The Predictive Performance of Tumor Morphological Features on MRI Combined With Serum CA19-9 for the Efficacy of TACE Treatment in Patients With Primary Liver Cancer

Ann. Ital. Chir., 2026 97, 1: 104–110
https://doi.org/10.62713/aic.4298

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AIM: To explore the predictive performance of magnetic resonance imaging (MRI) combined with serum carbohydrate antigen 19-9 (CA19-9) for the efficacy of transarterial chemoembolization (TACE) treatment in patients with primary liver cancer.
METHODS: In this retrospective study, a total of 174 patients with primary liver cancer who underwent TACE treatment at Hangzhou Xixi Hospital between January 2022 and January 2025 were selected as the study subjects. The patients were divided into an effective group and an ineffective group according to the treatment efficacy at 3 months postoperatively, and the clinical data of the two groups were compared. Multifactorial logistic regression analysis was conducted to identify factors affecting patient efficacy, and a predictive model was constructed. Receiver operating characteristic (ROC) curve analysis was used to evaluate the predictive performance of MRI combined with serum CA19-9 and the model.
RESULTS: Among the 174 patients, 50 cases achieved complete remission (CR) (28.74%), 29 cases attained partial remission (PR) (16.67%), 58 cases had stable disease (SD) (33.33%), and 37 cases experienced disease progression (PD) (21.26%). The results of multifactorial logistic regression analysis showed that low tumor differentiation, continuous multi-nodular tumor margins, incomplete tumor capsule, higher ALT levels, and high CA19-9 were risk factors for compromised efficacy of TACE treatment in patients with primary liver cancer ($p < 0.05$), while tumor tissue necrosis was a protective factor ($p = 0.001$). The area under the curves (AUCs) of MRI, CA19-9, MRI combined with CA19-9, and the model were 0.883, 0.772, 0.904, and 0.958, respectively; the sensitivities were 79.84%, 70.18%, 86.95%, and 89.96%, respectively; and the specificities were 82.69%, 67.88%, 84.02%, and 91.05%, respectively.
CONCLUSIONS: MRI demonstrates promising utility in predicting the efficacy of TACE treatment in patients with primary liver cancer, with its predictive performance enhanced by the combination with serum CA19-9.

Keywords: primary liver cancer; TACE; MRI; serum CA19-9; efficacy

Introduction

Primary liver cancer is one of the most common, life-threatening malignant tumors worldwide, with persistently high incidence and mortality rates [1]. The latest statistics from the World Health Organization [2] indicate an annual incidence rate of over 900,000 new liver cancer cases. Most patients are diagnosed at intermediate or advanced stages, often missing the window for curative surgical resection. For those with unresectable liver cancer at these stages, transarterial chemoembolization (TACE) is currently considered the first-line non-surgical treatment. TACE can effectively control tumor progression and prolong patient survival by blocking the blood supply to tumors and locally delivering chemotherapeutic drugs [3–5]. However, it has been reported that patients demonstrate varying degrees of response to TACE treatment, with some experiencing rapid progression or even recurrence [6–8]. Therefore, identifying reliable predictors of treatment efficacy is of great significance for developing personalized treatment plans.

With recent developments in medical imaging and molecular biology, multimodal evaluation strategies have shown promising application prospects in predicting the efficacy of liver cancer treatment. In terms of imaging assessment, magnetic resonance imaging (MRI), due to its excellent soft tissue resolution and functional imaging capabilities, has become an important tool for evaluating the efficacy of TACE [9]. Dong *et al.* [10] demonstrated that a multi-sequence model constructed based on multiparametric MRI radiomic features can accurately predict the refractoriness of hepatocellular carcinoma (HCC) response to TACE, with the predictive model achieving an area under the curve (AUC) of 0.905. Notably, the morphological features of tumors, such as capsule integrity, the degree

