

# Research Progress in Predicting Hepatocellular Carcinoma with Portal Vein Tumour Thrombus in the Era of Artificial Intelligence

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**Abstract:** Hepatocellular Carcinoma (HCC) is a condition associated with significant morbidity and mortality. The presence of Portal Vein Tumour Thrombus (PVTT) typically signifies advanced disease stages and poor prognosis. Artificial intelligence (AI), particularly Machine Learning (ML) and Deep Learning (DL), has emerged as a promising tool for extracting quantitative data from medical images. AI is increasingly integrated into the imaging omics workflow and has become integral to various medical disciplines. This paper provides a comprehensive review of the mechanisms underlying the formation and progression of PVTT, as well as its impact on clinical management and prognosis. Additionally, it outlines the advancements in AI for predicting the diagnosis of HCC and the development of PVTT. The limitations of existing studies are critically evaluated, and potential future research directions in the realm of imaging for the diagnostic prediction of HCC and PVTT are discussed, with the ultimate goal of enhancing survival outcomes for PVTT patients.

**Keywords:** hepatocellular carcinoma, portal vein tumour thrombus, imaging omics, prediction, artificial intelligence

## Background

Hepatocellular Carcinoma (HCC) ranks as the sixth most prevalent cancer globally and the third leading cause of cancer-related mortality, boasting a five-year survival rate of less than 20%.<sup>1,2</sup> Due to the inconspicuous clinical manifestations of early-stage liver cancer, a significant proportion of patients (70–80%) present at an advanced disease stage. Portal Vein Tumor Thrombus (PVTT) is recognized as a critical prognostic factor in HCC, often indicating rapid disease progression and leading to intrahepatic and extrahepatic spread, portal hypertension, jaundice, and refractory ascites. While surgical resection, Transhepatic Arterial Chemotherapy And Embolization (TACE), and systemic treatment have shown potential for improving the survival of patients with liver cancer, the presence of PVTT significantly limits treatment options. The overall survival rate for patients with PVTT is notably lower compared to those without PVTT.<sup>3</sup>

In China, the incidence of PVTT ranges from approximately 44% to 62.2%, and patients without intervention have a median survival of only 2.7 months.<sup>4</sup> Based on the findings of a comprehensive review conducted by Daniel Q. Huang et al, which encompassed 8598 articles and 40 studies involving 8218 patients predominantly from European and American nations, it was determined that the median survival following resection of HCC patients with macrovascular invasion (MVI) was 14.39 months. In contrast, the median survival for those with involvement of the main body was 6.41 months.<sup>5</sup> Presently,

there exists controversy regarding the safety and applicability of various treatment approaches, such as surgery, TACE, and immunotherapy, for liver cancer patients with PVTT.<sup>6</sup>

The advancement of artificial intelligence (AI) in the medical domain has led to an increase in studies aimed at enhancing risk prediction, diagnosis, and prognosis of HCC through AI, and introducing a novel model for improving clinical care for HCC.<sup>7</sup> Imaging omics and deep learning (DL) techniques have the capability to extract intricate information from medical images that may not be discernible to the human eye, thereby offering valuable guidance for clinical decision-making.<sup>8</sup>

The majority of existing research has concentrated on the management and outcome of HCC patients with PVTT, with limited investigations conducted on the prediction of PVTT in HCC patients without PVTT. This study elucidates the pathogenesis and development mechanism of PVTT and its impact on clinical management and prognosis. It provides an overview of the advancements in AI technology for predicting the diagnosis of HCC and the occurrence of PVTT. The primary objective is to enhance the comprehension of PVTT among medical professionals and radiologists, refine the diagnostic and therapeutic approaches for HCC patients, and establish a foundation for the implementation of personalized precision medicine.

