

## Review Article

# Research progress on machine algorithm prediction of liver cancer prognosis after intervention therapy

Feng Guo<sup>1\*</sup>, Hao Hu<sup>2\*</sup>, Hao Peng<sup>3</sup>, Jia Liu<sup>4</sup>, Chengbo Tang<sup>1</sup>, Hao Zhang<sup>5</sup>

<sup>1</sup>Department of Interventional Diagnosis and Treatment, Yongzhou Central Hospital, Yongzhou Clinical College, University of South China, Yongzhou 425000, Hunan, China; <sup>2</sup>Department of Gynecologic Oncology, Hubei Cancer Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430079, Hubei, China; <sup>3</sup>Department of Abdominal Oncology, The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture, Enshi 445000, Hubei, China; <sup>4</sup>Department of Oncology, The First People's Hospital of Changde City, Changde 415003, Hunan, China; <sup>5</sup>Department of Interventional Vascular Surgery, First Affiliated Hospital of Hunan Normal University (Hunan Provincial People's Hospital), Changsha 410000, Hunan, China. \*Equal contributors.

Received July 16, 2024; Accepted September 13, 2024; Epub September 25, 2024; Published September 30, 2024

**Abstract:** The treatment for liver cancer has transitioned from traditional surgical resection to interventional therapies, which have become increasingly popular among patients due to their minimally invasive nature and significant local efficacy. However, with advancements in treatment technologies, accurately assessing patient response and predicting long-term survival has become a crucial research topic. Over the past decade, machine algorithms have made remarkable progress in the medical field, particularly in hepatology and prognosis studies of hepatocellular carcinoma (HCC). Machine algorithms, including deep learning and machine learning, can identify prognostic patterns and trends by analyzing vast amounts of clinical data. Despite significant advancements, several issues remain unresolved in the prognosis prediction of liver cancer using machine algorithms. Key challenges and main controversies include effectively integrating multi-source clinical data to improve prediction accuracy, addressing data privacy and ethical concerns, and enhancing the transparency and interpretability of machine algorithm decision-making processes. This paper aims to systematically review and analyze the current applications and potential of machine algorithms in predicting the prognosis of patients undergoing interventional therapy for liver cancer, providing theoretical and empirical support for future research and clinical practice.

**Keywords:** Machine algorithms, liver cancer, interventional therapy, prognosis prediction

## Introduction

Liver cancer is one of the most common malignant tumors worldwide and ranks third among the leading causes of cancer-related deaths in humans [1]. According to estimates from the International Agency for Research on Cancer (IARC), there were approximately 870,000 new liver cancer cases and 760,000 deaths globally in 2022 [2]. Hepatocellular carcinoma (HCC) is the most common type of liver cancer, accounting for about 80% of all liver cancer cases, followed by intrahepatic cholangiocarcinoma (ICC), which accounts for approximately 15%, with other rare types of liver cancer making up around 5% [2, 3]. This review primarily focuses on HCC due to its predominant role in liver cancer; however, we also address ICC and

other less common types to provide a comprehensive overview of the current state of prognostic prediction models for liver cancer patients undergoing interventional treatments.

Interventional therapy for liver cancer, such as transcatheter arterial chemoembolization (TACE), is a crucial treatment method that can effectively control tumor growth and extend patient survival across early, intermediate, and advanced stages [4, 5]. Interventional treatment strategies for liver cancer are either vascular or non-vascular (**Figure 1**). Non-vascular interventional techniques include various ablation methods, such as microwave ablation (MWA), radiofrequency ablation (RFA), irreversible electroporation (IRE), cryoablation (CRA), high-intensity focused ultrasound (HIFU), and

# Research progress on machine algorithm prediction of prognosis for liver cancer

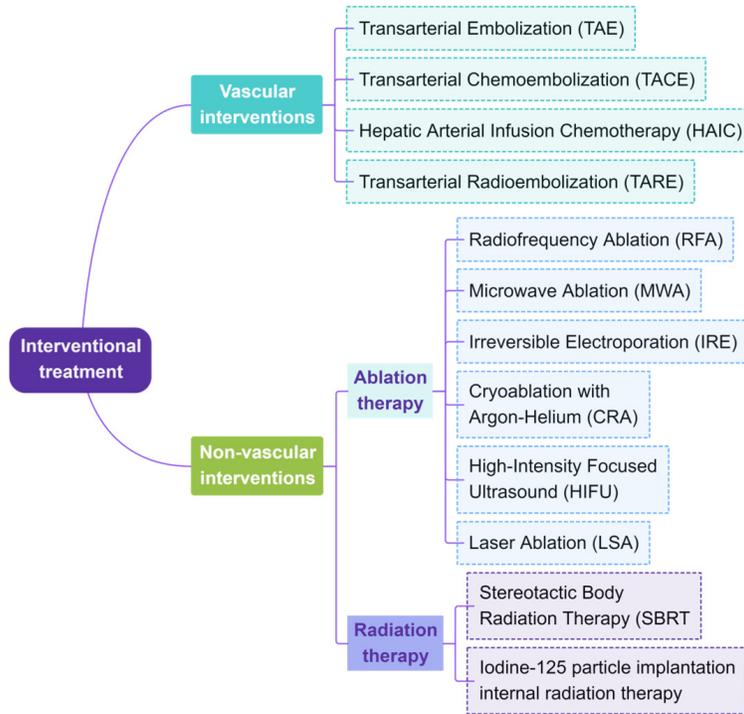


Figure 1. Main interventional treatment methods.

laser ablation (LSA) [6]. Additionally, radiotherapy, including stereotactic body radiotherapy (SBRT) and iodine-125 seed implantation brachytherapy, is also part of non-vascular interventional therapy. In the vascular interventional treatment domain, transhepatic arterial interventions, particularly TACE and hepatic arterial infusion chemotherapy (HAIC), are mainstream clinical choices due to their significant efficacy. However, patients' responses and prognoses to interventional treatments vary significantly, with objective response rates (ORRs) ranging from 40% to 80% and overall survival (OS) time varying from 13 to 48 months [7, 8] (Figure 1).

In recent years, with the development of artificial intelligence (AI) technology, machine learning (ML) has been increasingly applied in the medical field, providing new approaches for predicting the prognosis of liver cancer. ML processes large amounts of clinical and imaging data, allowing for advanced feature generation and quantitative radiomics parameter analysis, thus helping to identify hidden patterns in the data [9, 10]. Compared to traditional statistical methods, ML algorithms can detect complex patterns in liver cancer treatment data more clearly. These algorithms simulate human

learning process, effectively extracting and analyzing key features from multi-source data, such as tumor growth dynamics, changes in imaging performance, and post-treatment response [11, 12]. This review aims to explore the latest research advancements of ML algorithms in predicting the prognosis of patients undergoing interventional therapy for liver cancer by summarizing recent key clinical data on interventional treatment outcomes, and discussing how these algorithms can optimize clinical decision-making processes, so as to improve treatment personalization and precision. Flowchart of the study is shown in Figure 2.

## Overview of liver cancer interventional therapies

Interventional therapy plays a crucial role in managing intermediate and advanced HCC patients, especially for those who are ineligible for surgery or transplantation. Since early-stage HCC often lacks obvious symptoms, most patients are diagnosed at an advanced stage [13]. In the *Chinese Guidelines for the Diagnosis and Treatment of Primary Liver Cancer (2022 Edition)* [14], interventional therapy is recommended as a treatment strategy spanning from early to late-stage liver cancer, with TACE recognized as one of the most commonly used non-surgical treatments for liver cancer. Similarly, in the internationally recognized *Barcelona Clinic Liver Cancer (BCLC) Staging System and Treatment Strategy* [15], interventional therapy, particularly ablation therapy, is recommended as the first-line treatment for very early-stage liver cancer (single tumor  $\leq 2$  cm) in patients not suitable for liver transplantation.

Ablation therapy has been shown to provide efficacy comparable to surgical resection in early-stage liver cancer patients [16]. For intermediate and advanced liver cancer, downstaging conversion therapy strategies, especially local interventional therapy, have played a key role in converting initially unresectable liver

# Research progress on machine algorithm prediction of prognosis for liver cancer

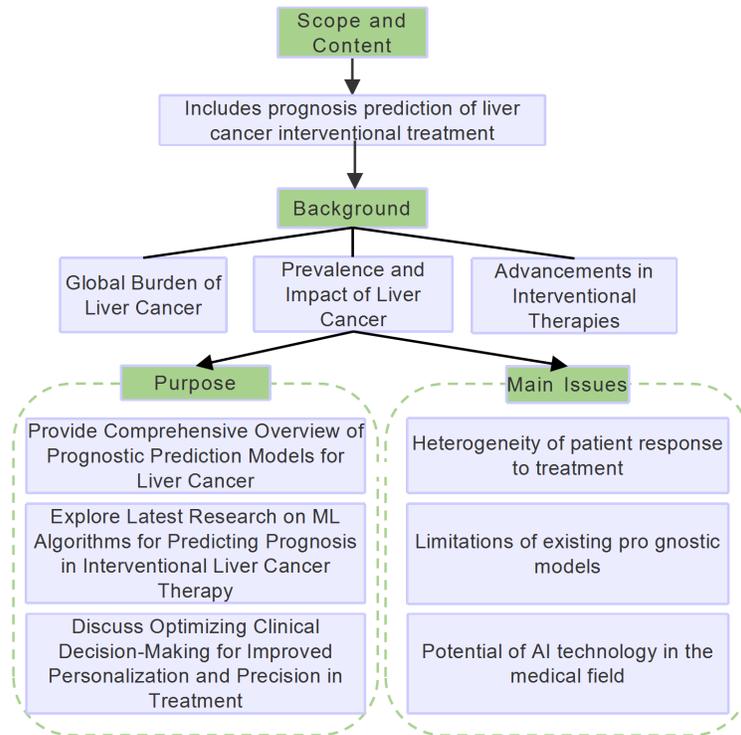


Figure 2. Flowchart of the study.

cancer into a resectable state [17]. After years of in-depth research, the combination of local interventional therapy and systemic targeted immunotherapy has been proven to significantly improve tumor response rates and conversion resection possibilities, becoming a crucial strategy for downstaging intermediate and advanced liver cancers [18]. A prospective phase II study in China (DoHAICs study, NCT05166772) evaluated the efficacy of HAIC combined with donafenib and sintilimab as a first-line treatment for unresectable liver cancer [19]. The results showed that the ORR of the combined treatment was 78.3%, with a conversion success rate of 65.2%. Recent studies have reported better tumor response rates at 1 month, 3 months, and 6 months following TACE combined with MWA treatment [7].

