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ORIGINAL ARTICLE

Relationship between Mayo endoscopic score and histological scores in ulcerative colitis: A prospective study

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Abstract

Background: The Mayo endoscopic score (MES) remains the most commonly used index in clinical practice, as well as in various clinical trials. Recently, two validated histological indices (Nancy Index [NI] and Robert Histological Index [RHI]) have been developed for ulcerative colitis (UC). We aim to study the relationship between MES with NI, RHI, and the established Geboes Index (GI) in patients with UC.

Methods: This was a prospective single-center study. MES was documented from the most involved area. Biopsy was taken from the same area and reported by a single gastrointestinal histopathologist who was blinded to the endoscopic score. Histological activity was reported using GI, NI, and RHI. Statistical analysis was performed using Spearman's correlation coefficient and Cohen's kappa coefficient using SPSS version 23.

Results: Median age of patients with UC (n = 96) was 36 years. Seventeen patients were in endoscopic remission (MES 0/1). Correlation coefficient between MES and GI/NI/RHI was only weak to moderate (rho = 0.381/0.389/0.442, respectively; $P < 0.001$ for all three correlations). In patients with endoscopic mucosal healing (n = 17), the agreement coefficient between MES and GI/RHI was weak (κ = 0.253/0.336, respectively; P = 0.001 for both agreements). However, there was no significant agreement coefficient between MES and NI (P = 0.573).

Conclusion: MES moderately correlated with histological scores. RHI had the best correlation with MES among all histological indices. Endoscopic mucosal healing is not strongly correlated with histological healing. Histological examination should be performed even in patients with mucosal healing to detect ongoing histological activity.

Introduction

Targets of therapy in ulcerative colitis (UC) have witnessed a paradigm shift from only symptomatic improvement to mucosal healing and, recently, even histological healing. Mucosal healing is defined as the absence of friability, erosions, and ulcers in all visualized segments of gut mucosa.[1] Mucosal healing is associated with the decreased risk of disease relapse and disease-related morbidity.[2,3] However, endoscopic inactivity does not always correlate with histological inactivity.[4] Ongoing histological activity may be associated with the increased risk of disease relapse, even in patients with endoscopically normal mucosa.[5,6] Moreover, histological inflammation has also been shown to be associated with increased risk of dysplasia in patients with UC.[7] So, it is of utmost importance to understand the relationship between commonly used endoscopic and histological indices in patients with UC. The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) has been recently developed and is a partially validated endoscopic score in patients with UC.[8,9] However, the Mayo endoscopic score (MES) remains the most commonly used endoscopic index in routine clinical practice, as well as in various clinical trials.[10–12] Although not validated, the Geboes Index (GI) still remains one of the most widely used histological scores in routine clinical practice.[13] The Nancy Index (NI) and Roberts Histological Index (RHI) are recently developed validated indices for histological evaluation in patients with UC.[14,15] Recently, one study has shown good correlation between the UCEIS score and these histological indices (NI [r = 0.84] and RHI [r = 0.86]).[16] However, the relationship of MES with these scoring systems has not been evaluated.

This study was conducted to find the relationship between MES and histological scores (GI, NI, and RHI) in patients with UC.

Methods

This was a single-center study performed at a tertiary care institution in North India. It was a prospective study with an inclusion

Table 1 Mayo endoscopic scoring system and data of individual scores in our study group[17]

Endoscopic appearance	Mayo endoscopic score
Normal mucosa	0
Decreased vascularity, mild friability, erythema	1
Absent vascular pattern, marked erythema, severe friability, erosions	2
Spontaneous bleeding, ulceration	3

Table 2 Geboes Index for histological scoring and data of individual scores in our study group[13]

Grade	Description
Grade 0	Structural (architectural changes)
0.0	No abnormality
0.1	Mild abnormality
0.2	Mild or moderate diffuse or multifocal abnormalities
0.3	Severe diffuse or multifocal abnormalities
Grade 1	Chronic inflammatory infiltrate
1.0	No increase
1.1	Mild but unequivocal increase
1.2	Moderate increase
1.3	Marked increase
Grade 2	Lamina propria neutrophils and eosinophils
2A	Eosinophils
2A.0	No increase
2A.1	Mild but unequivocal increase
2A.2	Moderate increase
2A.3	Marked increase
2B	Neutrophils
2B.0	No increase
2B.1	Mild but unequivocal increase
2B.2	Moderate increase
2B.3	Marked increase
Grade 3	Neutrophils in epithelium
3.0	None
3.1	<5% crypts involved
3.2	<50% crypts involved
3.3	>50% crypts involved
Grade 4	Crypt destruction
4.0	None
4.1	Probable local excess of neutrophils in part of crypt
4.2	Probable marked attenuation
4.3	Unequivocal crypt destruction
Grade 5	Erosion or ulceration
5.0	No erosion, ulceration or granulation tissue
5.1	Recovering epithelium + adjacent inflammation
5.2	Probable erosion – focally stripped
5.3	Unequivocal erosion
5.4	Ulcer or granulation tissue

