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ARTICLE

Predictive Value of PHRI for Recurrence within One Year after UC Treatment: A Retrospective Study

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Abstract

Aims/Background Accurate prediction of recurrence after treatment is crucial for controlling the progression and improving the prognosis of active ulcerative colitis (UC) patients. Previous studies have evaluated the therapeutic response in UC patients by assessing mucosal healing, using measures such as the Paddington International Virtual ChromoendoScopy Score (PICaSSO) and the PICaSSO Histological Remission Index (PHRI). The PHRI is effective for evaluating treatment response and disease control in UC patients, but its predictive value for short-term recurrence has not been reported in the literature. Therefore, this retrospective analysis of clinical data aims to explore the predictive value of the PHRI and provide a reference for improving the prognosis of UC patients.

Methods Clinical data of UC patients in clinical remission admitted to our hospital from June 2017 to June 2023 were retrospectively collected. Patients were divided into the recurrence group and the non-recurrence group, based on whether they experienced recurrence during the one-year follow-up. Clinical data, laboratory test results, and PHRI scores were collected. Variables that showed statistically significant differences between groups in univariate analysis were included in multivariate logistic regression analysis. The predictive value of PHRI was analyzed with receiver operating characteristic (ROC) curve analysis.

Results One hundred and two UC patients in the clinical remission stage were included in this study, and there were no cases of loss to follow-up. Among them, 36 patients (35.29%) experienced recurrence within the one-year follow-up, whereas 66 patients (64.71%) did not. Compared with the non-recurrence group, the recurrence group had a more number of cases with lesions in the left-sided colon and extensive colon, higher percentages of cases that were moderate or severe, and a significantly higher colonoscopy score ($p < 0.05$). Compared with the non-recurrence group, the PHRI score of the recurrence group was significantly higher ($p < 0.001$). Multivariate logistic regression analysis showed that that the lesion range (OR = 4.127, $p = 0.005$), disease severity (OR = 3.889, $p = 0.019$), colonoscopy score (OR = 6.128, $p < 0.001$), and PHRI score (OR = 5.466, $p < 0.001$) were independent risk factors for recurrence in UC patients. The results of ROC curve analysis showed that the area under the curve of the PHRI score in predicting the recurrence of UC patients was 0.838 (95% CI: 0.760–0.916). When the optimal cut-off value was 1 point, the sensitivity and specificity were the highest, which were 89.58% and 65.58%, respectively, indicating that PHRI score had good predictive value.

Conclusion The lesion extent, disease severity, endoscopic score, and PHRI score are associated with recurrence within one year in UC patients in the clinical remission stage, and the PHRI score has good predictive value.

Key words: PICaSSO Histological Remission Index; ulcerative colitis; recurrence; retrospective study

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Introduction

Ulcerative colitis (UC) is a type of chronic inflammatory bowel disease. It is an autoimmune disease that primarily affects the colonic mucosa, leading to intestinal inflammation and ulcer formation. UC severely affects patients' quality of life, and patients often experience such symptoms as diarrhea, abdominal pain, urgency, anemia, and weight loss (Segal et al, 2021). The incidence rates vary significantly by geographical area, an epidemiological study has indicated (Calmé-jane et al, 2023) that the incidence of UC has been steadily increasing in western countries, and there is also an upward trend in regions with previously lower incidence rates, such as Asia and the Middle East. The exact pathogenesis of UC is still unclear, but it is believed to be associated with genetic factors, oxidative stress, alterations in the gut microbiota, and other factors. Clinical management mainly involves medication and nutritional support measures (Chen et al, 2022). Active UC refers to a disease state in the course of UC, and most patients with active UC undergo a cycle of "remission, relapse, remission, and relapse" during the prolonged course of the disease. This disease course not only significantly affects intestinal function but can also lead to malnutrition, hypoalbuminemia, anemia, and other nutritional disorders, increasing the risk of gastrointestinal tumors (Ge et al, 2022). A meta-analysis showed that the probability of colorectal neoplasia in UC patients was 3.7%, and a disease duration of >10 years was an independent risk factor for colorectal neoplasia. Therefore, accurate prediction of recurrence after treatment for active UC is crucial for controlling disease progression and improving patient prognosis (Cortesi et al, 2023). Previous studies have mainly assessed the therapeutic response in UC patients by evaluating mucosal healing using measures such as the Paddington International Virtual ChromoendoScopy Score (PICaSSO) and the PICaSSO Histological Remission Index (PHRI) (Lenfant et al, 2024; Sood et al, 2022; Uchiyama et al, 2023). The PHRI focuses on neutrophil infiltration as an observation index and involves histological scoring of biopsy samples. It helps physicians understand the severity of the patient's condition and guides the development of treatment plans and monitoring of treatment efficacy. The PHRI is effective for assessing endoscopic activity and clinical outcomes in UC patients (Gui et al, 2022), but its predictive value for short-term recurrence in UC patients has not been reported in the literature. Therefore, this study aims to explore the predictive value of PHRI through a retrospective analysis of clinical data, providing a reference for improving the prognosis of UC patients.

