

Research Progress on Radiomics Combined Model for Predicting the Efficacy of Transcatheter Arterial Chemoembolization in Hepatocellular Carcinoma

Jiahao Sun¹, Yixiong Zhang¹, Jiaping Wang^{2*}

¹The Second Affiliated Hospital of Kunming Medical University, Kunming 650000, Yunnan, China

²Radiology Department of the Second Affiliated Hospital of Kunming Medical University, Kunming 650000, Yunnan, China

*Author to whom correspondence should be addressed.

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Abstract: Radiomics, a field that extracts quantitative features from medical images, plays a crucial role in predicting the efficacy of treatments like Transcatheter Arterial Chemoembolization (TACE) for hepatocellular carcinoma (HCC). Recent advancements have shown that combining radiomics with clinical and genetic data enhances predictive accuracy. This integration has significantly influenced current diagnostic and treatment strategies for HCC. Studies have demonstrated that these combined models provide more precise predictions, leading to improved patient outcomes. This review summarizes recent advances and current challenges in radiomics-based combined models for predicting outcomes after TACE in HCC. It systematically outlines key breakthroughs, including multimodal data fusion, improved methods for quantifying intratumoral heterogeneity, and enhanced model predictive performance. It also examines persistent bottlenecks: dataset-dependent feature standardization, limited model generalizability, clinical annotation bias, and high computational costs. The goal of this review was to guide researchers in addressing these technical barriers and optimizing model architectures, to provide evidence for individualized clinical decision-making, and to accelerate the translation of radiomics combined models from basic research into standardized clinical practice—ultimately improving post-TACE outcomes and long-term quality of life for HCC patients.

Keywords: Hepatocellular carcinoma; Transcatheter Arterial Chemoembolization; Radiomics combined model; Efficacy prediction

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1. Introduction

HCC ranks among the most prevalent and deadly cancers globally, with Asia experiencing particularly high incidence rates ^[1]. In China, HCC is the fourth most common cancer and the second leading cause of cancer-

related deaths^[2], with over 50% of cases diagnosed at advanced stages^[3]. TACE serves as a crucial local treatment for middle- and advanced-stage HCC^[4,5]. However, patient responses to TACE vary significantly. While some patients experience notable improvements, others see little benefit or even deterioration. Predicting treatment outcomes and selecting suitable patients remain challenging. Consequently, there is an urgent clinical need for an effective prediction model to aid in patient selection and enhance clinical decision-making for those requiring TACE treatment^[6].

Radiomics is a field that extracts quantitative features from medical images, such as CT and MRI, using advanced computer technology to process, analyze, and model these features. It holds significant potential for diagnosing and treating liver cancer. The primary goal is to identify imaging features not visible to the human eye, aiding in disease diagnosis, prognosis, and treatment evaluation and prediction. A single radiomics model's sensitivity and specificity in predicting post-TACE efficacy in HCC patients are somewhat limited^[7]. However, a combined prediction model, integrating radiomics features with clinical, pathological, immune, and genetic information, demonstrates superior predictive performance compared to standalone radiomics or clinical models. This approach offers valuable guidance for selecting personalized treatment options for liver cancer patients^[7,8].

2. Construction of the radiomics combined model

Radiomics features involve extracting numerous characteristics from target tumor Regions of Interest (ROIs) using manual or semi-automatic segmentation and specialized software or platforms. These features encompass multi-dimensional aspects such as morphology, texture, intensity statistics, and wavelet transforms^[9]. After extraction, the original image data undergoes pre-processing, like normalization, followed by dimensionality reduction. Quantitative features are then calculated using various algorithms^[10]. Ultimately, logistic regression, combined with feature selection methods, identifies the most predictive feature subset for model building^[11,12].

