Original Article

Development and nomogram prediction of early postoperative recurrence in hepatocellular carcinoma based on preoperative CT imaging radiomic features and serum features related to microvascular infiltration

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Background: Hepatocellular carcinoma (HCC) is characterized by high postoperative recurrence rates, and predicting early recurrence is crucial for improving clinical outcomes, yet remains challenging. Both preoperative computed tomography (CT) imaging radiomic features and serum biomarkers related to microvascular infiltration are important indicators of HCC prognosis. This study aimed to develop a nomogram model incorporating both preoperative CT radiomic features and serum biomarkers associated with microvascular infiltration to predict early postoperative recurrence in HCC patients.

Methods: The study included 156 HCC patients who underwent radical surgery at the Tumor Hospital Affiliated to Nantong University between January 2021 and January 2022. Preoperative CT imaging data were obtained for each patient, and radiomic features were extracted using the 3D Slicer software. Preoperative serum biomarkers related to microvascular invasion were collected, including alpha-fetoprotein (AFP), vascular endothelial growth factor A (VEGF-A), Speckled Protein 100 (SP100), and the Fibrosis-4 (FIB-4) index levels. Postoperative follow-up was conducted for 2 years, during which recurrence data were collected. The radiomics score was generated through dimensionality reduction and least absolute shrinkage and selection operator (LASSO) regression analysis. Univariate and logistic regression analyses were used to identify independent risk factors for early postoperative recurrence of HCC. The nomogram model was constructed using R language, and its predictive performance was evaluated using receiver operating characteristic curves, calibration curves, and decision curve analysis curves.

Results: Among the 156 patients, 60 experienced early recurrence, while 96 did not. Feature reduction through LASSO regression identified 10 optimal features from the venous phase and 4 optimal features from the arterial phase, leading to the development of a radiomics score formula. The early recurrence group had significantly higher radiomics scores than the non-early recurrence group [–1.35 (–2.29, 1.21) *vs.* 0.94 (–0.40, 1.87), P<0.001]. Logistic multivariate regression analysis identified lesion number, Edmondson grade, AFP and VEGF-A levels, and radiomics score as independent risk factors for early postoperative recurrence of HCC (P<0.05). The nomogram model demonstrated high predictive performance with area under the curve (AUC) values of 0.9265 and 0.9255 in the training and internal test sets, respectively. The model demonstrated good net benefit across a threshold range of 0.01–75%, effectively identifying high-risk patients for early postoperative recurrence.

Conclusions: The nomogram model based on preoperative serum biomarkers related to microvascular infiltration and CT radiomic features demonstrated high predictive performance for early postoperative recurrence of HCC. However, further studies, including external validation, are needed to establish the model's generalizability and clinical applicability.

Keywords: Computed tomography (CT); radiomics; microvascular infiltration; serum characteristics; hepatocellular carcinoma (HCC)

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Introduction

Hepatocellular carcinoma (HCC) is the sixth most common malignant tumor worldwide, and the fourth most common cancer in China, and thus poses a severe threat to the health and lives of the Chinese population (1,2). Current treatment options for liver cancer include radical surgery, local therapies (e.g., radiofrequency ablation, and transarterial chemoembolization), radiotherapy, and chemotherapy (3,4). However, due to the complex histological features, high tumor heterogeneity, and diverse invasive behavior of HCC, the recurrence rate remains high post-treatment. Indeed, research has reported that the recurrence rate after radical surgery is as high as 70% (5,6). Early recurrence of liver cancer typically refers to the reappearance or metastasis of HCC within two years of treatment (7). Early recurrence as a significant risk factor for a poor prognosis in HCC patients, who have worse outcomes than those with late recurrence (8). Therefore, risk assessment, appropriate monitoring, and the treatment of patients with postoperative recurrence are crucial for improving HCC patient outcomes.

Currently, predicting HCC recurrence relies primarily on pathological data and traditional imaging, such as tumor staging, infiltration degree, and microvascular infiltration (9). Microvascular infiltration is a research hotspot in the early recurrence of HCC, and is usually confirmed through postoperative pathological examination (9-11). Preoperatively, it can only be indirectly inferred from imaging features, such as unclear tumor boundaries or infiltrative growth. Recent studies have also identified serum markers associated with microvascular infiltration, including alpha fetoprotein (AFP), vascular endothelial growth factor A (VEGF-A), Speckled Protein 100 (SP100), and the fibrosis-4 (FIB-4) index (12-14). However, these markers alone cannot directly diagnose microvascular infiltration and offer limited predictive accuracy when used in isolation.