Although interventional therapy offers diverse treatment options and demonstrates good efficacy for HCC patients, challenges remain in predicting treatment response due to biological heterogeneity of tumors and complications, such as bleeding, liver and kidney function impairment, and ectopic embolization of embolic agents, which are crucial for ensuring patient safety and treatment efficacy [7, 20]. These

challenges highlight the importance of accurately predicting patient prognosis.

## Overview of machine algorithms

Machine algorithms, such as ML and deep learning, have shown significant achievements and application potential in medical prognosis prediction. ML technology can automatically learn and identify patterns from historical data, while deep learning simulates the human brain's working mechanisms, using complex algorithms to process and analyze data.

Logistic regression (LR), known for its simple model and high computational efficiency, is widely used in liver cancer diagnosis, prediction, and prognosis assessment [21, 22]. Support

vector machines (SVM) are powerful classification algorithms that find optimal hyperplanes in the feature space to differentiate between categories. In medical image processing, SVMs are often combined with feature extraction techniques [23]. Random forest (RF) algorithms improve classification accuracy and evaluate the importance of different clinical features by constructing multiple decision tree models [24]. Although the k-nearest neighbors (KNN) algorithm has limitations in computational efficiency, its simplicity and intuitive nature still make it suitable for classification tasks in small patient datasets [25]. Naive Bayes simplifies computation by assuming feature independence, making it useful for handling gene expression data with many features and helping identify relevant genetic markers [26]. Gradient boosting decision trees (GBDT) construct models through iterative optimization, accurately evaluating and guiding the latest model with annotations generated from privileged information [27].

Deep learning algorithms, such as convolutional neural networks (CNN), recurrent neural networks (RNN), and deep neural networks (DNN), automatically extract features in medical image

analysis, improving the accuracy of liver cancer diagnosis and metastasis prediction [28, 29]. Wu et al. [30] proposed a phase difference network (PDN), utilizing phase difference and multi-head self-attention mechanisms to distinguish HCC and ICC from four-phase CT images, showing better performance than traditional deep learning methods. The Transformer, a neural network model based on self-attention mechanisms, consists of multiple encoders and decoders. Tang et al. [31] developed a hybrid model combining graph neural networks and Transformer, which effectively utilized global context information from whole-slide images, significantly improving the accuracy and clinical value of HCC prognosis assessment.

Generative adversarial networks (GANs) demonstrate significant potential in medical image enhancement and data generation. The 2021 AI data challenge successfully showcased GANs' ability to generate numerous rare malignant tumor MRI images from a few real MRI samples, with qualitative and quantitative evaluations confirming its effectiveness [32]. Bayesian networks, with their advantages in handling uncertainty and causal relationship modeling, provide deeper insights into liver cancer prediction and treatment. Cai et al. [33] identified portal vein tumor thrombus as the most important predictor of survival time in HCC patients after liver resection using Bayesian networks and importance measurement methods.

The clinical application process of ML includes clinical data acquisition and preprocessing, feature selection, model training and tuning, model diagnosis, multi-model fusion, and deploying validated models into clinical practice to assist in diagnosis and treatment decisions (Figure 3). In clinical applications, the ML process must particularly focus on data representativeness and diversity, ensuring the model generalizability to different patient groups while considering interpretability, allowing doctors to understand and trust its outputs.

### **Application of ML algorithms in predicting prognosis for liver cancer patients undergoing interventional therapies**

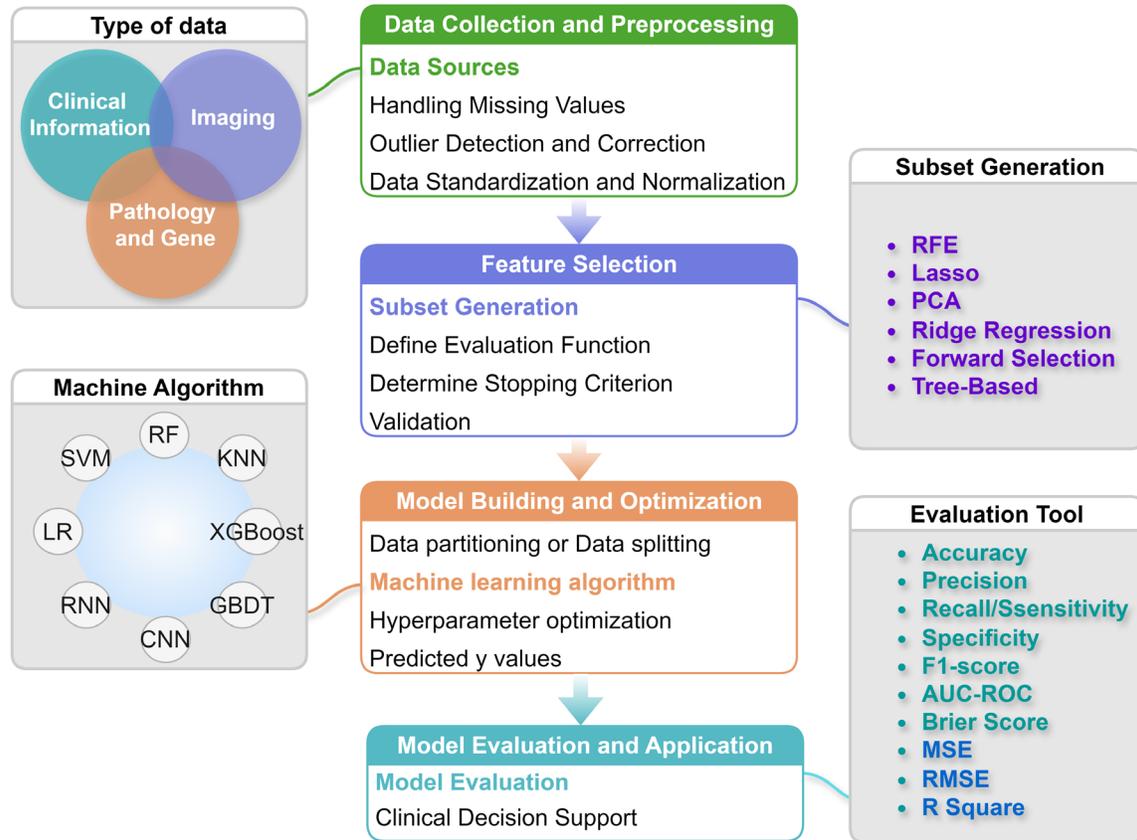
#### *TACE*

Many HCC patients are diagnosed at intermediate or advanced stages, missing the optimal

treatment window. TACE is the gold-standard treatment for intermediate HCC patients [34, 35], but patients' responses to TACE vary significantly, and not all benefit from it [36]. Therefore, developing models to predict the efficacy of TACE is crucial.

Previous studies have constructed various ML models using clinical and radiological variables to predict outcomes for HCC patients post-TACE. Spleen volume (SV) is an undervalued, automatically retrievable imaging biomarker. Muller et al. [37] used CNN algorithms to automatically assess SV and found that high SV correlated significantly with reduced survival in liver cancer patients. SV is also a strong predictor of hepatic decompensation post-TACE. Bartnik et al. [38] analyzed radiomics features from multiple organs of interest in liver cancer patients using deep learning, showing that their radiomics model outperformed traditional clinical models in predicting progression-free survival (PFS) after TACE. These studies highlight the importance of non-tumor regional features in clinical prediction. Bernatz et al. [39] analyzed CT images after three consecutive TACE procedures, combining radiomics features with clinical mHAP-II scores. Their RF model achieved an AUC of 0.70 and an accuracy of 0.72 at the lesion level, an AUC of 0.62 at the patient level, and a C-index of 0.67 for OS prediction, demonstrating potential in improving TACE response prediction. Dong et al. [40] selected clinical data from patients receiving their first TACE for unresectable liver cancer, identified three features (portal vein tumor thrombus type, albumin level, and intrahepatic tumor distribution) using the LASSO algorithm, and built various prognostic models (XGBoost, decision tree, SVM, RF, KNN, and ANN). Among them, the RF model performed best, with an AUC of 0.802, accuracy of 0.784, sensitivity of 0.904, and specificity of 0.480. Ma et al. [41] compared different machine algorithms for predicting responses in unresectable HCC patients receiving lenvatinib combined with TACE, finding that SVM and RF models performed best in accuracy and AUC. The RF model reached an AUC of 0.91, indicating high predictive accuracy. Peng et al. [42] emphasized the high accuracy of radiomics conventional ML and deep learning models in preoperative TACE response prediction (deep learning model AUC = 0.972, integrated model AUC = 0.994). Combining

## Research progress on machine algorithm prediction of prognosis for liver cancer



**Figure 3.** Flow of the machine learning algorithm. LR: Logistic Regression; SVM: Support Vector Machine; RF: Random Forest; KNN: K-Nearest Neighbors; XGBoost: eXtreme Gradient Boosting; GBDT: Gradient Boosting Decision Tree; CNN: Convolutional Neural Network; RNN: Recurrent Neural Network; RFE: Recursive Feature Elimination; PCA: Principal Component Analysis; AUC-ROC: Area Under the Receiver Operating Characteristic Curve; MSE: Mean Squared Error; RMSE: Root Mean Squared Error.

these models with clinical variables offers a novel and accurate method for predicting treatment responses in intermediate-stage liver cancer patients. Zhang et al. [43] developed and validated a fully automated deep learning framework to predict TACE response in real time for HCC patients. Overall, these studies demonstrate the potential of ML models in predicting TACE response and the importance of non-tumor regional features and automated imaging analysis. Relevant studies are summarized in **Table 1**.

