Endoscopic Score for Crohn's Disease for endoscopic evaluation, are recommended.
- The Rutgeerts index is used to assess the likelihood of postoperative recurrence in Crohn's disease.

remission and a decrease of more than 2 points considered a response to treatment (Supplementary Table 1).

Endoscopic Indices

Since mucosal remission is the ultimate goal in UC treatment, endoscopic assessment of the mucosa is crucial.

The Baron Index, though easy to calculate, provides a crude assessment as it does not account for mucosal ulcers. It is not a dynamic tool for evaluating treatment success, with a total score of 0–1 considered remission (Supplementary Table 2).[5]

The Rachmilewitz Index is a simple, observer-dependent tool that assesses granularity, submucosal vascular patterns, and mucosal damage. It has a total score range of 0–12, with scores below 4 indicating remission and scores above 4 indicating active disease (Supplementary Table 3).[6]

Table 2. Classification of Crohn's Disease Based on Age at Onset, Localization, Disease Behavior, and Growth/Development

	Montreal Classification	Paris Classification
Age at diagnosis (A)(years)	A1: < 17 A2: 17 - 40 A: > 40	A1a: < 10 A1b: 10 - 17 A2: 17 - 40 A3: > 40
Location (L)	L1: Terminal ileal + limited cecal disease L2: Colonic L3: Ileocolonic L4: Isolated upper disease	L1: Distal 1/3 ileal + limited cecal disease L2: Colonic L3: Ileocolonic L4a: Upper disease proximal to Ligamet of Tretiz L4b: Upper disease distal to ligament of Treitz and proximal to distal 1/3 ileum
Behavior (B)	B1: Non-stricturing, non-penetrating B2: Stricturing B3: Penetrating p: Perianal disease modifier	B1: Non-stricturing, non-penetrating B2: Stricturing B3: Penetrating B2 B3: Both penetrating and stricturing disease either at the same or different times
Growth (G)		G0: No evidence of growth delay G1: Growth delay

Table 3. Truelove and Witts Index

	Mild	Moderate	Severe
Bloody stools per day	< 4	>4	> 6
Pulse	< 90 /minute	< 90 /minute	> 90 / minute
Temperature	< 37.5 ºC	< 37.8 ºC	> 37.8 ºC
Hemoglobin	> 11.5 g/dL	>10.5 g/dL	< 10.5 g/dL
Erythrocyte Sedimentation rate	< 20 mm / h	< 30 mm/h	> 30 mm/h

UCEIS is similar to the Rachmilewitz Index but is a validated tool that effectively assesses inflammatory activity with minimal interobserver variability. This index evaluates parameters such as vascular patterns, bleeding, erosions, and ulcers, with a total score ranging from 0 to 8. A score below 1 is considered remission (Table 4).[7]

Combined Indices

Combined indices were developed based on the rationale that clinical or endoscopic findings alone may be insufficient for accurately assessing disease activity.

The Mayo Index, which includes the Total Mayo Index, Mayo Clinical Subscore, and Mayo Endoscopic Subscore, is widely used in current practice (Table 5). Although the subscores can be used independently, the Mayo Endoscopic Subscore is more commonly utilized. The Mayo Clinical Subscore assesses parameters such as stool frequency, rectal bleeding, and the clinician's overall assessment, with a score ranging from 0 to 9 points. A score of 1 or below indicates inactive disease, 2 to 4 signifies mild activity, 5 to 6 indicates moderate activity, and 7 to 9 reflects severe activity. The Mayo Endoscopic Subscore is a scale from 0 to 3, where scores of 0–1 indicate remission, and a score of 0 reflects endoscopic mucosal healing. The total Mayo Index ranges from 0 to 12, with scores of 3–5 indicating mild disease, 6–10 moderate disease, and 11–12 severe disease.[8] Clinical response is defined as a decrease in the initial Mayo score by at least 3 points, a 30% reduction from the initial score, and a reduction of at least one point on the rectal bleeding subscale or a rectal bleeding score of 0 or 1. Clinical remission is defined as a Mayo score of 2 or lower, with no individual subscore exceeding 1.[9] Despite its widespread use, the Mayo Index has limitations due to insufficient validation and potential subjectivity in the clinician's overall assessment.