period from August 2016 to December 2017. The study was approved by the Institutional Ethics Committee.

Consecutive patients of UC, with varying levels of disease severity, attending our gastroenterology outpatient services were included in the study. Patients underwent sigmoidoscopy or colonoscopy to assess their endoscopic disease activity. The MES was noted by trained fellows working in our department in the most affected area during endoscopic examination. They were educated regarding use of various endoscopic scoring systems before reporting of endoscopic activity (Table 1).[17] MES ≤ 1 was considered endoscopic remission (mucosal healing).[1] Biopsy was taken from the most affected area during endoscopic examination and was sent for histopathological examination. A single experienced gastrointestinal histopathologist blinded to the endoscopic activity reported the histological activity using the GI, NI, and RHI. The GI consists of six grades of histological activity, with grade < 3 considered histological remission (Table 2).[13] The NI consists of three histological parameters including acute inflammatory cells, chronic inflammatory cells, and ulceration, with score ranging from 0 to 9 and grade ranging from 0 to 4 (Table 3). Grade 0 or 1 represents the absence of acute inflammatory cells and histological remission, while grade 4 is suggestive of severe inflammation.[15] The RHI consists of four histological parameters: epithelial neutrophils, lamina propria neutrophils, chronic inflammatory cells, and erosions/ulceration (Table 4). The score varies from 0 to 33, with a score ≤ 3 suggestive of histological remission.[14]

Statistical Analysis. All the data were entered in Microsoft Excel format and then exported to SPSS version 23 (Chicago). Spearman correlation was calculated between MES, GI, RHI, and NI. Agreement between endoscopic and histological correlation was calculated by using Cohen's kappa coefficient. A coefficient of zero indicates that no linear relationship exists between two continuous variables, and a correlation coefficient of −1 or +1 indicates a perfect linear relationship. A value between 0 and 0.19 was regarded as very weak, 0.2–0.39 as weak, 0.40–0.59 as moderate, 0.6–0.79 as strong, and 0.8–1.0 as very strong correlation.[18]

Results

Baseline characteristics. A total of 96 patients of UC were included in the study, with a median age of 36 [interquartile range (IQR 15)] years; 51 (53.12%) patients were male. Mean duration of the disease was 35.65 ± 35.47 months. Among patient with UC, 82 (85.4%) patients had a relapsing, remitting type of disease course, and 14 (14.6%) patients had a continuous disease course. In our study group, 5 (5.2%) patients had proctitis, 57 (59.4%) patients had left-sided colitis, and 34 (35.4%) had extensive colitis (Table 5).

Correlation between endoscopic activity and histological indices. The correlation coefficient between MES and the GI/NI was weak, with rho = 0.381 (95% CI 0.20–0.57; $P < 0.001$) and 0.389 (95% CI 0.17–0.55; $P < 0.001$), respectively. The correlation coefficient between the MES and RHI was moderate with rho = 0.442 (95% CI 0.26–0.63; $P < 0.001$). The GI showed a strong correlation with the NI (rho = 0.635; 95% CI 0.47–0.81; $P < 0.001$) and RHI (rho = 0.708; 95% CI 0.59–0.87; $P < 0.001$). Correlation between the NI and RHI was

Table 3 Nancy Index for histological scoring and data of individual scores in our study group[15]

Grade	Acute inflammatory cells	Chronic inflammatory cells	Ulcerations
0	None (0 point)	None (0 point) Mild (1 point)	None (0 point)
1	None (0 point)	Moderate or marked increase (3 points)	None (0 point)
2	Mild (2 points)	Moderate or marked increase (3 points)	None (0 point)
3	Moderate (3 points) Severe (4 points)	Moderate or marked increase (3 points)	None (0 point)
4	Moderate (3 points) Severe (4 points)	Moderate or marked increase (3 points)	Yes (2 points)

also very strong, with rho = 0.872 (95% CI 0.75–0.96; $P < 0.001$) (Fig. 1 and Table 6).

