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ORIGINAL RESEARCH

A Nomogram Based on Laboratory Data, Inflammatory Bowel Disease Questionnaire and CT Enterography for Activity Evaluation in Crohn's Disease

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Background: Accurately assessing the activity of Crohn's disease (CD) is crucial for determining prognosis and guiding treatment strategies for CD patients.

Objective: This study aimed to develop and validate a nomogram for assessing CD activity.

Methods: The semi-automatic segmentation method and PyRadiomics software were employed to segment and extract radiomics features from the spectral CT enterography images of lesions in 107 CD patients. The radiomic score (rad-score) was calculated using the radiomic signature formula. Multivariate logistic regression analysis identified the independent risk factors of erythrocyte sedimentation rate, fecal calprotectin, and Inflammatory Bowel Disease Questionnaire (IBDQ), and a nomogram was constructed in combination with rad-score. The nomogram underwent evaluation and testing in the training set (n = 84) and validation set (n = 23), respectively.

Results: The discrimination performance of the combined (AUC 0.877) was marginally superior to that of IBDQ + clinical (AUC 0.854). However, there was no significant difference in AUC between the two models in the validation set (P = 0.206). IBDQ + clinical outperformed clinical (AUC 0.808), clinical outperformed IBDQ (AUC 0.746), and IBDQ outperformed radiomic signature (AUC 0.688). Significant differences in AUC were observed between the two models (radiomic signature vs clinical, P = 0.026; radiomic signature vs IBDQ + clinical, P = 0.011; radiomic signature vs combined, P = 0.008; in the validation set).

Conclusion: The nomogram, combined with laboratory data, IBDQ and rad-score, presents an accurate and reliable method for assessing CD activity.

Clinical Impact: The nomogram enhances the potential for personalized treatment plans and better disease management, making it a valuable tool for clinical practice.

Keywords: Crohn's disease, laboratory data, quality of life, nomogram, CT enterography

Introduction

Crohn's disease (CD) is a chronic, progressive, nonspecific inflammatory condition of the intestines characterized by recurrent episodes of activity and remission.[1] CD often affects various parts of the intestine, mainly the terminal ileum and ileocecal region, with characteristics such as segmental, skip, and asymmetric ulcerative lesions.[2] Prolonged active disease stages can lead to irreversible intestinal damage, including thickening and stenosis of the intestinal wall. Prolonged active disease stages can also increase the risk of surgery, disability, and significantly impact patients' quality

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of life and increase economic burden.[3–5] Therefore, accurate and effective monitoring and assessment of CD disease activity is essential for the effective management and treatment adjustment of CD patients.

Various methods, such as endoscopy, CT enterography (CTE), and MR enterography (MRE), are employed to evaluate the severity of CD activity. Although endoscopy is the gold standard, its invasiveness, time-consuming nature, expense, associated risks of complications, and patients' discomfort, particularly with repeated procedures, pose significant challenges.[6,7] CTE and MRE, with comparable specificity and sensitivity in diagnosing CD and assessing activity, are suggested alternatives to endoscopy.[8,9] While MRE utilizes the magnetic resonance index of activity for assessment, its lengthy examination duration, susceptibility to abdominal breathing artifacts compromising image quality, and the need for substantial patient cooperation are notable limitations. CTE holds promise over MRE due to its shorter examination duration, superior spatial and temporal resolution, and reduced cost.[10] Nonetheless, the imaging diagnosis of both CTE and MRE is susceptible to bias from individual experience and subjective visual interpretation. Thus, a pressing need exists for a reproducible, accurate, and validated method to assess CD activity.

Radiomics, involving the high-throughput extraction of numerous advanced quantitative imaging features from medical images and subsequent analysis, elucidates the molecular biology's heterogeneity.[11,12] There are several radiomics models applied to CD, such as the prediction of activity, mucosal healing in patients treated with infliximab, and the degree of intestinal fibrosis.[13–15] These studies underscore the potential utility of radiomics in CD management.

To our knowledge, prior studies have not incorporated the Inflammatory Bowel Disease Questionnaire (IBDQ), a health-related quality of life measure, as a predictor. The IBDQ contains 32 disease-specific items, which can be used to measure the patient's feeling of the disease and the effect of treatment through the answers given by the patients, without the need for complex medical evaluation.[16] Recent treatment objectives and activity indicators in CD strive to normalize health-related quality of life and eradicate disability.[17,18]

Therefore, this study aimed to develop and validate a nomogram for assessing CD activity based on a combination of laboratory data, IBDQ, and CTE.

Materials and Methods

Study Design and Patients

This research strictly adhered to the Helsinki Declaration throughout the process, conformed to its regulatory norms, and safeguarded the rights and interests of the participates in all aspects. The study received approval from our institutional review board (Clinical Medical Research Ethics Committee of the First Affiliated Hospital of Anhui Medical University), and informed consent was obtained from all participants. We conducted a single-center, prospective cohort study using data from CD patients admitted to our hospital between July 2023 and April 2024.

The patient inclusion criteria comprised of: 1) patients with CD diagnosis confirmed following the ECCO guidelines;[19] 2) completion of the IBDQ and spectral CTE; 3) undergoing both endoscopy and spectral CTE within 3 days; 4) no prior abdominal surgery preceding CTE examination. The exclusion criteria included: 1) undergoing routine CTE examination; 2) inadequate bowel preparation and suboptimal CTE image quality; 3) presence of jejunal lesions; 4) coexisting conditions such as inflammation, tumors or liver cirrhosis (Figure 1).

Disease status in all CD patients was classified as either remission or active based on the Simplified Endoscopic Score for Crohn's disease (SES-CD) criteria using endoscopy examination.[20] Among the 107 CD patients, 46 were in remission and 61 were active. Of the patients, 79 were male and 28 were female.