The American College of Gastroenterology (ACG) has proposed a new scoring system called the UCAI. This index combines the Truelove and Witts Index with additional clinical parameters, including urgency affecting quality of life, fecal calprotectin as a biochemical marker, and either the Mayo Endoscopic Subscore or UCEIS for endoscopic evaluation.[10] In this system, remission is clearly defined, and fulminant colitis is distinctly categorized from moderate to severe ulcerative colitis (Supplementary Table 4).

After total proctocolectomy with ileal pouch-anal anastomosis, inflammation occurs in the created pouch in approximately 50% of cases. To evaluate this inflammation, the Pouchitis Disease Activity Index was developed, incorporating clinical, endoscopic, and histological parameters (Supplementary Table 5). According to this system, a total score ≥7 indicates active disease, while an endoscopic subscore ≤1 and a total score ≤2 indicate remission.[11]

Table 4. Ulcerative Colitis Endoscopic Severity Index (UCEIS)

Descriptor (score most severe lesions)	Definition
Vascular patern	0 Normal vascular pattern with arborizations of capillaries clearly defined 1 Patchy obliteration ov vascular pattern 2 Complete obliteration of vascular pattern
Bleeding	0 No visible blood 1 Some spots or streaks of coagulated blood on the surface of the mucosa, which can be washed away 2 Some free liquid blood in the lümen 3 Frank blood in thje lümen or visible oozing from mucosa after washing intraluminal blood, or visible oozing from hemorrhagic mucosa
Eroions and ulcers	0 Normal mucosa, no visible erosions or ulcers 1 Small defects in the mucosa (≤ 5 mm), white or yellow, white edge 2. Large defects in the mucosa (> 5 mm), discrete fibrin covered, remain superficial 3 Deeper excavated defects in the mucosa, with a raised edge

Table 5. Total MAYO Index in Ulcerative Colitis

Mayo index	0	1	2	3
Bowel frequency	normal	1-2/day more than normal	3-4/day more than normal	5/day more than normal
Rectal bleeding	none	streaks of blood with stool less than half the time	obvious blood with stool most of the time	blood alone passed
Mucosal appearance at endoscopy	normal	mild disease (erhytema, decreased vascular patern, mild friability)	moderate disease (marked erhytema, absent vascular pattern, friability, erosions)	severe disease (spontaneous bleeding, ulceration)
Physician's global assessment	normal	mild disease	moderate disease	severe disease

Table 6. Harvey Bradshaw index

1. General well-being
(0= very well, 1= Slightly below average, 2= Poor, 3= Very poor, 4= Terrible)

2. Abdominal pain
(0= None, 1= Mild, 2= Moderate, 3= Severe)

3. Number of liquid stool per day
(1 for each liquid stool per day)

4. Abdominal mass
(0= None, 1= Dubious, 2= Definite, 3= definite with tenderness)

5. Complications, 1 point for each
(Artralgia, uveitis, erhytema nodosum, aphtous ulcers, pyoderma gangrenosum, anal fissure, new fistula, apscess)

Table 7. Simple Endoscopic Score for Crohn's Disease (SES-CD)

Variables	Score			
	0	**1**	**2**	**3**
Persence and size of ulcers	None	Aphtous ulcers (< 0.5 cm)	Large ulcers (0.5 – 2 cm)	Very large ulcers (> 2 cm)
Extend of ulcerated surface	None	< % 10	% 10 – 30	>% 30
Extend of affected surface	Unaffected	< % 50	% 50 – 75	>%75
Presence and type of narrowings	None	Single, can be passed	Multiple, can be passed	Cannot be passed