Radiomics, a rapidly evolving field, transforms medical imaging data into high-throughput quantitative features that capture tumor heterogeneity beyond what is observable through conventional imaging (15). By integrating radiomic features derived from preoperative computed tomography

Highlight box

Key findings

- A predictive nomogram model was established that combines preoperative serum biomarkers and computed tomography radiomic features. This model was shown to effectively predict early postoperative recurrence in hepatocellular carcinoma (HCC) patients.
- The key predictive factors included Kiel 67 (Ki-67) levels, tumor diameter, alpha fetoprotein and vascular endothelial growth factor levels, the fibrosis-4 index, multifocality, abnormal enhancement around the tumor, and a specifically derived radiomics score.
- The model demonstrated excellent predictive accuracy with area under the curve values of 0.9265 and 0.9255 for the training and internal test sets, respectively.

What is known and what is new?

- Early postoperative recurrence of HCC is a major factor affecting patient survival, and traditional prognostic models have limited accuracy.
- This study introduced a novel nomogram that incorporates advanced radiomics and serum biomarkers related to microvascular infiltration, offering significant improvements in predicting early recurrence of HCC.

What is the implication, and what should change bow?

- The introduction of this nomogram that identifies patients at high risk of early recurrence into clinical practice could enable personalized surgical planning and follow-up strategies.
- Clinical guidelines may need to be updated to incorporate radiomic and biomarker analyses as standard preoperative assessments in HCC treatment protocols.

(CT) imaging, clinicians can non-invasively assess tumor biology and prognosis. However, radiomic features alone may not fully reflect the systemic and biochemical environment of the tumor, which is captured by serum markers. Therefore, combining radiomic features with serum biomarkers associated with microvascular infiltration offers a complementary approach to enhance the prediction of early recurrence.

This study addresses the limitations of existing models by developing a multidimensional predictive model that integrates preoperative CT radiomic features with serum biomarkers related to microvascular infiltration. This novel combination leverages the strengths of both modalities: radiomics provides a non-invasive, quantitative assessment of tumor heterogeneity, while serum markers reflect underlying biological processes, such as angiogenesis and tumor invasiveness. By bridging these complementary domains, the proposed model aims to improve the accuracy and clinical utility of early recurrence prediction, providing clinicians with a robust, personalized tool to guide postoperative management and improve patient outcomes. We present this article in accordance with the TRIPOD and STROBE reporting checklists (available at https://jgo.amegroups.com/article/view/10.21037/jgo-2024-914/rc).

Methods

Research subjects

This study was a single-center, retrospective analysis. A total of 156 HCC patients who were hospitalized and underwent radical surgery at the Tumor Hospital Affiliated to Nantong University between January 2021 and January 2022 were included in the study. The inclusion criteria for the study were: (I) have pathologically confirmed HCC; (II) have undergone preoperative CT imaging within 2 weeks prior to surgery; (III) have CT images of adequate quality; and (IV) have provided informed consent. Patients were excluded from the study if they met any of the following exclusion criteria: (I) had received preoperative HCC treatment; (II) had incomplete clinical data; and/or (III) were lost to follow-up within 2 years. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Tumor Hospital Affiliated to Nantong University (No. 2024-029), and informed consent was obtained from all the patients.

Follow-up assessment

Patients were regularly followed up by outpatient visits, and telephone calls, and reference to their medical records. Postoperative imaging included ultrasound, CT, magnetic resonance imaging, or hepatic artery angiography to detect recurrence. Early recurrence was defined as new liver lesions or metastases within 2 years after surgery, confirmed by imaging and pathology.

Clinical data collection

The following preoperative data were collected for this study: (I) basic information: gender, age, liver cirrhosis history, hepatitis history, etc.; (II) pathological data: Barcelona Clinic Liver Cancer (BCLC) stage, Kiel 67 (Ki-67), and Edmondson grade; (III) Preoperative imaging data: CT images and CT signs (e.g., tumor diameter, number of lesions, tumor location, abnormal enhancement around the tumor, and hepatosplenomegaly); and (IV) preoperative AFP, VEGF-A, SP100, FIB-4 index levels.

CT examination method

CT imaging of the upper abdomen was performed with both unenhanced and contrast-enhanced scans. The specific scanning parameters were as follows: slice thickness: 5 mm; slice spacing: 5 mm; matrix: 512×512; tube voltage: 120 kV; tube current: 210 mAs; and reconstruction slice thickness: 1.25 mm. A routine unenhanced scan was first conducted, followed by contrast injection. A Ulrich Missouri dual-channel power injector (Ulrich Medical, Germany) was used to inject iopromide (1.1 mL/kg) at a flow rate of 2.4 m/s into the antecubital vein. Subsequently, 20 mL of saline was injected at the same flow rate to flush the catheter. Scans were performed at arterial phase, venous phase, and delayed phase at 25, 60, and 120 seconds after contrast injection, respectively.