2.1. Data fusion strategy of the joint model

- (1) Fusion of Imaging and Clinical Baseline Features: A prediction model was developed by combining imaging features with clinical baseline data, such as blood routine, coagulation indicators, biochemical markers, and tumor markers. This approach is prevalent in current research due to its accessibility and capacity to gather extensive patient information.
- (2) Multi-Omics Data Fusion: Beyond clinical baseline features, this method integrates molecular data, including genomics, pathomics, and immunomics. Some studies have also incorporated signaling pathway mutation loads and radiomics features to build survival prediction models^[13].
- (3) Multi-Modal Imaging Fusion: This technique utilizes the complementary nature of different imaging modalities, such as CT and MRI, and the supplementary features obtained at various stages (arterial, portal venous, and venous phases) of the same imaging examination. Features extracted from each modality undergo fusion analysis^[14]. Data fusion typically occurs at the feature level (early fusion) or the model prediction level (late fusion). The primary challenge is addressing the scale differences between features from each modality and merging redundant features after removing duplicates to create suitable features for classification models^[15,16].

2.2. Model construction process and common algorithms

The process of constructing a combined model begins with data preparation. Clinical, imaging, and other relevant data are collected from either a single center or multiple centers. This data is then divided into a training set and a validation set, typically in a 7:3 ratio^[17]. For multi-center cases, an independent external validation cohort may be established^[18]. Feature screening follows, where important features are selected and standardized. Common dimensionality-reduction methods, such as Least Absolute Shrinkage and Selection Operator (LASSO) and Principal Component Analysis (PCA), are employed to reduce dimensions and select features^[19]. Next, a combined model is chosen. This involves selecting from basic machine learning algorithms like Logistic Regression (LR), Random Forest (RF), Support Vector Machine (SVM), eXtreme Gradient Boosting (XGBoost), and K-Nearest Neighbors (KNN)^[20]. The prediction performance of the combined model is enhanced using weighted or voting methods^[21]. During the model training and validation phase, cross-validation (internal validation) and independent external cohort validation are used to ensure the model's generalization ability^[22]. Subsequently, the model's performance and interpretability are optimized. For performance, hyperparameter tuning is conducted based on project requirements, and ensemble learning's boosting method is considered to enhance robustness^[23]. To improve interpretability, tools like nomograms, SHAP (Shapley value), and LIME are utilized to clarify the model's predictions and identify key influencing factors^[24].

3. Analysis of the main types and efficacy of radiomics combined models

3.1. CT radiomics combined model

The CT radiomics combined model is developed by delineating the region of interest in preoperative three-phase enhanced CT scans (arterial, portal venous, and delayed phases). Features are extracted and screened using software, then combined with clinical features such as alpha-fetoprotein, Child grading, liver function indicators, platelets, immune-related indicators, and pathological markers. An ROC curve is drawn to predict the efficacy of TACE in patients with HCC. This combined model addresses the limitations of single models, allowing for better generalization in clinical practice. It ultimately facilitates precise patient selection, individualized treatment, and improved patient prognosis. Zhao et al. investigated the value of CT radiomics in predicting the efficacy of the first TACE in advanced HCC patients^[25]. Their findings indicated that the combined model (radiomics features + AFP) outperformed the single clinical model and the radiomics model in both the training set (AUC = 0.92) and validation set (AUC = 0.815), compared to the single clinical model (AUC = 0.65/0.60) and radiomics model (AUC = 0.86/0.755). They also developed an early prediction model based on clinical-radiomics features. Huang et al. integrated a model combining clinical imaging features, signal pathway mutation load, and radiomics features^[26]. This model effectively predicted overall survival and progression-free survival in patients with intermediate-advanced HCC treated with TACE and tyrosine kinase inhibitors, offering a valuable tool for clinical decision-making and patient management. Numerous studies have highlighted that, for predicting efficacy post-TACE, the combined model generally surpasses single models by capturing multi-dimensional information and compensating for the limitations of single imaging features^[27,28].