Submitted: 11 August 2025 Revised: 4 November 2025 Accepted: 18 November 2025 Published: 10 January 2026
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Editor: Giulio Illuminati

of intra-tumoral necrosis, and arterial phase enhancement heterogeneity, are closely related to the efficacy of TACE treatment [11]. In terms of serum biomarkers, carbohydrate antigen 19-9 (CA19-9), as a broad-spectrum tumor marker, has gained increasing attention due to its promising clinical values. Du *et al*. [12] found that serum CA19-9 levels are significantly associated with the prognosis of liver cancer patients, providing new evidence for the application of serum biomarkers in predicting treatment efficacy. The predictive efficacy of a single indicator is often limited, and combining multimodal indicators may improve predictive accuracy. Currently, the predictive performance of MRI functional parameters combined with CA19-9 in predicting TACE treatment efficacy, as well as the mechanism of their synergistic effect, remains unknown.

This study aims to systematically evaluate the predictive performance of MRI morphological features combined with serum CA19-9 levels for the efficacy of TACE treatment in patients with primary liver cancer. It is expected to provide clinicians with more accurate tools for predicting treatment outcomes, optimizing therapeutic decisions, and ultimately improving patient prognosis. The results of this study will help advance precision medicine in liver cancer and provide an important reference for the development of personalized treatment plans.

Methods

Study Subjects

In this retrospective study, a total of 174 patients with primary liver cancer who underwent TACE treatment at Hangzhou Xixi Hospital from January 2022 to January 2025 were selected as the study subjects. All patients were deemed ineligible for curative surgical resection due to one or more of the following reasons: intermediate to advanced stage disease (Barcelona Clinic Liver Cancer [BCLC] stage B or C), multifocal tumors not amenable to complete resection, insufficient future liver remnant, proximity of tumors to major vascular structures, or presence of comorbidities that contraindicated major surgery. Inclusion criteria of this study include: (1) meeting the diagnostic criteria of primary liver cancer [13], as confirmed using laboratory tests, imaging, and pathological examinations. All 174 patients underwent pathological assessment via biopsy or surgical specimen examination, in adherence to the international gold standard for HCC diagnosis. Intrahepatic cholangiocarcinoma (ICC) or combined hepatocellular cholangiocarcinoma (HCC-CCA) was explicitly excluded based on histological assessment; (2) meeting the indications for TACE treatment and receiving TACE for the first time; (3) with an expected survival time of more than 3 months; (4) with complete clinical data. Exclusion criteria are as follows: (1) cachexia; (2) distant metastasis; (3) liver function classified as Child–Pugh grade C; (4) presence of systemic diseases; (5) active infection; (6) cognitive impairment; (7) recurrent liver cancer. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Hangzhou Xixi Hospital (Approval No. 2025-096). Written informed consent was obtained from every participant prior to participation in the study.

Sample Size Calculation

The sample size was determined based on the Event Per Variable (EPV) principle. Assuming an EPV of 10 and expecting an inclusion of six independent variables in the multivariate logistic regression, the calculation referenced the study by Xie *et al*. [14], which reported a 38.00% objective response rate (ORR) to TACE treatment in primary liver cancer. Considering a 10% attrition rate, the total required sample size was calculated as $10 \times 6 \div 38.00\% \times (1 + 10\%) = 174$ cases.

TACE Treatment Method

At the beginning of the TACE treatment, the patient was placed in a supine position, followed by anesthesia administration, routine disinfection, and draping. The right femoral artery was punctured, and under the guidance of digital subtraction angiography (DSA), a catheter was inserted into the celiac artery, hepatic artery, and feeding artery. A mixture of 40 mg epirubicin hydrochloride (National Medicine Standard HZ20000496, Pfizer) and 20 mL iodized oil (National Medicine Standard HJ20171362, Guerbet) was emulsified and infused for embolization. Angiography was performed again under DSA to examine the embolization effect. The procedure was concluded upon observing satisfactory outcomes. Local hemostatic compression was applied, followed by liver-protective and supportive treatments.

