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RESEARCH

Prediction of vedolizumab efficacy in ulcerative colitis: a nomogram incorporating pathological feature and serological marker

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Abstract

Vedolizumab (VDZ) is a humanized, gut-selective biologic used in the treatment of ulcerative colitis (UC). However, data on predictive factors for treatment response are limited. This study aims to develop a nomogram to predict VDZ treatment responsiveness in UC. We retrospectively collected clinical data from patients with moderate-to-severe active UC who received VDZ induction therapy at Chongqing General Hospital from December 2020 to March 2024. Full-slide images of colon biopsies from UC patients prior to VDZ treatment were analyzed to quantify mean mucosal eosinophil density (MMED). Based on clinical response 14-week post-treatment, patients were categorized into responsive and non-responsive groups. In total, 84 UC patients were analyzed, with 58 responding to VDZ treatment and 26 not responding. Significant differences were observed in pathological indices, with MMED showing a statistically significant difference between the groups ($p < 0.001$). Serum biomarkers, including C-reactive protein (CRP), also showed a significant difference ($P = 0.015$), as did the CRP/albumin (CRP/ALB) ratio ($P = 0.018$). Additionally, UCEIS scores differed significantly between the groups ($P = 0.025$). Independent risk factors identified through multivariate logistic regression analysis were used to establish a predictive model, presented as a nomogram. The area under the curve (AUC) for the combined MMED and CRP predictive model was 0.867 (95% CI: 0.781–0.953, $p < 0.001$), indicating high accuracy in predicting VDZ efficacy. These data are easily accessible even in primary healthcare settings, allowing our predictive model to support improved treatment decisions for patients.

Keywords Vedolizumab · Ulcerative colitis · Prediction model · Mean mucosal eosinophil density · CRP

Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) with an unclear etiology. Evidence indicates that its pathogenesis is closely linked to genetic predisposition, environmental factors, gut microbiota alterations, and immune dysregulation [1]. The incidence of UC has been rising annually in Asia, particularly in newly industrialized countries, placing a substantial economic burden on both patients and society [2]. UC is characterized by recurrent episodes of inflammation and remission in the colonic and rectal mucosa, leading to mucosal damage, including crypt structural abnormalities, erosions, and ulcers, as well as infiltration of inflammatory cells such as neutrophils and eosinophils [3]. Current treatment options include 5-aminosalicylic acid agents, corticosteroids, thiopurines, and biologic agents (such as anti-TNF, IL-12, IL-23 inhibitors, and anti-integrins), as well as small molecule agents, including Janus kinase inhibitors and sphingosine-1-phosphate receptor modulators [1, 4].

Biologics are currently utilized as first-line treatments for moderate-to-severe UC, playing a crucial role in managing active disease phases and maintaining remission [5]. Vedolizumab (VDZ) is a humanized, gut-specific monoclonal antibody that selectively binds to the α4β7 integrin, thereby

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inhibiting its interaction with the mucosal addressin cell adhesion molecule-1 (MAdCAM-1). This binding reduces inflammation in intestinal tissues by preventing eosinophil and lymphocyte adhesion to the intestinal vascular endothelium and their subsequent migration into the gut tissue [6]. VDZ has been demonstrated to be an effective and safe therapeutic option for moderate-to-severe UC. However, a subset of UC patients does not achieve a clinical response by week 14 of VDZ therapy. Data from two single-center, retrospective real-world studies conducted in China indicated that the clinical remission rates of vedolizumab for UC at week 14 were 63.1% and 65.6% [7, 8].

Accurate prediction of response to VDZ therapy in UC patients could substantially improve clinical decision making. A study observed that IBD patients with a favorable response to VDZ therapy exhibited a significant increase in specific butyrate-producing bacteria [9]. However, the variability in intestinal flora across populations and the timing of sample collection limit the reproducibility of these findings. Another study, which analyzed memory and regulatory T cells from peripheral blood and lamina propria mononuclear cells using RNA sequencing in VDZ-treated UC patients, demonstrated that gene expression profiles in peripheral blood Tregs could serve as predictors of response to VDZ therapy [10]. However, genetic testing requires considerable time and is costly, posing limitations for clinical application.

Histopathological examination of intestinal sections offers valuable insights into the microstructure of tissues and cells. Eosinophil counts in intestinal biopsies have emerged as a promising and reproducible tool for predicting the efficacy of VDZ treatment, providing actionable insights that may serve as clinical predictors and contribute to further research. Eosinophils, a type of granulocyte produced in the bone marrow, play a key role in the inflammatory response. They adhere to inflamed tissues by expressing specific proteins like integrins. The α4β7 integrin on eosinophils binds to the MAdCAM-1 molecule on intestinal endothelial cells, promoting eosinophil accumulation in intestinal tissues and contributing to mucosal damage and repair processes [11]. IBD patients with high levels of eosinophils in the gut were found to have a negative correlation with the efficacy of vedolizumab treatment in one study [12], and in another study, it was shown that in adults with UC, severe eosinophilic infiltration on colon biopsy was the most significant predictor of poor outcome of first-line treatments, including mesalamine and corticosteroids [13]. Eosinophil activation and increased numbers of intestinal mucosal eosinophils are common in patients with UC [14], and by participating in the inflammatory response, eosinophils may play an important role in the damage and repair process of the intestinal mucosa [15].