TACE models typically combine clinical, radiological, and radiomics features, with non-tumor regional features (such as spleen volume) serving as important predictors. These models employ deep learning and conventional ML algorithms, with RF models showing excellent performance in several studies. AUC values range from 0.62 to 0.994, with most studies

reporting AUCs above 0.8. Key predictive features include portal vein tumor thrombus, albumin levels, and intrahepatic tumor distribution. Automated imaging analysis and deep learning frameworks demonstrate significant potential, offering new perspectives for predicting TACE efficacy.

### HAIC

HAIC involves catheterizing the hepatic artery supplying the tumor and continuously infusing chemotherapeutic agents. It is advantageous for advanced liver cancer with portal vein tumor thrombus, arterio-venous fistula, and poorly vascularized liver metastases [35].

Recent advances show that combining deep learning with radiomics features significantly improves the predicted accuracy of HAIC treatment response. Xu et al. [44] developed the DLRN model, integrating deep learning,

## Research progress on machine algorithm prediction of prognosis for liver cancer

**Table 1.** ML-based prognostic model characteristics of HCC patients after TACE

Author	ML Algorithms	Prediction Targets	Key Predictors	Main Results/Performance Indicators	Model Validation and Interpretability	Other Important Findings
Muller 2022 [32]	CNN	OS, PFS, TTUP	SV	Significant correlation between SV and survival rates	Internal validation, Sørensen Dice score, Bland-Altman plot	Spleen volume significantly correlates with risk of liver dysfunction after TACE
Bartnik 2024 [33]	DL, RSF, COX	OS, PFS	Tumor VOI and non-tumor VOI	OS: C-index range 0.616 to 0.640. PFS: C-index 0.713	Cross-validation, XAI	Multiple VOI features extracted from CT images, overcoming manual segmentation limitations
Bernatz 2023 [34]	RF	TACE response, OS	Radiomic features and clinical mHAP-II score	Lesion-level AUC 0.70, Accuracy 0.72; Patient-level AUC 0.62; C-index 0.67	Reliability and redundancy analysis	Supports the potential of lipid deposition as an imaging biomarker
Dong 2021 [35]	XGBoost, Decision Tree, SVM, RF, KNN, ANN	Early treatment response post first cTACE	Portal vein tumor thrombus type, Albumin level, Tumor distribution in liver	RF model performed best, AUC 0.802, Accuracy 0.784, Sensitivity 0.904, Specificity 0.480	5-fold cross-validation	Portal vein tumor thrombus type is the most important factor for predicting response to first cTACE treatment
Ma 2023 [36]	CART, AdaBoost, XGBoost, RF, SVM	Response to combination therapy (lenvatinib + TACE)	K, LDL, D-D, Red blood cells, ALT, ALB, Mono, Tumor size, TG, and Age	RF model AUC 0.91, SVM and RF performed best	SHAP algorithm enhanced model interpretability	Lower serum K, older age, higher BMI, and larger tumor size correlate with better efficacy of combination therapy
Peng 2021 [37]	Linear model, LR, SVM, GBM, RF, DL	TACE treatment response	Tumor size	DL model AUC 0.972, Integrated model AUC 0.994	Multicenter data validated model robustness	Tumor size significantly correlates with initial treatment response, while AFP levels do not
Zhang 2022 [38]	ResNet18 and Multilayer Perceptron	TACE treatment response	DSA video information, Demographics, and liver function parameters	Accuracy rates on internal and external validation sets were 78.2% and 75.1% respectively	Internal and external validation	Predictive model performance using segmentation results as input is slightly lower than using true segmentation results, but not significantly

ML: Machine Learning; CNN: Convolutional Neural Network; OS: Overall Survival; PFS: Progression-Free Survival; TTUP: Time to Tumor Progression; SV: Segmentation Volume; TACE: Transarterial Chemoembolization; VOI: Volume of Interest; DL: Deep Learning; RSF: Random Survival Forest; COX: Cox Proportional Hazards Model; RF: Random Forest; AUC: Area Under the Curve; mHAP-II: Modified Hepatoma Arterial Embolization Prognostic Score; SVM: Support Vector Machine; KNN: k-Nearest Neighbors; GBM: Gradient Boosting Machine; LR: Logistic Regression; DL: Deep Learning (used in the context of the algorithm name); AFP: Alpha-Fetoprotein; ALT: Alanine Aminotransferase; ALB: Albumin; Mono: Monocytes; TG: Triglyceride; BMI: Body Mass Index; DSA: Digital Subtraction Angiography; AUC: Area Under the Receiver Operating Characteristic Curve; XAI: Explainable Artificial Intelligence; SHAP: SHapley Additive exPlanations.

radiomics features, and key clinical variables, achieving high accuracy in training, internal, and external validation cohorts (AUCs of 0.988, 0.915, and 0.896, respectively). The model also predicted survival based on treatment response, with the median OS in the response group significantly higher than in the non-response group. Quan et al. [45] used the InceptionV4 CNN model with preoperative MRI data and clinical factors (HAIC cycle count, tumor thrombus, neutrophil-lymphocyte ratio, and gamma-glutamyltransferase), achieving an AUC of 0.871 in the training cohort and 0.826 in the internal validation cohort. Another retrospective study used a combination model of MRI radiomics and ALBI score to predict HAIC treatment response, providing a nomogram to assess PFS [46]. Patients with high scores had a median PFS of 6.0 months, significantly shorter than 9.0 months in low-score patients. He et al. [47] further explored radiomics features extracted from dual-phase contrast-enhanced CT (CECT), combined with clinical variables and MTM subtypes, and established a multi-task deep learning radiomics (MDLR) model to provide accurate HAIC prognostic risk stratification for HCC patients. Relevant studies are summarized in **Table 2**.

HAIC models often integrate deep learning, radiomics features, and clinical variables, commonly using pre-treatment MRI and CT images for feature extraction. These models achieve AUC values ranging from 0.826 to 0.988, with key predictive features including HAIC cycle count, tumor thrombus, neutrophil-lymphocyte ratio, and gamma-glutamyltransferase. MDLR models exhibit high accuracy, capable of predicting both treatment response and survival outcomes, providing personalized prognostic assessment tools for HAIC treatment.

### TARE

Transarterial radioembolization (TARE), also known as selective internal radiation therapy (SIRT), involves injecting the radioactive isotope yttrium-90 (90Y) to treat liver cancer.

Roll et al. [48] extracted and analyzed radiomics features from pre-TARE CT images of patients with colorectal cancer liver metastases. Two independent radiomics features (energy and maximum correlation coefficient) reflected tumor heterogeneity. Their multivariate LR

model successfully distinguished high-risk from low-risk patients, with an AUC of 0.75, providing a new prognostic assessment tool. Ince et al. [49] found that ML models (SVM, LR, RF, LightGBM) combining radiomics features from pre-treatment contrast-enhanced MRI and clinical data significantly improved TARE response prediction. Kobe et al. [50] used features from pre-TARE CBCT images, achieving high sensitivity (94.2%) and moderate specificity (67.7%) with a multi-layer perceptron ANN in an external test set. Marinelli et al. [51] collected baseline and early post-TARE MRI of HCC patients, using semi-automatic segmentation to extract radiomics features. Their XGBoost model showed high accuracy (AUC = 0.89) in an independent validation cohort, particularly outperforming models using only clinical parameters and conventional imaging features in predicting complete response. Balli et al. [52] combined dynamic MRI radiomics scores with clinical features using LASSO feature selection and LR to build a radiomics model. Triple cross-validation optimized parameters, with the model predicting response to 90Y TARE in intrahepatic cholangiocarcinoma patients, showing that responders had significantly lower radiomics scores. Axial T2W with fat suppression sequence achieved an AUC of 0.839, indicating high predictive accuracy. Aujay et al. [53] compared the European Association for the Study of the Liver (EASL) criteria, using radiomics combined with MRI data to assess treatment response in patients with locally advanced HCC undergoing TARE. They found that long emphasis, short axis length, surface area, and gray-scale non-uniformity in arterial phase images could accurately predict early treatment response, demonstrating the potential of radiomics combined with LR in predicting TARE efficacy. Relevant studies are summarized in **Table 3**.