Radiomics analysis

Feature extraction

The collected CT image data were resampled and standardized for gray scale. A senior radiologist with over five years of experience in abdominal imaging manually delineated the regions of interest (ROI) along the edges of the target lesions on the CT plain, arterial, venous, and delayed phase images using the open-source software 3D

Slicer. Subsequently, the Radiomics plugin in 3D Slicer was used for feature extraction, which included: (I) first-order statistics: these provide basic information about tumor density and heterogeneity. (II) Shape features (3D): these offer geometric information about the tumor, such as maximum diameter and volume, which are crucial for assessing the tumor's growth pattern and its invasive properties. (III) Texture analysis, including the gray level co-occurrence matrix (GLCM), gray level size zone matrix (GLSZM), gray level run length matrix (GLRLM), gray level dependence matrix (GLDM), and neighboring gray tone difference matrix (NGTDM). These texture features are closely associated with the tumor's microvascular structure. Microvascular invasion often correlates with higher image texture heterogeneity, indicating a more disordered and complex tumor microenvironment.

Feature reduction and selection

After feature extraction, we used the Mann-Whitney *U* test for statistical analysis to select radiomic features significantly associated with early recurrence of HCC. We employed the Spearman rank correlation coefficient to detect correlations between features, thereby avoiding redundancy in the model. Additionally, we standardized all features to ensure they were on the same scale, facilitating comparison and analysis. Subsequently, we utilized the least absolute shrinkage and selection operator (LASSO) algorithm for feature selection and dimensionality reduction. This method helped us identify the key features that best predict early HCC recurrence from a large set of radiomic features. This process optimized our predictive model by minimizing unnecessary information, ensuring the model was both accurate and practical. Finally, based on the importance of the selected features, we calculated each patient's radiomic score using a formula (referred to as the radiomic scoring formula). This score integrates multiple imaging features, aiding physicians in assessing the risk of early postoperative recurrence in patients.

Statistical analysis

Data analysis was performed using IBM SPSS 26.0 (International Business Machines Corporation, USA) Normality was tested. Non-normally distributed continuous data are presented as [median (M25, M75)], and comparisons between groups were conducted using the Mann-Whitney rank-sum test. Categorical data are presented as n (%), and comparisons between groups were performed using the Chi-squared test. Logistic regression analysis was performed to identify independent risk factors for early postoperative recurrence. The nomogram model was developed using R language (R Foundation for Statistical Computing, Austria), and its area under the curve (AUC) value was obtained by receiver operating characteristic (ROC) curve to evaluate its performance. The threshold interpretation of AUC values was as follows: AUC (<0.6) indicates poor differentiation. AUC (0.6 to <0.7) indicates average differentiation. AUC (0.7to <0.8) indicates moderate discrimination. AUC (0.8 to <0.9) indicates good discrimination. AUC 0.9–1.0 indicates excellent discrimination. A calibration curve was generated to evaluate the goodness of fit of the model, and the consistency of the calibration curve was evaluated using Hosmer-Lemeshow test, with P>0.05 indicating a good fit. The net benefit of the model was evaluated using decision curve analysis.

Results

Comparison of clinical data between non-early recurrence and early recurrence patients

In this study, 60 patients (38.46%) experienced early recurrence, and 96 patients (61.54%) did not. The early recurrence patients had a significantly higher tumor diameter, Ki-67, AFP, and VEGF-A levels, FIB-4 index, number of lesions, and abnormal enhancement around tumors than the non-recurrence patients (P<0.05). Differences in the Edmondson grading distribution were also significant (P<0.05) (*Tables 1-3*).

Radiomic features

After the dimensionality reduction and LASSO regression, four arterial-phase and 10 venous-phase radiomic features associated with early postoperative recurrence were identified. The lambda with the smallest standard error of the distance was 0.03 (*Figure 1*). The imaging score formula corresponding to the model variables is expressed as follows:

–7.372–0.325 × V-Shape-Maximum – 3Ddiameter + 2.015 × A-Shape-Sphericity –1.421 × A-Firstorder-12Percentile – 1.587 × V-Firstorder-Kurtosis + 0.4 × V-Firstorder-Median + 0.898 × V-Firstorder-Robust Mean TAbsolute Deviation + 2.118 × V-GLCM – Difference Variance + 0.067 × A-GLCM – Inverse Variance + 5.168 × V-GLCM – Joint Energy + 1.159 × GLCM – Maximum Probability + 4.72 × V-GLSZM – Gray-Level Non