Methods

Research Objects

For this retrospective study, clinical data of 102 patients with UC admitted to our hospital from June 2017 to June 2023 were collected. The inclusion criteria were as follows: (1) patients with a clinical diagnose of UC; (2) patients with a previous colonoscopy; (3) patients in clinical remission; (4) patients aged over 18 years; (5) patients with regular follow-up and complete clinical data. The exclusion criteria were as follows: (1) patients with concomitant gastrointestinal diseases like

peptic ulcers or irritable bowel syndrome; (2) patients with concomitant autoimmune diseases or hepatic/renal dysfunction; (3) patients with malignant tumors; (4) patients with incomplete clinical data; (5) pregnant or lactating women. All patients were followed up through outpatient visits or telephone interviews, starting from discharge until the first diagnosis of recurrence or the end of the 1-year follow-up period. After drug treatment or natural remission, recurrence was defined as reappearance of active UC symptoms (abdominal pain, diarrhea, bloody stools, etc.). Based on whether patients experienced a recurrence during the 1-year follow-up period, they were divided into the recurrence group and the non-recurrence group. The Mayo Overall score was used to evaluate the clinical activity of the disease. A Mayo score >2 indicated that the UC condition was in a moderate active period (Lamb et al, 2019). The content of this study is in compliance with the 'Helsinki Declaration', and the study has been approved by the Medical Ethics Committee of Beijing Friendship Hospital Capital Medical University (BFHHZS20240182).

Data Collection

Patient data including gender, age, smoking history, alcohol consumption history, extent of UC lesion and severity, endoscopic scores, and laboratory test results were collected through electronic medical records. The severity assessment was based on the Mayo Overall Score, and laboratory tests included white blood cell count (WBC), albumin, platelet count (PLT), high-sensitivity C-reactive protein (hs-CRP), and others.

PHRI Assessment Method (Iacucci et al, 2021)

The PHRI assesses neutrophil infiltration as the observation index. Surface epithelial infiltration, crypt epithelial infiltration, crypt abscess, and lamina propria infiltration are each scored as 1 point, with a total score of 4 points. It emphasizes that cryptitis is defined as neutrophil infiltration in any number of crypts or glands, and crypt abscess is defined as neutrophil overflow into the crypt lumen, or any degree of crypt epithelial cell damage in the presence of cryptitis. PHRI assessments were performed by two senior pathologists who were unaware of the details of this study and independently evaluated the pathological slides.

Statistical Methods

Data analysis was performed with SPSS 27.0 (IBM Corp., Armonk, NY, USA) in this study. Normally distributed continuous variables are presented as $\bar{x} \pm s$, and group comparisons were conducted using independent sample *t*-tests. Categorical variables are presented as "n (%)", and comparisons were performed using χ^2 tests. In the univariate analysis, variables that showed statistically significant group differences in the univariate analysis were included in multivariate logistic regression analysis. Additionally, the predictive value of PHRI was assessed using receiver operating characteristic (ROC) curve analysis. The significance level was set at $\alpha = 0.05$.

Table 1. Comparison of clinical data between recurrence group and non-recurrence group.

Item		Recurrence group (n = 36)	Non-recurrence group (n = 66)	χ^2/t value	p value
Gender [n (%)]	Male	15 (41.67)	30 (45.45)	0.136	0.713
	Female	21 (58.33)	36 (54.55)		
Age (years, $\bar{x} \pm s$)		45.18 ± 8.15	44.28 ± 9.02	0.498	0.620
Smoking history [n (%)]	Yes	11 (30.56)	18 (27.27)	0.123	0.725
	No	25 (69.44)	48 (72.73)		
Alcohol consumption [n (%)]	Yes	9 (25.00)	16 (24.24)	0.007	0.932
	No	27 (75.00)	50 (75.76)		
Extent of lesion [n (%)]	Rectal	3 (8.33)	21 (31.82)	7.643	0.022
	Left-sided colon	23 (63.89)	28 (42.42)		
	Extensive colon	10 (27.78)	17 (25.76)		
Disease severity [n (%)]	Mild	4 (11.11)	25 (37.88)	8.203	0.017
	Moderate	25 (69.44)	32 (48.48)		
	Severe	7 (19.44)	9 (13.64)		
Endoscopic score [n (%)]	>1 point	27 (75.00)	28 (42.42)	9.949	0.002
	≤1 point	9 (25.00)	38 (57.58)		