Observation Indicators

A range of observation indicators were included in this study:

(1) General information, including gender, age, body mass index (BMI), liver cirrhosis, and liver function based on the Child–Pugh classification.

(2) Pathological characteristics, including tumor diameter, tumor location, degree of tumor differentiation, number of tumors, and tumor type.

(3) MRI features: Prior to TACE treatment, patients underwent liver plain and enhanced scans using a GE Prime Elite 1.5T scanner (General Electric, Milwaukee, WI, USA). The MRI characteristics obtained were assessed independently by two experienced abdominal radiologists who were blinded to the clinical data and patient outcomes. The specific criteria for evaluating key morphological features include:

• Tumor margins: The presence of a "continuous multinodular tumor margin" was defined as a tumor border consisting of multiple contiguous, small nodular components on post-contrast images, often indicating an invasive

Table 1. Comparison of clinical data between the effective and ineffective groups.

Indicator	Effective group (n = 79)	Ineffective group (n = 95)	t/χ^2	p
Gender, n (%)			0.821	0.365
Male	48 (60.76)	64 (67.37)		
Female	31 (39.24)	31 (32.63)		
Age (years)	47.12 ± 5.08	47.36 ± 4.95	0.315	0.753
BMI (kg/m^2)	24.58 ± 2.18	24.73 ± 2.34	0.434	0.665
Liver cirrhosis, n (%)			0.408	0.523
No	47 (59.49)	61 (64.21)		
Yes	32 (40.51)	34 (35.79)		
Liver function based on Child–Pugh classification, n (%)			2.865	0.091
Grade A	46 (58.23)	67 (70.53)		
Grade B	33 (41.77)	28 (29.47)		
Tumor diameter, n (%)			0.640	0.424
<5 cm	31 (39.24)	43 (45.26)		
≥5 cm	48 (60.76)	52 (54.74)		
Tumor location, n (%)			3.150	0.207
Left lobe of the liver	29 (36.71)	25 (26.32)		
Right lobe of the liver	31 (39.24)	37 (38.95)		
Left and right hepatic lobes	19 (24.05)	33 (34.74)		
Degree of tumor differentiation, n (%)			15.194	0.001
Well differentiated	40 (50.63)	35 (36.84)		
Moderately differentiated	29 (36.71)	23 (24.21)		
Poorly differentiated	10 (12.66)	37 (38.95)		
Number of tumors, n (%)			0.292	0.589
Single lesion	39 (49.37)	43 (45.26)		
Multiple lesions	40 (50.63)	52 (54.74)		
Tumor type, n (%)			1.442	0.486
Mass type	16 (20.25)	18 (18.95)		
Diffuse type	24 (30.38)	37 (38.95)		
Nodular type	39 (49.37)	40 (42.11)		
Tumor tissue necrosis, n (%)			50.235	<0.001
No	11 (13.92)	64 (67.37)		
Yes	68 (86.08)	31 (32.63)		
Continuous multinodular tumor margins, n (%)			25.301	<0.001
No	63 (79.75)	40 (42.11)		
Yes	16 (20.25)	55 (57.89)		
Incomplete tumor capsule, n (%)			33.386	<0.001
No	65 (82.28)	37 (38.95)		
Yes	14 (17.72)	58 (61.05)		
AST (IU/L)	28.52 ± 4.31	29.01 ± 4.45	0.734	0.464
ALT (IU/L)	23.26 ± 5.64	29.93 ± 4.74	8.477	<0.001
CA19-9 (U/L)	32.77 ± 5.80	37.38 ± 5.54	5.350	0.001
AFP (ng/mL)	277.87 ± 73.45	299.72 ± 81.03	1.847	0.066
PIVKA-II (mIU/mL)	2357.56 ± 437.18	2465.93 ± 402.55	1.700	0.091

Notes: Data are expressed as mean ± standard deviation (SD), unless otherwise indicated.