Data Acquisition and Evaluation

Figure 2 shows the workflow of radiomics. Prior to the CTE scan, patients underwent standardized bowel preparation, which included a 12-hour fast and the administration of 500mL of isotonic solution at 45, 30, and 15 minutes before the scan. Ten minutes before scanning, patients received a 20mg intravenous infusion of raceanisodamine hydrochloride solution to minimize artifacts resulting from gastrointestinal peristalsis. Iodinated contrast medium (320 mg/mL, 1.5mL/kg) was injected into the antecubital vein using a high-pressure syringe at a rate of 3.0mL/s. All CTE examinations were conducted using Revolution CT or Optima CT 680 (GE Healthcare) with the following dual-energy spectral scanning

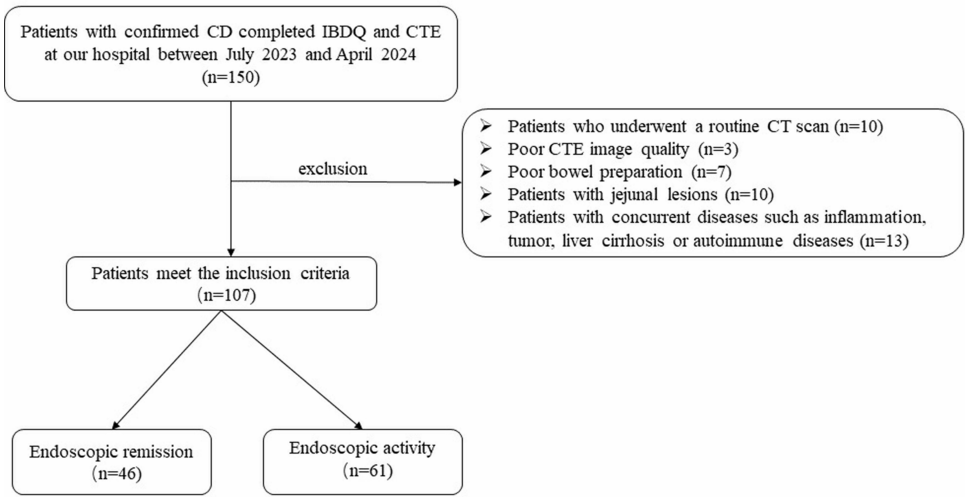

Figure 1 Flow chart of the patient cohort inclusion.

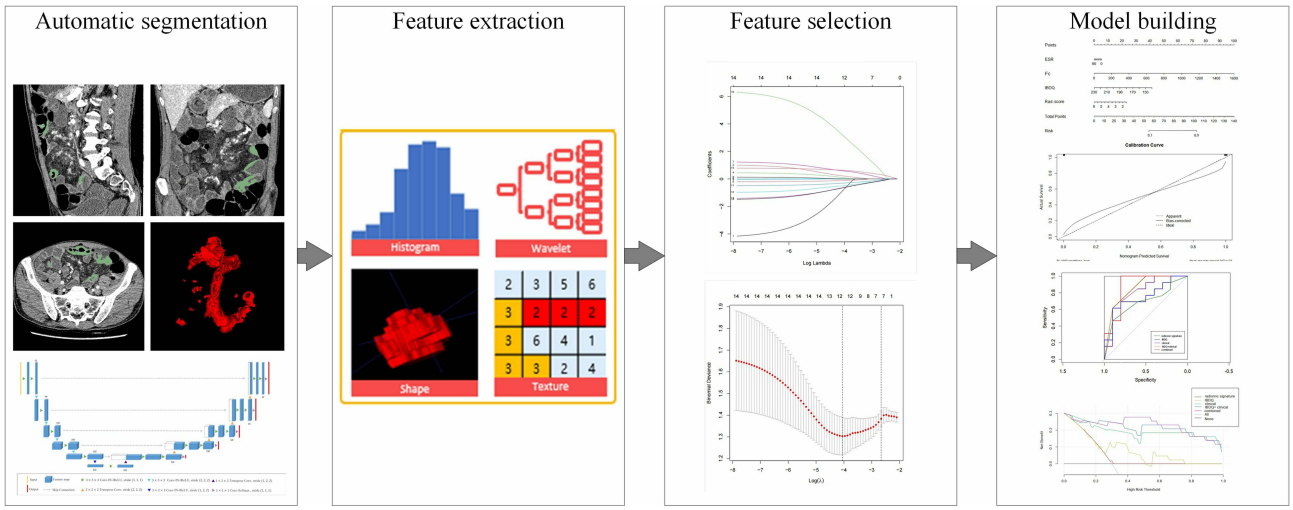

Figure 2 Radiomics workflow implemented in this study.

parameters: fast tube voltage switching between 80 and 140 KVP, tube current ranging from 150 to 300 mA, matrix of 512 × 512, detector collimation of 64×0.625, slice thickness of 5 mm, and slice spacing of 5 mm. Scans were obtained at 45 seconds post-contrast injection for the intestinal phase, and at 70 seconds for the venous phase.

CD activity was assessed based on the following CTE parameters: 1) mural hyperenhancement; 2) mural stratification; 3) mesenteric hypervascularity; 4) mesenteric fibrofatty proliferation; 5) increased fat density; 6) bowel fistula; 7) bowel stricture; 8) enlarged mesenteric lymph nodes. Their presence or absence was assessed by 2 experienced radiologists according to previously reported established criteria.[21]

Clinical parameters collected in this study included IBDQ, multiple continuous variables (age, disease duration, C-reactive protein-CRP, erythrocyte sedimentation rate-ESR, hemoglobin-Hb, albumin-Alb, platelet-PLT, fecal calprotectin-FC), and two binary variables (sex, perianal lesions).

Endoscopy was conducted by two experienced gastroenterologists. Patients underwent bowel cleansing the night before the examination, receiving 3000 to 4000 mL of complex polyethylene glycol and electrolyte solution. The two physicians independently scored all acquired endoscopic images according to SES-CD criteria and then averaged the scores.[20] Endoscopic remission was defined as a score of 0–2, while a score of 3–56 indicated endoscopic activity (Supplement 1).