A previous study developed a clinical decision-support tool to predict the efficacy of VDZ in treating UC , incorporating variables such as prior exposure to tumor necrosis factor (TNF) antagonists, disease duration, baseline endoscopic activity, and baseline albumin concentration [16]. However, the lower limit of the confidence interval for the performance of this model was not ideal, resulting in limited predictive power. To further optimize the model for predicting the effectiveness of VDZ in treating UC, we incorporated the mucosal eosinophil. We aim to enhance the accuracy and reliability of the prediction model by integrating histopathological and serological indicators, thereby providing a clinically actionable framework to guide treatment decisions in the management of UC patients.

Materials and methods

Study design and participants

This study was a clinical single-center retrospective cohort study. A total of 84 UC patients from December 1, 2020, to March 31, 2024, were included in the study after approval by the Medical Ethics Committee of Chongqing General Hospital (KY S2022-113-01). Inclusion criteria: (1) adults over 18 years; (2) patients with a confirmed diagnosis of ulcerative colitis according to 2023 Chinese national clinical practice guideline on diagnosis and management of ulcerative colitis [17]; (3) VDZ treatment was initiated between December 1, 2020, and March 31, 2024, with documented follow-up on therapy and treatment outcomes available in our center's electronic medical records, and (4) colonic and/or rectum biopsies collected during an initial colonoscopy within 6 months before starting vedolizumab therapy were available. Exclusion criteria: (1) patients who underwent intestinal biopsy within 4 weeks before colonoscopy but received oral hormone therapy and (2) lack of 14 weeks of treatment and follow-up of treatment results. This study was approved by the Ethics Review Committee of Chongqing General Hospital.

Variables

General clinical data of UC patients were collected, including age, sex, BMI (measured at the time of the patient's first VDZ infusion), disease duration, history of smoking, site of disease according to the Montreal Classification (E1, E2, and E3), opportunistic infections prior to the current VDZ treatment, previous hormone therapy, previous anti-TNF and immunosuppressive use, modified mayo score, laboratory tests, and other relevant data.

Evaluation of eosinophil number and density

Hematoxylin and eosin (HE)-stained pathology sections from colonic/rectal biopsies of UC patients before VDZ treatment were digitized for analysis. The baseline HE-stained pathology sections were independently reviewed by two pathologists in a blinded manner. In cases where their assessments differed significantly, a third senior pathologist performed a subsequent review. Biopsies were selected from the most inflamed bowel segments to determine the mean eosinophil density, following these steps:

1. Sections were first examined at low magnification to identify hotspot areas of eosinophil infiltration.
2. Eosinophils were then quantified within a single high magnification field of view, with each field covering an area of 0.24 mm^2.
3. Eosinophil density was defined as the number of eosinophils per field area (mm^2).
4. Eosinophil counts were recorded across five high magnification fields of view within hotspot areas, and the average was calculated to obtain the mean eosinophil density.

This method provided a precise assessment of eosinophil infiltration in the most inflamed regions [18].

Outcomes

Clinical outcomes at 14 weeks of VDZ treatment were grouped according to the presence or absence of a clinical response: a clinical response was defined as a decrease of $\geq 30\%$ in the modified mayo score [19] relative to the baseline value as well as a score of ≥ 3 and a decrease of ≥ 1 in the sub-score for blood in stools or a score of 0 or 1 for this sub-score, and vice versa for no response.

Statistical analysis

Data analysis was conducted using SPSS version 26.0. Categorical variables were expressed as frequencies and percentages (n, %) and analyzed with the chi-square test. The normality of each variable was assessed using the Shapiro–Wilk test. Continuous variables with normal distribution were presented as mean ± standard deviation (SD) and analyzed using the independent samples t-test. Non-normally distributed continuous variables were reported as median and interquartile range (IQR) and analyzed with the Mann–Whitney U test. A p-value < 0.05 was considered statistically significant. A collinearity analysis was meticulously conducted for significant variables, with variance inflation factors (VIF) and tolerances. A VIF value below 5 and a tolerance above 0.1 were used as criteria to signify an absence of notable collinearity. The significant factors were incorporated into the multivariate logistic regression model. With the Akaike information criterion (AIC) serving as the judgment criterion, a stepwise regression was employed to screen variables, thereby obtaining the final model. Internal validation was performed using cross-validation. To validate the accuracy and clinical utility of the nomogram model constructed, a series of evaluations were conducted. The model's discriminative ability was measured by the area under the receiver operating characteristic (ROC) curve, and its calibration was assessed by comparing predicted outcomes with actual observations using calibration plots. Decision curve analysis (DCA) provided standardized net benefits across different risk thresholds to assess the model's practical clinical value.