Table 1 Comparison of the baseline data of patients with non-early recurrence and early recurrence

Clinical features	Non-early relapse group (n=96)	Early relapse group (n=60)	Z/χ^2	P
Age (years)	60.00 (55.00, 65.00)	61.00 (54.75, 66.00)	–1.5191	0.13
Gender				
Male	28 (29.17)	18 (30.00)	0.0123	0.91
Female	68 (70.83)	42 (70.00)		
Cirrhosis				
No	74 (77.08)	50 (83.33)	0.8846	0.35
Yes	22 (22.92)	10 (16.67)		
History of hepatitis				
No	67 (69.79)	38 (63.33)	0.6999	0.40
Yes	29 (30.21)	22 (36.67)		
Drinking history				
No	74 (77.08)	42 (70.00)	0.9716	0.32
Yes	22 (22.92)	18 (30.00)		
BCLC staging				
0	40 (41.67)	21 (35.00)	3.624	0.16
A	54 (56.25)	34 (56.67)		
B	2 (2.08)	5 (8.33)		
Ki-67				
≤20	71 (73.96)	27 (45.00)	13.2568	<0.001
>20	25 (26.04)	33 (55.00)		
Edmondson grade				
I	73 (76.04)	7 (11.67)	61.26	<0.001
II	21 (21.88)	48 (80.00)		
III	2 (2.08)	5 (8.33)		

Data are presented as median (M25, M75) or n (%). BCLC, Barcelona Clinic Liver Cancer.

Uniformity – 0.299 × V-GLSZM – High Gray-Level Zone Emphasis + 2.702 × V-GLSZM –Small Area Emphasis – 0.897 × A-GLSZM – Small Area High Gray-Level Emphasis + 2.39 × V-GLSZM – Small Area Low Gray-Level Emphasis.

Note: V, volume-based; A, area-based; GLCM: gray-level co-occurrence matrix; GLSZM: gray-level size zone matrix.

Calculations showed that the radiomic scores of the patients without early recurrence were significantly lower than those of the patients with early recurrence [–1.35 (–2.29, 1.21) *vs.* 0.94 (–0.40, 1.87), P=0.0001].

Logistic multi-factor analysis

The logistic analysis results showed that the number of lesions, Edmondson grade, AFP and VEGF-A levels, and radiomics score were independent risk factors for early postoperative recurrence in HCC patients (P<0.05) (*Table 4*).

Nomogram model establishment

Based on the results of the logistic multivariate analysis, 156 subjects were randomly divided into a training set and an internal test set at a ratio of 8:2 using the R language rms package (R Foundation for Statistical Computing,

Table 2 Comparison of CT signs between patients with non-early recurrence and patients with early recurrence

CT signs	Non-early relapse group (n=96)	Early relapse group (n=60)	Z/χ^2	P
Tumor diameter				
≤5 cm	69 (71.88)	24 (40.00)	15.5820	<0.001
>5 cm	27 (28.12)	36 (60.00)		
Number of lesions				
Single	88 (91.67)	43 (71.67)	10.97	<0.001
Multiple	8 (8.33)	17 (28.33)		
Abnormal enhancement around the tumor				
No	87 (90.62)	34 (56.67)	24.4673	<0.001
Yes	9 (9.38)	26 (43.33)		
Tumor location				
Left lobe	38 (39.58)	23 (38.33)	0.2614	0.88
Right lobe	48 (50.00)	32 (53.33)		
Left lobe + right lobe	10 (10.42)	5 (8.33)		
Lesion morphology and margin				
Regular	57 (59.38)	26 (43.33)	3.816	0.051
Irregular	39 (40.62)	34 (56.67)		
Tumor pseudocapsule				
Yes	49 (51.04)	22 (36.67)	3.077	0.08
None	47 (48.96)	38 (63.33)		
Hepatosplenomegaly				
No	64 (66.67)	40 (66.67)	0.0000	>0.99
Yes	32 (33.33)	20 (33.33)		

Data are presented as n (%). CT, computed tomography.

