

# TRACE Model: Predicting Treatment Response to Transarterial Chemoembolization in Unresectable Hepatocellular Carcinoma

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**Purpose:** To develop and validate a predictive model for predicting six-month outcome by integrating pretreatment MRI features and one-month treatment response after TACE.

**Methods:** A total of 108 patients with 160 hCCs from a single-arm, multicenter clinical trial (NCT03113955) were analyzed and served as the training cohort. An external multicenter dataset (ChiCTR2100046020) consisting of 63 patients with 99 hCCs served as the test dataset. Radiomics model was constructed based on the selected features from pretreatment MR images. Univariate and multivariate logistic regression analysis of clinical and radiological factors were used to identify the independent predictors for the 6-month treatment response. A combined model was further constructed by incorporating one-month treatment response, selected clinical and radiological factors and radiomics signature.

**Results:** Among all the clinical and radiological features, only corona enhancement and one-month treatment response were selected. The combined model, named TRACE model (Treatment response at 1 month, RAdiomics and Corona Enhancement), with AUCs of 0.91 (training cohort) and 0.84 (test cohort). The TRACE model demonstrated a significantly higher AUC than the radiomics model ( $P = 0.001$ ). High-risk and low-risk groups stratified by using the TRACE model also exhibited significant differences in overall survival (OS) ( $P < 0.001$ ). In contrast, none of the published scoring systems, including ART, SNACOR or ABCR score, demonstrated significant differences between the risk groups in OS prediction.

**Conclusion:** The TRACE model exhibited favorable predictive capability for six-month TACE response, and holds potential as a marker for long-term survival outcomes.

**Keywords:** hepatocellular carcinoma, treatment response, transarterial chemoembolization, radiomics



## Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and a leading cause of cancer-related deaths.<sup>1</sup> The majority of HCC patients is diagnosed at unresectable stages in Asia despite efforts to improve availability of screening.<sup>2</sup> Transarterial chemoembolization (TACE), as has been recommended as the first-line therapy for most intermediate-stage HCC,<sup>3,4</sup> blocks the blood supply to the tumor by embolizing the feeding artery, leading to tumor ischemia and necrosis.<sup>3</sup> TACE has been widely accepted as an effective strategy to control tumor growth, downgrade the tumor stage, and extend survival of unresectable HCC patients.<sup>4</sup> While TACE combined with systemic therapy has become increasingly popular for advanced HCC treatment in recent years, TACE remains a cornerstone due to the strong implications of its treatment response for the subsequent use of systemic therapy.<sup>5–7</sup> Reliable predictions of treatment responses to TACE are crucial to help clinicians make timely adjustments to their treatment strategies.

However, the response to TACE varies in patients due to tumor heterogeneity. Several scoring systems have been proposed to predict post-TACE response and guide treatment decisions. Some are based on pre-treatment information, including clinical, laboratory and imaging features, such as the STATE-score,<sup>8</sup> modified Hepatoma Arterial-embolization Prognostic (mHAP),<sup>9</sup> and albumin-bilirubin grade (ALBI).<sup>10</sup> Some others combined short-term post-treatment response with pre-treatment features, such as the ART score,<sup>11</sup> the SNACOR score<sup>12</sup> and the ABCR score.<sup>13</sup> However, the performance of these existing scoring systems is less than satisfactory as they often fail in external validation and reflecting intra-tumoral heterogeneity. Models with improved predictive accuracy and generalizability are needed to identify potential candidates who may benefit from TACE and develop tailored treatment strategy.

Radiomics is an emerging and promising methodology that enables the quantitative assessment of tumor heterogeneity by converting medical images into data that can be analyzed in a high-throughput manner.<sup>14,15</sup> Previous radiomics studies on HCC have demonstrated substantial potential in predicting tumor characteristics, treatment response, and prognosis.<sup>16–19</sup> Several previous MRI-based HCC radiomics studies were conducted in a limited number of centers, leading to moderate predictive power and limited generalizability.<sup>20–23</sup>

The objective of this study was to develop radiomics and combined models to predict the six-month outcome based on Liver Imaging Reporting and Data System treatment response algorithm version 2024 (LI-RADS TRA v2024) after TACE.

## Materials and Methods

This multicenter, retrospective study was reviewed and approved by the Institutional Review Board/Ethics Committee of the participating study centers (Identifier: 2017ZDSYLL022-P01). The study also conformed with Good Clinical Practice (GCP) guidelines, the Declaration of Helsinki, and applicable local laws. Each patient provided written informed consent before enrollment.