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Image Preprocessing and Lesion Semi-Automatic Segmentation

The nnU-Net, a biomedical segmentation model based on deep learning, demonstrated excellent performance in our previous research.[22,23] In the previous study, only CD patients in the active stage (SES-CD > 2) were chosen for automatic segmentation.[22] According to previous research, this study selected the venous phase monochromatic images at 50 keV, with window level and width set at 40 hounsfield units (Hu) and 400 hu, respectively. The nnU-Net was employed for full 3D segmentation of CD lesions, followed by manual adjustment (Supplement 2). The nnU-Net code is accessible at https://github.com/MIC-DKFZ/nnUNet.

Image Normalization and Radiomic Feature Extraction

First, PyRadiomics software (version 3.0.1; https://pypi.org/project/pyradiomics/) was used for the 3D region-of-interest feature extraction. All images underwent resampling to achieve a voxel size of 1 × 1×1 mm^3. A total of 1168 radiomics features, including shape features, first-order statistical features, and texture features, were extracted. The z-score method was employed for feature standardization.

Model Building

The collected imaging data were randomly divided into a training set (n = 84) and a validation set (n = 23) at a ratio of 8:2. Feature selection and nomogram construction were conducted using R statistical software (version 4.3.3). Initially, the maximum correlation and minimum redundancy (mRMR) algorithm was employed to eliminate irrelevant and redundant features, retaining those with high correlation and low redundancy.

Subsequently, the least absolute shrinkage and selection operator (LASSO) regression analysis method was applied to select the most predictive features from the remaining set. Finally, radiomic scores (rad-scores) were computed based on the selected features, and the corresponding LASSO coefficient-weighted rad-score for each patient was calculated through linear combination. The area under the receiver operating characteristic (ROC) curve (AUC) in both the training and validation sets was utilized to demonstrate the accuracy of rad-score classification.

Clinical and CTE parameters underwent assessment using chi-square tests (for binary variables) and Wilcoxon tests (for continuous variables). Univariate logistic analysis was conducted to identify characteristics with $P < 0.05$ and determine risk factors for CD lesion activity. Multivariate logistic regression was further employed to analyze independent risk factors, IBDQ and rad-scores, and to finally establish a predictive nomogram.

Nomogram Evaluation and Validation

The classification performance of the nomogram was evaluated separately on the training set and the validation set.

Calibration curves were used to assess the goodness of fit of the nomogram. AUC was utilized to quantify the classification performance of the nomogram. The Delong test was employed to evaluate the model performance in AUC across different models: radiomic signature, IBDQ, clinical, IBDQ + clinical, and combined. Net Reclassification improvement (NRI) and Integrated discrimination improvement (IDI) were employed to evaluate and quantify the gains of the new model in risk prediction by comparing the performance of the above models.[24]

Decision curve analysis (DCA) is a method used to plot decision curves based on threshold probability. It is employed to assess the robustness of the nomogram for clinical practice.

Statistical Analysis

Either an independent *t*-test or Wilcoxon test was employed to analyze continuous variables. The chi-square test or Fisher's test was used to analyze binary variables. Univariate and multivariate analyses were conducted to assess the relationship between clinical and CTE parameters and the activity of CD lesions. Statistical analysis was performed using R statistical software (version 4.3.3; https://www.Rproject.org). $P < 0.05$ was considered statistically significant.

Results

Demographic Characteristics

A total of 107 patients were included in the study. The training set (n = 84) comprised 61 males and 23 females, with a mean age of 32 years (range: 24–41 years). Endoscopic remission was observed in 36 cases, while activity was observed in 48 cases. The validation set (n = 23) consisted of 18 males and 5 females, with an average age of 34 years (range: 24–47 years). Ten patients achieved endoscopic remission, while 13 patients exhibited activity.

Clinical and CTE Parameters Features

Table 1 displays the clinical and CTE parameters of the 107 patients. Univariate analysis of clinical and CTE parameters ($P < 0.05$) identified the following as risk factors for active CD: CPR, ESR, Hb, Alb, FC, mural stratification, and mesenteric hypervascularity (Table 2).

Table 1 Clinical and CTE Parameters Features of the Classification Cohort

Features		Training Set	Validation Set	*P* value
Gender				0.585
	Male	61	18	
	Female	23	5	
Age, y		32 (24–41)	34 (24–47)	0.906
Disease duration, mo		28 (12–48)	12 (4–36)	0.197
CRP, mg/L		6.36 (1.31–13.00)	4.14 (1.07–10.55)	0.353
ESR, mm/h		14.00 (7.50–23.00)	10.00 (14.00–18.00)	0.857
Hb, g/L		127.00 (115.00–143.25)	106.00 (127.00–140.00)	0.657
Alb, g/L		40.88±5.02	41.04±4.41	0.893
PLT, $\times 10^9$/L		243.88±74.03	272.96±83.46	0.129
FC, ug/g		357.05 (87.99–788.79)	357.05 (121.60–594.46)	0.958
Perianal lesions				0.896
	–	56	15	
	+	28	8	
Mural hyperenhancement				1.000
	–	6	2	
	+	78	21	
Mural stratification				0.368
	–	28	10	
	+	56	13	
Mesenteric hypervascularity				0.391
	–	39	13	
	+	45	10	
Mesenteric fibrofatty proliferation				0.861
	–	60	16	
	+	24	7	
Increased fat density				0.861
	–	60	16	
	+	24	7	
Bowel fistula				0.953
	–	74	21	
	+	10	2	
Bowel stricture				0.773
	–	61	16	
	+	23	7	

(*Continued*)

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Table 1 (Continued).

Features		Training Set	Validation Set	*P* value
Enlarged mesenteric lymph nodes				0.488
	–	23	8	
	+	61	15	
IBDQ		181.61±24.98	189.96±19.68	0.167
Activity				0.957
	Endoscopic remission	36	10	
	Endoscopic activity	48	13	

Notes: Values are n, mean ± SD, median (interquartile range).
Abbreviations: CRP, C reactive protein; ESR, Erythrocyte sedimentation rate; Hb, Hemoglobin; Alb, Albumin; PLT, Platelet; FC, Fecal calprotectin; IBDQ, Inflammatory Bowel disease Questionnaire.