TARE models utilize pre-treatment imaging (CT, MRI, CBCT) for radiomics feature extraction, with the combination of radiomics features and clinical data significantly improving prediction accuracy. These models employ various ML algorithms, including SVM, LR, RF, LightGBM, and XGBoost, with AUC values ranging from 0.75 to 0.89. The models can predict both overall response and complete response, with key radiomics features reflecting tumor heterogeneity. These models offer new perspectives for

## Research progress on machine algorithm prediction of prognosis for liver cancer

**Table 2.** ML-based prognostic model characteristics of HCC patients after HAIC

Author	ML Algorithms	Prediction Target	Key Predictive Factors	Main Results/Performance Metrics	Model Validation & Interpretability	Other Important Findings
Xu 2022 [39]	DL, XGBoost	OR	APE, RVI, R score, DL score	AUC in training set = 0.988, internal validation set AUC = 0.915, external validation set AUC = 0.896	Internal and external validation	Radiological parameters (APE and RVI) may predict the efficacy of HAIC better than clinical characteristics
Quan 2024 [40]	Incep-tionV4-CNN	HAIC response	MRI data, HAIC cycles, cancer thrombus, NLR	AUC in training cohort = 0.871, internal validation cohort AUC = 0.826	Cross-validation and independent validation, CAM used for visualization	Age, HAIC cycle number, tumor thrombus, extrahepatic spread, and AST level are independent predictors
Zhao 2023 [41]	LR	PFS	Radiomic score (Radscore) and ALBI score	Combined model AUC in training and validation sets are 0.79 and 0.75, respectively	Internal validation	NA
He 2023 [42]	MDLR	Post-HAIC patient prognosis	CECT radiomic features, portal vein cancer thrombus, HAIC response, HAIC cycles	AUC for survival prediction model in internal and external validation sets are 0.87 and 0.83	Internal and external validation	Tumor burden and distribution as well as tumor microenvironment features are associated with prognosis

XGBoost: Extreme Gradient Boosting; OR: Objective Response; APE: Asymmetry of Parenchymal Enhancement; RVI: Reduction in Viable Tumor on Initial; R score: Radiographic Response Score; DL score: Deep Learning Score; HAIC: Hepatic Arterial Infusion Chemotherapy; MRI: Magnetic Resonance Imaging; NLR: Neutrophil-to-Lymphocyte Ratio; CAM: Class Activation Mapping; PFS: Progression-Free Survival; Radscore: Radiomic Score; ALBI: Albumin-Bilirubin Grade; MDLR: Multitask Deep Learning Radiomics; CECT: Contrast-Enhanced Computed Tomography; AST: Aspartate Aminotransferase; NA: Not Available.

**Table 3.** ML-based prognostic model characteristics of HCC patients after TARE

Author	ML Algorithms	Prediction Target	Key Predictive Factors	Main Results/Performance Metrics	Model Validation & Interpretability	Other Important Findings
Roll 2024 [43]	Multivariate LR	Treatment Response and Survival Outcome	Energy, Maximal Correlation Coefficient	AUC: 0.75	Feature selection with Boruta algorithm	Radiomic analysis can quantify tumor heterogeneity, including blood supply, cellular vitality, density, and fibrosis
Ince 2023 [44]	SVM, LR, RF, LightGBM	Treatment Response	8 Radiomic features, 4 Clinical features	AUC: 0.88-0.94	5-fold cross-validation	Age and preoperative total bilirubin level significantly correlate with TARE treatment response
Kobe 2021 [45]	Multilayer Perceptron, ANN	Disease Control (PR/SD) and PD	104 Texture Analysis Features from CBCT, 15 features after selection	AUC: 0.85, Sensitivity 94.2%, Specificity 67.7%	10-fold cross-validation	NA
Marinelli 2023 [46]	XGBoost	Treatment Response at 4-6 Months Post-Treatment	Radiomic features from baseline and early post-treatment (1-2 months) MRI images	AUC: 0.89	NA	Combined baseline and early follow-up MRI radiomic data better predict patient treatment response
Balli 2024 [47]	LASSO, LR	Radiological Response at 6 Months Post-Treatment	Rad-score, Bifurcation Lesions	AUC: 0.696-0.880	DeLong test, NRI, IDI	First study to use MRI radiomics to predict TARE treatment response in ICC patients
Aujay 2022 [48]	LR	Treatment Response	Longitudinal Emphasis, Minor Axis Length, Surface Area, and Gray Level Non-uniformity	AUC: 1	Cross-validation	Heterogeneity parameters in arterial and portal venous phase images before and after treatment not significantly different between responders and non-responders

LightGBM: A gradient boosting framework that uses tree-based learning; ANN: Artificial Neural Network; PR: Partial Response; SD: Stable Disease; PD: Progressive Disease; CBCT: Cone Beam Computed Tomography; ICC: Intrahepatic Cholangiocarcinoma; TARE: Transarterial Radioembolization; NRI: Net Reclassification Improvement; IDI: Integrated Discrimination Improvement.

## Research progress on machine algorithm prediction of prognosis for liver cancer

predicting TARE treatment efficacy, aiding in personalized treatment decisions.

### RFA

Treatment guidelines from BCLC, CNLC, and NCCN emphasize RFA as the preferred method for early HCC with small tumors. Studies indicate that the five-year survival rate for RFA-treated patients ranges from 26% to 56.7%, and the five-year disease-free survival rate is between 15% and 28.7% [54-56]. However, the high recurrence rate, rapid tumor growth, and invasiveness post-recurrence remain to be clinical concerns [57].

Recent research explores ML in predicting outcomes for HCC patients undergoing RFA. One study used the XGBoost algorithm on multidimensional data from patients receiving localized RFA between 2018 and 2022 [58]. Their model achieved an accuracy of 78.9% and an AUC of 0.80 in an independent validation set. Tong et al. [59] compared five algorithms (LR, decision tree, GBDT, RF, GBM) in predicting overall mortality post-RFA, and identified platelet count, Alpha-Fetoprotein (AFP), age, tumor size, and total bilirubin as key prognostic factors. GBM was found to have the highest accuracy (0.681), indicating the potential and differences of various algorithms in predicting HCC patient prognosis. Sato et al. [60] developed a transformer-based ML model analyzing data from 1778 treatment-naïve HCC patients undergoing RFA, aiming to improve the prediction of OS. This model used clinical and pathological features, evaluated by Harrel's c-index, showing superior discrimination compared to traditional deep learning models. Results indicated the transformer's high discriminative ability in external validation cohorts and its capacity to provide personalized cumulative recurrence prediction curves. Another study analyzed 898 early-stage HCC patients using Lasso and Cox regression analysis to identify independent risk factors like age, gender, BCLC stage, tumor size, globulin, and  $\gamma$ -glutamyl transpeptidase [61]. The nomogram, validated by C-index, ROC, calibration, and decision curve analysis (DCA), showed excellent discrimination, consistency, and clinical utility. RFA treatment showed potential in improving long-term survival for solitary HCC patients with tumor diameters  $\leq 5$  cm. He et al. [62] revealed the

effectiveness of RFA in improving 5-year OS and cancer-specific survival (CSS) rates compared to radiotherapy, chemotherapy, and blank control groups by analyzing data from the SEER database. Further Cox regression analysis and the development of the XGBoost model identified key prognostic factors such as age, race, marital status, grade, cirrhosis, tumor size, and AFP level, and constructed a valid predictive model. The XGBoost model demonstrated good predictive performance in the validation cohort through ROC curve, calibration plot, and DCA, providing a personalized CSS predictive tool for patients with isolated HCC with a diameter of less than 5 cm. The relevant studies are listed in **Table 4**.

RFA models utilize multidimensional clinical and pathological data, comparing various algorithms including XGBoost, LR, decision tree, GBDT, RF, and GBM. AUC values range from 0.68 to 0.80, with key prognostic factors including platelet count, AFP, age, tumor size, and total bilirubin. Transformer-based models show promise in predicting OS. These models can predict both overall mortality and cancer-specific survival, providing powerful tools for prognostic assessment following RFA treatment.

### MWA

MWA is a commonly used ablation method, particularly for tumors with diameters ranging from 3 to 5 cm. It has been shown to have high efficacy and ablation efficiency. Compared to radiofrequency ablation (RFA), MWA significantly shortens the procedure time and is less sensitive to the heat-sink effect of blood flow, thereby reducing the risk of incomplete ablation in the treatment of larger tumors [55]. However, despite its advantages in ablation efficiency, MWA does not show significant differences in local efficacy, complication rates, or long-term survival outcomes compared to RFA [63].

In a study predicting local tumor progression (LTP) in early-stage HCC patients post-MWA, Ren et al. [64] analyzed the clinicopathological data and ablation parameters of 607 untreated early HCC patients. They developed predictive models using four ML algorithms, including CatBoost, RF, XGBoost, and LR. Among these models, the CatBoost algorithm, which combined nine key variables - tumor number, albu-

## Research progress on machine algorithm prediction of prognosis for liver cancer

**Table 4.** ML-based prognostic model characteristics of HCC patients after RFA

Author	ML Algorithms	Prediction Target	Key Predictive Factors	Main Results/Performance Metrics	Model Validation & Interpretability	Other Important Findings
Hamed 2024 [53]	XGBoost	Disease control at 12 months	Child-Pugh score, WBC count, Heparan concentration, Diabetes, Hypertension, Tumor size, AFP	Accuracy and AUC are 78.9% and 0.80, respectively	Internal validation	1-year survival and local control rates are 94.6% and 61.3%, respectively
Tong 2021 [54]	RF, LR, LightGBM, GBDT, Decision Tree	Total mortality	PLT, AFP, Age, Tumor size, Total bilirubin	GBDT has the highest accuracy (0.681), precision (0.721), AUC: 0.714	Internal validation	NA
Sato 2024 [55]	Transformer-based ML model (SurvTRACE)	OS	Age, Gender, Number and size of tumors, Liver function indicators (Albumin, Total bilirubin, AST, ALT), Tumor markers (AFP, DCP), Hepatitis virus infection status, Platelet count, Prothrombin time	C-index of 0.69	Internal and external validation	5-year and 10-year survival rates are 63.7% and 30.4%, respectively. 1-year, 3-year, and 5-year local tumor recurrence rates are 1.7%, 5.3%, and 6.5%, respectively
Zhang 2024 [56]	Lasso regression and Cox regression analysis	RFS	Age, Gender, BCLC stage, Tumor size, Glob, $\gamma$ -GT	AUC for 1-year, 3-year, and 5-year RFS are 0.721, 0.756, and 0.779, respectively	Internal validation	NA
He 2023 [57]	LR, SVM, RF, KNN, XGBoost	CSS	Liver cirrhosis, Tumor size, AFP level, Age, Marital status	XGBoost model's AUC for predicting 1-year, 3-year, and 5-year CSS are 0.88, 0.81, and 0.79, respectively	Internal validation	Compared to other treatment modalities, RFA shows better performance in improving OS and CSS for patients with single HCC $\leq$ 5 cm, but still lower than hepatectomy

RFA: Radiofrequency Ablation; RF: Random Forest; PLT: Platelet Count; DCP: Des gamma Carboxyprothrombin; RFS: Recurrence-Free Survival; BCLC: Barcelona Clinic Liver Cancer; Glob: Globulin;  $\gamma$ -GT:  $\gamma$ -Glutamyl Transpeptidase; CSS: Cancer-Specific Survival; c-index: Concordance Index; AFP: Alpha-Fetoprotein.