Abbreviations: AFP, alpha-fetoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CA19-9, carbohydrate antigen 19-9; PIVKA-II, protein induced by vitamin K absence or antagonist-II.

growth pattern. A smooth, pushing border was considered negative for this feature.

• Tumor capsule: An "incomplete tumor capsule" was identified as a disruption or an absence of the hypointense rim (the "capsular" sign) surrounding the tumor on T1-weighted or delayed phase images. A completely hypointense rim encircling the tumor was considered a complete capsule. Any discrepancies in assessment between the two radiologists were resolved through consensus discussion.

(4) Preoperative serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), CA19-9, alpha-fetoprotein (AFP), and protein induced by vitamin K ab-

sence or antagonist-II (PIVKA-II): The upper limit of normal (ULN) for these serum markers, as established by our institutional laboratory, was defined as follows: AST, 40 IU/L; ALT, 40 IU/L; CA19-9, 37 U/L; AFP, 7 ng/mL; and PIVKA-II, 40 mIU/mL.

Clinical Efficacy Evaluation

At 3 months after TACE, clinical efficacy was evaluated using the solid tumor response evaluation criteria (RECIST 1.1) [15]. We acknowledge that the modified RECIST (mRECIST) criteria are more specifically recommended for assessing tumor response in HCC following locoregional therapies like TACE, as they account for tumor viability by focusing on the enhancement of arterial phase contrast images. However, RECIST 1.1 was employed in this study due to its consistent application throughout our institution's radiology department during the patient enrollment period, ensuring uniform assessment across all subjects. The criteria are defined as follows:

(1) Complete response (CR): Disappearance of all target lesions (undetectable by imaging), with the short axis of every pathological lymph node (whether target or non-target) measuring less than 10 mm.

(2) Partial response (PR): A reduction of at least 30% in the sum of the diameters of target lesions compared to the baseline.

(3) Progressive disease (PD): An increase of at least 20% in the sum of the diameters of target lesions compared to the smallest sum recorded during the study (including baseline), with an absolute increase of at least 5 mm, or the appearance of one or more new lesions.

(4) Stable disease (SD): Neither sufficient shrinkage to qualify as PR nor sufficient tumor growth to qualify as PD, using the smallest sum of diameters recorded during the study as a reference.

The ORR was determined by finding the sum of the CR and PR rates. Patients achieving CR or PR at 3 months postoperatively are classified into the effective group, while the remaining patients are classified into the ineffective group.

Statistical Methods

Data analysis was performed using SPSS version 22.0 software (IBM Corporation, Armonk, NY, USA). The normality of data distribution for continuous variables was assessed using the Shapiro–Wilk test. Data conforming to a normal distribution are expressed as mean ± standard deviation (SD), and comparisons between groups were conducted using the independent samples *t*-test. Categorical data are expressed as counts and percentages, and comparisons between groups were conducted using the χ^2 test. Multivariate logistic regression analysis was used to identify factors affecting the clinical efficacy of patients, and separate models were constructed: an MRI model and a combined model (MRI features + serum CA19-9 levels). Receiver operating characteristic (ROC) curves were used to evaluate the predictive performance of MRI, CA19-9, the combination of MRI and CA19-9, and the model. Internal validation was performed using bootstrapping with 1000 resamples to assess model stability and correct for overoptimism. The bootstrap-corrected C-index was reported as a measure of predictive performance. A *p*-value of less than 0.05 was considered statistically significant.

Results

Analysis of Post-TACE Treatment Efficacy in Patients With Primary Liver Cancer

The efficacy evaluation results showed that among the 174 patients, 50 cases (28.74%) achieved CR, 29 cases (16.67%) achieved PR, 58 cases (33.33%) had SD, and 37 cases (21.26%) experienced PD, with an ORR of 45.40%.