Variables	Ileum	Right colon	Transvers colon	Left colon	Rectum	Total
Persence and size of ulcers (0- 3)	0 - 3	0 - 3	0 - 3	0 - 3	0 - 3	0 - 15
Extend of ulcerated surface (0- 3)	0 - 3	0 - 3	0 - 3	0 - 3	0 - 3	0 - 15
Extend of affected surface (0- 3)	0 - 3	0 - 3	0 - 3	0 - 3	0 - 3	0 - 15
Presence and type of narrowings (0- 3)	0 - 3	0 - 3	0 - 3	0 - 3	0 - 3	0 - 15

Sum of the variables = 0 - 60
Affected segment number: n
Total – 1.4 x n = SES-CD

Table 8. Rutgeerts score

Score	Lesion
i0	No lesions
i1	≤5 aphthous ulcers
i2	> 5 aphtous ulcers with normal intervening mucosa, or large lesions confined to the anastomosis
i3	Diffusely inflamed mucosa with aphtous ileitis
i4	Diffuse inflamation large ulcers/nodules/narowing

INDICES USED IN CROHN'S DISEASE

The most commonly used clinical indices for Crohn's disease are the Harvey-Bradshaw Index (HBI), the Crohn's Disease Activity Index (CDAI), and the Perianal Crohn's Disease Activity Index (PDAI). Among the endoscopic indices, the Crohn's Disease Endoscopic Index of Severity (CDEIS), the Simple Endoscopic Score for Crohn's Disease (SES-CD), and the Rutgeerts score for assessing postoperative recurrence are widely used.

Clinical Activity Indices

CDAI evaluates disease activity over a 7-day period, incorporating parameters such as the daily count of liquid or unformed stools, daily abdominal pain severity, the patient's subjective sense of well-being, presence of complications, use of anti-diarrheal medications, abdominal mass, hematocrit level decrease, and weight loss, with each parameter weighted by a coefficient (Supplementary Table 6). The total score ranges from 0 to 600. Disease activity is classified as follows: remission is defined by a CDAI score below 150, mild activity ranges from 150 to 220, moderate activity from 220 to 450, and severe activity is indicated by scores above 450. A reduction of 70–100 points is considered a response to treatment in clinical trials. However, the CDAI has notable limitations: it reflects a 7-day period, requires high patient compliance, and is inadequate for cases of fistulizing, fibrostenotic, and perianal Crohn's disease, as well as in patients with stomas or those who have undergone resection.[9]

The Harvey-Bradshaw Index (HBI) is a simple, easy-to-calculate tool suitable for bedside assessment and correlates with the CDAI (Table 6).[12] However, it is insufficient for evaluating perianal Crohn's disease and the fibrostenotic and fistulizing phenotypes.[8] Additionally, the HBI may overestimate disease activity when Crohn's disease coexists with functional bowel disorders.[13] An HBI score of <3 indicates remission, while a score of >8–9 reflects severe disease.

PDAI was developed to address the inadequacies of the CDAI and HBI in assessing perianal disease and fistulas. This index evaluates key parameters, including fistula discharge, pain/restriction in activities, restriction in sexual activity, type of perianal disease, and degree of induration. Each parameter is scored on a scale from 0 to 4, with a total score ranging from 0 to 20. Higher scores indicate more severe disease (Supplementary Table 7).[14]

Endoscopic Indices

Endoscopic indices in Crohn's disease are used not only to assess disease severity but also to predict postoperative recurrence. The CDEIS and SES-CD are employed to evaluate inflammatory activity, while the Rutgeerts score is used to predict postoperative recurrence.

The Crohn's Disease Endoscopic Activity Score is a mathematical system that assesses deep ulcers, superficial ulcers, and lesion surface area across five segments: the rectum, sigmoid-descending colon, transverse colon, ascending colon, and ileum (Supplementary Table 8). Scores range from 0 to 44, with a score below 6 indicating endoscopic remission and a score below 3 indicating complete remission. The CDEIS is characterized by its complexity, time requirements, and the need for specialized expertise, which limits its use in routine practice. It is primarily employed in clinical trials.[13,15] This index does not correlate with the Crohn's Disease Activity Index and does not provide a description of mucosal healing.[8]

SES-CD is less complex and correlates with the CDEIS. It uses well-defined parameters to evaluate ulcer size, area affected, and stricture characteristics across five anatomical regions (Table 7).[16] Inactive disease (remission) is defined by a score of 0–3, mild activity by a score of 4–10, moderate activity by a score of 11–19, and severe activity by a score of 20 or higher. The SES-CD has undergone validation but lacks a definition for mucosal healing.