**Table 5.** ML-based prognostic model characteristics of HCC patients after MWA

Author	ML Algorithms	Prediction Target	Key Predictive Factors	Main Results/Performance Metrics	Model Validation & Interpretability	Other Important Findings
Ren 2023 [59]	CatBoost, SVM, RF, LR	LTP	Number of tumors, Albumin, AFP, Tumor size, Age, INR	Best performance by CatBoost model, AUC of 0.898	Internal and external validation	NA
An 2022 [60]	LR, RF, SVM, XGBoost	ER	Tumor number, Platelets, AFP, Comorbidity score, WBC, ChE, PT, Neutrophils, Etiology	Best performance by XGBoost model, AUC 0.74 (internal) and 0.76 (external)	Internal and external validation, SHAP and LIME algorithms for model explanation	NA
Shahveranova 2023 [61]	LR	LTP	Preoperative extrahepatic metastasis, Tumor size, CA 19-9	Combined Model 2 (clinical data and Phase 2 radiomic features) has the highest discriminative performance for LTP prediction (AUC 0.981)	NA	LTP group patients have significantly higher radiomic scores in both MRI phases (Phase 1 and Phase 2)

CatBoost: A machine learning algorithm based on decision trees; LTP: Local Tumor Progression; INR: International Normalized Ratio; ER: Early Recurrence; ChE: Cholinesterase; PT: Prothrombin Time; WBC: White Blood Cell Count; CRLM: Colorectal Liver Metastasis; CA 19-9: A tumor marker for gastrointestinal malignancies; LIME: Local Interpretable Model-agnostic Explanations; AFP: Alpha-Fetoprotein.

min and alpha-fetoprotein levels, tumor size, age, and international normalized ratio - exhibited the highest predictive accuracy (AUC: 0.898). The study suggested that precise ablation planning and personalized treatment based on these predictive factors could significantly reduce the risk of LTP, thereby improving the success rate of MWA in treating early-stage HCC.

Another study [65] employed ML techniques to predict early recurrence (ER) risk by analyzing the clinical data of 1,574 early HCC patients who underwent MWA. This study constructed ML models, including RF, support vector machine (SVM), and XGBoost, and enhanced their interpretability using SHAP and LIME algorithms. The XGBoost model performed best in predicting ER, accurately identifying key risk factors such as tumor number, platelet count, and alpha-fetoprotein level. Their XGBoost-based prediction system is available online, providing clinicians with a practical tool (<http://114.251.235.51:8001/>).

In the study on the predictability of LTP after MWA in colorectal cancer liver metastases, clinical data and MRI radiomic features were analyzed to develop two combined models [66]. Model 2, which incorporated T2 fat-suppressed and early arterial phase T1 fat-suppressed features, showed better performance in predicting LTP, with an AUC of 0.981. These highly accurate models offer new perspectives for clinical practice, but the studies also emphasize the need for further large-scale research to validate the generalizability and reliability of these models. Related research is summarized in **Table 5**.

MWA models focus primarily on predicting LTP and ER, utilizing various ML algorithms including CatBoost, RF, XGBoost, and LR. AUC values range from 0.898 to 0.981, with key predictive features including tumor number, albumin levels, AFP, tumor size, and platelet count. These models combine clinical data with MRI radiomics features, with some studies providing online prediction tools for clinical use, offering important references for prognostic assessment and personalized treatment following MWA.

Overall, these ML-based prognostic models for HCC patients undergoing interventional thera-

pies share common characteristics. They typically combine clinical, radiological, and radiomics features to improve prediction accuracy. Various ML algorithms are applied, with RF and XGBoost frequently performing well. Pre-treatment imaging (CT, MRI) is commonly used for feature extraction. These models can predict various outcomes, including treatment response, survival, and recurrence. AUC values generally range from 0.7 to 0.9, indicating good to excellent predictive performance. Furthermore, there is an increasing trend towards using deep learning and multi-task learning approaches, providing more precise and personalized tools for prognostic assessment following HCC interventional treatments.

In summary, DL and ML models have demonstrated high accuracy in predicting outcomes for various liver cancer treatments. For instance, in PFS prediction, models by Bartnik et al. [38] and Quan et al. [45] outperformed traditional clinical models. In predicting treatment response, studies by Muller et al. [37] and Peng et al. [42] highlighted the advantages of radiomics combined with deep learning. For OS prediction, models by Ma et al. [41] and Sato et al. [60] showed strong predictive capabilities. Additionally, in LTP prediction, the models by Ren et al. [64] and those incorporating MRI radiomics features [66] demonstrated exceptionally high accuracy (**Table 6**).

### Conclusion

Currently, the application of ML algorithms in predicting the prognosis of interventional therapy for liver cancer focuses on two main areas. The first is the prognostic evaluation based on imaging features, such as analyzing CT and MRI imaging data to identify tumor size, morphology, and vascular characteristics, thereby predicting treatment efficacy and recurrence risk [67]. For instance, deep learning algorithms have demonstrated remarkable ability in analyzing liver cancer CT images, accurately identifying tumor boundaries and vascular invasion [68-70]. The second area involves integrating multidimensional clinical information of patients, including age, gender, tumor stage, and liver function, to construct complex prognostic models that help determine the optimal treatment plan.

## Research progress on machine algorithm prediction of prognosis for liver cancer

**Table 6.** Predictive accuracy of machine algorithm models for liver cancer outcomes

Prediction Target	Author	Machine algorithm	AUC/C-index
PFS	Bartnik [38]	Deep Learning	-
PFS	Quan [45]	Deep Learning	0.826
Treatment Response	Muller [37]	CNN	-
Treatment Response	Peng [42]	Deep Learning	0.994
Treatment Response	Xu [39]	DLRN	0.988
CR Prediction	Marinelli [46]	XGBoost	0.89
OS	Ma [41]	RF	0.91
OS	Sato [60]	Transformer Model	-
LTP	Ren [64]	CatBoost	0.898
LTP	Shahveranova [66]	-	0.981

PFS: Progression-Free Survival; LTP: Local Tumor Progression; CNN: Convolutional Neural Network.

We found that models integrating clinical, imaging, and radiomics features exhibit superior predictive accuracy. Although RF and XGBoost algorithms perform well in many cases, researchers are exploring a range of algorithms from traditional ML to advanced deep learning methods. Imaging, particularly pre-treatment CT and MRI, plays a crucial role in feature extraction across most models. These models predict not only treatment response but also survival and recurrence risk, demonstrating good to excellent predictive capabilities, with AUC values typically ranging from 0.7 to 0.9. As deep learning and multi-task learning approaches become more prevalent, prediction accuracy and personalization are continually improving.

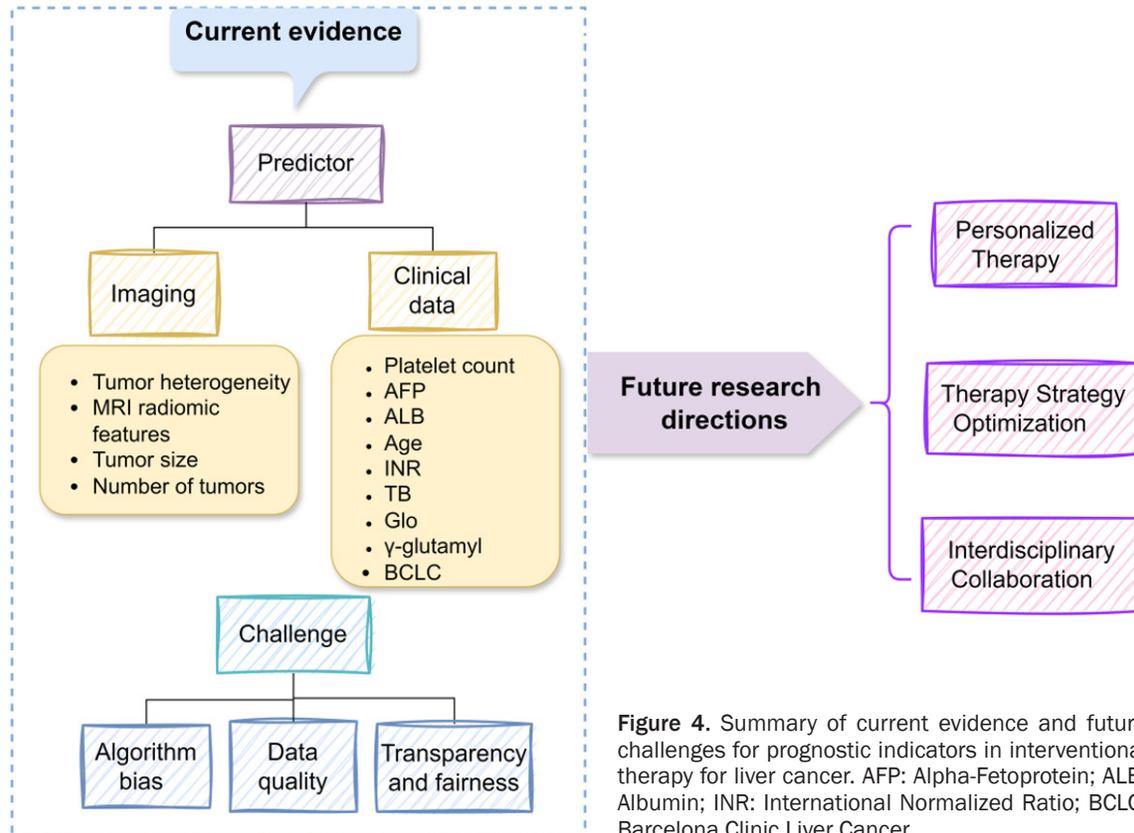
However, despite the significant advances in applying ML to HCC and ICC interventional treatments, there are areas needing further investigation. For instance, many studies rely on single-center data, so multi-center, large-scale studies are necessary to validate models across different patient populations. Additionally, while certain features (e.g., tumor characteristics, liver function markers) consistently emerge as important predictors across various interventions, a deeper understanding of their biological basis is needed.