## Study Population

The first trial (NCT03113955) was a prospective, single-arm, multicenter trial conducted in patient with HCC at 10 clinical centers in China with enrollment between October 24, 2017, and December 7, 2018, and served as the training set. The research results were published in the *Cardiovasc Intervent Radiology*.<sup>24</sup> The other trial (ChiCTR2100046020) was a prospective, multicenter study and was utilized as the test set. Both of these clinical trials were originally designed to evaluate the efficacy of respective treatment. In the training set, patients were performed with drug-eluting microsphere TACE (DEM-TACE) using Tandem (Boston Scientific Corporation, Massachusetts, United States) embolic microspheres loaded with epirubicin. In the test set, patients were randomly assigned to the following three groups: lipiodol + epirubicin hydrochloride (conventional TACE [cTACE]), TP21 (a platinum drug) + lipiodol, TP21 + lipiodol + epirubicin hydrochloride.

Inclusion criteria were as follows: 1) aged between 18 and 75 years old; 2) initially diagnosed with HCC without treatment; 3) recurrence of HCC after previous curative surgery or ablation; 4) Child-Pugh class A or B and Eastern Cooperative Oncology Group (ECOG)  $\leq 2$ . Exclusion criteria included: 1) the presence of vascular invasion or extra-hepatic metastases, or diffused tumors or coexisted with arteriovenous fistulae; 2) any contraindication to TACE or

epirubicin treatment. In addition, the training set further requested: single tumor diameter <7 cm, multiple tumors up to 3 in total and sum of tumor diameters <10 cm, while diffused tumors were defined as involving over 50% of the liver. In the test set, patients with a single tumor diameter >5 cm in BCLC stage A and all patients in BCLC stage B were included. Diffused tumors were defined as involving more than 70% of the liver. [Figure 1](#) shows the patient enrollment flowchart.

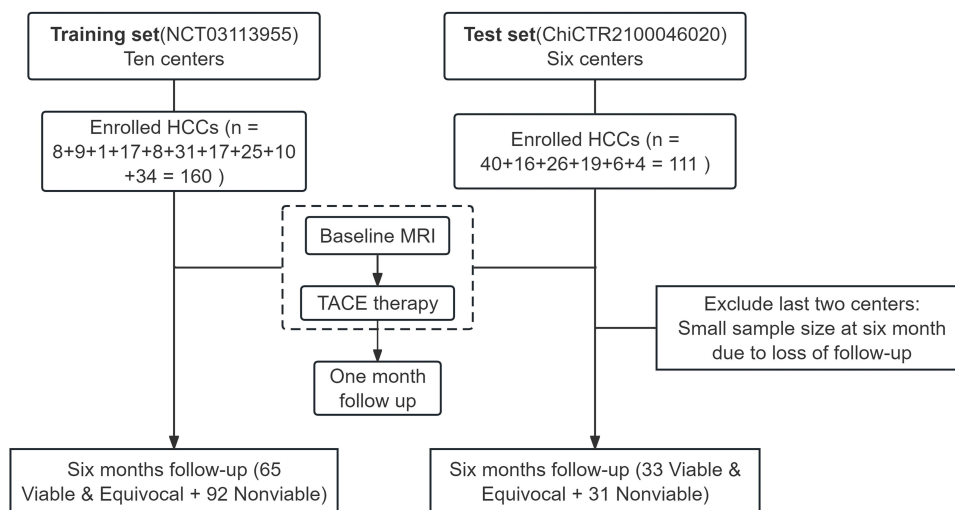
Demographic, clinical information and laboratory tests in baseline and one-month follow-up were recorded for each HCC patient, including age, gender, Child-Pugh score, history of cirrhosis, ECOG, total bilirubin, direct bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, albumin, total protein, alpha-fetoprotein (AFP) and prothrombin time.

## MRI Protocol

All MRI scans were performed using 1.5T or 3.0T MR scanners from different vendor. MRI sequences included coronal T2-weighted imaging (T2WI), fat-suppressed transverse T2WI, in and out of phase fast-spoiled gradient-recalled echo T1-weighted imaging (T1WI), diffusion weighted imaging (DWI) and dynamic contrast-enhanced (DCE) imaging. Details about imaging equipment and scanning parameters are shown in [Tables E1](#) and [E2](#), respectively. During scanning, mild adjustment of the sequence parameters (eg, field of view) was allowed in each center according to specific circumstances.

## Evaluation of TACE Response

Tumor response at one-month was estimated based on the pre- and post-TACE MRI images by two radiologists (reader 1, QJ.Y., with 5 years of experience in liver imaging; reader 2, Y.P., with 6 years of experience in liver imaging). It is the longest diameter of the baseline HCC and the viable portion of the tumor at 1 month. Viable tumor is defined as tumor showing enhancement in the arterial phase (AP) of DCE-MRI.<sup>25,26</sup> For disagreements between the two readers, a senior radiologist (reader 3, YC.W., with 15 years of experience in liver imaging) determined the final results. The treatment response at 1 month was classified into four categories according to the mRECIST criteria (modified Response Evaluation Criteria in Solid Tumors), as complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD). Tumor response at 6 month based on LI-RADS TRA was evaluated by the above three radiologists as well.