Results

Comparison of Clinical Data between Recurrence Group and Non-Recurrence Group

One hundred and two patients with UC were included in this study, and none of them were lost to follow-up. During the 1-year follow-up period, 36 patients (35.29%) experienced a recurrence, whereas 66 patients (64.71%) did not. Compared with the non-recurrence group, the recurrence group had a more number of cases with lesions in the left-sided colon and extensive colon, higher percentages of cases that were moderate or severe, and a significantly higher colonoscopy score ($p < 0.05$). There was no significant difference in gender, age, or other data between the two groups ($p > 0.05$). See Table 1 for details.

Comparison of Laboratory Test Results and PHRI Scores between Recurrence Group and Non-Recurrence Group

Compared with the non-recurrence group, the PHRI score of the recurrence group was significantly higher ($p < 0.001$). There was no significant difference in laboratory examination data such as WBC count and albumin between the two groups ($p > 0.05$). See Table 2 for details.

Multivariate Logistic Regression Analysis of Factors Affecting UC Recurrence

Multivariate logistic regression analysis was performed with the variables that showed statistically significant differences in the univariate analysis as independent variables. The dependent variable was whether UC patients experienced recurrence (1 = yes, 0 = no). The results showed that the lesion range [odds ratio (OR) = 4.127, $p = 0.005$], disease severity (OR = 3.889, $p = 0.019$), colonoscopy score (OR =

Table 2. Comparison of laboratory test results and PHRI scores between recurrence group and non-recurrence group ($\bar{x} \pm s$).

Item	Recurrence group (n = 36)	Non-recurrence group (n = 66)	*t* value	*p* value
WBC ($\times 10^9$/L)	9.88 ± 1.65	9.42 ± 1.92	1.213	0.228
Albumin (g/L)	52.27 ± 4.47	53.36 ± 4.96	1.097	0.275
PLT ($\times 10^9$/L)	288.15 ± 71.66	280.75 ± 75.49	0.482	0.631
hs-CRP (mg/L)	22.63 ± 2.65	21.79 ± 3.18	1.349	0.180
PHRI score (Point)	1.69 ± 0.27	0.75 ± 0.28	16.406	<0.001

WBC, white blood cell; PLT, platelet count; hs-CRP, high-sensitivity C-reactive protein; PHRI, PI-CaSSO Histological Remission Index; PICaSSO, Paddington International Virtual ChromoendoScopy Score.

Table 3. Multivariate logistic regression analysis of factors affecting UC recurrence.

Factor	β	SE	Wald χ^2	*p*	OR	95% CI
Extent of lesion	1.418	0.489	8.403	0.005	4.127	1.583–10.764
Disease severity	1.358	0.541	6.302	0.019	3.889	1.347–11.229
Endoscopic score	1.813	0.456	15.805	<0.001	6.128	2.507–14.979
PHRI score	1.699	0.408	17.331	<0.001	5.466	2.457–12.161

UC, ulcerative colitis; SE, standard error; OR, odds ratio; CI, confidence interval.

6.128, $p < 0.001$), and PHRI score (OR = 5.466, $p < 0.001$) were independent risk factors for recurrence in UC patients. See Table 3 for details.

ROC Curve Analysis of PHRI Score in Predicting UC Recurrence

With UC recurrence within 1 year as the outcome variable (1 = yes, 0 = no), and the PHRI score as the diagnostic variable, a ROC curve was plotted. The results of ROC curve analysis showed that the area under the curve (AUC) of the PHRI score in predicting the recurrence of UC patients was 0.838 (95% CI: 0.760–0.916). When the optimal cut-off value was 1 point, the sensitivity and specificity were the highest, which were 89.58% and 65.58%, respectively, indicating that PHRI score had good predictive value. See Fig. 1 for details.