Table 2 Positive Results of Univariate& Multivariate Logistic Regression Analysis for Activity in CD

Features	Univariate		*P* value	Multivariate		*P* value
	OR	95% CI		OR	95% CI	
Gender	1.591	0.588–4.303	0.360			
Age	1.014	0.978–1.050	0.451			
Disease duration, mo	1.002	0.988–1.015	0.810			
CRP	1.094	1.025–1.167	0.007	0.997	0.781–1.273	0.983
ESR	1.131	1.056–1.211	<0.001	1.208	0.945–1.544	0.031
Hb	0.942	0.912–0.973	<0.001	0.989	0.808–1.211	0.918
Alb	0.760	0.665–0.869	<0.001	0.621	0.335–1.152	0.131
PLT	1.006	0.999–1.012	0.092			
FC	1.015	1.008–1.022	<0.001	1.019	1.003–1.035	0.023
Perianal lesions	1.000	0.400–2.501	1.000			
Mural hyperenhancement	0.647	0.112–3.744	0.627			
Mural stratification	3.800	1.462–9.875	0.006	19.059	0.100–3621.984	0.271
Mesenteric hypervascularity	5.519	2.148–14.180	<0.001	2.387	0.026–220.268	0.706
Mesenteric fibrofatty proliferation	1.750	0.651–4.704	0.267			
Increased fat density	1.750	0.651–4.704	0.267			
Bowel fistula	1.143	0.297–4.392	0.846			
Bowel stricture	0.466	0.176–1.233	0.124			
Enlarged mesenteric lymph nodes	1.682	0.640–4.419	0.292			
IBDQ				0.941	0.853–1.037	0.028
Rad-score				10.254	0.337–312.156	0.018

Abbreviations: CRP, C reactive protein; ESR, Erythrocyte sedimentation rate; Hb, Hemoglobin; Alb, Albumin; PLT, Platelet; FC, Fecal calprotectin; IBDQ, Inflammatory Bowel disease Questionnaire, CI, confidence interval, OR, odd ratio.

Radiomic Feature Selection, and Rad-Score Establishment

The mRMR algorithm analysis retained 30 features characterized by high correlation and low redundancy.

The LASSO logistic regression model selected 12 relevant features with the highest predictive power in the training set, as shown in Figure 3a and b. Additionally, rad-scores were computed for each patient and utilized for predicting CD activity (Supplement 3).

Nomogram Establishment, Evaluation, and Validation

Multivariate logistic regression analysis revealed that ESR, FC, IBDQ, and rad-scores were independent indicators for active CD, as depicted in Table 2. These factors were integrated to develop a combined model, as illustrated in Figure 4a.

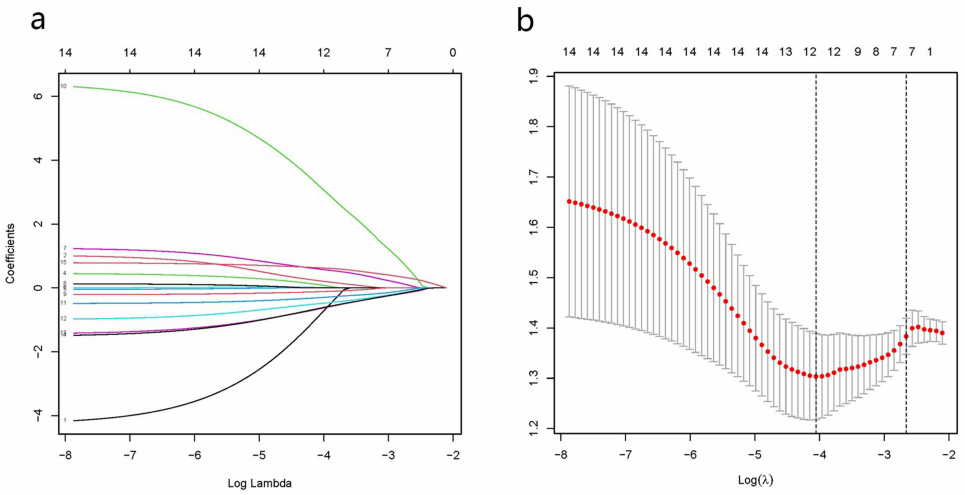

Figure 3 Selection of textural features to subject to the least absolute shrinkage selection operator logistic regression. (**a**) The coefficients are plotted versus ln(λ), displaying features with non-zero coefficients. (**b**) The tuning parameter (λ) in the LASSO model is chosen via 10-fold cross-validation following the minimum criterion. The binomial deviances from the LASSO regression cross-validation model are plotted as a function of ln(λ). The y-axis presents binomial deviances, and the x-axis presents ln(λ). The numbers above the x-axis denote the average number of predictors. Red dots signify the average deviance values of each model for a given λ, and the vertical bars through the red dots represent the deviance range. The vertical black lines mark the optimal λ values where the model fits the data best.

The combined model demonstrated excellent differentiation performance in both the training set (AUC 0.969) and the validation set (AUC 0.877). The calibration curve depicted in Figure 4b illustrates the good fit of the combined model.

DCA of the combined model is presented in Figure 5. Within threshold probabilities ranging from 0.1 to 0.9, the combined model outperformed the other four models.

Performance Comparison Between Models

Figure 6 displays the results of the ROC analyses. The combined model exhibited the highest AUC in both the training set (AUC 0.969) and the validation set (AUC 0.877). The combined model demonstrated strong predictive ability in distinguishing CD activity. As depicted in Table 3, the accuracy, sensitivity, and specificity of the combined model in the training set was 0.91, 0.94, and 0.86, respectively, while in the validation set, the accuracy, sensitivity, and specificity was 0.70, 0.62, and 0.80, respectively.