Agreement between endoscopic mucosal healing and histological healing. In our study group, 17 patients were in endoscopic remission (MES 0/1). Agreement between endoscopic remission and histological remission was calculated. The agreement coefficient between MES and GI/RHI was weak, with $\kappa = 0.253$ and 0.336, respectively ($P = 0.001$). However, agreement between MES and NI was statistically nonsignificant ($\kappa = 0.053$; $P = 0.573$).

Discussion

Mucosal healing, a recently defined target of therapy in inflammatory bowel disease (IBD), has been associated with a decreased rate of hospitalization, reduced incidence of colorectal carcinoma, and decreased need of surgery.[2,19] Histological healing is still an evolving concept in the management of UC. Few studies have shown that histological healing as a target of therapy is associated with better outcomes, even in patients with mucosal healing.[5,20] Moreover, ongoing histological activity may be associated with increased disease relapse rates in patients with endoscopically normal mucosa.[5,6] A few previous studies have shown conflicting results on the relationship between endoscopic and histological activity due to the use of heterogeneous, nonvalidated endoscopic and histological indices.[21–23]

In our study, MES correlates with the GI, RHI, and NI. However, the strength of the correlation was weak with the GI and NI and moderate with the RHI. The RHI is a recently developed, validated histological index. It includes a wide range of histological activity from 0 to 33, which might be the reason for better expression of various stages of histological activity compared to the other two scoring systems and better correlation with endoscopic activity compared to the other two scoring systems. A similar study was conducted by Lemmens *et al*., where they had evaluated the correlation between MES with that of the GI and the Riley Histological Index in 131 patients with UC. In their study as well, the correlation between MES and the histological index was moderate, with $r = 0.482$ ($P < 0.001$).[24] Simsek *et al*. have studied the relationship between the Rachmilewitz Endoscopic Activity Index (EAI) and Harpaz Histopathological Activity Scoring System (HSS) in 109 patients with UC. In that study, they have found poor agreement between endoscopic and histological scoring systems.[21] In a study by Kovach *et al*., the correlation between MES and GI was weak to moderate for different parameters (rho = 0.14–0.48).[22] However, a recent study by Irani *et al*. evaluated the correlation between UCEIS score

Table 4 Roberts Histological Index for histological scoring and data of individual scores in our study group[14]

Components	Scoring
Epithelial neutrophils	0 = None 1 = <5% crypts involved 2 = <50% crypts involved 3 = >50% crypts involved
Lamina propria neutrophils	0 = None 1 = Mild but unequivocal increase 2 = Moderate increase 3 = Marked increase
Chronic inflammatory cell infiltrate	0 = No increase 1 = Mild but unequivocal increase 2 = Moderate increase 3 = Marked increase
Erosion or ulceration	0 = No erosions or ulceration 1 = Recovering epithelium 1 = Probable erosion-focally stripped 2 = Unequivocal erosion 3 = Ulcer or granulation tissue

Calculation of RHI: RHI = 1 × chronic inflammatory cell infiltrate (4 levels) + 2 × Lamina propria neutrophils (4 levels) + 3 × Epithelial neutrophils (4 levels) + 5 × Erosions or ulceration (4 levels).
Total score: 0–33.

Table 5 Baseline characteristic of patients with ulcerative colitis (UC)

Baseline characteristics	Frequency (n = 96) (%)
Age (median) (IQR)	36 years (IQR 15)
Male	51 (53.12%)
Course of disease	
Relapsing remitting	82 (85.4)
Continuous	14 (14.6)
Extent of disease	
Proctitis	5 (5.2)
Left-sided colitis	57 (59.4)
Extensive colitis	34 (35.4)
Extraintestinal manifestation	
Arthritis	12 (12.5)
Oral Ulcers	2 (2.1)
None	82 (85.4)