Results

Baseline characteristics of UC patients

A total of 95 patients with UC were included in this study. According to the established criteria, eight patients had received hormone therapy prior to intestinal biopsy, and three patients were lost to follow-up. Consequently, 84 patients with UC were ultimately enrolled (Fig. 1). Among these, there were 51 males (60.7%) and 33 females (39.3%). The median age at diagnosis of the disease was 36 years. The median duration of the disease was 6 years. A total of 18 patients had a history of smoking (21.4%). The average age of individuals who initiated treatment with VDZ was 42 years. Additionally, there were 77 patients with rectal involvement. In this cohort, 4 patients (4.7%) had a history of Clostridioides difficile infection, 2 patients (2.4%) had previously been infected with Cytomegalovirus (CMV), and 14 patients (16.7%) had a history of Epstein-Barr virus (EBV) infection. Furthermore, 13 patients (15.5%) had prior exposure to anti-TNF therapy, while 4 patients (4.7%) had received VDZ therapy, and 3 patients (3.6%) had been treated with both anti-TNF and VDZ therapies. The overall mean mucosal eosinophil density in colonic was 209.2(112.1,332.9)eosinophils/mm^2, and the mean value of CRP was 3.40(1.16,7.48)mg/L (Table 1).

The characteristics in responsive and unresponsive patient cohort to treatment with VDZ

Overall, 58 out of 84 (69.05%) UC patients achieved a clinical response and remained on vedolizumab 14 weeks after the initiation of therapy. The mean eosinophil density in the mucosa significantly differed between the two groups (181.67[102.50, 265.63] vs. 340.00 [232.92,

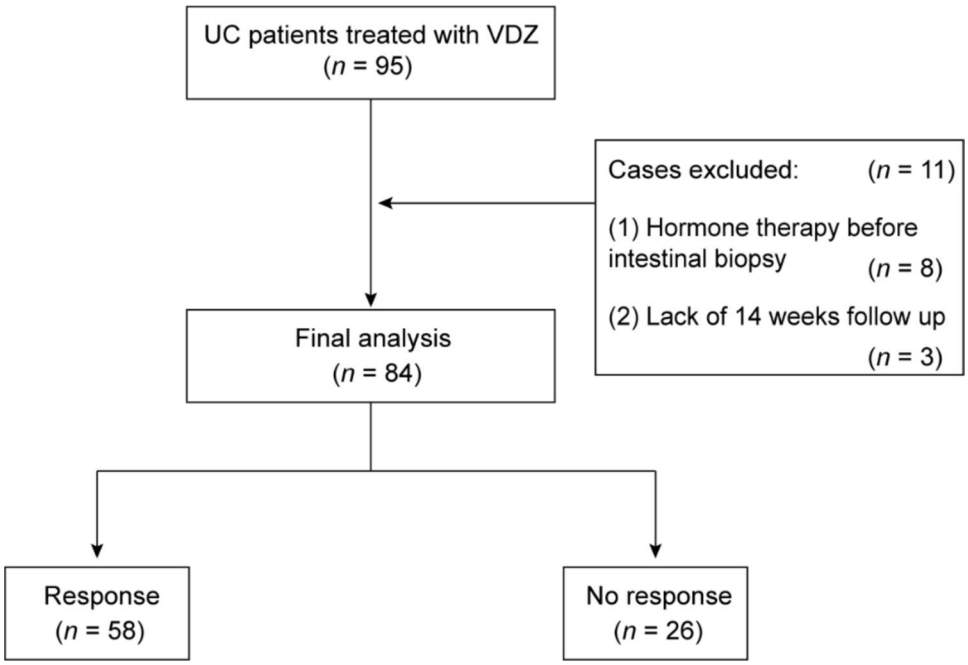

Fig. 1 Flow chart of participants included and excluded in this study. UC, ulcerative colitis; VDZ, vedolizumab

491.04], $p < 0.001$). And, C-reactive protein (CRP) levels were significantly different between the groups (2.71 [0.80, 4.77] vs. 5.92 [2.56, 18.80], $P = 0.008$), as was the CRP/ALB (0.06 [0.02, 0.11] vs. 0.14 [0.07, 0.50], $P = 0.008$). Additionally, UCEIS scores were significantly different between the groups (5[3, 6] vs. 6[4, 7], $P = 0.025$). In contrast, no significant differences were observed in clinical data between the two groups regarding gender, age at diagnosis, disease duration, smoking history, BMI, age at the start of VDZ, vasculitis antibody profile, modified mayo score, Montreal classification, history of opportunistic infections prior to treatment, previous biologic therapy, or serological examinations, including hemoglobin, ESR, WBC count, peripheral eosinophil count, and PLT count (Table 2).