The discrimination performance of the combined model (AUC 0.877) was marginally superior to that of the IBDQ + clinical model (AUC 0.854). As indicated in Table 4, there was no significant difference in AUC between the two models in the validation set ($P = 0.206$). The IBDQ + clinical model was superior to the clinical model (AUC 0.808), and there was no significant difference in AUC between the two models in the validation set ($P = 0.376$). The clinical model outperformed the IBDQ model (AUC 0.746), although there was no significant difference in AUC between the two models in the validation set ($P = 0.677$). The IBDQ model was superior to the radiomic signature (AUC 0.688), and there was no significant difference in AUC between the two models in the validation set ($P = 0.170$). On the other hand, the clinical model, IBDQ + clinical model, and combined model significantly outperformed the radiomic signature in the validation set (radiomic signature vs clinical model, $P = 0.026$; radiomic signature vs IBDQ + clinical model, $P = 0.011$; radiomic signature vs combined model, $P = 0.008$). The NRI values were 1.192 (95% CI 0.707–1.678), 1.646 (95% CI 1.226–2.067) and 1.723 (95% CI 1.324–2.122), respectively, all $P < 0.001$. The IDI values were 0.593 (95% CI 0.382–0.805), 0.793 (95% CI 0.611–0.975) and 0.814 (95% CI 0.632–0.997), respectively, all $P < 0.001$.

Discussion

This study compared five models for assessing CD activity. The combined model demonstrated the highest performance in both the training and validation sets. In addition, the IBDQ + clinical model outperformed all individual models. The clinical model surpassed both the IBDQ model and radiomic signature. Lastly, the IBDQ model outperformed the

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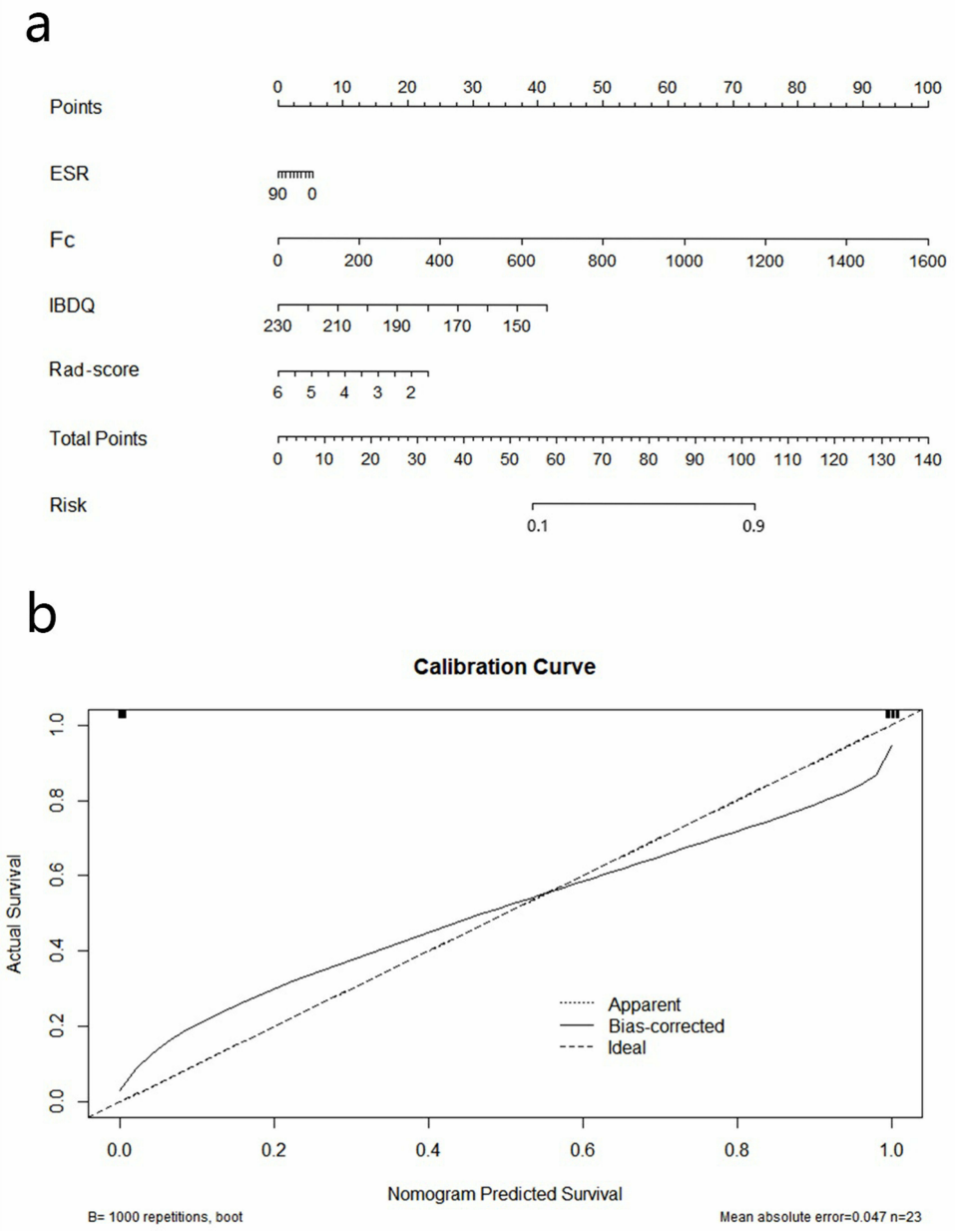

Figure 4 Nomogram for predicting activity of Crohn's disease (**a**). Calibration curves of the nomogram in the validation set (**b**).

radiomic signature. The combined model, integrating laboratory data, IBDQ, and CTE, effectively and reliably distinguished active endoscopic CD from remission endoscopic CD.