**Figure 1** Flowchart of the study population.

## Evaluation of Radiological Features

Two radiologists (WL.W. and SH.Z., with 3 and 2 years of experience in liver imaging, respectively) evaluated the imaging features of pre-treatment MRI images. They were informed of the HCC diagnosis but were blinded to clinical information, laboratory test, imaging report, treatment response and survival outcomes. The following radiological features were recorded: 1) shortest distance from the tumor boundary to the liver capsule; 2) tumor size (largest diameter of the tumor); 3) tumor shape (regular or irregular); 4) tumor margin (smooth or non-smooth); 5) intratumoral fat; 6) intratumoral hemorrhage and/or necrosis; 7) corona enhancement, defined as peritumoral enhancement in the AP, the enhancement is contiguous with and surrounds all or part of the tumor; 8) pseudo-capsule, visible as an enhancing rim in portal venous phase (PVP), delayed phase, or transitional phase. Among these features, 5) to 8) were qualitative categorical variables, recorded as present or absent. Features 7) and 8) were defined according to Liver Imaging Reporting and Data System (LI-RADS).

## Tumor Segmentation and Radiomics Feature Extraction

The three-dimensional tumor region at baseline MR images (T2WI, T1WI-AP and -PVP) was manually delineated by the two above mentioned radiologists (WL.W. and SH.Z) using open-source software ITK-SNAP (version 3.8.0, <http://www.itksnap.org/>). A total of 105 radiomics features (18 histogram-based, 14 shape-based, and 73 texture-based) complying with the image biomarker standardization initiative<sup>27</sup> were extracted using FAE, an integrated open-source software for radiomics (Feature Explorer, version 0.5.2, <https://github.com/salan668/FAE>). To ensure an optimal feature selection process, shape features were extracted only on PVP images, thereby preventing repeated selection of similar shape features across different phases.

## Feature Selection, Radiomics Model Construction and Radiomics Quality Score

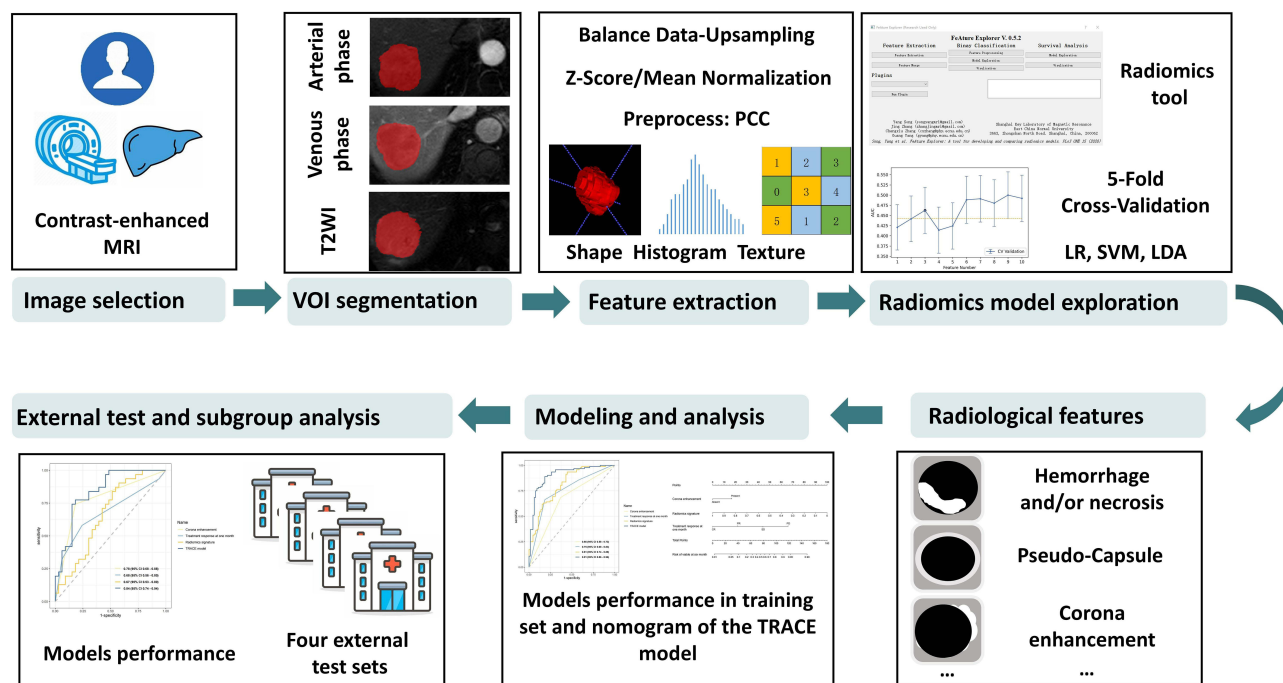
First, the Pearson correlation coefficient was applied to exclude the redundant features. Next, the logistic regression, support vector machine and linear discriminant analysis algorithm, with penalty parameter tuning conducted by 5-fold cross-validation, were further performed to identify the top ranked and most valuable features to build the predictive model. The radiomics models were constructed using the selected features extracted from each sequence and their combination via the logistic regression analysis. All the above procedures were also performed in FAE software.

