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How to Grade IBD Disease Activity in Your Daily Practice



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Inflammatory bowel disease (IBD) is a chronic inflammatory condition caused by immune dysregulation. Measurement of disease activity, which refers to the inflammatory burden and its impact on the patient at any one point in time, is a crucial step in the assessment of patients and factors into decision making regarding therapy. Categorizing disease activity into three domains – quality of life, clinical symptoms and endoscopic inflammation – can help the clinician follow disease activity using objective and standardized grading systems. This in turn can help assess response to treatment, which is increasingly important as the paradigm of management in IBD shifts to a “treat-to-target” approach. A clear understanding of disease activity can facilitate better care for IBD patients by addressing the impact of disease as well as risk of progression. The aim of this review is to discuss accessible measures of disease activity in IBD that can be used regularly in the office with the goal of facilitating consistent clinic care, use of a shared vocabulary for IBD activity and to provide an objective basis for treatment and assessment of treatment response.

INTRODUCTION

Inflammatory bowel disease (IBD), a progressive and chronic condition, is driven by immune dysregulation of the digestive tract which results in chronic inflammation and disease activity.^{1,2} A significant challenge is how to describe disease activity and severity in a way that is reproducible and actionable. An additional challenge is determining if disease activity and severity is best described

using symptoms, colonoscopy findings, or impact of the disease on quality of life. The aim of this review is to discuss accessible measures of disease activity in IBD that can be used regularly in the office with the goal of facilitating consistent clinic care, use of a shared vocabulary for IBD activity and to provide an objective basis for treatment and assessment of treatment response.

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Disease Activity Versus Severity in IBD

A fundamental, though often misunderstood, concept in the understanding of IBD disease scoring is the difference between disease activity and severity. Disease activity refers to a measure of the inflammatory burden and its impact at any one point in time and disease severity is a measure of the cumulative impact of the inflammatory burden over time.⁴ While disease activity and severity can be related, they are separate concepts that should not be used interchangeably. The focus of this article will be on disease scoring and tracking disease activity as it influences daily care by aiding in decisions for management and monitoring response to treatment.

Three Domains of Disease Activity

A recent review divides disease activity into three domains: quality of life (QOL), clinical symptoms, and inflammation⁵ as shown in Table 1. Each domain has specific measures for ulcerative colitis (UC) and Crohn's disease (CD). It is useful to think of these domains separately, though admittedly they overlap and are interrelated. However, considering them separately allows for a standardized approach to disease activity scoring.

Quality of Life

Quality of life (QOL) is a critical component of disease activity as it evaluates the patient's social and emotional well-being, behavior and

attitudes, and physical disease related symptoms and is the ultimate goal of therapy.⁵ Because many QOL measures are lengthy and cumbersome, we recommend only measures which are fast to complete, valid, reliable, and acceptable to patients. Measurement tools for QOL in IBD fall into three categories: psychological distress, disease adaptation and global QOL.

Measures of psychological distress are not IBD-specific and include the Patient Health Questionnaire-9 (PHQ-9) and the Hospital Anxiety and Depression Scale. The PHQ-9 was validated for diagnosing and monitoring major depressive disorder, but is easy to use in a clinical setting and given the high prevalence of comorbid depression in IBD⁶ is relevant. The Hospital Anxiety and Depression Scale was validated to screen for depression, anxiety and emotional distress in the outpatient setting utilizing just 14 questions and is commonly used, though never validated, in IBD-related research. A recent study confirmed prevalent depression and anxiety in IBD patients, but recognition of the symptoms by gastroenterologists was only fair.⁷ We believe routine use of a standardized measure will help in the identification of patients who would benefit from addressing their comorbid psychiatric conditions.