The Rutgeerts score is designed to predict the likelihood of postoperative recurrence by endoscopically evaluating changes on the ileal side of the anastomosis in patients who have undergone resection surgery (Table 8).[17] It is not intended to be used as an activity index. A Rutgeerts score greater than i2 is associated with a significantly higher risk of postoperative recurrence, indicating the need for prophylactic treatment. Since mucosal changes near the anastomosis may result from factors such as ischemia, the i2 score has been further refined. The i2a category refers to isolated anastomotic lesions, while i2b refers to more than five aphthous lesions in the ileum, whether or not they are associated with the anastomotic site. However, studies have found no significant difference in postoperative recurrence between these subcategories.[18]

PATIENT-REPORTED OUTCOME MEASURES

Inflammatory bowel diseases are chronic inflammatory conditions that significantly impact patients' quality of life. In IBD cases, symptoms may persist even in the absence of significant disease activity or inflammation. Therefore, patient-centered assessment indices, known as Patient-Reported Outcome Measures (PROMs), have been developed. PROMs are defined as information provided directly by the patient about their health status, without any interpretation by clinicians or others and without the use of laboratory findings.[19]

PROMs reflect the effectiveness of treatment and changes in quality of life from the patient's perspective. For assessing disease activity in UC and CD, two-parameter PROMs have been developed. UC-PRO2 evaluates stool frequency and bloody stools, while CD-PRO2 focuses on abdominal pain and stool frequency. In PRO3, a general well-being parameter is added to these assessments.[20]

Peer-review: Internally peer-reviewed.

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Supplementary Tables

Supplementary Table 1. Simple Clinical Colitis Activity Index (SCCAI)

Symptom	Score
Bowel Frequency (day)	
1 – 3	0
4 – 6	1
7 – 9	2
> 9	3
Bowel Frequency (night)	
1 – 3	1
4 – 6	2
Urgency of Defecation	
Hurry	1
immediately	2
incontinence	3
Blood in the stool	
Trace	1
Occasionally frank	2
Usually frank	3
General well being	
Very well	0
Slightly below par	1
Poor	2
Very poor	3
Terrible	4
Extracolonic features	1 per manifestation

Supplementary Table 2. Baron Index

Score	Endoscopik Findings
0	Normal
1	Mild (erythema, granularity, friability)
2	Moderate (loss of fasculary patern , scattered ulcers)
3	Severe (spontaneous bleeding, compound ulcers)

Supplementary Table 3. Rachmilewitz Endoscopic Index

Endoscopic finding	Point
Granulation	
None	0
Yes	1
Vascular patern	
Normal	0
Faded/disturbed	1
Completely absent	2
Vulnerability of mucosa	
None	0
Slightly increased (contact bleeding)	2
Generally increased (spontaneous bleeding)	4
Mukosal damage (mucus,fibrin,exudate, erosion, ulcer)	
None	0
Slight	2
Pronounced	4
Total	12

Supplementary Table 4. Ulcerative Colitis Activity Index (UCAI)

	Remission	Mild	Moderate-Severe	Fulminant
Stool frequency (per day)	Formed stool	< 4	>6	>10
Blood in stool	None	Intermittent	Frequent	Continuous
Urgency	None	Mild/occasional	Often	Continuous
Hemoglobin	Normal	Normal	%75 of normal	Transfusion required
Eritrocyte sedimantation rate	< 30	< 30	> 30	>30
C-reactive protein	Normal	Elevated	Elevated	Elevated
Fecal Calprotectin (mg/ gr)	< 150 - 200	> 150-200	> 150-200	> 150-200
MAYO endoscopic score	0 - 1	1	2 - 3	3
Ulcerative Colitis Endoscopic Severity Index (UCEIS)	0 - 1	2 - 4	5 - 8	7 - 8