Finally, the overall process evaluation of radiomics was performed and the score was calculated in [Figure E1 online](#) according to the radiomics workflow scoring criteria.<sup>15</sup> The complete workflow of the study is presented in [Figure 2](#).

## Statistical Analysis

Statistical analyses were performed to compare continuous and categorical variables between the training and test cohorts. Student's *t* test and Mann–Whitney *U*-test were used for continuous variables, while the chi-square test was used for categorical variables. Discriminatory performance of prediction models was evaluated using the receiver operating characteristic (ROC) curves, and key metrics such as area under the curve (AUC), accuracy, sensitivity, specificity, and calibration curves were calculated. Decision curve analysis was used to assess the clinical utility of radiomics based on its net benefit.<sup>28</sup> Comparisons between the AUCs of the various models were performed using the Delong's test. To evaluate overall survival (OS) across different treatment response models, Kaplan–Meier survival curves were constructed and compared using the Log rank test. Interobserver agreement of radiological feature evaluation was assessed by using the intraclass correlation coefficient as follows: 0.40 or less, poor agreement; 0.41–0.75, moderate agreement; and greater than 0.75, almost perfect agreement.

Statistical analyses were carried out using SPSS statistical software version 25 (IBM, Chicago, IL, USA) and R statistics (version 3.6.1, <http://www.R-project.org>), with statistical significance set at a two-sided *P* value < 0.05.



**Figure 2** Flowchart of the study. TRACE model, a model based on the Treatment response at one month, Radiomics signature and Corona Enhancement. **Abbreviations:** VOI, volume of interest; PCC, Pearson correlation coefficient; LR, logistic regression; SVM, support vector machine; LDA, linear discriminant analysis.

## Results

### Baseline Characteristics and MRI Features of HCCs

A total of 108 patients, comprising 87 men and 21 women, with a median age of 60 years (range: 31–75 years), were enrolled in the training set. There were 160 hCC lesions identified on baseline MR images. According to the LR-TRA, 92 (59%) lesions showed nonviable and 65 (41%) lesions showed viable and equivocal at 6 months after TACE. The demographic data, clinical laboratory information and radiological features of the viable and equivocal and nonviable groups at 6 months were summarized in [Table 1](#). Among all the variables, only the corona enhancement was found to be statistically significant between the viable and equivocal and nonviable groups ( $P < 0.001$ ). [Table E3](#) demonstrates the interobserver agreement on HCC radiological features, indicating a moderate-to-high level of consistency.

### Predictive Performance of Radiomics Signature

The ultimate radiomics model comprised shape feature from the PVP sequences and other features extracted from the AP, PVP, and T2WI sequences. In total, 21 features were selected, consisting of 4 shape features only from PVP, 8 features from AP, 3 features other than shape from PVP, and 6 features from T2WI. Details of these features are provided in [Table E4](#).

The performance of the radiomics model in predicting six-month response post-TACE in both the training and test datasets are presented in [Table E5](#). The performance of radiomics model combining shape, AP, PVP and T2WI features outperformed those based on each individual sequence, yielding AUCs of 0.81 (95% confidence interval [CI]: 0.74, 0.88) in the training set and 0.67 (95% CI: 0.53, 0.80) in the external test set.