Comparison of Clinical Data Between the Effective and Ineffective Groups

The ineffective group showed a significantly lower proportion of tumor tissue necrosis compared with the effective group ($p < 0.05$). Conversely, the ineffective group had significantly higher proportions of poorly differentiated tumors, continuous multinodular tumor margins, and incomplete tumor capsules, as well as elevated serum ALT and CA19-9 levels than those in the effective group ($p < 0.05$), as shown in Table 1.

Multivariate Logistic Regression Analysis of Factors Affecting Patients' Clinical Efficacy

The multivariate logistic regression analysis incorporated indicators showing statistically significant differences between the effective and ineffective groups in the univariate analysis as independent variables, and the clinical efficacy at 3 months after TACE (effective = 0, ineffective = 1) as the dependent variable. Multivariate logistic regression analysis showed that poor tumor differentiation, continuous multinodular tumor margins, incomplete tumor capsule, higher ALT levels, and high CA19-9 levels were risk factors for ineffective TACE treatment in patients with primary liver cancer ($p < 0.05$), while tumor tissue necrosis was a protective factor ($p = 0.001$). Based on these results, the predictive model was constructed as follows: Logit(P) = –14.546 – 0.163 × moderate tumor differentiation (no=0, yes=1) + 1.592 × poor tumor differentiation (no = 0, yes = 1) – 1.814 × tumor tissue necrosis (no = 0, yes = 1) + 1.584 × continuous multinodular tumor margins (no = 0, yes = 1) + 2.634 × incomplete tumor capsule (no = 0, yes = 1) + 0.297 × ALT + 0.166 × CA19-9. Detailed results are shown in Table 2.

Predictive Performance of MRI Combined With Serum CA19-9 and the Model for Patients' Clinical Efficacy

The AUCs for MRI, CA19-9, the combination of MRI and CA19-9, and the model were 0.883 (95% CI: 0.834–0.933, $p < 0.001$), 0.772 (95% confidence Interval [CI]:

Table 2. Multivariate logistic regression analysis of factors affecting patients' clinical efficacy.

Indicator	β	SE	Wald χ^2	p	OR (95% CI)
Degree of tumor differentiation			6.514	0.038	
Well differentiated					1.000
Moderately differentiated	−0.163	0.629	0.067	0.795	0.849 (0.248–2.914)
Poorly differentiated	1.592	0.706	5.080	0.024	4.915 (1.231–19.624)
Tumor tissue necrosis	−1.814	0.565	10.312	0.001	0.163 (0.054–0.493)
Continuous multinodular tumor margins	1.584	0.575	7.584	0.006	4.873 (1.579–15.043)
Incomplete tumor capsule	2.634	0.616	18.266	<0.001	13.929 (4.162–46.611)
ALT	0.297	0.071	17.647	<0.001	1.346 (1.172–1.546)
CA19-9	0.166	0.054	9.590	0.002	1.181 (1.063–1.312)
Constant	−14.546	3.262	19.882	<0.001	-

OR, odds Ratio; CI, confidence Interval; SE, standard error.

-, the OR for the intercept (constant) is not reported because it does not have a meaningful clinical interpretation.

0.647–0.797, $p < 0.001$), 0.904 (95% CI: 0.858–0.950, $p < 0.001$), and 0.958 (95% CI: 0.932–0.984, $p < 0.001$), respectively. Accordingly, the sensitivities of these strategies were 79.84%, 70.18%, 86.95%, and 89.96%, and their specificities were 82.69%, 67.88%, 84.02%, and 91.05%, respectively. The predictive performance of the combined MRI and CA19-9 was superior to either strategy when used alone. The comprehensive multivariate model integrated all significant predictors. Fig. 1 shows the ROC curves of all the tested strategies. Internal validation suggested that the model had good predictive performance (C-index: 0.939 [95% CI: 0.912–0.973]).