Table 3 Comparison of preoperative serological characteristics related to microvascular infiltration between patients with non-early recurrence and early recurrence

Index	Non-early relapse group (n=96)	Early relapse group (n=60)	Z/χ^2	P
AFP (μg/L)	304.20 (245.14, 420.22)	417.03 (251.93, 525.42)	–2.8213	0.005
VEGF-A (pg/mL)	127.71 (95.49, 159.95)	121.35 (86.60, 152.61)	–2.5372	0.01
S100P (μg/L)	14.40 (11.78, 16.86)	14.00 (11.44, 16.60)	–1.9580	0.050
FIB-4 Index	2.06 (1.69, 2.39)	1.96 (1.64, 2.33)	–2.2713	0.02

Data are presented as median (M25, M75). AFP, alpha fetoprotein; VEGF-A, vascular endothelial growth factor A; FIB-4, fibrosis-4.

Austria), and a nomogram model for predicting the risk of early postoperative recurrence in HCC patients was constructed (*Figure 2A*). In the nomogram, "0" on the "number of lesions" axis represents a single lesion, and "1" represents multiple lesions; "0" on the "Edmondson stage" axis represents Edmondson stage I, "1" represents Edmondson stage II, and "2" represents Edmondson stage III; the "VEGF-A" axis represents the actual preoperative

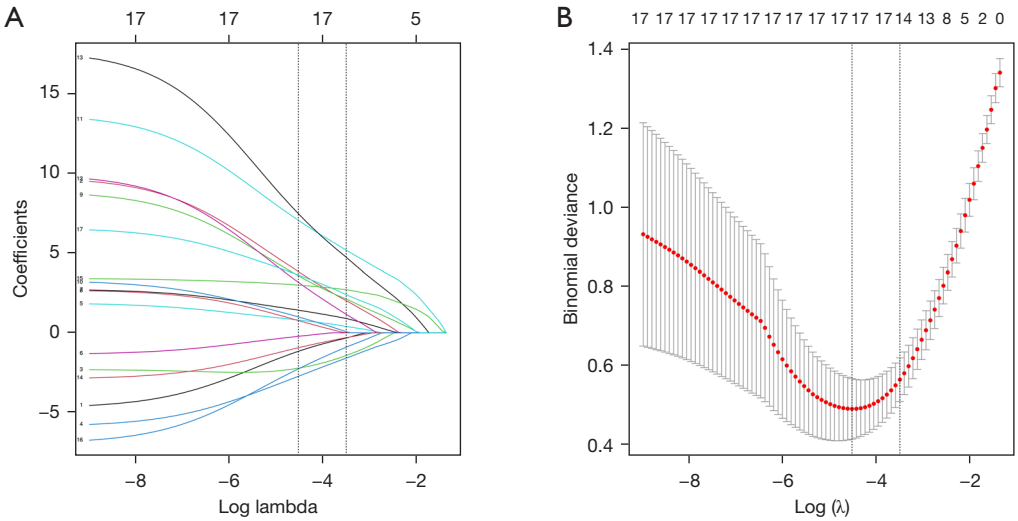

Figure 1 LASSO regression analysis. (A) LASSO regression path diagram illustrating the shrinkage of coefficients for various predictors as the penalty parameter (log lambda) increases. The vertical dashed lines represent the values of lambda that minimize the cross-validated error. (B) Cross-validation curve for LASSO regression, showing the binomial deviance plotted against the log lambda. The red dots indicate the mean deviance values for each lambda, while the error bars represent standard errors. The two vertical dashed lines denote the minimum deviance and the largest value of lambda within one standard error of the minimum. LASSO, least absolute shrinkage and selection operator.

Table 4 Logistic multivariate analysis to screen independent risk factors for early postoperative recurrence in HCC patients

Variables	β	SE	Z	P	OR (95% CI)
Intercept	–7.2647	1.7147	–4.2367	<0.001	0.0007 (0.0000–0.0202)
Number of lesions	1.5285	0.6772	2.2570	0.02	4.6111 (1.2228–17.3884)
Abnormal enhancement around the tumor	1.0073	0.6131	1.6430	0.10	2.7382 (0.8234–9.1056)
Edmondson stage	2.8924	0.6151	4.7022	<0.001	18.0362 (5.4021–60.2179)
Ki-67	0.7350	0.5139	1.4301	0.16	2.0854 (0.7616–5.7104)
Tumor diameter	0.3703	0.5346	0.6927	0.49	1.4482 (0.5079–4.1292)
AFP	0.0042	0.0021	2.0330	0.042	1.0042 (1.0001–1.0082)
VEGF-A	0.0132	0.0063	2.0833	0.04	1.0133 (1.0008–1.0259)
FIB-4	0.3872	0.4693	0.8250	0.41	1.4728 (0.5870–3.6950)
Radiomics score	0.3876	0.1232	3.1464	0.002	1.4734 (1.1574–1.8757)

HCC, hepatocellular carcinoma; SE, standard error; OR, odds ratio; CI, confidence interval; AFP, alpha fetoprotein; VEGF-A, vascular endothelial growth factor A; FIB-4, fibrosis-4.