### Predictive Performance of TRACE Model

After univariate and multivariate logistic regression analysis of all baseline and 1-month laboratory parameters and radiological features, only corona enhancement ( $P = 0.03$ ) and one-month treatment response ( $P < 0.001$ ) were identified as independent predictors for treatment response at 6 months ([Table E6](#)). The combined model, named TRACE model, was constructed using the Treatment response at 1 month, Radiomics signature and Corona Enhancement. The AUCs of corona enhancement, treatment

**Table 1** Patient Baseline Characteristics in the LR-TR Viable & Equivocal and Nonviable Groups at 6 month After TACE

Variables	Viable & Equivocal (n = 65)	Nonviable (n = 92)	P value
Patient demographics			
Age	61 (56, 65.5)	61 (54, 68)	0.81
Sex (Male)	53 (81.5)	79 (85.9)	0.47
Cirrhosis	50 (76.9)	60 (65.2)	0.12
Laboratory parameters			
Child-Pugh grade			0.82
A	58 (89.2)	81 (88.0)	
B	7 (10.8)	11 (12.0)	
ECOG			0.46
0	59 (90.8)	80 (87.0)	
I	6 (9.2)	12 (13.0)	
Additional TACE treatment	39 (60.0)	47 (51.1)	0.27
Total bilirubin (μmol/L)	14.8 (10.2, 21.5)	14.3 (10.3, 20.8)	0.91
Direct bilirubin (μmol/L)	5.2 (4.1, 7.9)	5.1 (4.1, 7.7)	0.90
Aspartate aminotransferase (U/L)	28.0 (21.5, 39.0)	26.0 (21.0, 37.8)	0.44
Alanine aminotransferase (U/L)	27.0 (19.0, 35.0)	29.0 (17.3, 38.0)	0.54
Alkaline phosphatase (U/L)	87.5 (72.0, 103.0)	88.0 (67.0, 107.0)	0.65
Albumin (g/L)	40.4 (17.5, 44.2)	38.1 (4.1, 43.4)	0.37
Total protein (g/L)	69.7 (65.0, 76.8)	70.1 (64.5, 74.8)	0.99
Alpha-fetoprotein (μg/L)	15.7 (4.9, 141.1)	16.3 (3.9, 134.1)	0.75
Prothrombin time	12.4 (11.8, 13.8)	12.5 (11.8, 13.5)	0.85
Total amount of TANDEM + Epirubicin delivered (mL)	5.0 (2.5, 12.5)	6.0 (3.0, 10.0)	0.92
Radiological features			
Distance of the tumor from the capsule (cm)	1.9 (1.3, 2.9)	2.0 (1.2, 3.0)	0.74
Tumor long diameter (cm)	2.7 (1.7, 4.6)	2.3 (1.6, 3.2)	0.10
Shape			0.32
Regular	41 (63.1)	65 (70.7)	
Irregular	24 (36.9)	27 (29.3)	
Margin			0.64
Smooth	44 (67.7)	59 (64.1)	
Non-smooth	21 (32.3)	33 (35.9)	
Intratumoral fat			0.59
Present	12 (18.5)	14 (15.2)	
Absent	53 (81.5)	78 (84.8)	
Intratumoral hemorrhage and/or necrosis			0.06
Present	23 (35.4)	20 (21.7)	
Absent	42 (64.6)	72 (78.3)	
Corona enhancement			<0.001
Present	41 (63.1)	29 (31.5)	
Absent	24 (36.9)	63 (68.5)	
Pseudo-Capsule			0.29
Absent	34 (52.3)	56 (60.9)	
Present	31 (47.7)	36 (39.1)	

**Note**—Data are medians with interquartile range in parentheses, or number of patients with percentage in parentheses.

**Abbreviations:** LR-TR, Liver Imaging Reporting and Data System treatment response; TACE, Transarterial chemoembolization; ECOG, Eastern Cooperative Oncology Group.



response at 1 month, radiomics signature, and TRACE model were 0.66, 0.75, 0.81 and 0.91 in the training set (Figure 3A) and 0.78, 0.68, 0.67 and 0.84 in the test set, respectively (Figure 3B). The TRACE model demonstrated a significantly higher AUC than the radiomics model ( $P = 0.001$ ,  $P = 0.01$ ), the corona enhancement ( $P < 0.001$ ,  $P = 0.04$ ) and the treatment response at 1 month ( $P < 0.001$ ,  $P = 0.01$ ) both in the training and test cohort.