Discussion

In this study, 102 UC patients were included for follow-up observation. The results showed that 36 out of 102 patients experienced recurrence within one year, accounting for 35.29%, whereas 66 patients did not experience recurrence, accounting for 64.71%. These findings were similar to the results reported by Park et al (2022); however, the recurrence rate of our study was lower than the recurrence rate of 45.8% reported by Kurimoto et al (2023). This difference is mainly attributed to the duration of follow-up. In the present study, the focus was on the recurrence within one year after treatment in UC patients. A previous study has revealed (Gu et al, 2024) that UC is a risk factor for colorectal cancer, and frequent recurrences in UC patients can further exacerbate the disease, increase the difficulty of treatment,

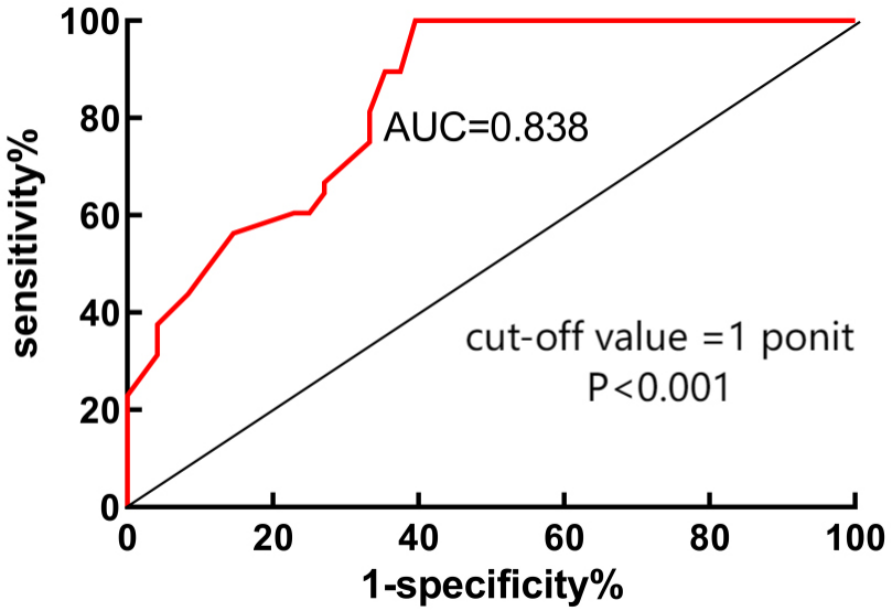

Fig. 1. ROC curve of PHRI score for predicting UC recurrence. ROC, receiver operating characteristic; UC, ulcerative colitis; AUC, the area under the curve.

and impose a significant burden on patients, seriously affecting their quality of life. Therefore, accurately predicting the recurrence of UC patients at an early stage is helpful in adjusting treatment strategies promptly, effectively controlling the disease, reducing the recurrence rate, and minimizing the negative impacts (Moda et al, 2022). By comprehensively evaluating treatment outcomes, disease activity, treatment compliance, as well as potential genetic and environmental factors, doctors can more accurately predict the risk of recurrence in patients, thereby achieving personalized management and intervention (Shimodaira et al, 2022).

In this study, through univariate and multivariate logistic regression analysis, the results showed that the extent of lesions, disease severity, endoscopic score, and PHRI score are independent risk factors for UC recurrence. Previous research (Lindgren et al, 1998) has indicated that among patients with chronic recurrent UC, the proportion of lesions involving the left colon and extensive colon is significantly higher than that involving the rectum, which is consistent with the findings of this study. A study conducted in Europe showed that patients with extensive colon UC have significantly shorter recurrence times, compared to patients with left-sided or rectal UC, with 100% recurrence after 5 years in rectal UC patients and 100% recurrence after 9 years in pancolitis UC patients (Wu et al, 2024). A relevant study has pointed out that the severity of UC is closely associated with disease recurrence, and severe disease is considered an independent risk factor for frequent recurrence in UC patients (Narula et al, 2020). The endoscopic score directly reflects the degree and activity of inflammation in the patient's intestines. Numerous studies have indicated that a high endoscopic score usually indicates severe inflammation and active disease, which increases the risk of recurrence after treatment (Jangi et al, 2021; Wang et al, 2023). Previous studies have often evaluated treatment outcomes in UC patients based on mucosal healing. However, some studies have found that even