With increasing model complexity, ensuring interpretability is crucial for clinical adoption. Techniques such as SHAP and LIME, used in some studies, should be more widely implemented. Moreover, despite promising results, integrating these models into clinical decision-making remains a challenge. Future research should focus on developing user-friendly interfaces and decision support tools.

Most current models emphasize short-term outcomes, so developing models that can predict long-term outcomes and account for changes in patient status over time is a crucial next step. With the growing use of combination therapies, models capable of predicting outcomes for these complex treatment regimens will be increasingly valuable.

Furthermore, the high accuracy of personalized treatment plans highlights the potential for highly individualized therapy. Future research should concentrate on developing dynamic models that can adapt recommendations as patient conditions evolve. For example, Zhang et al.'s [43] automated deep learning framework for TACE response prediction points to the possibility of real-time treatment outcome prediction, potentially allowing immediate adjustments during the procedure.

In the realm of liver cancer prognosis prediction, ML algorithms face core challenges including algorithm bias, data quality, and ethical considerations (**Figure 4**). Algorithm bias primarily manifests as models potentially overfitting specific datasets, impacting their applicability across diverse patient populations [71]. Addressing this issue requires rigorous cross-validation and generalization capability assessments to ensure model robustness. On the data front, diversity and consistency of data are crucial for enhancing model performance [72]. Promoting multicenter studies and establishing unified data standards can help expand dataset scope and improve model generalizability. Additionally, algorithm transparency and fairness are critical ethical considerations, necessitating that model decision processes be inter-



**Figure 4.** Summary of current evidence and future challenges for prognostic indicators in interventional therapy for liver cancer. AFP: Alpha-Fetoprotein; ALB: Albumin; INR: International Normalized Ratio; BCLC: Barcelona Clinic Liver Cancer.

pretable and unbiased, with effective oversight mechanisms in place [71, 73-75].

Looking ahead, liver cancer treatment will become more personalized and precise. The integration of high-resolution imaging technologies and advanced ML algorithms will foster the development of intelligent decision support systems based on imaging features. Furthermore, emerging therapies such as targeted therapies and immunotherapies, along with in-depth research into biomarkers and molecular mechanisms, will drive the optimization of liver cancer treatment strategies, improving treatment outcomes and patient quality of life. Interdisciplinary collaboration and in-depth research are essential for continued progress in this field.

#### Disclosure of conflict of interest

None.

**Address correspondence to:** Hao Peng, Department of Abdominal Oncology, The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture, Enshi

445000, Hubei, China. E-mail: penghao202203@163.com; Jia Liu, Department of Oncology, The First People's Hospital of Changde City, Changde 415003, Hunan, China. E-mail: 572630988@qq.com

#### References

- [1] Sidali S, Trepo E, Sutter O and Nault JC. New concepts in the treatment of hepatocellular carcinoma. *United European Gastroenterol J* 2022; 10: 765-774.
- [2] Global cancer burden growing, amidst mounting need for services. World Health Organization; 2024.
- [3] Rungay H, Ferlay J, de Martel C, Georges D, Ibrahim AS, Zheng R, Wei W, Lemmens VEPP and Soerjomataram I. Global, regional and national burden of primary liver cancer by subtype. *Eur J Cancer* 2022; 161: 108-118.
- [4] Cassinotto C, Nogue E, Morell M, Panaro F, Molinari N and Guiu B. Changing trends in hepatocellular carcinoma management: results from a nationwide database in the last decade. *Eur J Cancer* 2021; 146: 48-55.
- [5] Duan R, Gong F, Wang Y, Huang C, Wu J, Hu L, Liu M, Qiu S, Lu L and Lin Y. Transarterial chemoembolization (TACE) plus tyrosine kinase inhibitors versus TACE in patients with hepato-

## Research progress on machine algorithm prediction of prognosis for liver cancer

- cellular carcinoma: a systematic review and meta-analysis. *World J Surg Oncol* 2023; 21: 120.
- [6] Childs A and Meyer T. Hepatocellular Carcinoma: Treatment. 2019. pp. 703-714.
- [7] Ji J, Yang W, Shi HB, Liu S and Zhou WZ. Transcatheter arterial chemoembolization alone versus combined with microwave ablation for recurrent small hepatocellular carcinoma after resection: a retrospective comparative study. *BMC Gastroenterol* 2022; 22: 321.
- [8] Guo Y, Ren Y, Chen L, Sun T, Zhang W, Sun B, Zhu L, Xiong F and Zheng C. Transarterial chemoembolization combined with camrelizumab for recurrent hepatocellular carcinoma. *BMC Cancer* 2022; 22: 270.
- [9] Mokrane FZ, Lu L, Vavasasseur A, Otal P, Peron JM, Luk L, Yang H, Ammari S, Saenger Y, Rousseau H, Zhao B, Schwartz LH and Derclé L. Radiomics machine-learning signature for diagnosis of hepatocellular carcinoma in cirrhotic patients with indeterminate liver nodules. *Eur Radiol* 2020; 30: 558-570.
- [10] Zou ZM, Chang DH, Liu H and Xiao YD. Current updates in machine learning in the prediction of therapeutic outcome of hepatocellular carcinoma: what should we know? *Insights Imaging* 2021; 12: 31.
- [11] Dong B, Zhang H, Duan Y, Yao S, Chen Y and Zhang C. Development of a machine learning-based model to predict prognosis of alpha-fetoprotein-positive hepatocellular carcinoma. *J Transl Med* 2024; 22: 455.
- [12] Calderaro J, Zigutyte L, Truhn D, Jaffe A and Kather JN. Artificial intelligence in liver cancer - new tools for research and patient management. *Nat Rev Gastroenterol Hepatol* 2024; 21: 585-599.
- [13] Demir T, Lee SS and Kaseb AO. Systemic therapy of liver cancer. *Adv Cancer Res* 2021; 149: 257-294.
- [14] Zhou J, Sun H, Wang Z, Cong W, Zeng M, Zhou W, Bie P, Liu L, Wen T, Kuang M, Han G, Yan Z, Wang M, Liu R, Lu L, Ren Z, Zeng Z, Liang P, Liang C, Chen M, Yan F, Wang W, Hou J, Ji Y, Yun J, Bai X, Cai D, Chen W, Chen Y, Cheng W, Cheng S, Dai C, Guo W, Guo Y, Hua B, Huang X, Jia W, Li Q, Li T, Li X, Li Y, Li Y, Liang J, Ling C, Liu T, Liu X, Lu S, Lv G, Mao Y, Meng Z, Peng T, Ren W, Shi H, Shi G, Shi M, Song T, Tao K, Wang J, Wang K, Wang L, Wang W, Wang X, Wang Z, Xiang B, Xing B, Xu J, Yang J, Yang J, Yang Y, Yang Y, Ye S, Yin Z, Zeng Y, Zhang B, Zhang B, Zhang L, Zhang S, Zhang T, Zhang Y, Zhao M, Zhao Y, Zheng H, Zhou L, Zhu J, Zhu K, Liu R, Shi Y, Xiao Y, Zhang L, Yang C, Wu Z, Dai Z, Chen M, Cai J, Wang W, Cai X, Li Q, Shen F, Qin S, Teng G, Dong J and Fan J. Guidelines for the diagnosis and treatment of primary liver cancer (2022 Edition). *Liver Cancer* 2023; 12: 405-444.
- [15] Reig M, Forner A, Rimola J, Ferrer-Fabrega J, Burrel M, Garcia-Criado A, Kelley RK, Galle PR, Mazzaferro V, Salem R, Sangro B, Singal AG, Vogel A, Fuster J, Ayuso C and Bruix J. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. *J Hepatol* 2022; 76: 681-693.
- [16] Yang B, Xi X, Yu H, Jiang H, Liang Z, Smayi A, Wu B and Yang Y. Evaluation of the effectiveness of surgical resection and ablation for the treatment of early-stage hepatocellular carcinoma: a retrospective cohort study. *Cancer Rep (Hoboken)* 2024; 7: e2030.
- [17] Karachaliou GS, Dimitrakakis N and Moris DP. Downstaging strategies for unresectable hepatocellular carcinoma. *World J Gastroenterol* 2024; 30: 2731-2733.
- [18] Li M, Bhoori S, Mehta N and Mazzaferro V. Immunotherapy for hepatocellular carcinoma: the next evolution in expanding access to liver transplantation. *J Hepatol* 2024; 81: 743-755.
- [19] Zhang W, Gao W, Liu C, Li G and Zhang Q. Donafenib combined with hepatic artery infusion chemotherapy (HAIC) and sintilimab for unresectable hepatocellular carcinoma (uHCC): a prospective, single-arm phase II trial (DoHAICs study). *J Clin Oncol* 2023; 41: e16165.
- [20] Della Corte A, Rimini M, Steidler S, Palumbo D, Ratti F, Aldrighetti L, Cascinu S, Casadei-Gardini A and De Cobelli F. Combined loco-regional and systemic treatment strategies for hepatocellular carcinoma: from basics to new developments. *Cardiovasc Intervent Radiol* 2023; 46: 175-186.
- [21] Ksiazek W, Gandor M and Plawiak P. Comparison of various approaches to combine logistic regression with genetic algorithms in survival prediction of hepatocellular carcinoma. *Comput Biol Med* 2021; 134: 104431.
- [22] Jin Z, Chen L, Zhong B, Zhou H, Zhu H, Zhou H, Song J, Guo J, Zhu X, Ji J, Ni C and Teng G. Machine-learning analysis of contrast-enhanced computed tomography radiomics predicts patients with hepatocellular carcinoma who are unsuitable for initial transarterial chemoembolization monotherapy: a multicenter study. *Transl Oncol* 2021; 14: 101034.
- [23] Chowdhary CL and Acharjya DP. Segmentation and feature extraction in medical imaging: a systematic review. *Procedia Comput Sci* 2020; 167: 26-36.
- [24] Svetnik V, Liaw A, Tong C, Culberson JC, Sheridan RP and Feuston BP. Random forest: a classification and regression tool for compound classification and QSAR modeling. *J Chem Inf Comput Sci* 2003; 43: 1947-1958.