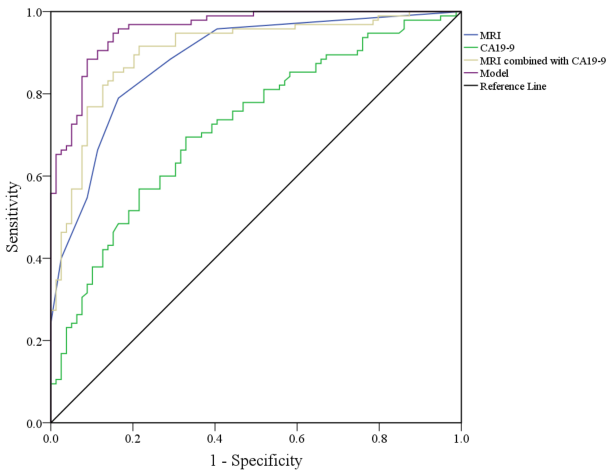

Fig. 1. ROC curves of MRI, CA19-9, MRI combined with serum CA19-9, and the multivariate model for predicting clinical efficacy in patients. ROC, receiver operating characteristic; MRI, magnetic resonance imaging.

Discussion

In recent years, predicting the efficacy of TACE treatment in patients with intermediate to advanced primary liver cancer has become a hot topic in clinical research. Conventionally, imaging approaches or assessments of single serum biomarkers are primarily employed to facilitate treatment response prediction, but their predictive performance is often less than satisfactory [16–18]. In this context, multimodal joint prediction strategies have gradually gained attention, as they integrate biological information from different dimensions and are expected to overcome the limitations of single indicators. This study innovatively combines MRI morphological features with serum CA19-9 levels, providing a new approach for establishing a more accurate method for predicting efficacy. This method not only reflects the morphological characteristics of the tumor but also incorporates its molecular biological features, comprehensively evaluating the tumor's potential response to treatment from both macroscopic and microscopic perspectives. Notably, in line with the prevailing concept of precision medicine, employing a multi-parameter predictive model has gradually been mainstreamed as an important avenue for evaluating treatment efficacy in cancer patients; nevertheless, its clinical application value requires further validation through robust investigations.

The results of this study showed that among 174 patients with primary liver cancer who received TACE treatment, the treatment efficacy rate was 45.40%, which is generally consistent with previously reported TACE outcomes [14]. Multivariate analysis revealed that tumor tissue necrosis was a protective factor against TACE treatment failure, while poor tumor differentiation, continuous multinodular tumor margins, incomplete tumor capsule, and elevated serum ALT and CA19-9 levels were identified as risk factors. This finding has important clinical significance. Tumor tissue necrosis, as a protective factor, may be directly related to the therapeutic mechanism of TACE. Our findings are corroborated by the study by Mosenthal *et al.* [19], which demonstrated that patients without complete pathologic necrosis had a markedly higher recurrence rate (16%, 6/37) compared to those with complete pathologic necrosis (3%, 1/36), underscoring the critical role of extensive necrosis in achieving durable local control post-