Development of the nomogram

The variables of significance in the univariate analysis were subjected to a collinearity test. After it was determined that there was no collinearity (Supplementary Table 1), these variables were incorporated into the multiple logistic regression model. (Table 3). The results indicated that MMED was an independent predictor ($p < 0.001$, OR = 0.983, 95% CI: 0.975–0.992). The final model was obtained through stepwise regression (Table 4). The predictive variables identified by logistic regression were incorporated into the nomogram to construct the final model.

The results are presented in Fig. 2. The calibration curve of the combined model closely aligns with the ideal 45-degree diagonal, indicating good agreement between predicted and observed outcomes. The C-index value of the model is 0.751 (95% CI: 0.551–0.802), demonstrating acceptable discriminatory ability. Although some bias was observed in predicting extremely low and high risks, the overall prediction accuracy is sufficient for the model to function as an effective clinical risk assessment tool (Fig. 3).

Validation the performance of the nomogram

The AUC predicted by MMED alone was 0.796 (95% CI:0.685 ~ 0.906, $P < 0.001$) and CRP alone was 0.683 (95% CI:0.556 ~ 0.809, $P = 0.008$), whereas the AUC predicted by MMED combined with CRP was 0.867 (95% CI. 0.781 ~ 0.953, $p < 0.001$). The above results suggested that the prediction of VDZ for UC based on mucosal eosinophils combined with CRP was well differentiated (Fig. 4).

On the decision curve, the combined predictive model of MMED and CRP had a higher net gain than either metric alone. The net gain of the combined model was consistently higher than that of the no-intervention strategy (i.e., assuming that all patients were invalid) and the all-intervention strategy (i.e., assuming that all patients were valid) over most of the range of threshold probabilities. In particular, the net gain of the joint model was highest at threshold probabilities of 0.2–0.9, showing good clinical application. In practical application, the use of this joint model can more effectively identify those who are effective and ineffective for VDZ treatment of UC, thus improving the efficiency and effectiveness of clinical interventions (Fig. 5).

Table 1 Baseline characteristics of UC patient (n = 84)

Characteristics	Results
Gender	
Male (n, %)	51 (60.7%)
Female (n, %)	33 (39.3%)
Age at diagnosis	36(28,47)
Disease duration	6 (2,10)
BMI (kg/m^2)	21.01(18.91, 23.38)
Smoking history	
Yes	18 (21.4%)
No	66 (78.6%)
Age at VDZ start	42(33,54)
Modified mayo score	8(7, 10)
UCEIS score	5(4,6)
UC Montreal classification	
E1	8 (9.5%)
E2	28 (33.3%)
E3	48 (57.2%)
Rectal involvement	
Yes	77 (91.7%)
No	7 (8.3%)
Opportunistic infection before treatment	
C-diff	4 (4.7%)
CMV	2 (2.4%)
EBV	14 (16.7%)
no infection	64 (76.2%)
Prior steroid therapy	
Yes	18 (21.4%)
No	66 (78.6%)
Previous biologic therapy	
Anti-TNF	13 (15.5%)
VDZ	4 (4.7%)
Anti-TNF and VDZ	3 (3.6%)
No	64 (76.2%)
Pathological indicator	
MMED (eos/mm^2)	209.2 (112.1, 332.9)
Serological indicators	
CRP (mg/L)	3.40 (1.16, 7.48)
ALB (g/L)	42.65(38.75, 45.45)
CRP/ALB (mg/g)	0.08 (0.03, 0.21)
25-hydroxyvitamin-D3 (nmol/L)	19.00(12.75,26.01)
Other Laboratory values	
Hemoglobin (g/L)	133.00(116.75, 146.75)
ESR (mm/h)	14.50(6.00, 30.50)
WBC (10^9/L)	6.45(4.90,7.87)
EO*10^9/L	0.12 (0.60, 0.19)
NEUT*10^9/L	4.14 (3.14, 5.43)
PLT (10^9/L)	269.00 (213.75, 330.75)

UC, ulcerative colitis; BMI, body mass index; VDZ, vedolizumab; MMED, Mean mucosal eosinophil density; C-diff, Clostridium difficile; CMV, Cytomegalovirus; EBV, Epstein-Barr virus; CRP, C-reaction protein; ALB, Albumin; ESR, Erythrocyte sedimentation rate; WBC, White blood cell count; EO, Eosinophils; NEUT, Neutrophil count; PLT, Platelet

Discussion

With the rapid expansion of targeted treatment options for UC, one of the primary goals of UC management is to achieve precision therapy. Predicting the response to biologics, such as VDZ, has become a major focus of current research. In this study, we retrospectively analyzed the clinical data and colonic MMED of UC patients treated with VDZ at a tertiary care hospital to identify predictive factors for VDZ efficacy. The results demonstrated that higher MMED level was independent risk factor for treatment failure after 14 weeks of VDZ therapy. The combination of MMED and CRP proved to be highly accurate in predicting the therapeutic response to VDZ in UC patients.