in UC patients who have achieved mucosal healing criteria, approximately 24% to 40% of patients still have histologically active lesions. The current histological scoring systems have limitations such as the need to evaluate multiple parameters, as well as being cumbersome to perform and time-consuming, which can affect the interpretation of histological scores and expert reassessment (Yoon et al, 2020). The PHRI score is a new histological scoring system developed by endoscopic and pathological experts, and is validated through long-term follow-up studies. It can better reflect tissue remission, is relatively simple to assess, and can avoid subjective bias of evaluators. By evaluating the most severe lesion site, it reflects the overall disease activity of the intestine and avoids repetitive biopsies of multiple segments. It has the advantages of simplicity and strong reproducibility (Iacucci et al, 2023; Parigi et al, 2023). Chronic inflammation can lead to the continuous activation of the local immune system, which may promote the continuation of the pathological process. The continuous activation of the immune system can make the colon mucosa more prone to recurrence when encountering UC triggers. The PICaSSO index can reflect the repair of colonic mucosa. If the histological score is high, it means that the repair process of the colonic mucosa may not be complete, resulting in a persistent inflammatory environment. This environment may make the colonic mucosa more sensitive to disease recurrence.

The present study evaluated the application value of the PHRI score in predicting UC recurrence in patients with ROC curve analysis. The results showed that the AUC of the PHRI score in predicting UC recurrence was 0.838, which was similar to the results reported by Nardone et al (2022). This suggests that the PHRI score has good predictive value for UC recurrence, possibly because it objectively reflects the histological remission of patients by assessing the histological characteristics of the intestinal mucosa, including the degree of inflammation and healing. These factors directly relate to disease activity and the risk of recurrence. However, in a review of UC endoscopy scores published by Mohammed Vashist et al (2018), it was pointed out that compared with the Mayo score and PHRI score, the endoscopic severity index (UCEIS) of ulcerative colitis had higher accuracy in predicting the severity of UC patients. The reason may be that the PHRI score needs to be evaluated by endoscopy and histopathological experts, and it is necessary to interpret the physician's degree of experience in endoscopy or histopathological scoring, which may easily lead to observer consistency bias between endoscopy scores. Secondly, although UC is a continuous lesion, it can show discontinuous lesions after treatment. Therefore, endoscopic observation and histological score of a single site cannot represent the overall condition, which may be the reason why the accuracy of the PHRI score is lower than that of the UCEIS.

When the PHRI score ≥ 1, it means that the patient's histological inflammation is not completely relieved, and there is still a certain degree of inflammation or pathological changes; these factors have predictive value for the recurrence of UC. This helps doctors identify high-risk patients earlier and take corresponding management strategies. Residual inflammation indicates that the disease is not completely controlled and may provide conditions for future recurrence. Even if the clinical symptoms are alleviated, chronic inflammation in the mucosa may still

lead to disease recurrence in the long term. Regularly using the PHRI for evaluation can help doctors monitor the treatment effect and disease progression, and adjust the treatment plan in time to maintain the histological remission status. This is of great significance for reducing intestinal inflammation, reducing the risk of complications, and improving the quality of life of patients.

There are some limitations in this study. It is a retrospective single-center study with a small sample size. There are many related studies on the influencing factors of recurrence in UC patients. However, the application of the PHRI score in UC patients is relatively lacking. There are many studies related to the influencing factors of relapse in UC patients, which may cause certain bias in the research results. Therefore, in the future research, it is necessary to consider more influencing factors and construct a multi-level interrelated model for in-depth study.

Conclusion

In conclusion, the lesion range, disease severity, colonoscopy score, and PHRI score are related to the recurrence of UC patients within 1 year. The PHRI score has a good predictive value, which provides evidence for the clinical application value of PHRI, helps to provide clinicians with more accurate histological information, supports the implementation of personalized treatment management strategies, and thus brings better clinical results and quality of life of patients.

Key Points

- Patients with recurrent ulcerative colitis (UC) have significantly higher scores on the PICaSSO Histological Remission Index (PHRI) in comparison to non-recurrent patients.
- The extent of the lesion, disease severity, endoscopic score, and PHRI score are closely associated with recurrence within one year in UC patients.
- The PHRI has good predictive value for recurrence within one year in patients with ulcerative colitis.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

KZ and JX designed the research study and formulated the research plan. MJ and KZ collected research cases, related articles and data statistical analysis. JX and JZ contributed to the inspection and scoring of sections. KZ drafted the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Medical Ethics Committee of Beijing Friendship Hospital Capital Medical University (BFHHZS20240182). The entire experimental procedure adhered to the principles of informed consent, with patients of their family members being provided with information about the study and informed consent was obtained from all study participants.

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Conflict of Interest

The authors declare no conflict of interest.

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