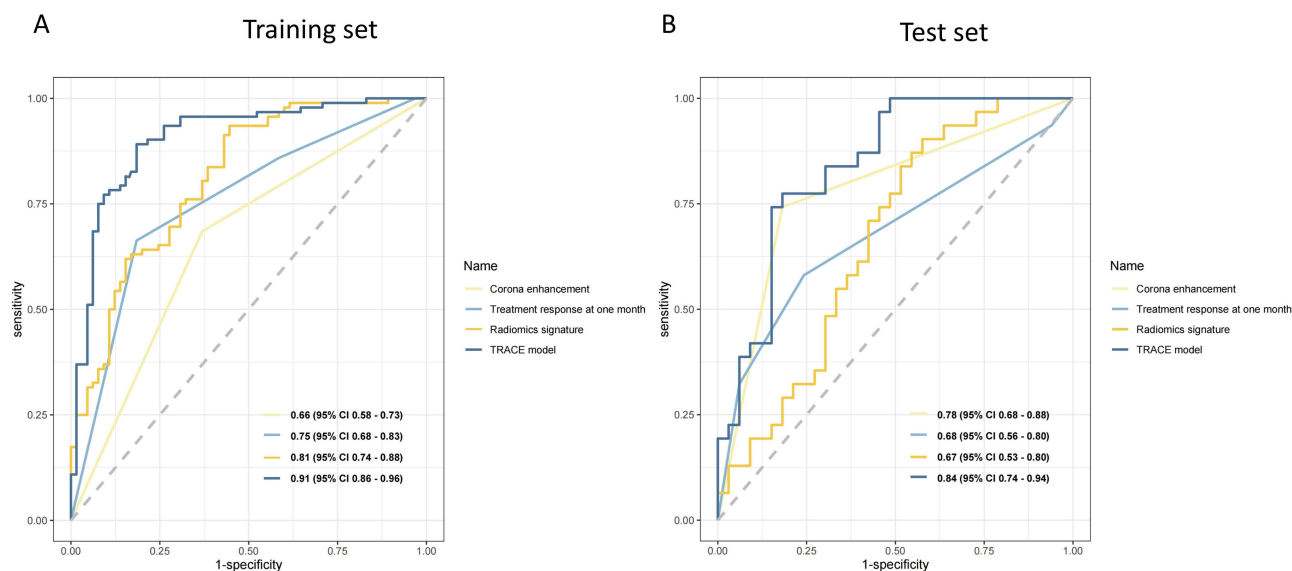
Further subgroup analyses in the test set were performed according to different centers and treatment groups (Table 2). The AUCs for the TRACE model ranged from 0.56 (95% CI: 0.20, 0.93) to 0.90 (95% CI: 0.76, 1.00) in different centers and 0.66 (95% CI: 0.40, 0.91) to 0.93 (95% CI: 0.84, 1.00) in different treatment groups. The nomogram based on the TRACE model was developed to predict the treatment response at 6 months after the initial TACE procedure (Figure E2 online).

The decision curves illustrate the performance of the TRACE model in the training set (Figure E3A online) and test set (Figure E3B online). Notably, the TRACE model exhibited more favorable performance. Additionally, the calibration curves were also drawn and confirmed the reliable calibration of the TRACE model in both the training (Figure E3C online) and test cohorts (Figure E3D online).

Two representative patients are shown in Figure E4 online with different treatment response at 6 months. The HCC in Figure E4A online had a low TRACE model score and nonviable at 6 months, whereas the HCC in Figure E4B online had a high TRACE model score and viable at 6 months.

## Evaluation of Overall Survival (OS)

Subsequently, the Jorden index was employed to identify the optimal cut-off values for each model, enabling the classification of patients into high-risk and low-risk groups based on their predicted outcomes. For patients with multiple lesions, sum of prediction scores from each lesion were assigned to these patients. The analysis revealed significant differences in OS (Figure 4A) between the low-risk and high-risk groups as stratified by the TRACE model ( $P < 0.001$ ). On the contrary, when stratifying patients using the ABCR score ( $P = 0.11$ ), the SNACOR score ( $P = 0.14$ ) or the ART score ( $P = 0.24$ ), none of these models could distinguish OS between the high and low-risk groups (Figure 4B-4D). Considering the multiple factors that affect OS, we conducted a multivariable regression based on baseline clinical information and TRACE model score. The forest plot in Figure E5 online indicates that compared to other factors, the TRACE model remains a significant predictor.



**Figure 3** ROC curves for models based on the Corona enhancement, treatment response at one month, radiomics signature and TRACE model in the training cohort (A) and test set (B) at six months.

**Table 2** Discriminative Predictive Performance of TRACE Model in Test Set Subgroups at Six month After TACE

Subgroups	Number of HCC			AUC (95% CI)
	Baseline	One Month	Six Month	TRACE Model
Centers				
Center one	40	40	16	0.56 (0.20–0.93)
Center two	14	14	12	0.88 (0.67–1.00)
Center three	26	26	20	0.90 (0.76–1.00)
Center four	19	19	16	0.87 (0.67–1.00)
Treatment groups				
Lipiodol + epirubicin hydrochloride	36	36	17	0.90 (0.74–1.00)
TP21 (a platinum drug) + lipiodol	22	22	19	0.66 (0.40–0.91)
TP21 + lipiodol + epirubicin hydrochloride	41	41	28	0.93 (0.84–1.00)
All tumors	99	99	64	0.84 (0.74–0.94)

**Abbreviations:** TACE, Transarterial chemoembolization; TRACE model, a model based on the treatment response at one month, radiomics signature and corona enhancement; AUC, area under the curve; CI, confidence interval.