In our study, 84 patients with moderate-to-severe UC were included, and the clinical response rate to VDZ was 69.05%. Our findings are consistent with a real-world study conducted in China involving 64 patients with moderate-to-severe UC treated with VDZ, which reported that 73.4% of patients achieved a clinical response after 14 weeks of treatment [7].

Eosinophils are a type of leukocyte that constitutes a component of the innate immune system and are primarily found in mucosal tissues, particularly in the gastrointestinal tract. These cells are highly sensitive to their environment and can respond to pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs) during the immune response. This suggests that eosinophils play a crucial role in responding to pathogens and tissue damage resulting from focal infections. Activated eosinophils release a variety of biological substances, including granule proteins, cytokines, chemokines, enzymes, and growth factors, which mediate the diverse biological activities of eosinophils in infection and inflammation [20]. In patients with active UC , a marked increase in the number of eosinophils in the colorectal mucosa has been observed [21]. The Nancy scoring system, which is used to assess the degree of histologic inflammation in UC, includes a description of eosinophils [22]. Furthermore, studies have demonstrated that an increase in mucosal neutrophils, eosinophils, ulcers, and plasma cells is predictive of UC recurrence [23, 24]. Additionally, eosinophils are implicated in the chronic inflammation and fibrosis of the intestinal tract [25]. All of these findings suggest that tissue eosinophils are closely associated with the development and activity of UC. Histological evaluation is increasingly being utilized to predict the risk of recurrence in patients in clinical remission and has become a therapeutic target in various histologic grading systems in several studies [26, 27]. The results of the present study indicated that higher mucosal mean eosinophil

Table 2 Baseline characteristics between responsive (n = 58) and unresponsive (n = 26) patient cohort to treatment with VDZ

	Response ($n=58$)	No response ($n=26$)	p-value
Gender			0.285
Male	33 (56.9%)	18 (69.2%)	
Female	25 (43.1%)	8 (30.8%)	
Age at diagnosis	40(29–50)	33(26–42)	0.201
Disease duration	5(2,7)	8 (2, 10)	0.144
BMI (kg/m^2)	20.81 (19.15, 23.34)	21.24 (18.19, 23.60)	0.731
Smoking history			0.742
Yes	45 (77.6%)	21 (80.8%)	
No	13 (22.4%)	5 (19.2%)	
Age at VDZ start	45(32,55)	41(34,48)	0.408
Modified mayo score	8(6, 10)	8 (7, 10)	0.205
UCEIS score	5(3,6)	6(4,7)	0.025
UC Montreal classification			0.455
E1	7 (12.07%)	1 (3.85%)	
E2	18 (31.03%)	10 (38.46%)	
E3	33 (56.90%)	15 (57.69%)	
Rectal involvement			0.319
Yes	52(89.7%)	1 (3.8%)	
No	6 (10.3%)	25 (96.2%)	
Opportunistic infection before treatment			0.509
Yes	15(25.86%)	5(19.23%)	
No	43(74.14%)	21(80.77%)	
Prior steroid therapy			0.742
Yes	13 (22.4%)	5 (19.2%)	
No	45 (77.6%)	21 (80.8%)	
Previous biologic therapy			0.316
Yes	12(20.7%)	8 (30.8%)	
No	46 (79.3%)	18 (69.2%)	
Pathological examination			
MMED (eos/mm^2)	181.67(102.50,265.63)	340.00(232.92,491.04)	< 0.001
Serological examination			
CRP (mg/L)	2.71 (0.80, 4.77)	5.92 (2.56, 18.80)	0.008
ALB (g/L)	43.50 (40.38, 45.50)	40.90 (35.50, 45.03)	0.158
CRP/ALB (mg/g)	0.06 (0.02, 0.11)	0.14 (0.07, 0.50)	0.008
25-hydroxyvitamin-D3 (nmol/L)	20.17 (12.62, 28.00)	17.44 (13.00, 22.31)	0.450
Other Laboratory values			
Hemoglobin (g/L)	135.00(120.50,147.25)	130.50 (98.00, 146.50)	0.416
ESR (mm/h)	10.50 (6.00, 26.50)	18.00 (10.00, 35.00)	0.090
WBC (10^9/L)	6.07 (4.75, 7.84)	6.64 (5.41, 7.95)	0.172
EO*10^9/L	0.10 (0.06, 0.17)	0.15 (0.07, 0.25)	0.167
NEUT*10^9/L	4.02(3.04,5.33)	4.49(3.28,5.64)	0.225
PLT (10^9/L)	262.00(210.75,334.00)	280.00(217.25,331.50)	0.158

C-diff, CMV, and EBV were combined into opportunistic infection. Anti-TNF, VDZ, anti-TNF and VDZ were combined into previously used biologic. UC, ulcerative colitis; BMI, body mass index; VDZ, vedolizumab; MMED, Mean mucosal eosinophil density; C-diff, Clostridium difficile; CMV, Cytomegalovirus; EBV, Epstein-Barr virus; CRP, C-reaction protein; ALB, Albumin; ESR, Erythrocyte sedimentation rate; WBC, White blood cell count; EO, Eosinophils; NEUT, Neutrophil count; PLT, Platelet

density was negatively correlated with moderate-to-severe UC treated with VDZ, independent of peripheral blood eosinophil levels, which is consistent with findings from similar previous studies [12].