Radiomics and deep learning are revolutionizing various aspects of radiology. Currently, the primary applications in CD include automatic detection and segmentation of typical lesions, evaluation of activity, and detection of enteral and parenteral complications, stratified based on patient severity.[25] Previous studies have primarily relied on manual segmentation of CD lesions, which is not only time-consuming and laborious but also results in incomplete biological information, as typically only the representative part of the lesion is segmented. In this study, applying a deep learning automatic segmentation nnU-Net model based on dual-energy spectral CTE resulted in obtaining more comprehensive biological information, as it accurately identified and segmented all lesions in CD patients. Recognizing the promise of radiomics as a tool, we constructed radiomic signature based on the 50keV spectral CTE of 107 CD patients to extract numerous quantitative features for assessing disease activity. However, the AUC value in the validation set for the single

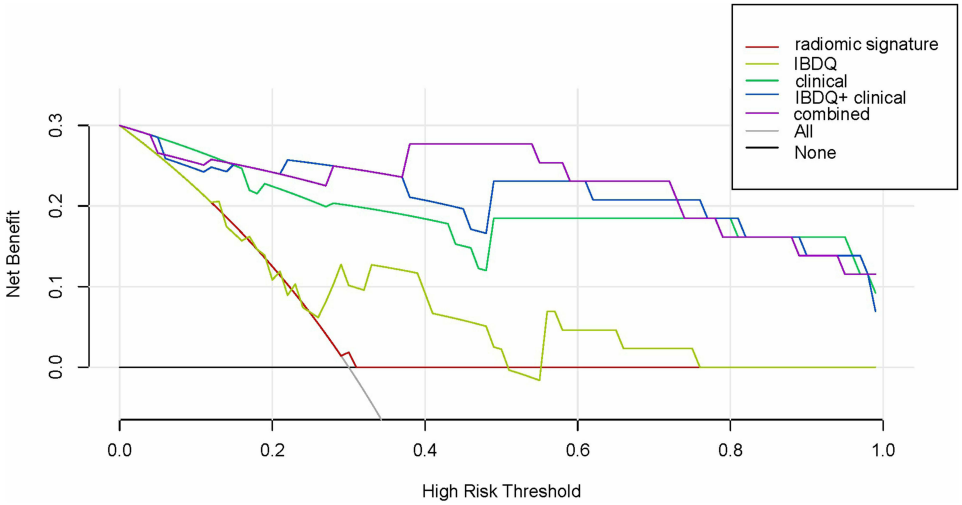

Figure 5 Decision curve analysis for the models.

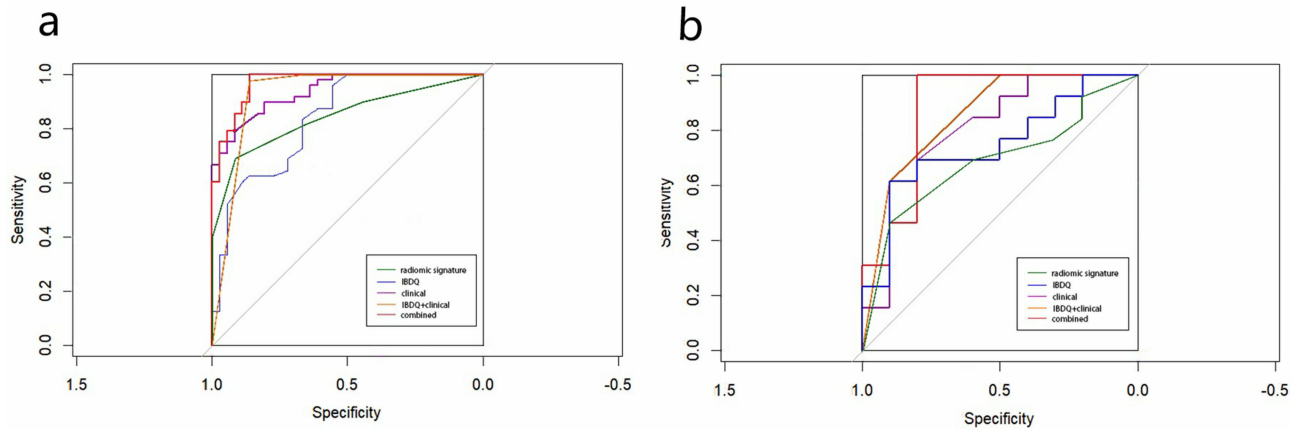

Figure 6 Models performance of 107 cases in the training set (**a**) and validation set (**b**), respectively.

radiomics signature was only 0.688. There may be two primary reasons for this outcome. Firstly, the limited data size and single-center sourcing, may have contributed. Secondly, despite manual adjustments to the nnU-Net model's segmentation, errors may persist.

Table 3 Results of Models Predictive Ability for Distinguishing CD Activity

		AUC (95% CI)	Accuracy	Sensitivity	Specificity	PPV	NPV
radiomic signature	Train	0.844 (0.763–0.926)	0.786	0.688	0.917	0.917	0.688
	Test	0.688 (0.468–0.909)	0.652	0.692	0.600	0.692	0.600
IBDQ	Train	0.838 (0.752–0.925)	0.762	0.854	0.639	0.759	0.767
	Test	0.746 (0.536–0.956)	0.739	0.615	0.900	0.889	0.643
clinical	Train	0.938 (0.893–0.984)	0.833	0.854	0.806	0.854	0.806
	Test	0.808 (0.615–1.000)	0.696	0.846	0.500	0.688	0.714
IBDQ + clinical	Train	0.927 (0.869–0.986)	0.929	0.979	0.861	0.904	0.969
	Test	0.854 (0.704–1.000)	0.739	0.615	0.900	0.889	0.643
combined	Train	0.969 (0.938–1.000)	0.905	0.938	0.861	0.900	0.912
	Test	0.877 (0.707–1.000)	0.696	0.615	0.800	0.800	0.615

Abbreviations: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

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Table 4 Delong Test Comparison Between Models of AUCs in the Validation Set

	P value				
	Radiomic Signature	**IBDQ**	**Clinical**	**IBDQ + Clinical**	**Combined**
Radiomic signature		0.170	0.026	0.011	0.008
IBDQ	0.170		0.677	0.165	0.681
Clinical	0.026	0.677		0.376	0.835
IBDQ + clinical	0.011	0.165	0.376		0.206
Combined	0.008	0.681	0.835	0.206	

The Selecting Therapeutic Targets in Inflammatory Bowel Disease initiative (STRIDE-II) outlines that the primary treatment goals for patients with inflammatory bowel disease (IBD) are to sustain long-term health-related quality of life by attaining clinical response and remission, endoscopic healing, and normalization of CRP, ESR, and FC levels.[26] The objective of patient-reported outcome (PRO) measures, such as questionnaires like the IBDQ, is to ultimately enhance the quality of life of IBD patients post-treatment, aiming for a quality of life comparable to that before the onset of illness. Consequently, the treatment objective of STRIDE II is to achieve favorable PROs, with a primary focus on enhancing quality of life. In our study, the freely available IBDQ was utilized as a predictor to formulate a model for assessing endoscopic activity. In the validation set, the AUC of the single IBDQ model was 0.746, surpassing that of the single radiomic signature, rendering it a natural, reliable, and scientifically supported predictor.