3.2. MRI radiomics combined model

The MRI radiomics combined model leverages multiple MRI sequences, including T1WI, T2WI, T1WI fat suppression, diffusion, and liver-specific contrast enhancement, using pre-operative plain and contrast-enhanced

MRI images. This approach allows for precise delineation of regions of interest and extensive feature extraction and screening through specialized software. By integrating these features with clinical data, a combined model is developed, and the ROC curve is used to predict the efficacy of HCC treatment post-TACE [29,30]. Wang et al. constructed a prediction model utilizing deep-learning radiomics from pre-operative multi-phase contrast-enhanced MRI and conventional manually delineated radiomics, combined with clinical features [31]. They successfully predicted early peritumoral recurrence in HCC patients after drug-eluting microsphere transarterial chemoembolization within a multi-center cohort. Their findings indicated that the combined model excelled in both the training set (AUC = 0.802) and validation set (AUC = 0.770), demonstrating high calibration and outperforming the single clinical model ($P < 0.05$). Decision curve analysis (DCA) confirmed the model's clinical utility, showing a higher net benefit than other models. Luo et al. were pioneers in exploring the prediction of disease progression in HCC treated with lenvatinib combined with TACE, based on multi-parameter MRI radiomics [32]. By integrating radiomics features with clinical factors, they enhanced the sensitivity of their prediction model. Liu et al. developed a model by combining MRI radiomics with clinical factors such as BCLC stage and ALBI grade [33]. This model effectively predicted tumor response and long-term survival outcomes for HCC patients post-TACE, with T2WI sequence radiomics features making significant contributions. It provided a reliable tool for personalized treatment decision-making. The MRI radiomics combined model, with its advantage of utilizing multiple sequences and minimizing interference from lipiodol embolization in images, is increasingly employed to predict efficacy after TACE [34].

3.3. Cross-modal/Multi-dimensional joint model

With advancements in research, numerous studies now predict responses, efficacy, and complex issues like the tumor microenvironment and microvascular invasion after TACE for HCC [35]. These predictions utilize a combination of examinations, tests, tumor-specific characteristics, and advanced algorithms, such as AI deep learning. Bartnik et al. introduced a fully automatic multi-organ radiomics method that effectively predicted progression-free survival in HCC patients post-TACE [36]. This approach, for the first time, applied fully automatic deep-learning multi-organ segmentation to TACE prognosis prediction. It overcame the traditional focus on tumor areas by systematically analyzing the prognostic value of non-tumor organ characteristics and enhancing model transparency with interpretable AI. Liu et al. combined deep neural networks with radiomics to develop a nomogram for predicting TACE efficacy [37]. They systematically compared traditional machine learning and deep neural network models, integrating independent clinical risk factors to enhance prediction performance. Li et al. created a TACE efficacy prediction model by integrating tumor growth patterns, intratumoral and peritumoral radiomics features, and the ALBI score [38]. They confirmed the significant role of peritumoral radiomics features in improving prediction performance and established a visual nomogram to aid clinical decision-making. Beyond traditional tumor markers like alpha-fetoprotein and abnormal prothrombin, which assist in diagnosing but not effectively predicting TACE efficacy, Wang et al. developed a transcriptomic marker, TFS, composed of five genes [39]. This marker effectively predicts TACE efficacy in HCC patients and relates to pre-treatment radiomics features, the tumor immune microenvironment, and responses to immune/targeted therapy. The development of multi-modal and multi-dimensional combined models extracts more information, providing a robust theoretical foundation for screening TACE patients and formulating individualized treatment strategies [40].

4. Conclusion

The radiomics combined model, known for its non-invasive and convenient nature, holds significant potential in clinical practice for predicting the efficacy of TACE. It enables accurate pre-TACE classification of patients with hepatocellular carcinoma, thereby enhancing the precision of treatment response predictions. Furthermore, advancements in genomics and immunomics have facilitated mutual verification with radiomics, further improving the model's accuracy and applicability.

The clinical application of the radiomics combined model faces several limitations and challenges:

- (1) Most studies are retrospective and conducted at single centers, lacking validation from prospective, multi-center research.
- (2) Many studies constructing the combined model involve small sample sizes and some lack external validation.
- (3) The extraction and analysis of radiomics features are significantly influenced by researchers' subjectivity, with notable variations in scanning equipment, parameters, and analysis software. Currently, standardized guidelines are lacking.

With technological advancements and the establishment of relevant standards, the radiomics combined model is expected to become more accurate in predicting the efficacy of TACE in HCC patients. This model will significantly enhance its generalization ability, allowing for precise identification of patients who will benefit. Consequently, it will enable the formulation of personalized diagnosis and treatment plans.

Disclosure statement

The authors declare no conflict of interest.

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