CRP is an acute time-phase response protein synthesized by the liver, which is elevated in inflammatory infections, traumas, stress reactions, fever, etc., and enhances phagocyte phagocytosis and activation of complement,

Table 3 Multivariate logistic regression results

	β	S.E	P	OR (95%CI)
MMED	−0.017	0.004	<0.001	0.983 (0.975~0.992)
CRP	−0.168	0.101	0.098	0.846 (0.693–1.031)
CRP/ALB	2.762	2.67	0.301	15.836 (0.085–2965.19)
UCEIS Score	−0.049	0.221	0.823	0.952 (0.617–1.468)

Table 4 Prediction model

	β	S.E	Z	P	OR (95%CI)
Pathological feature (MMED)	0.02	0	4.12	<.001	0.985 (0.982~0.993)
Serological marker (CRP)	0.08	0.02	3.55	<.001	0.932 (0.891~0.972)

etc., during inflammatory reactions, and is one of the commonly used indicators to assess the inflammatory state of the body in clinical practice, and one of the most important biomarkers to assess the inflammatory activity of UC. CRP is one of the most important biomarkers for assessing inflammatory activity in UC and is often used to monitor UC disease activity. CRP testing during treatment predicts the patient's response to treatment and risk of complications (e.g., hospitalization and surgery) [28]. A population-based study conducted by the IBSEN Study Group demonstrated that in patients with ulcerative colitis, a CRP level above 10 mg/L at 1-year predicted an increased risk of surgery over the following 4 years. In patients with total colonic ulcerative colitis, a CRP level above 23 mg/L at diagnosis predicted an increased risk of colectomy during the first 5 years of follow-up. ALB, which is also synthesized by the liver, is widely used as an indicator of nutritional status and to monitor liver function, and the rate of synthesis is directly affected by the severity of acute infections [29]. Low levels of ALB interfere with immune mechanisms such as humoral and cellular immunity and phagocytosis. phagocytosis. A study showed that lower levels of ALB as well as higher levels of CRP reduced the likelihood of endoscopic remission in IFX-treated patients with IBD [30]. CRP and ALB, referred to as positive and negative acute-phase reactants, respectively, have been recognized in septic patients as a novel inflammation-based score, which, compared with CRP or albumin alone, provides more useful inflammatory status Information [31]. Other studies have shown that the CRP/ALB ratio is strongly correlated with IBD disease activity and is a highly valuable biomarker for assessing disease activity [32, 33]. The present study showed that higher serum CRP and higher CRP/ALB ratio were negatively correlated with the efficacy of VDZ in the treatment of UC, which may be due to the fact that high serum CRP levels and low albumin levels indicate a more severe disease state and poorer nutritional status, which further indicates a more refractory disease state, and thus may be the reason for the poor efficacy of VDZ.

Previous studies in the treatment of moderate-to-severe ulcerative colitis with VDZ have shown that prior treatment with TNF antagonists affects the efficacy of VDZ [34], but this was not observed in the present study, and it was considered that there may have been fewer patients with prior use of TNF antagonists in the present study, which did not reflect a statistical difference.

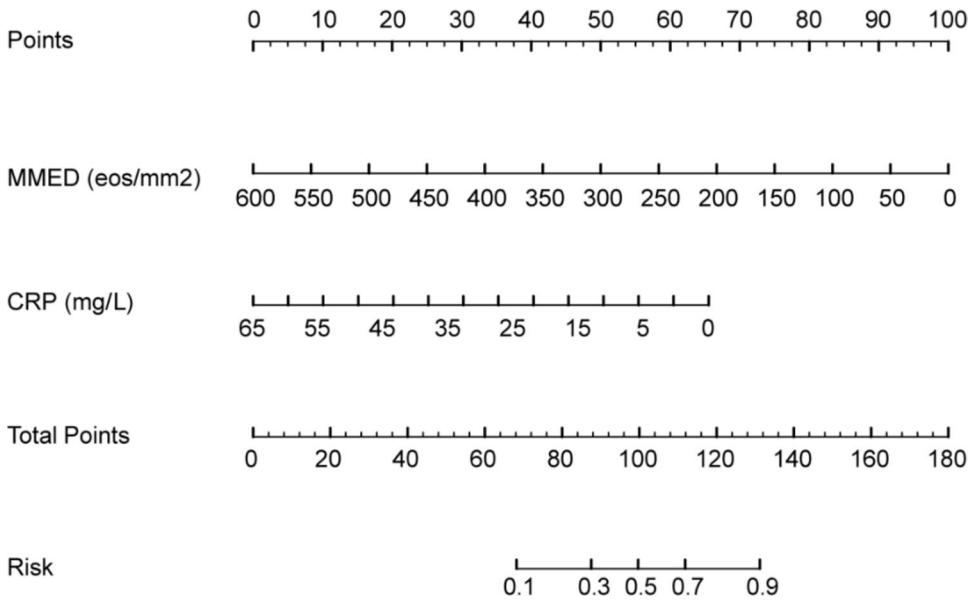

Fig. 2 Nomogram for predicting the efficacy of UC treated with Vedolizumab. MMED, mucosal mean eosinophil density; CRP, C-reactive protein