This study identified noninvasive biomarkers, ESR and FC, as the significant factors associated with the endoscopic activity of CD through feature selection. ESR stands out as a reliable indicator of systemic inflammatory response. ALPERA et al demonstrated that while ESR, as a dichotomous variable, closely correlated with the clinical, endoscopic, and histological activity of CD patients, its continuous counterpart was solely linked to endoscopic and histological activity.[27] ESR was incorporated as a continuous variable to discern endoscopic activity. Recently, FC has emerged as an ideal non-invasive biomarker for assessing CD disease activity.[28] Previous studies have consistently demonstrated FC's ability to effectively differentiate between patients in remission and active stages, highlighting its high patient acceptance and operational convenience.[28–30] Hence, this study developed a clinical model based on ESR and FC predictors, yielding an AUC of 0.808 in the validation set, surpassing that of the single IBDQ model. Nonetheless, ESR and FC also pose drawbacks. Firstly, ESR is contingent upon plasma concentration and red blood cell count and volume, rendering it susceptible to influences such as smoking, age, and medications. Secondly, the FC evaluation value is influenced by the location of CD lesions, with relatively lower accuracy observed in small intestinal lesions.[31] False positive FC values may arise in patients with inflammatory polyps within 3 months post-surgery, within 2 weeks post-colonoscopy, and in those using nonsteroidal anti-inflammatory drugs or proton-pump inhibitors.[32]

Our study is the first to explore the integration of the dependable IBDQ with laboratory data as predictors to develop an IBDQ + clinical model for assessing CD activity. Notably, the AUC of the IBDQ + clinical model in the validation set reached 0.854, surpassing that of any individual model. Consequently, our study proceeded to develop a combined model integrating free IBDQ, non-invasive laboratory data, and CTE. Our study marks the inaugural use of IBDQ as a predictor in a nomogram for assessing CD activity. Ultimately, the combined model exhibited an AUC of 0.877 in the validation set, marginally surpassing that of the IBDQ + clinical model. However, the difference in AUC between the two models lacked statistical significance. The findings suggested that the IBDQ + clinical model could serve as a viable alternative to the combined model in cases where CTE examination is not available.

Limitations

Our study has some limitations. Firstly, the study suffered from a small sample size with the validation set originated from a same center. Secondly, the study's categorization of CD into solely active and remission stages lacked further granularity, a limitation attributed to the small sample size and the highly uneven distribution across mild, moderate, and

severe active stages, potentially introducing calculation bias. Future investigations, encompassing multiple centers and larger sample sizes, are imperative to delineate more refined classifications within the active stage. Thirdly, segmenting lesions through a combination of deep learning segmentation models and manual adjustments, albeit prone to errors, might impacts radiomic feature extraction, radiomic signature and nomogram performance. In subsequent research, efforts will focus on refining an automatic segmentation model covering the entire intestine, encompassing all intestinal wall lesions.