VEGF-A level of the patient; the "AFP" axis represents the actual preoperative AFP level of the patient; the "radiomics score" axis represents the radiomics score of the patient's preoperative CT image; and the "risk" axis represents the risk of early postoperative recurrence in HCC patients predicted by the model.

The ROC curve of the nomogram model was plotted (*Figure 2B*), and the results showed that the AUC value of the training set was 0.9265 (0.8799–0.9731). The internal validation of the nomogram was performed by 1000-bootstrap analyses, and the AUC value was 0.9255 (0.8376–1.0000), indicating that the model has good accuracy (*Figure 2B*, b-d). In addition, the ROC curves of simple clinical characteristics, microvascular infiltration

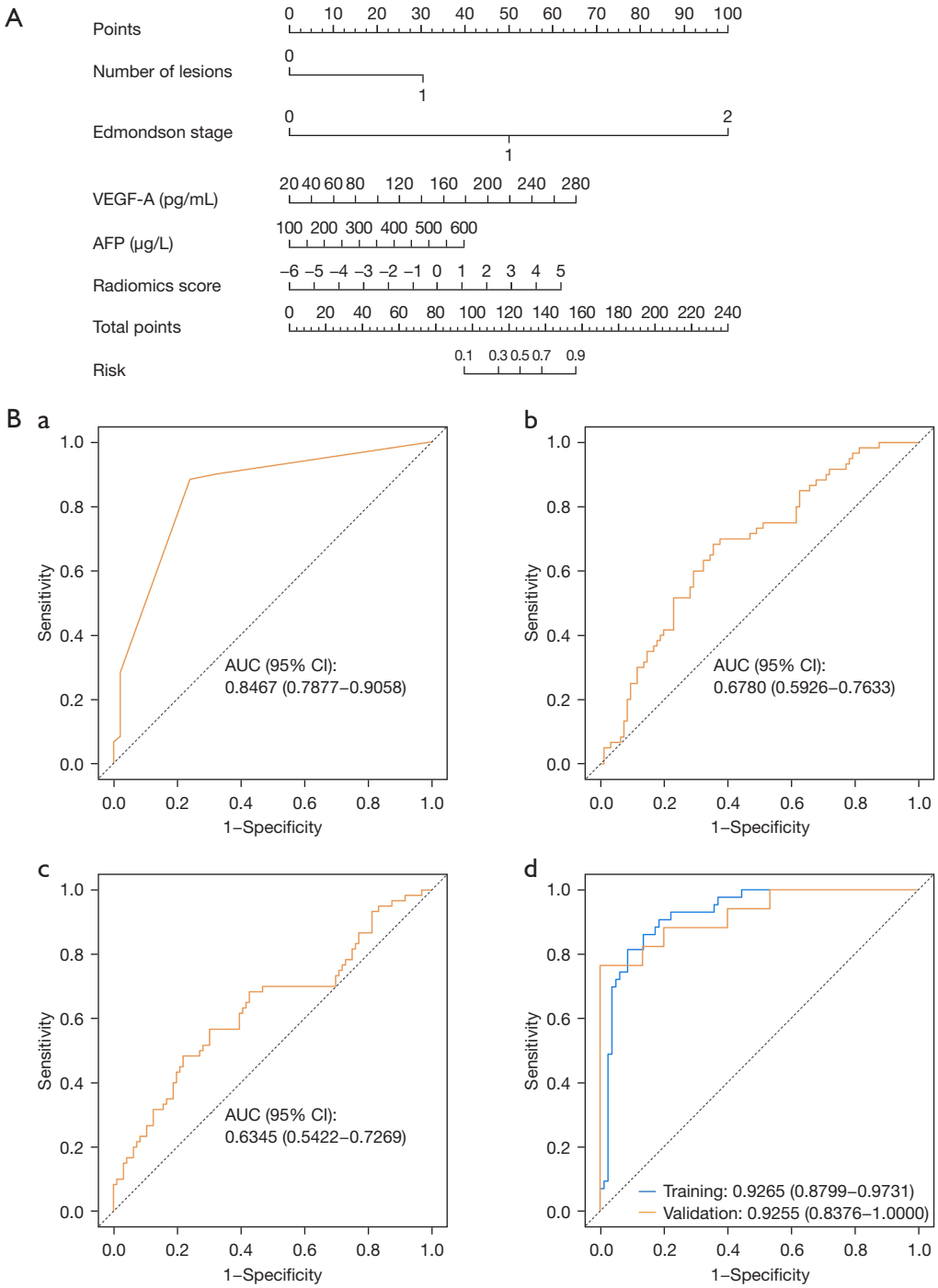

Figure 2 Nomogram model and ROC curve for predicting early postoperative recurrence in HCC patients. (A) Nomogram model for predicting the risk of early postoperative recurrence in HCC patients. (B) ROC curve analysis: (a) ROC curve of clinical characteristics (number of lesions and Edmondson stage) for predicting early postoperative recurrence of HCC. (b) ROC curve of microvascular infiltration serological characteristics (AFP and VEGF-A) for predicting early postoperative recurrence of HCC. (c) ROC curve of the radiomics score for predicting early postoperative recurrence of HCC. (d) ROC curve of the integrated nomogram prediction model for predicting early postoperative recurrence of HCC, comparing training and validation datasets. VEGF-A, vascular endothelial growth factor A; AFP, alpha fetoprotein; AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic; HCC, hepatocellular carcinoma.

Table 5 Prediction performance of training set and internal test set

Dataset	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Cut-off value
Training set	0.9265 (0.8799–0.9731)	0.9136 (0.8524–0.9748)	0.8140 (0.6976–0.9303)	0.4610
Internal test set	0.9255 (0.8376–1.0000)	0.8667 (0.6946–1.0000)	0.7647 (0.5631–0.9663)	0.4610

AUC, area under the curve; CI, confidence interval.