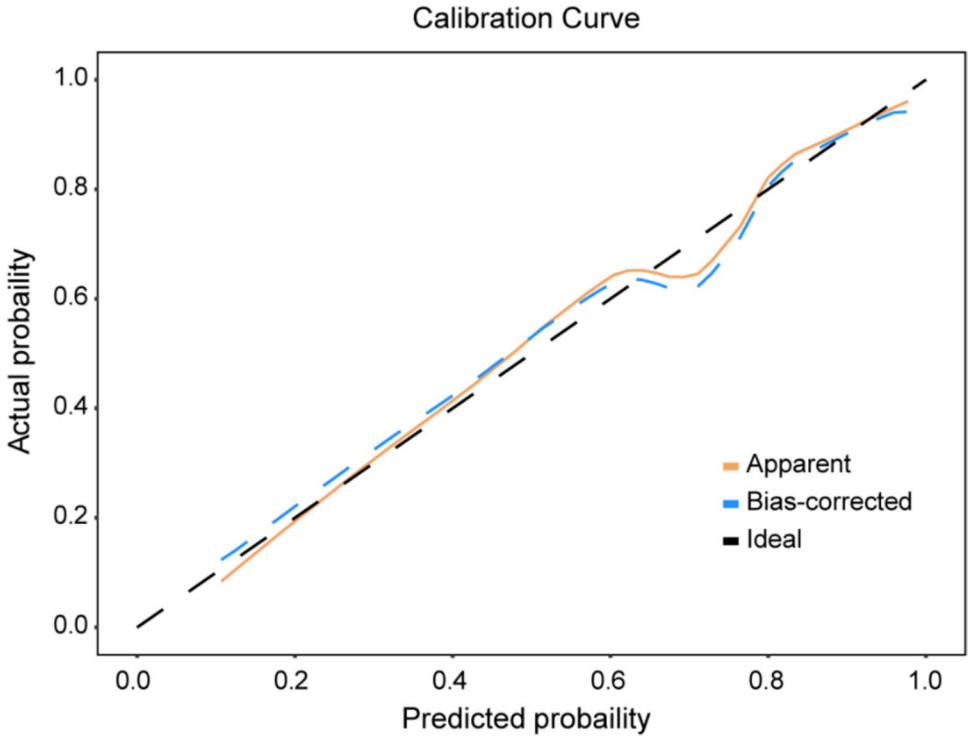

Fig. 3 The calibration plot for the prediction model

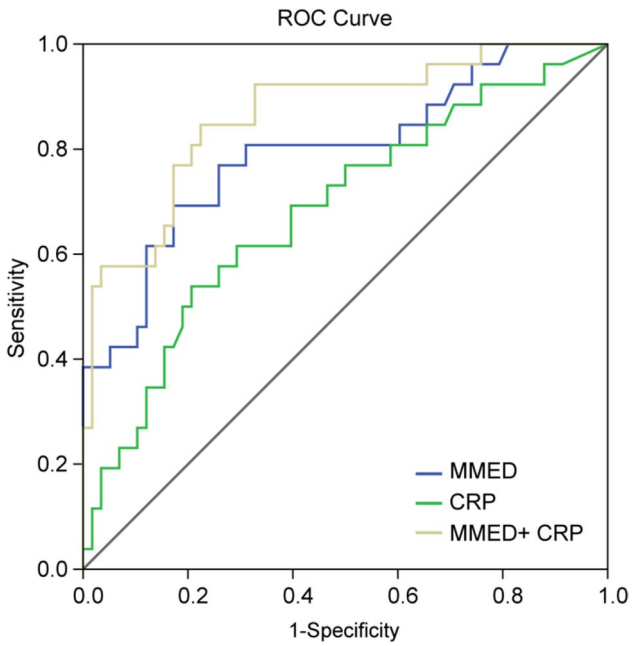

Fig. 4 ROC analysis of the nomogram for the efficacy of UC treated with Vedolizumab. The AUC values for predicting were 0.796 (MMED), 0.683 (CRP), and 0.867 (MMED + CRP). MMED, mucosal mean eosinophil density; CRP, C-reactive protein

In order to further promote individualized treatment, save treatment costs, improve the efficiency of VDZ in the treatment of UC, and assist doctors and patients to jointly develop treatment strategies, we produced a prediction model for the 14-week efficacy of VDZ in the treatment of patients with moderate-to-severe UC and plotted columnar line graphs for clinical reference. Logistic regression analysis was used in this study, which was mainly used to identify risk factors for VDZ treatment failure and to predict and assess VDZ efficacy. This model is effective in controlling confounding factors when quantitatively analyzing the relationship between study variables and study outcomes. The model was internally validated using ten-fold cross-validation. By evaluating the adjusted consistency index (C-index) and constructing calibration curves, we found that the model performed well in terms of differentiation and calibration. In addition, the results of the Hosmer–Lemes how test indicated that the model was well fitted.