Conclusion

In conclusion, our study utilized semi-automatic segmentation method to extract radiomic features for establishing and validating a nomogram based on laboratory data, IBDQ, and CTE. The nomogram is capable of effectively discerning active and remissive CD states to serve as a straightforward, accurate, and dependable method for assessing disease severity in CD patients.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Torres J, Bonovas S, Doherty G, et al. ECCO Guidelines on Therapeutics in Crohn's Disease: medical Treatment. *J Crohns Colitis*. 2020;14(1):4–22. doi:10.1093/ecco-jcc/jjz180
2. Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. *LANCET*. 2017;389(10080):1741–1755. doi:10.1016/S0140-6736(16)31711-1
3. van der Valk ME, Mangen MJ, Leenders M, et al. Risk factors of work disability in patients with inflammatory bowel disease--a Dutch nationwide web-based survey: work disability in inflammatory bowel disease. *J CROHNS COLITIS*. 2014;8(7):590–597. doi:10.1016/j.crohns.2013.11.019
4. Magro F, Magalhaes D, Patita M, et al. Subclinical Persistent Inflammation as Risk Factor for Crohn's Disease Progression: findings From a Prospective Real-World Study of 2 Years. *CLIN GASTROENTEROL H*. 2022;20(9):2059–2073. doi:10.1016/j.cgh.2021.12.004
5. El OS, Baker ME, Lyu R, et al. Validation of stricture length, duration and obstructive symptoms as predictors for intervention in ileal stricturing Crohn's disease. *UNITED EUR GASTROENT*. 2022;10(9):958–972. doi:10.1002/ueg2.12314
6. Flynn S, Eisenstein S. Inflammatory Bowel Disease Presentation and Diagnosis. *SURG CLIN N AM*. 2019;99(6):1051–1062. doi:10.1016/j.suc.2019.08.001
7. Buisson A, Gonzalez F, Poullenot F, et al. Comparative Acceptability and Perceived Clinical Utility of Monitoring Tools: a Nationwide Survey of Patients with Inflammatory Bowel Disease. *INFLAMM BOWEL DIS*. 2017;23(8):1425–1433. doi:10.1097/MIB.0000000000001140
8. Ma L, Shen X, Chen YJ, Zhang Q, Li B, Zhang W. Computed tomography enterography for crohn's disease: correlation between the imaging findings and histopathologic scoring system. *ABDOM RADIOL*. 2021;46(9):4121–4129. doi:10.1007/s00261-021-03112-w
9. Yu H, Wang Y, Wang Z, Li J, Lu J, Hu D. Prospective comparison of diffusion-weighted magnetic resonance enterography and contrast enhanced computed tomography enterography for the detection of ileocolonic Crohn's disease. *J GASTROEN HEPATOL*. 2020;35(7):1136–1142. doi:10.1111/jgh.14945
10. Del GA, Fletcher JG, Yu L, et al. Reducing radiation dose in CT enterography. *RADIOGRAPHICS*. 2013;33(4):1109–1124. doi:10.1148/rg.334125074
11. Gillies RJ, Kinahan PE, Hricak H. Radiomics: images Are More than Pictures, They Are Data. *RADIOLOGY*. 2016;278(2):563–577. doi:10.1148/radiol.2015151169
12. Kumar V, Gu Y, Basu S, et al. Radiomics: the process and the challenges. *MAGN RESON IMAGING*. 2012;30(9):1234–1248. doi:10.1016/j.mri.2012.06.010
13. Zhu C, Hu J, Wang X, et al. A novel clinical radiomics nomogram at baseline to predict mucosal healing in Crohn's disease patients treated with infliximab. *EUR RADIOL*. 2022;32(10):6628–6636. doi:10.1007/s00330-022-08989-9
14. Ruiqing L, Jing Y, Shunli L, et al. A Novel Radiomics Model Integrating Luminal and Mesenteric Features to Predict Mucosal Activity and Surgery Risk in Crohn's Disease Patients: a Multicenter Study. *ACAD RADIOL*. 2023;30(1):S207–S219. doi:10.1016/j.acra.2023.03.023
15. Meng J, Luo Z, Chen Z, et al. Intestinal fibrosis classification in patients with Crohn's disease using CT enterography-based deep learning: comparisons with radiomics and radiologists. *EUR RADIOL*. 2022;32(12):8692–8705. doi:10.1007/s00330-022-08842-z
16. Guyatt G, Mitchell A, Irvine EJ, et al. A new measure of health status for clinical trials in inflammatory bowel disease. *GASTROENTEROLOGY*. 1989;96(3):804–810. doi:10.1016/0016-5085(89)90905-0
17. Kishi M, Hirai F, Takatsu N, et al. A review on the current status and definitions of activity indices in inflammatory bowel disease: how to use indices for precise evaluation. *J GASTROENTEROL*. 2022;57(4):246–266. doi:10.1007/s00535-022-01862-y
18. Gavrilescu O, CC P, Dranga M, IV P, Mihai C. Impact of COVID-19 Pandemic on the Quality of Life of IBD Patients. *MEDICINA*. 2022;58(5):562.
19. Maaser C, Sturm A, Vavricka SR, et al. ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: initial diagnosis, monitoring of known IBD, detection of complications. *J CROHNS COLITIS*. 2019;13(2):144–164. doi:10.1093/ecco-jcc/jjy113
20. Daperno M, D'Haens G, Van Assche G, et al. Development and validation of a new, simplified endoscopic activity score for Crohn's disease: the SES-CD. *GASTROINTEST ENDOSC*. 2004;60(4):505–512. doi:10.1016/S0016-5107(04)01878-4

21. Sakurai T, Katsuno T, Saito K, et al. Mesenteric findings of CT enterography are well correlated with the endoscopic severity of Crohn's disease. *EUR J RADIOL*. 2017;89:242–248. doi:10.1016/j.ejrad.2016.10.022
22. Gao Y, Zhang B, Zhao D, et al. Automatic Segmentation and Radiomics for Identification and Activity Assessment of CTE Lesions in Crohn's Disease. *INFLAMM BOWEL DIS*. 2023;30:1957–1964.
23. Isensee F, Jaeger PF, Kohl S, Petersen J, Maier-Hein KH. nnU-Net: a self-configuring method for deep learning-based biomedical image segmentation. *NAT METHODS*. 2021;18(2):203–211. doi:10.1038/s41592-020-01008-z
24. Pencina MJ, D'Agostino RS, D'Agostino RJ, Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. *STAT MED*. 2008;27(2):157–172,207–212. doi:10.1002/sim.2929
25. Kilcoyne A, Kaplan JL, Gee MS. Inflammatory bowel disease imaging: current practice and future directions. *World J Gastroenterol*. 2016;22 (3):917–932. doi:10.3748/wjg.v22.i3.917
26. Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: an Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): determining Therapeutic Goals for Treat-to-Target strategies in IBD. *GASTROENTEROLOGY*. 2021;160(5):1570–1583. doi:10.1053/j.gastro.2020.12.031
27. Alper A, Zhang L, Pashankar DS. Correlation of Erythrocyte Sedimentation Rate and C-Reactive Protein With Pediatric Inflammatory Bowel Disease Activity. *J PEDIATR GASTR NUTR*. 2017;65(2):e25–e27. doi:10.1097/MPG.0000000000001444
28. Khaki-Khatibi F, Qujeq D, Kashifard M, Moein S, Maniati M, Vaghari-Tabari M. Calprotectin in inflammatory bowel disease. *CLIN CHIM ACTA*. 2020;510:556–565. doi:10.1016/j.cca.2020.08.025
29. Li J, Xu M, Qian W, et al. Clinical value of fecal calprotectin for evaluating disease activity in patients with Crohn's disease. *FRONT PHYSIOL*. 2023;14:1186665. doi:10.3389/fphys.2023.1186665
30. Lin JF, Chen JM, Zuo JH, et al. Meta-analysis: fecal calprotectin for assessment of inflammatory bowel disease activity. *INFLAMM BOWEL DIS*. 2014;20(8):1407–1415. doi:10.1097/MIB.0000000000000057
31. Sakurai T, Saruta M. Positioning and Usefulness of Biomarkers in Inflammatory Bowel Disease. *DIGESTION*. 2023;104(1):30–41. doi:10.1159/000527846
32. Singh S, Ananthakrishnan AN, Nguyen NH, et al. AGA Clinical Practice Guideline on the Role of Biomarkers for the Management of Ulcerative Colitis. *GASTROENTEROLOGY*. 2023;164(3):344–372. doi:10.1053/j.gastro.2022.12.007