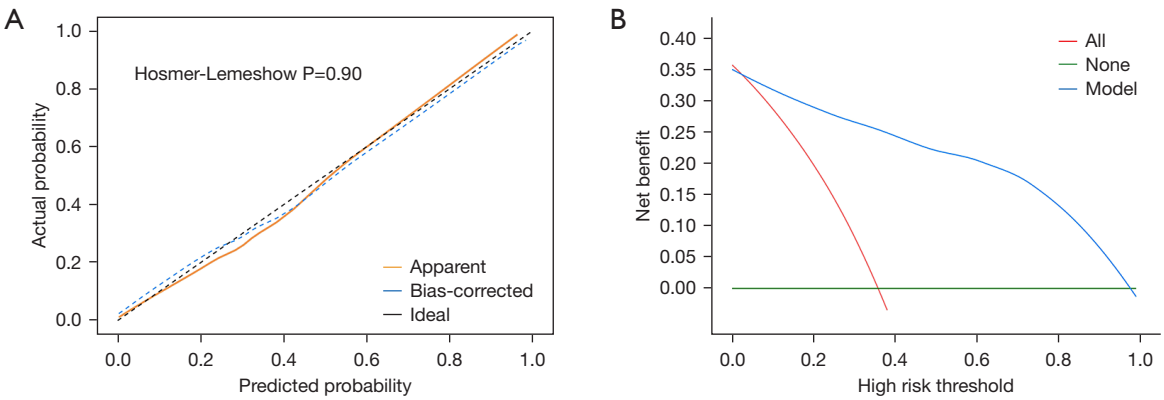

Figure 3 Calibration and DCA for the prediction model. (A) Calibration curve assessing the agreement between the predicted and actual probabilities of early postoperative recurrence in HCC patients. The curve shows the model's performance (orange line), bias-corrected performance (blue dashed line), and the ideal line (black dashed line). The Hosmer-Lemeshow P value indicates the goodness of fit. (B) DCA showing the net benefit of the prediction model across different high-risk thresholds compared to treating all patients (red line) and treating no patients (green line). The blue line represents the net benefit of using the prediction model. DCA, decision curve analysis; HCC, hepatocellular carcinoma.

serological characteristics, and the radiomics score for predicting early postoperative recurrence of HCC were plotted simultaneously. The results showed that the AUC value of the nomogram prediction model was greater than the AUC value of the simple clinical characteristics, microvascular infiltration serological characteristics, and radiomics score (*Figure 2B*), indicating that the nomogram model has better predictive efficiency. As *Table 5* shows, the cut-off value of the model was 0.4610. In this study, risk scores ≥0.4610 points indicated a high risk of early postoperative recurrence in HCC patients, and risk scores <0.4610 points indicated a low risk of early postoperative recurrence in HCC patients.

Performance evaluation

The Hosmer-Lemeshow test results (χ^2=3.460, P=0.90) indicated that there was no significant difference between the predicted and actual values. The calibration curves also demonstrated that the predicted probabilities were generally consistent with the actual probabilities (*Figure 3A*). The clinical decision curves (*Figure 3B*) showed that within the threshold probability range of 0.01% to 75.00% (where the blue line was above the red and green lines), the model offered a net benefit and was effective at identifying patients at high risk of early postoperative recurrence for HCC surgery.