Measurement of disease adaptation is important in the assessment of QOL in chronic diseases such as IBD as they have the potential

Table 1. Domains of Disease Activity

Domain	Measures	Clinically accessible Indices
Inflammation	Endoscopy	UCEIS, Mayo score, SES-CD, Rutgeerts post-operative score
	Imaging	MRI/MRE, CTE
	Biomarkers	CRP, fecal calprotectin
Quality of life	Psychological distress	PHQ-9, Hospital Anxiety and Depression Scale
	Disease adaptation	Brief Illness Perception Questionnaire
	Global quality of life	Short Inflammatory Bowel Disease Questionnaire
Clinical symptoms	Phenotype/Disease Extent	Montreal Classification
	Intestinal and extra-intestinal symptoms	HBI, SCCAI

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to capture important changes that are difficult to otherwise to identify. The Brief Illness Perception Questionnaire is one such measure with nine items that has the added benefit of being positively associated with medication adherence⁸ and thus serves as a potential target to improve outcomes.

The Short Inflammatory Bowel Disease Questionnaire is an IBD-specific measure of global QOL that consists of 10 items that address bowel symptoms, emotional health, systemic symptoms

Table 2. Harvey Bradshaw Index (HBI) for Crohn’s Disease

Descriptor	Description	Score
General well-being	Very well	0
	Slightly below par	1
	Poor	2
	Very poor	3
	Terrible	4
Abdominal pain	None	0
	Mild	1
	Moderate	2
	Severe	3
Liquid stools daily	1 per occurrence	–
Abdominal mass	None	0
	Dubious	1
	Definite	2
	Definite and tender	3
Complications	1 per item	–
	Arthralgia	
	Uveitis	
	Erythema Nodosum	
	Aphthous ulcer	
	Pyoderma gangrenosum	
	Anal fissure	
	New fistula	
	Abscess	
Total (out of 19)		

and social function. It is easy to use, validated, reproducible and responsive and correlates well with longer IBD-specific questionnaires.⁹ It is subject to license so does require a fee to use.

Clinical Symptoms

In clinical practice, assessment of symptoms predominates patient encounters and thus it is crucial to objectively assess symptoms as they relate to disease activity to guide precision in decision making.¹⁰ There are over 20 indices of clinical symptoms in UC and CD, some of which are cumbersome to use in clinical practice and require complex calculations like the Crohn’s Disease Activity Index. We present the indices we have found to be straight-forward and easy to integrate into daily practice.

An important first step in clinical symptom assessment is determining disease extent in UC patients and the phenotype of CD patients as this helps understand the cause of symptoms or guide investigation into complications that may be driving the onset of new symptoms. The Montreal Classification is a simple tool that categorizes UC patients based on disease extent – E1 disease is limited to the rectum (proctitis), E2 disease is limited to the splenic flexure (left-sided) and E3 disease extends beyond the splenic flexure (extensive).¹¹ Similarly, CD is categorized based on age of disease onset (A1: ≤ 16 years, A2: 17-40 years, A3 >40 years), location (L1: ileal, L2: colonic, L3: ileocolonic, L4: isolated upper gastrointestinal), and behavior (B1: non-stricturing, non-penetrating, B2: stricturing; B3: penetrating, +p if perianal disease present).

We recommend use of the Harvey Bradshaw Index (HBI) for symptom assessment in CD given it is simple to use and correlates well the complex Crohn’s Disease Activity Index, which has been an outcome measure in many of the studies of treatments for CD. The HBI has five variables and items are scored based on the previous making it easy to use as shown in Table 2. The major limitation is that perianal disease is a low contributor to the total score, which may underestimate the more severe phenotype. HBI scores greater than 16 are consistent with severe disease activity, whereas scores between 5-7 suggest mild activity and 8-16

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Table 3. Simple Clinical Colitis Activity Index (SCCAI)