## Research progress on machine algorithm prediction of prognosis for liver cancer

- [25] Zhang S, Li X, Zong M, Zhu X and Wang R. Efficient kNN classification with different numbers of nearest neighbors. *IEEE Trans Neural Netw Learn Syst* 2018; 29: 1774-1785.
- [26] Ziemski M, Wisanwanichthan T, Bokulich NA and Kaehler BD. Beating naive bayes at taxonomic classification of 16S rRNA gene sequences. *Front Microbiol* 2021; 12: 644487.
- [27] Li X, Du B, Zhang Y, Xu C and Tao D. Iterative privileged learning. *IEEE Trans Neural Netw Learn Syst* 2020; 31: 2805-2817.
- [28] Said D, Carbonell G, Stocker D, Hectors S, Vietti-Violi N, Bane O, Chin X, Schwartz M, Tabrizian P, Lewis S, Greenspan H, Jegou S, Schiratti JB, Jehanno P and Taouli B. Semiautomated segmentation of hepatocellular carcinoma tumors with MRI using convolutional neural networks. *Eur Radiol* 2023; 33: 6020-6032.
- [29] Albaradei S, Thafar M, Alsaedi A, Van Neste C, Gojobori T, Essack M and Gao X. Machine learning and deep learning methods that use omics data for metastasis prediction. *Comput Struct Biotechnol J* 2021; 19: 5008-5018.
- [30] Wu Y, Chen G, Feng Z, Cui H, Rao F, Ni Y, Huang Z and Zhu W. Phase difference network for efficient differentiation of hepatic tumors with multi-phase CT. *Annu Int Conf IEEE Eng Med Biol Soc* 2023; 2023: 1-5.
- [31] Tang L, Diao S, Li C, He M, Ru K and Qin W. Global contextual representation via graph-transformer fusion for hepatocellular carcinoma prognosis in whole-slide images. *Comput Med Imaging Graph* 2024; 115: 102378.
- [32] Mule S, Lawrance L, Belkouchi Y, Vilgrain V, Lewin M, Trillaud H, Hoeffel C, Laurent V, Ammari S, Morand E, Faucoz O, Tenenhaus A, Cotten A, Meder JF, Talbot H, Luciani A and Lassau N. Generative adversarial networks (GAN)-based data augmentation of rare liver cancers: the SFR 2021 artificial intelligence data challenge. *Diagn Interv Imaging* 2023; 104: 43-48.
- [33] Cai ZQ, Si SB, Chen C, Zhao Y, Ma YY, Wang L and Geng ZM. Analysis of prognostic factors for survival after hepatectomy for hepatocellular carcinoma based on a bayesian network. *PLoS One* 2015; 10: e0120805.
- [34] Cho Y, Choi JW, Kwon H, Kim KY, Lee BC, Chu HH, Lee DH, Lee HA, Kim GM, Oh JS, Hyun D, Lee IJ and Rhim H; Research Committee of the Korean Liver Cancer Association. Transarterial chemoembolization for hepatocellular carcinoma: 2023 expert consensus-based practical recommendations of the Korean Liver Cancer Association. *Clin Mol Hepatol* 2023; 29: 521-541.
- [35] Clinical Guidelines Committee of Chinese College of Interventionalists. Chinese clinical practice guidelines for transarterial chemoembolization of hepatocellular carcinoma (2023 edition). *Zhonghua Yi Xue Za Zhi* 2023; 103: 2674-2694.
- [36] Mendez Romero A, van der Holt B, Willemsen FEJA, de Man RA, Heijmen BJM, Habraken S, Westerveld H, van Delden OM, Klumpen HJ, Tjwa ETTL, Braam PM, Jenniskens SFM, Vanwolleghem T, Weytjens R, D'Archambeau O, de Vos-Geelen J, Buijsen J, van der Leij C, den Toom W, Sprengers D, IJzermans JNM and Moelker A. Transarterial chemoembolization with drug-eluting beads versus stereotactic body radiation therapy for hepatocellular carcinoma: outcomes from a multicenter, randomized, phase 2 trial (the TRENDY trial). *Int J Radiat Oncol Biol Phys* 2023; 117: 45-52.
- [37] Muller L, Kloeckner R, Mahringer-Kunz A, Stoehr F, Duber C, Arnhold G, Gairing SJ, Foerster F, Weinmann A, Galle PR, Mittler J, Pinto Dos Santos D and Hahn F. Fully automated AI-based splenic segmentation for predicting survival and estimating the risk of hepatic decompensation in TACE patients with HCC. *Eur Radiol* 2022; 32: 6302-6313.
- [38] Bartnik K, Krzyzinski M, Bartczak T, Korzenowski K, Lamparski K, Wroblewski T, Grat M, Holowko W, Mech K, Lisowska J, Januszewicz M and Biecek P. A novel radiomics approach for predicting TACE outcomes in hepatocellular carcinoma patients using deep learning for multi-organ segmentation. *Sci Rep* 2024; 14: 14779.
- [39] Bernatz S, Elenberger O, Ackermann J, Lenga L, Martin SS, Scholtz JE, Koch V, Grunewald LD, Herrmann Y, Kinzler MN, Stehle A, Koch I, Zeuzem S, Bankov K, Doering C, Reis H, Flinner N, Schulze F, Wild PJ, Hammerstingl R, Eichler K, Gruber-Rouh T, Vogl TJ, Dos Santos DP and Mahmoudi S. CT-radiomics and clinical risk scores for response and overall survival prognostication in TACE HCC patients. *Sci Rep* 2023; 13: 533.
- [40] Dong Z, Lin Y, Lin F, Luo X, Lin Z, Zhang Y, Li L, Li ZP, Feng ST, Cai H and Peng Z. Prediction of early treatment response to initial conventional transarterial chemoembolization therapy for hepatocellular carcinoma by machine-learning model based on computed tomography. *J Hepatocell Carcinoma* 2021; 8: 1473-1484.
- [41] Ma J, Bo Z, Zhao Z, Yang J, Yang Y, Li H, Yang Y, Wang J, Su Q, Wang J, Chen K, Yu Z, Wang Y and Chen G. Machine learning to predict the response to lenvatinib combined with transarterial chemoembolization for unresectable hepatocellular carcinoma. *Cancers (Basel)* 2023; 15: 625.
- [42] Peng J, Huang J, Huang G and Zhang J. Predicting the initial treatment response to transarterial chemoembolization in intermediate-stage hepatocellular carcinoma by the integration of