Discussion

HCC exhibits significant tumor heterogeneity, which contributes to its tendency for recurrence following treatment. A recent study has categorized HCC recurrence into early recurrence and late recurrence (14). Early recurrence is often associated with undetected micro-metastases or residual tumor cells prior to surgery, and may also be closely related to the tumor's biological characteristics such as high invasiveness, active tumor angiogenesis, and genetic mutations. It is one of the key factors contributing to a poor prognosis in HCC patients (16). Therefore, reducing postoperative recurrence

rates is a crucial component in improving overall treatment efficacy.

In recent years, researchers have focused on identifying risk factors for early recurrence to better predict recurrence risk. This study preliminarily identified the tumor diameter, Ki-67, AFP, and VEGF-A levels, FIB-4 index, lesion number, tumor-enhancing abnormalities, and Edmondson grading as factors associated with early HCC recurrence through the univariate analysis. These indicators are closely related to tumor invasiveness and biological behavior, further supporting their predictive ability for early HCC recurrence.

Radiomics is an emerging field that explores potential relationships between medical images and tumors non-invasively. In recent years, numerous researchers have identified and applied a variety of radiomics features related to HCC for early diagnosis and prognosis prediction (17-21). This is primarily because radiomics analysis facilitates the extraction of quantitative features from imaging data that cannot be observed with the naked eye, which are correlated with pathological characteristics of HCC, such as microvascular density and histological subtypes (22). In this study, after the dimensionality reduction, 10 venous-phase and four arterial-phase radiomic features associated with early recurrence were identified. These features describe tumor geometry, density distribution, and texture structure, helping to capture tumor heterogeneity and predict tumor biological behavior or clinical outcomes (e.g., recurrence risk and prognosis). The radiomics score formula derived from these features indicated that the imaging radiomics scores of patients without early recurrence were significantly lower than those with early recurrence. The radiomics score was identified as an independent risk factor for early postoperative recurrence of HCC. Thus, the radiomics score could potentially be used to predict early HCC recurrence.

Nomograms are statistical tools that combine radiomic features with other clinical variables (e.g., pathological features and serum markers) to construct individualized predictive models. By providing a simple graphical representation, nomograms enable the intuitive prediction of patient outcomes (e.g., survival rates and recurrence risks). For instance, Mao *et al.* (21) showed that radiomic features can be used to non-invasively indicate the potential relationship between CT images and HCC pathological grading. When the radiomics models were combined with clinical factors for training machine-learning models, the AUC value was 0.8014, indicating a significant increase in model performance and the effective prediction of preoperative pathological grading in HCC.

In this study, a nomogram model was established to predict early postoperative recurrence of HCC based on preoperative microvascular infiltration-related serological and CT radiomic features. This model demonstrated excellent classification performance not only in the training set but also in the internal validation set (AUC >0.9), significantly outperforming a model that only included conventional clinical and pathological data (23,24), proving its strong predictive and classificatory abilities. Moreover, the combined model significantly improved predictive efficacy over single factor-based models, indicating the synergistic effect of combining various risk factors for early HCC recurrence prediction. The model did not exhibit significant systemic bias. Its predicted risk probabilities closely aligned with the actual incidence rates, showing its reasonable and accurate prediction capability across different risk levels.

However, this study had some limitations. This study is a single-center retrospective study with a relatively small sample size, which may affect the external validity and generalizability of the results (25). Although the study demonstrated high predictive ability, the lack of external validation samples limits the model's applicability and stability. Future multicenter studies and validation with larger sample sizes will help further assess the external validity of the model. Additionally, the study did not consider postoperative lifestyle factors, emotional status, or patient adherence to medical advice, which could significantly impact HCC recurrence. Future research should include these potential confounding factors to improve the model's predictive capability. Therefore, while this model demonstrates good predictive performance in internal validation, further studies are needed to verify its external validity and facilitate its application in a broader clinical context.

Conclusions

This study developed a multidimensional nomogram model incorporating CT radiomic features, microvascular infiltration-related serological markers, and conventional clinical parameters. The integrative innovation of this model significantly enhances the prediction accuracy for early postoperative recurrence of HCC and holds the potential to provide strong support for the management and treatment decisions of patients with early recurrence of HCC.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-2024-914/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Tumor Hospital Affiliated to Nantong University (No. 2024-029), and informed consent was obtained from all the patients.

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