## Discussion

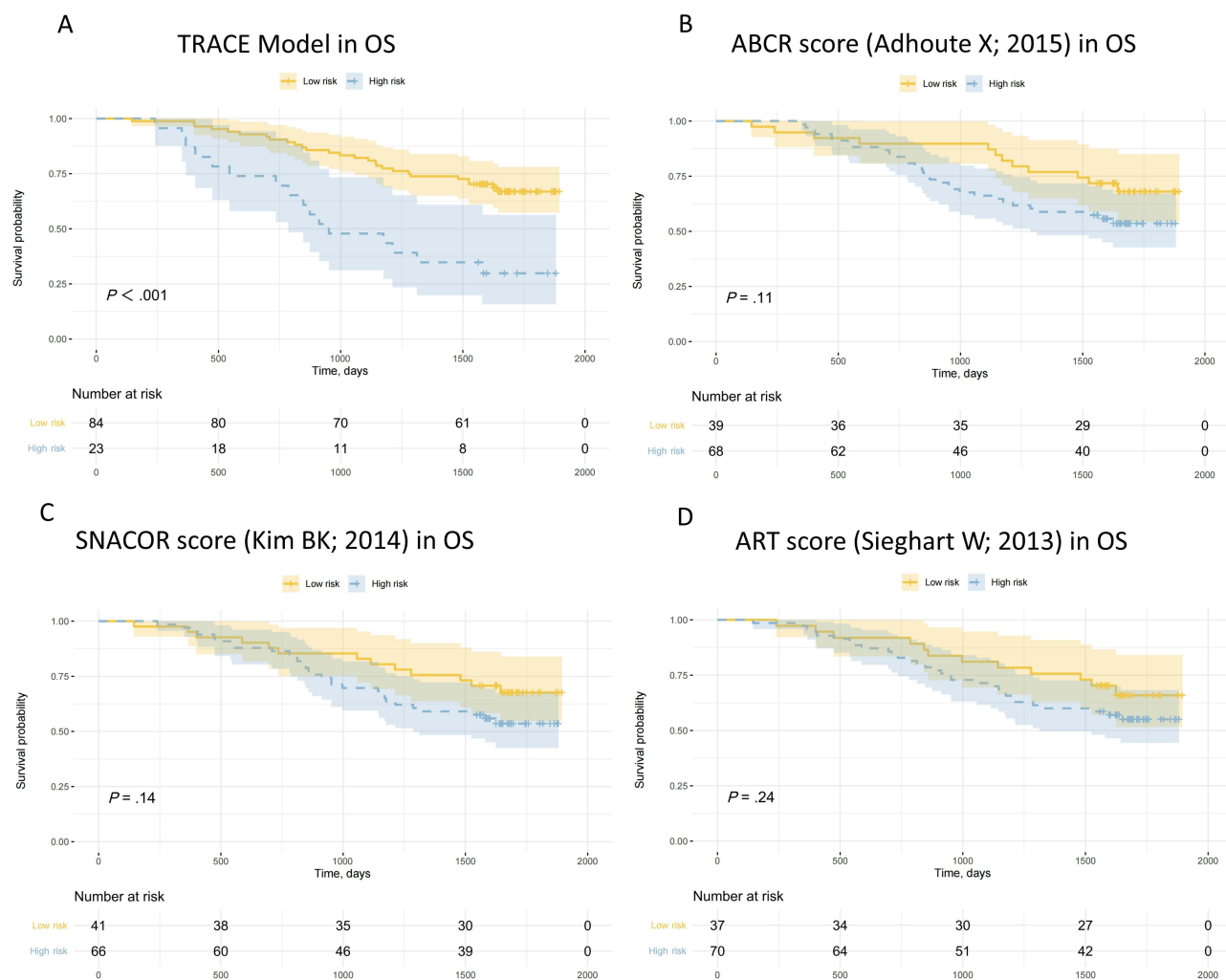
In the present study, we established a comprehensive TRACE model incorporating the radiological characteristics, radiomics score from pretreatment MRI and one-month treatment response to predict six-month outcome after TACE. The predictive performance of the model was evaluated in both training and test cohorts, yielding satisfactory results with AUCs of 0.91 and 0.84, respectively.