Descriptor	Description	Score
Bowel frequency (day)	0-3	0
	4-6	1
	7-9	2
	>9	3
Bowel frequency (night)	0	0
	1-3	1
	4-6	2
Urgency to defecate	none	0
	hurry	1
	immediately	2
	incontinent	3
Blood in stool	none	0
	trace	1
	occasionally frank	2
	usually frank (>50%)	3
General well-being	very well	0
	slightly below par	1
	poor	2
	very poor	3
	terrible	4
Extracolonic Features	<u>Arthritis</u>	
	yes	1
	no	0
	<u>Uveitis</u>	
	yes	1
	no	0
	<u>Erythema nodosum</u>	
	yes	1
	no	0
	<u>Pyoderma gangrenosum</u>	
yes	1	
no	0	
Total (out of 19)		

suggest moderate activity. Response to therapy is defined by a reduction in the score by 3 points or more.^{5,12,13} As shown in Table 3, the Simple Clinical Colitis Activity Index (SCCAI) is an easy to use index for the assessment of clinical symptoms in UC. This can be filled out by patients without the need for lab values, endoscopy results or physician assessment, making it our preferred measurement tool for clinical symptoms in UC. It includes nocturnal bowel movements and urgency to defecate which are omitted in other indices, but, in our experience, are vitally important to patients. It is the best non-invasive index for validity, reliability, feasibility with the added benefit of being able to measure responsiveness, or change in disease activity.^{5,14} A score of two or less on the SCCAI indicates remission.

Inflammation

Inflammation is closely linked to progression of disease and therefore impacts severity of disease; it is one of the hallmarks of IBD disease activity and the gold-standard for measurement is endoscopy. Complementary measures of inflammation include histology (which is obtained via endoscopy),

Table 4. UC Endoscopic Index of Severity (UCEIS)

Most Severely Affected Area on Endoscopy	Score
Vascular pattern	
0 = Normal	
1 = Patchy obliteration	
2 = Obliterated	
Bleeding	
0 = None	
1 = Mucosal	
2 = Luminal, mild	
3 = Luminal, moderate or severe	
Erosions and Ulcers	
0 = None	
1 = Erosions	
2 = Superficial ulcer	
3 = Deep Ulcer	
Sum	

imaging (such as magnetic resonance and computed tomography imaging) and biomarkers (such as C-reactive protein and fecal calprotectin). Various endoscopic scoring systems exist and are specific for UC and CD, which will be the focus of this review.

We recommend use of either the UC Endoscopic Index of Severity¹⁵ (UCEIS) or the Mayo endoscopic sub-score to assess inflammation activity in UC. The UCEIS is the only validated endoscopic index in UC, is simple to use, and has high inter-observer reproducibility. The endoscopist grades the inflammation, without considering disease extent, based on the most severe area in three categories: vascular pattern, bleeding, and erosions and ulcers as shown in Table 4. While the UCEIS does not

further classify the activity as mild, moderate, or severe, the target score for remission is one or less.^{3,5,16} An alternative endoscopic index for UC that is commonly utilized in clinical practice is the endoscopic sub-score of the Mayo index, which is simple to use but lacks strong inter-observer reliability and is not a validated measure of mucosal healing.^{3,5,16} Endoscopic activity is graded in each segment of the examined colon as normal (Mayo 0), mild (Mayo 1: erythema, mild friability and loss of vascular pattern), moderate (Mayo 2: presence of erosions and marked erythema, friability) and severe (Mayo 3: spontaneous bleeding and ulcers). Endoscopic remission corresponds to a Mayo 0 or 1. In our endoscopy unit, the Mayo endoscopic sub-score is widely used to grade disease activity

Table 5. Simple Endoscopic Score for Crohn's Disease (SES-CD)

Size of Ulcers, cm	Ileum	R colon	TV colon	L colon	Rectum	Total
0 = none						
1 = aphthous						
2 = large (0.5-2)						
3 = very large (>2)						
Ulcerated Surface, %						
0 = none						
1 = <10						
2 = 10 - 30						
3 = >30						
Affected Surface, %						
0 = unaffected						
1 = <50						
2 = 50 - 75						
3 = >75						
Presence of Narrowing						
0 = none						
1 = single, passable						
2 = multiple, passable						
3 = cannot be passed						
						SES-CD

Right (R), Transverse (TV), Left (L)

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to standardize assessment across physicians.