This study offers several strengths: (1) The analysis integrates clinical indicators, laboratory tests, and pathological indicators, all of which are objective test results and scales, ensuring high accuracy and practicality. Furthermore, eosinophil density in colonic tissues has been verified for inter-observer consistency [18]; (2) Currently, there are few studies on predicting the efficacy of biologics (including VDZ) for Chinese UC populations. This study is the first to establish an efficacy prediction model for VDZ in Chinese UC patients, complete with a clinical reference nomogram; (3) To ensure accuracy, all patients who used steroids within 4 weeks prior to biopsy were excluded to avoid potential bias from steroid's effects on eosinophil counts in intestinal tissues. However, the study has certain limitations. First, the sample size is small, as VDZ has only

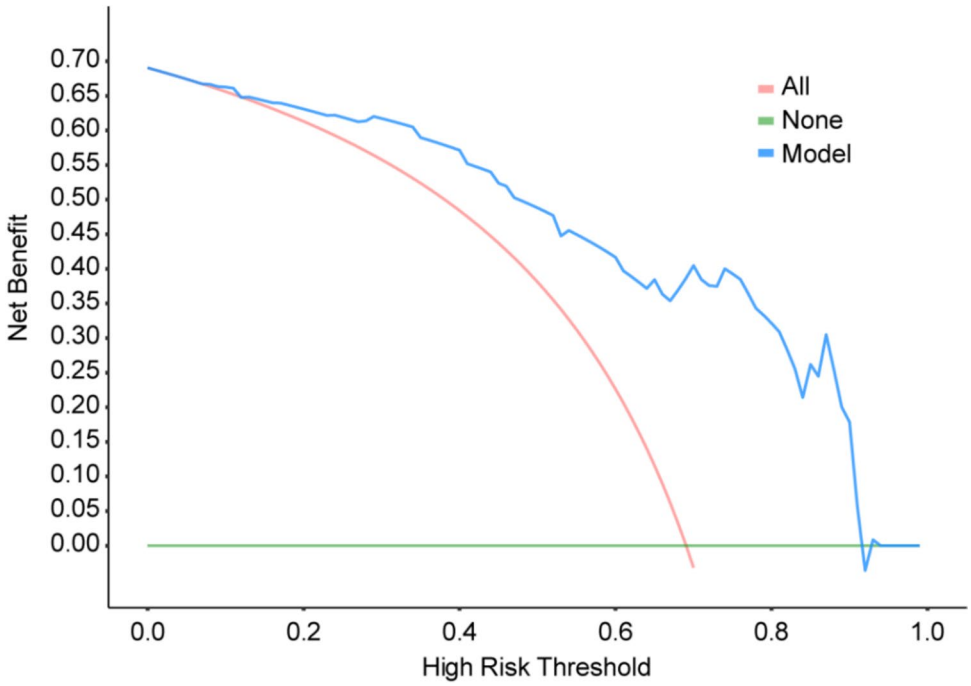

Fig. 5 The decision curve for the prediction model

recently been introduced in the Chinese market, with health insurance coverage available for just a year. This has limited the patient pool, with data derived from a single center and stringent inclusion criteria. Second, although the established prediction model demonstrates good differentiation and calibration, it has only undergone internal validation due to the limited sample size and lacks external validation. This limitation impacts the model's reliability and generalizability. A multicenter study with a larger sample size would provide a solid data foundation to further validate and improve the model, ultimately enhancing its predictive accuracy and stability. Third, in clinical practice, most biopsies are typically performed during routine monitoring. It may be acknowledged that the 6-month biopsy collection window for eosinophils may introduce potential confounding factors due to concomitant treatments. To address this limitation, future prospective studies we will optimize the timing of biopsies, restricting the biopsy collection period to within 2 weeks prior to treatment.

Conclusion

In conclusion, higher MMED was significantly and negatively correlated with clinical response at 14 weeks in patients with UC treated with VDZ, and the MMED (pathological feature) combined with CRP (serological marker) had good accuracy in predicting VDZ efficacy. This study explores a new way to construct a cost-effective predictive model and looks forward to validation in a larger patient cohort.

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Author contributions All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Tian Wang, Min Zou, Yan Liu, and Wei Tan. The first draft of the manuscript was written by Tian Wang, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author/s.

Declarations

Competing Interests The authors declare no competing interests.

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