Radiomics focuses on improvement of image analysis by extracting large amount of quantitative features through different mathematical algorithms.<sup>14</sup> In the current study, each of the radiomics models based on shape, AP, PVP and T2WI features at baseline demonstrates predictive value in six-month post-TACE treatment response. These findings are in line with previous studies, which also demonstrated the ability of AP- and PVP-based radiomics to predict treatment response in HCC.<sup>29,30</sup> It has been proposed that radiomics can reflect tumor heterogeneity and thus correlated to the invasiveness and treatment response.<sup>31</sup> In addition, the radiomics model based on multiple sequences including AP, PVP, and T2WI outperforms those based on single sequence in this study. This proves the complementary value of each sequence to the others and highlights the combination usage of these sequences in the clinical practice.

Previous predictive studies regarding treatment response to TACE have identified an array of clinical and laboratory biomarkers, including AFP, albumin-bilirubin (ALBI) score, Child-Pugh score, BCLC stage, and among others.<sup>23,30–32</sup> However, none of these biomarkers was found to be statistically significant in this study. This discrepancy may be attributed to two factors. First, the data used in this study was from prospective clinical trials with a high level of concordance in clinical information, distinguishing it from previous studies. Second, patients in the training set received DEM-TACE, which differs from the cTACE used in previous studies. Regarding the radiological features, only corona enhancement exhibited a reverse correlation with tumor response to TACE. A study by Xu et al<sup>33</sup> demonstrated that corona enhancement is a robust predictor of microvascular invasion in HCC, suggesting its potential correlation with increased aggressiveness and poorer treatment response.

One-month treatment response has been shown a powerful predictor of survival and prognosis in HCC patients, such as the ART score, the SNACOR score and the ABCR score.<sup>11–13</sup> The main reasons for the poor performance of these models on our data may include: 1) the above published models are based on HCC patients with diverse stages from early to advanced, while our cohorts are of BCLC class A and B. 2) compared to these models, the proposed TRACE model in this study has incorporated radiomics signature which may potentially reflect tumor heterogeneity. Nonetheless, the TRACE models should be further tested and compared in more multicenter datasets. This study concentrated on lesion-level research, which is why the six-month LR-TRA results were chosen as the study endpoint. The decision to not utilize LR-TRA results for the one-month treatment response is because changes in the size of viable tumors more





**Figure 4** The Kaplan–Meier curve for HCC patients’ survival after TACE. The Kaplan–Meier curves for low risk and high risk by the TRACE model (**A**) the other prediction score (ABCR score, SNACOR score and ART score) (**B–D**) for OS in training set. The optimal cut-off values for each model were determined by the Jordan index (−2.0 for ABCR score; 1.0 for SNACOR score; 2.5 for ART score).

accurately indicate tumor response. However, since mRECIST is patient-level evaluation, the assessment of the one-month treatment response partly relies on mRECIST.

In the subgroup analysis, the performance of the TRACE model in center one was relatively poor, possibly due to its high rate of lost to follow-up (24 out of 40 patients) at 6 months. In different treatment groups, the TRACE model performance was relatively poor in the TP21 (a platinum drug) + lipiodol group. It is possibly because patients in this group have not received epilubicin/doxorubicin, the chemotherapy drugs commonly used in TACE procedure, which might exert impact on the treatment efficacy. The TRACE model showed strong predictive ability for OS. The study avoided directly predicting OS by utilizing short-term treatment response to forecast six-month treatment response, resulting in a model with high interpretability and confidence. In contrast, a model that directly predicted OS would have reduced confidence due to the numerous factors influencing OS.

There are several limitations to be addressed. First, the study’s retrospective design and the relatively small sample size may impact on the robustness of the findings. Second, the external test set in this study utilized three different treatment regimens, which is different from the DEM-TACE used in the training set. However, comparable treatment efficacy of both TACE procedures has been widely reported.<sup>33,34</sup> Third, given that the recognized median survival time for HCC patients at BCLC stage B is roughly 16–20 months,<sup>34</sup> TACE response after longer period (eg 12 months) are worthy of investigation in the future. Finally, given that systemic therapy may cause certain side effects,<sup>35,36</sup> and the

combination of TACE and systemic therapy has become an prevailing strategy in unresectable HCC, the predictive model for response to this combination therapy entailed further exploration.<sup>37</sup>

In summary, our study introduced the TRACE model to predict the HCC treatment response at 6 months after TACE, showing outstanding performance that surpassed traditional scoring systems. The TRACE model can assist in identifying appropriate candidates for TACE treatment, predicting TACE response as early as 1 month, and making timely adjustments to treatment plans for HCC patients.

## Abbreviations

HCC, Hepatocellular carcinoma; LI-RADS TRA, Liver Imaging Reporting and Data System treatment response algorithm; OS, Overall survival; TACE, Transarterial chemoembolization.

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## Disclosure

The authors report no conflicts of interest in this work.

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