TACE. TACE induces tumor cell necrosis by blocking the blood supply to tumors and locally releasing chemotherapeutic drugs; therefore, early occurrence of tumor tissue necrosis following the procedure often indicates a better treatment outcome. Conversely, poor tumor differentiation was identified as a risk factor for compromised efficacy of TACE in patients with primary liver cancer, consistent with the findings reported by Wu *et al*. [20]. Poorly differentiated tumors often exhibit stronger proliferative activity and invasiveness. Continuous multinodular tumor margins and incomplete tumor capsules may indicate high tumor invasiveness or a complex blood supply, posing a challenge for TACE to completely block the tumor's blood supply, thereby reducing treatment efficacy. Elevated serum CA19-9 levels are typically associated with a high tumor burden or greater malignancy, which explains its role as a risk factor. Our results align with the broader prognostic significance of CA19-9 in HCC. Specifically, Han *et al*. [21] demonstrated that a high serum CA19-9 level was an independent risk factor for shortened recurrence-free survival in HCC patients classified as BCLC stage B, a key patient population for whom TACE is the standard first-line treatment. This consistency across studies strengthens the clinical relevance of CA19-9 as a robust biomarker for identifying tumors with more aggressive biological behavior that may respond poorly to locoregional therapies like TACE. The identification of a higher ALT level as a risk factor, even within the normal range, warrants careful interpretation. This is because a higher ALT level is unlikely to reflect overt liver dysfunction; instead, it may indicate a state of subclinical hepatic inflammation or heightened parenchymal stress. In the context of TACE treatment, liver function may affect the metabolism and tolerance of chemotherapeutic drugs, thereby indirectly influencing treatment outcomes. Additionally, higher ALT levels may also indicate more significant tumor infiltration and destruction of the liver parenchyma. The clinical importance of our finding—that a higher baseline ALT level predicts ineffective treatment response—is strongly supported by its association with long-term survival. Notably, Kaewdech *et al*. [16] identified ALT as a key factor influencing 6-month mortality in HCC patients after TACE. This convergence of evidence suggests that a higher baseline ALT level, even within the normal range, may be a marker of underlying hepatic vulnerability that not only affects initial tumor response but also ultimately impacts patient survival, underscoring its critical value in pre-TACE risk stratification.

Our ROC curve analysis showed that the AUCs for MRI and CA19-9 were 0.883 and 0.772, respectively, which were lower than the AUC of their combination, measuring 0.904, coupled with significant improvements in both sensitivity and specificity. These results fully demonstrate that combining imaging features with serum biomarkers can significantly enhance predictive accuracy. MRI, with its excellent soft tissue resolution and functional imaging capabilities, can clearly display the morphological characteristics of tumors, providing an important basis for efficacy prediction. Serum CA19-9, as a molecular marker reflecting tumor biological behavior, offers complementary information from another dimension. The combined application of both achieves a complementary advantage, providing a more comprehensive reference for clinical decision-making.

The innovation of this study lies in combining MRI morphological features with serum CA19-9 levels to construct a more comprehensive predictive model, and this approach offers a new perspective for clinical practice. With a focus on the innovative amalgamation of imaging features with serum biomarkers to create a predictive model, the current research provides a template for future treatment efficacy prediction studies involving other tumor types, holding significant academic value and clinical significance. However, the study also has some limitations. First, the relatively small sample size may compromise the reliability of our results. Second, the use of RECIST 1.1 instead of mRECIST for treatment response assessment may facilitate a more conservative estimation of the TACE treatment response, as RECIST 1.1 is not capable of differentiating between viable and necrotic tumor tissue, which may lead to the misclassification of some responders into the "ineffective" group. Future studies could employ larger sample sizes, a bigger set of parameters, and the mRECIST criteria to validate and refine this predictive model, as part of the effort to promote the further development of precision medicine for liver cancer. Lastly, the brief follow-up period did not allow for the assessment of long-term treatment efficacy.

Conclusions

This study demonstrates that specific MRI morphological features—such as continuous multinodular tumor margins, incomplete tumor capsule, and tumor tissue necrosis—and serum CA19-9 levels are significant independent predictors of TACE efficacy in patients with primary liver cancer. This multivariate predictive model exhibits superior performance in the preoperative prediction of treatment efficacy, providing a valuable tool for clinical optimization of treatment strategy, which is critical for improving patient management. Further validation in larger, prospective cohorts is warranted to confirm its clinical utility.

Availability of Data and Materials

All data included in this study can be obtained by contacting the corresponding author if needed.

Author Contributions

MHS designed the research study. WDZ performed the research. HHS participated in the data collection. BW ana-

lyzed the data and drafted the manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted following the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Hangzhou Xixi Hospital (Approval No. 2025-096). Written informed consent was obtained from all participants.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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