Supplementary Table 5. Pouchitis Disease Activity Index

Criteria	Score
Clinic:	
Stool frequency	0 = usual postoperative stool frequency
	1 = 1 – 2 stool/day > postoperative usual
	2 = ≥3 stool/day > postoperative usual
Rectal bleeding	0 = None or rate, 1 = Present daily
Fecal Urgency/ Abdominal cramps	0 = None, 1 = Occasional, 2 = Usual
Fever (≥37.8 ^{0}C / 100.5 ^{0}F)	0 = Absent, 1 = Present.
Endoscopic inflammation	Edema, granularity, friality, loss of vascular pattern, mucous exudate, ulceration - 1 point for each
Patological findings:	
Polymorphonuclear leucocyte infiltration	1 = mild, 2 = moderate + crypt abscess, 3 = severe + crypt abscess
Ulceration per low power field (mean)	1 = < %25, 2 = % 25 - 50, 3 = > % 50

Supplementary Table 6. Crohn's Disease Activity Index (CDAI)

Clinical or laboratory variables	Weighting factor
Number of liquid or soft stools each day for 7 days	x 2
Abdominal pain each day for 7 day (graded from 0 to 3 based on severity)	x 5
General well being, subjectively assessed from 0 (well) to 4 (terrible) each day for 7 days	x 7
Complications* (one point for each)	x20
Use of diphenoxilate or opiates for diarrhea	x30
An abdominal mass (0 = none, 2 = questionable, 5 = definite)	x10
Absolute deviation of hematocrit (<%42 in women, <% 47 in men)	x 6
Percentage deviation from standart weight	x 1

*:arthralgia or arthritis; iritis or uveitis; erythema nodosum, pyodermagangrenosum or aphtous ulcers; anal fissures, fistulas or abscess; other fistulas; fever (>100 °F)- during previous week

Supplementary Table 7. Perianal Crohn's Disease Activity Index (PDAI)

	Score and parameter
Fistula drainage	0 No drainage 1 Minimal mucus drainage 2 Frequent mucus or purulent drainage 3 Abundant drainage 4 Fecaloid drainage
Pain / aktivity restriction	0 No activity restriction 1 Discomfort, no activity restriction 2 Frequent discomfort, occasional activity restriction 3 Discomfort and significant limited activity 4 Pain and significant activity restriction
Restricted sexual activity	0 No 1 Occasional restriction 2 Frequent limitation of sexual activity 3 Significant limitation of sexual activity 4 Incapable of sexual activity
Type of perianal disease	0 No disease 1 Anal fissure 2 < 3 perianal fistulae 3 > 3 perianal fistulae 4 Anal ulcer or fistula with significant perianal skin involvment
Degree of induration	0 No induration 1 Mild induration 2 Significant induration 3 Noticeable induration 4 Absscess

Supplementary Table 8. Crohn's Disease Endoscopic Activity Score (CDEIS)

Variables	Rektum	Sigmoid end left colon	Transvers colon	Right colon	Ileum	Total
Deep ulceration (0= absent, 12= present)	0 or 12	0 or 12	0 or 12	0 or 12	0 v or 12	Total 1
Superficial ulceration (0= ülser yok, 6= var	0 or 6	0 or 6	0 or 6	0 or 6	0 or 6	Total 2
Surface involved by the disease (0 – 10 cm)	0 - 10	0 - 10	0 - 10	0 - 10	0 - 10	Total 3
Ulcerated surface (0 – 10 cm)	0 - 10	0 - 10	0 - 10	0 - 10	0 - 10	Total 4

Total1 + Total2 + Total3 + Total4 = Total A

Number of segments totally or partialy explored (1-5) = n

Total A / n = Total B

Quote 3 if ulcerated stenosis anywhere, 0 if not = Toplam C

Quote 3 if non ulcerated stenosis anywhere, 0 if not = Toplam C

TOTAL B + C + D = CDEIS