## Research progress on machine algorithm prediction of prognosis for liver cancer

- radiomics and deep learning. *Front Oncol* 2021; 11: 730282.
- [43] Zhang L, Jiang Y, Jin Z, Jiang W, Zhang B, Wang C, Wu L, Chen L, Chen Q, Liu S, You J, Mo X, Liu J, Xiong Z, Huang T, Yang L, Wan X, Wen G, Han XG, Fan W and Zhang S. Real-time automatic prediction of treatment response to transcatheter arterial chemoembolization in patients with hepatocellular carcinoma using deep learning based on digital subtraction angiography videos. *Cancer Imaging* 2022; 22: 23.
- [44] Xu Z, An C, Shi F, Ren H, Li Y, Chen S, Dou J, Wang Y, Yan S, Lu J and Chen H. Automatic prediction of hepatic arterial infusion chemotherapy response in advanced hepatocellular carcinoma with deep learning radiomic nomogram. *Eur Radiol* 2023; 33: 9038-9051.
- [45] Quan B, Li J, Mi H, Li M, Liu W, Yao F, Chen R, Shan Y, Xu P, Ren Z and Yin X. Development and preliminary validation of a novel convolutional neural network model for predicting treatment response in patients with unresectable hepatocellular carcinoma receiving hepatic arterial infusion chemotherapy. *J Imaging Inform Med* 2024; 37: 1282-1296.
- [46] Zhao Y, Huang F, Liu S, Jian L, Xia X, Lin H and Liu J. Prediction of therapeutic response of unresectable hepatocellular carcinoma to hepatic arterial infusion chemotherapy based on pretherapeutic MRI radiomics and Albumin-Bilirubin score. *J Cancer Res Clin Oncol* 2023; 149: 5181-5192.
- [47] He X, Li K, Wei R, Zuo M, Yao W, Zheng Z, He X, Fu Y, Li C, An C and Liu W. A multitask deep learning radiomics model for predicting the macrotrabecular-massive subtype and prognosis of hepatocellular carcinoma after hepatic arterial infusion chemotherapy. *Radiol Med* 2023; 128: 1508-1520.
- [48] Roll W, Masthoff M, Kohler M, Rahbar K, Stegger L, Ventura D, Morgul H, Trebicka J, Schafers M, Heindel W, Wildgruber M and Schindler P. Radiomics-based prediction model for outcome of radioembolization in metastatic colorectal cancer. *Cardiovasc Intervent Radiol* 2024; 47: 462-471.
- [49] Ince O, Onder H, Gencturk M, Cebeci H, Golzarian J and Young S. Prediction of response of hepatocellular carcinoma to radioembolization: machine learning using preprocedural clinical factors and mr imaging radiomics. *J Vasc Interv Radiol* 2023; 34: 235-243, e3.
- [50] Kobe A, Zraggen J, Messmer F, Puipe G, Sartoretti T, Alkadhi H, Pfammatter T and Mannil M. Prediction of treatment response to transarterial radioembolization of liver metastases: radiomics analysis of pre-treatment cone-beam CT: a proof of concept study. *Eur J Radiol Open* 2021; 8: 100375.
- [51] Marinelli B, Chen M, Stocker D, Charles D, Radell J, Lee JY, Fauveau V, Bello-Martinez R, Kim E and Taouli B. Early prediction of response of hepatocellular carcinoma to Yttrium-90 radiation segmentectomy using a machine learning MR imaging radiomic approach. *J Vasc Interv Radiol* 2023; 34: 1794-1801, e2.
- [52] Balli HT, Piskin FC, Puren Yücel S, Sozutok S, Ozgul D and Aikimbaev K. Predictability of the radiological response to Yttrium-90 transarterial radioembolization by dynamic magnetic resonance imaging-based radiomics analysis in patients with intrahepatic cholangiocarcinoma. *Diagn Interv Radiol* 2024; 30: 193-199.
- [53] Aujay G, Etchegaray C, Blanc JF, Lapuyade B, Papadopoulos P, Pey MA, Bordenave L, Trillaud H, Saut O and Pinaquy JB. Comparison of MRI-based response criteria and radiomics for the prediction of early response to transarterial radioembolization in patients with hepatocellular carcinoma. *Diagn Interv Imaging* 2022; 103: 360-366.
- [54] Xiong Y, Zhang Y and Hu C. Radiofrequency ablation versus microwave ablation for hepatocellular carcinoma with cirrhosis: a propensity score analysis. *Transl Cancer Res* 2024; 13: 1807-1820.
- [55] Chong CCN, Lee KF, Cheung SYS, Chu CCM, Fong AKW, Wong J, Hui JWY, Fung AKY, Lok HT, Lo EYJ, Chan SL, Yu SCH, Ng KKC and Lai PBS. Prospective double-blinded randomized controlled trial of microwave versus radiofrequency ablation for hepatocellular carcinoma (McRFA trial). *HPB (Oxford)* 2020; 22: 1121-1127.
- [56] Chen JJ, Jin ZC, Zhong BY, Fan W, Zhang WH, Luo B, Wang YQ, Teng GJ and Zhu HD. Locoregional therapies for hepatocellular carcinoma: the current status and future perspectives. *United European Gastroenterol J* 2024; 12: 226-239.
- [57] Yang Y, Chen Y, Ye F, Cao X, Xin Y, Wang Y, Lei Y, Li X, Feng D, Zhou X and Fan Q. Late recurrence of hepatocellular carcinoma after radiofrequency ablation: a multicenter study of risk factors, patterns, and survival. *Eur Radiol* 2021; 31: 3053-3064.
- [58] Hamed AA, Muhammed A, Abdelbary EAM, Elsharkawy RM and Ali MA. Can machine learning predict favorable outcome after radiofrequency ablation of hepatocellular carcinoma? *JCO Clin Cancer Inform* 2024; 8: e2300216.
- [59] Tong J, Liu P, Ji M, Wang Y, Xue Q, Yang JJ and Zhou CM. Machine learning can predict total death after radiofrequency ablation in liver cancer patients. *Clin Med Insights Oncol* 2021; 15: 11795549211000017.
- [60] Sato M, Moriyama M, Fukumoto T, Yamada T, Wake T, Nakagomi R, Nakatsuka T, Minami T,

## Research progress on machine algorithm prediction of prognosis for liver cancer

- Uchino K, Enooku K, Nakagawa H, Shiina S, Koike K, Fujishiro M and Tateishi R. Development of a transformer model for predicting the prognosis of patients with hepatocellular carcinoma after radiofrequency ablation. *Hepatol Int* 2024; 18: 131-137.
- [61] Zhang H, Sheng S, Qiao W, Sun Y and Jin R. Nomogram built based on machine learning to predict recurrence in early-stage hepatocellular carcinoma patients treated with ablation. *Front Oncol* 2024; 14: 1395329.
- [62] He Q, Xiong Y, Xia P, Yang X, Yu Y and Chen Z. Efficacy of radiofrequency ablation for solitary hepatocellular carcinoma 5 cm or smaller and construction of prognostic model by machine learning: a retrospective cohort study. *Research Square*; 2023.
- [63] Glassberg MB, Ghosh S, Clymer JW, Qadeer RA, Ferko NC, Sadeghirad B, Wright GW and Amaral JF. Microwave ablation compared with radiofrequency ablation for treatment of hepatocellular carcinoma and liver metastases: a systematic review and meta-analysis. *Oncotargets Ther* 2019; 12: 6407-6438.
- [64] Ren H, An C, Fu W, Wu J, Yao W, Yu J and Liang P. Prediction of local tumor progression after microwave ablation for early-stage hepatocellular carcinoma with machine learning. *J Cancer Res Ther* 2023; 19: 978-987.
- [65] An C, Yang H, Yu X, Han ZY, Cheng Z, Liu F, Dou J, Li B, Li Y, Li Y, Yu J and Liang P. A machine learning model based on health records for predicting recurrence after microwave ablation of hepatocellular carcinoma. *J Hepatocell Carcinoma* 2022; 9: 671-684.
- [66] Shahveranova A, Balli HT, Aikimbaev K, Piskin FC, Sozutok S and Yucel SP. Prediction of local tumor progression after microwave ablation in colorectal carcinoma liver metastases patients by MRI radiomics and clinical characteristics-based combined model: preliminary results. *Cardiovasc Intervent Radiol* 2023; 46: 713-725.
- [67] Jiang Y, Liang X, Han Z, Wang W, Xi S, Li T, Chen C, Yuan Q, Li N, Yu J, Xie Y, Xu Y, Zhou Z, Poultsides GA, Li G and Li R. Radiographical assessment of tumour stroma and treatment outcomes using deep learning: a retrospective, multicohort study. *Lancet Digit Health* 2021; 3: e371-e382.
- [68] Huang H, Xie Y, Wang G, Zhang L and Zhou W. DLNLF-net: denoised local and non-local deep features fusion network for malignancy characterization of hepatocellular carcinoma. *Comput Methods Programs Biomed* 2022; 227: 107201.
- [69] Kucukkaya AS, Zeevi T, Chai NX, Raju R, Haider SP, Elbanan M, Petukhova-Greenstein A, Lin M, Onofrey J, Nowak M, Cooper K, Thomas E, Santana J, Gebauer B, Mulligan D, Staib L, Batra R and Chapiro J. Predicting tumor recurrence on baseline MR imaging in patients with early-stage hepatocellular carcinoma using deep machine learning. *Sci Rep* 2023; 13: 7579.
- [70] Xia T, Zhao B, Li B, Lei Y, Song Y, Wang Y, Tang T and Ju S. MRI-based radiomics and deep learning in biological characteristics and prognosis of hepatocellular carcinoma: opportunities and challenges. *J Magn Reson Imaging* 2024; 59: 767-783.
- [71] Daneshjou R, Smith MP, Sun MD, Rotemberg V and Zou J. Lack of transparency and potential bias in artificial intelligence data sets and algorithms: a scoping review. *JAMA Dermatol* 2021; 157: 1362-1369.
- [72] Corti C, Cobanaj M, Dee EC, Criscitiello C, Tolaney SM, Celi LA and Curigliano G. Artificial intelligence in cancer research and precision medicine: applications, limitations and priorities to drive transformation in the delivery of equitable and unbiased care. *Cancer Treat Rev* 2023; 112: 102498.
- [73] Saadat A, Siddiqui T, Taseen S and Mughal S. Revolutionising impacts of artificial intelligence on health care system and its related medical in-transparencies. *Ann Biomed Eng* 2024; 52: 1546-1548.
- [74] Pecqueux M, Riediger C, Distler M, Oehme F, Bork U, Kolbinger FR, Schoffski O, van Wijnngaarden P, Weitz J, Schweipert J and Kahlert C. The use and future perspective of Artificial Intelligence-a survey among German surgeons. *Front Public Health* 2022; 10: 982335.
- [75] Hantel A, Walsh TP, Marron JM, Kehl KL, Sharp R, Van Allen E and Abel GA. Perspectives of oncologists on the ethical implications of using artificial intelligence for cancer care. *JAMA Netw Open* 2024; 7: e244077.