The gold-standard for the endoscopic assessment of disease activity in CD is the CD Endoscopic Index of Severity (CDEIS), which is reproducible, validated and used extensively in clinical trials.^{4,5,17} However, because it is cumbersome to use we don't routinely measure it as part of clinical care in our practice. Instead, we recommend measurement of the Simple Endoscopic Score for CD (SES-CD), which is validated, correlates with the CDEIS and is easier to use, though admittedly still takes time. Each part of the colon as well as the ileum are graded on four categories (size of ulcers, ulcerated surface area, affected surface area and presence of narrowing) and the total score correlates with remission (0-2), mild (3-6), moderate (7-16), and severe (>16) as shown in Table 4. A response is defined by at least 50% reduction in the score.^{3, 18} In post-operative CD patients, the Rutgeert's post-operative endoscopic score is an important activity index because it correlates with risk of recurrence and thus helps inform decision-making regarding post-operative treatment of CD.¹⁹ The Rutgeert's grade (i0-i4), as shown in Table 5, is based on the number and nature of ulcers at the neoterminal ileum and i0 and i1 grades are considered remission given the low risk of recurrence at five years.

Integrating Assessment of Disease Activity into Clinical Practice

Armed with an accurate, objective and reproducible assessment of disease activity in IBD, the clinician is able to understand the risks and benefits of

continuing or changing therapies for their patients. Recently, an evidence-based expert consensus process was conducted to examine potential treatment targets in IBD with a focus on a "treat-to-target" clinical management strategy and the results of their discussions were published as the Selective Therapeutic Targets in IBD (STRIDE) recommendations.¹² The rationale behind a "treat-to-target" approach is to focus on achieving remission and low disease activity; accordingly, physicians and patients should discuss the targets and work to achieve them within set time frames in order to improve outcomes (in all domains of disease activity, as previously described).

In UC, the STRIDE recommendation is to treat to a target of clinical symptomatic remission and patient reported outcomes as well as endoscopic remission (UCEIS ≤ 1 or Mayo endoscopy subscore of ≤ 1). Clinical symptoms and QOL should be assessed at least every three months during active disease and endoscopic evaluation should be performed every three months until remission. For CD, similarly the target was clinical remission (defined by clinical symptoms and QOL indices) as well as endoscopic remission or resolution of inflammation objectively documented on cross-sectional imaging. As in UC, clinical symptoms of QOL should be assessed at least every 3 months, but endoscopic evaluation can be performed in 6-9 month intervals until resolution.

The Role of Disease Severity

The STRIDE recommendations did not specify treatment modalities and instead focused on

Table 6. Rutgeert's Post-operative Endoscopic Score for Crohn's Disease

Rutgeerts Grade	Endoscopic Finding	Risk of Recurrence at 5 Years
i0	No lesions in distal ileum	6%
i1	No more than 5 aphthous ulcers in distal ileum	6%
i2	More than 5 aphthous ulcers with normal mucosa between lesions or skip areas of larger lesions up to 1 cm confined to the anastomosis	27%
i3	Diffuse aphthous ileitis with diffusely inflamed intervening mucosa	63%
i4	Diffuse inflammation with large lesions, large ulcers and/or nodules and/or narrowing/stenosis	100%

treatment targets. Decisions on which treatment to choose in IBD is complex and requires an understanding of both disease activity as well as severity since an assessment of current and prior activity as well as prognostication for long-term complications factors into risk assessment of patients with low and high severity of disease.

CONCLUSION

The three domains of disease activity (quality of life, clinical symptoms, and inflammation) present an opportunity to capture activity longitudinally to help care for IBD patients. Using a standardized approach to measurement of disease activity allows objective assessment of response to treatment and standardizes practice and facilitates comparisons between endoscopies and treating physicians with the ultimate goal of providing better care for IBD patients by addressing not only impact of the disease but also the risk of progression. ■

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