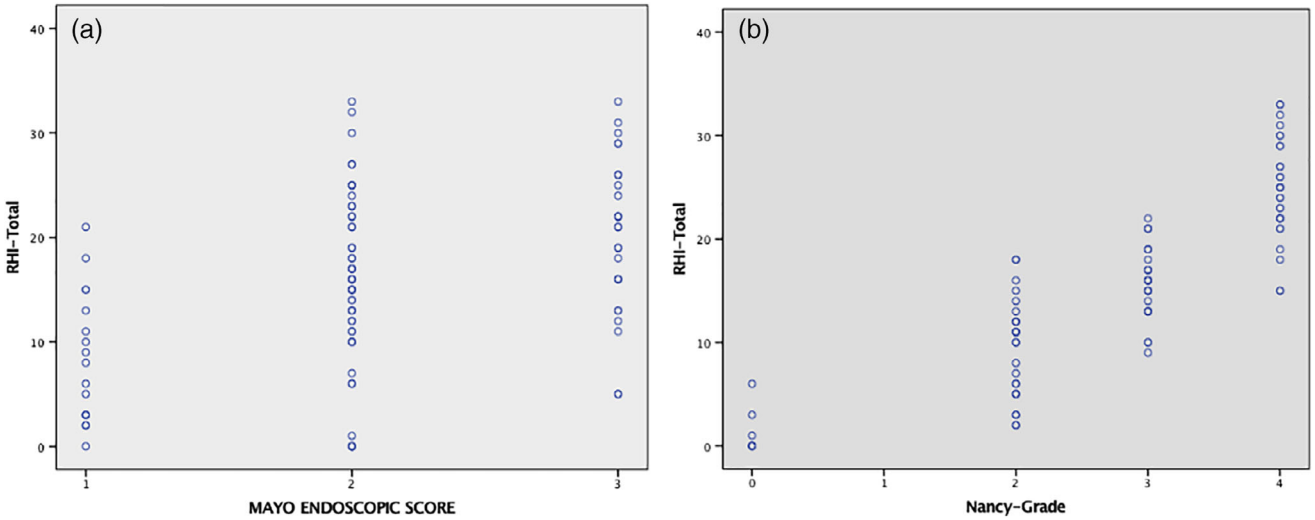

Figure 1 (a) Correlation between Mayo endoscopic score and Roberts Histological Index (RHI) is moderate [r = 0.442 (95% CI 0.26–0.63; P < 0.001)]; (b) Correlation between RHI and Nancy grading is strong [r = 0.872 (95% CI 0.75–0.96; P < 0.001)].

Table 6 Comparison of Mayo endoscopic score with histological indices

Mayo endoscopic score	Roberts Histological Index†	Nancy Index†	Geboes Index†
1 (n = 17)	8 (0–21)	2 (0–4)	3 (0–5)
2 (n = 52)	16 (0–33)	3 (0–4)	5 (0–5)
3 (n = 27)	21(5–33)	4 (2–4)	5 (3–5)

†Values expressed as median (range).

and the RHI and NI. In their study, a strong correlation between endoscopic and histological indices was found (r = 0.86 and r = 0.84 respectively; P < 0.001).[16] UCEIS is a more extensive and validated score, which might be why there is better correlation with histological indices compared to MES. However, other studies have found only a weak to moderate correlation between MES and histological indices similar to our study results.

In our study 17 patients were in endoscopic remission. We computed agreement between endoscopic and histological remission. We had used the definition of endoscopic remission (MES ≤ 1) as per standard criteria and use in different studies.[1,10,12] Endoscopic remission and histological remission by GI and RHI showed weak agreement. However, agreement between MES and NI was statistically nonsignificant. However, in our study, all 17 patients with endoscopic remission had an MES of 1. In a study by Lemmens *et al*., an MES of 1 showed poor correlation with histological activity, and patients with an MES of 1 had different grades of histological activity. In study by Simsek *et al*., they had also found poor agreement between endoscopic remission and histological remission.[21] In our study, none of the patients had an MES of 0, which might be why there is poor agreement between endoscopic and histological indices. Moreover, this also suggests that an MES of 1 is a poor predictor for histological remission.

Our study has few limitations. We have not evaluated interobserver variation in MES reporting, which might be why there is moderate correlation of MES with histological activity. None of the patients were had an MES of 0, which might be the reason for poor agreement between endoscopic and histological remission. Moreover, being a single-center study, large multicenter studies are needed for the validation of results of this study.

To conclude, MES only moderately correlated with histological scores. The RHI had the best correlation with MES among all histological indices. An MES of 1 poorly correlated with histological remission. Histological examination should be performed even in patients with mucosal healing to detect ongoing histological activity. A better validated endoscopic index is needed for defining endoscopic activity and remission.

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