## Mechanism and Development Mechanism of PVTT Formation

The physiological and anatomical features of HCC render hepatocellular carcinoma cells susceptible to invading the hepatic vasculature, particularly the portal vein system, resulting in the development of portal vein cancer thrombus.<sup>9</sup> The exact mechanism underlying the formation of PVTT remains unclear. (In multiple clinical factors) Lv et al employed unifactorial and multivariate logistic regression analyses to examine the association between PVTT and 18 routine clinical parameters. Their findings indicated a higher prevalence of PVTT among individuals under the age of 50 (RR:0.373; 95% CI:0.146–0.954;  $P = 0.040$ ), those with elevated levels of  $\gamma$ -Gamma-Glutamyltransferase (GGT) (RR:4.091; 95% CI:1.448–11.553;  $P = 0.008$ ), and those presenting with S3 segmental lesions (RR:4.625; 95% CI:1.916–11.165;  $P = 0.001$ ) and microvascular infiltration (RR:20.912; 95% CI:4.745–92.172;  $P < 0.01$ ).<sup>10</sup> (In genetic research) Shortly thereafter, Liu et al employed sophisticated microRNA and cDNA microarray methodologies to investigate the expression profiles of microRNAs and mRNAs in PVTT tissues. Their findings revealed the significant involvement of miR-135a in facilitating PVTT tumorigenesis, thereby indicating the prospective utility of miR-135a in PVTT therapeutic interventions.<sup>11</sup> (In spectral imaging) Pan et al employed perfusion indicators and spectral parameters to assess the blood supply characteristics of PVTT, categorizing PVTT into proximal and distal groups based on the distance from the tumor thrombus to the central portal vein. Ultimately, the researchers determined that both PVTT and primary liver lesions receive blood supply from the hepatic artery, with minimal heterogeneity observed between distal PVTT and primary lesions ( $P < 0.001$ ).<sup>12</sup> Sun et al examined the mechanism and clinical significance of Circulating Tumor Cells (CTCs) in predicting MVI in HCC. Their findings suggest that the progression of vascular invasion by tumor cells is associated with a higher risk of postoperative recurrence in cases of HCC with macrovascular infiltration. Conversely, cases with only microvascular infiltration may still have a favorable prognosis with potential for curative treatment. The presence of tumor blood vessels plays a crucial role in providing essential nutrients and creating an immune microenvironment that promotes tumor growth and accelerates malignant transformation.<sup>13</sup> (In the study of tumor markers) Chao et al enrolled 1009 patients from 5 hospitals who received Hepatic Artery Infusion Chemotherapy (HAIC) and alpha-fetoprotein (alpha-fetoprotein). In HCC patients who were repeatedly measured 3–10 times, the team used the LCGM model to identify three distinct trajectories for serum AFP: high stability (37.0%;  $n = 373$ ), low stability (15.7%;  $n = 159$ ) and sharply decreased (47.3%;  $n = 477$ ), multivariate Cox proportional risk regression analysis found that ALBIstage 2 to 3, BCLC-C stage and highly stable AFP trajectories were correlated with OS, and finally concluded that AFP trajectories based on longitudinal changes in AFP performed well in predicting survival outcomes after HAIC treatment in large HCC patients. This also provides a potential monitoring tool for improving clinical decision-making.<sup>14</sup> Stefano Mazza et al employed multivariate COX regression analysis to categorize the AFP threshold values of 266 HCC patients undergoing radical treatment, utilizing AFP values of 20, 200, 400, and 1000 ng/mL as reference points. An AFP level of  $\geq 1000$  ng/mL was found to be correlated with a decrease in overall survival (1-year OS: 67% vs 88%, 5-year OS: 1% vs 43%;  $p = 0.005$ ). The study concluded that baseline AFP levels were significantly associated with clinical outcomes in

HCC patients. This could help identify patients at higher risk for a poorer prognosis who might benefit from personalized monitoring and treatment plans.<sup>15</sup>

Previous research has established that the development of PVTT arises from the interplay among the patient, tumor cells, and the microenvironment. The formation of PVTT encompasses various mechanisms, including anatomical factors, hemodynamics, and internal molecular processes. Research has indicated that PVTT originates from malignant cells within primary tumor cells, with some studies suggesting an association with portal vein reflux (PVCC). Additionally, emerging evidence suggests that the tumor microenvironment significantly influences the formation of PVTT.<sup>3,16,17</sup> However, the comprehension of PVTT formation and progression remains in its nascent stages and requires additional investigation.

## Effect of PVTT on Clinical Treatment and Prognosis of HCC

The prognosis of patients with HCC is closely associated with the location and extent of PVTT. In a study conducted by Chen et al, 438 HCC patients with PVTT were categorized into two groups based on the proximity of PVTT to the central portal vein. Group A consisted of patients with PVTT located within the hepatectomy area or extending less than 1cm beyond the resection line into the first branch of the central portal vein, while Group B included patients with PVTT extending into the central portal vein. Thrombectomy was performed on all subjects, and the results revealed a significantly higher overall survival rate in Group A compared to Group B ( $P < 0.02$ ).<sup>18</sup> Shortly thereafter, Takizawa et al carried out a multicenter study involving 193 patients diagnosed with HCC and PVTT. Utilizing the Kaplan-Meier method and Cox proportional risk model, they analyzed the clinical characteristics, prognosis, and survival outcomes of these patients. The 1-year, 2-year, 3-year and 5-year survival rates of 193 PVTT patients were 37.5%, 24.0%, 18.9% and 8.3%, ultimately determining that HCC patients with PVTT exhibited a dismal prognosis.<sup>19</sup> Subsequent research by Mahringer-Kunz et al further delineated the spectrum of PVTT based on the classification established by the Japanese Liver Cancer Research Group, confirming the association between PVTT in HCC patients and poor prognosis, the median OS without PVTT was 35.7 months, significantly longer than that of PVTT patients (7.2 months,  $P < 0.001$ ) with even mild PVTT resulting in an unfavorable prognosis.<sup>20</sup>

There is currently no universally accepted consensus or standardized guidelines for the treatment of HCC with PVTT. Sorafenib is commonly recommended for HCC patients with PVTT according to the Barcelona Clinic Liver Cancer (BCLC) classification.<sup>21</sup> However, experts, particularly in China, advocate for a multidisciplinary approach to treating HCC with PVTT, which may include surgery, TACE, radiotherapy (RT), molecularly targeted drugs, and/or immune checkpoint inhibitors. Neoadjuvant therapy and tumor-down staging are strategies believed to extend the survival of patients with PVTT, representing a current focal point in HCC research that warrants further scientific investigation.<sup>3,9,22–29</sup>

## Progress of Artificial Intelligence in Imaging Prediction of PVTT

### Use of Artificial Intelligence and Imaging Omics to Diagnose HCC

HCC can be diagnosed without histological examination due to its distinctive radiological characteristics. The imaging diagnosis of liver cancer primarily relies on the “fast in and fast out” enhancement technique of dynamic enhanced scans. Dynamic enhanced CT and multi-parameter MRI demonstrate consistently or variably enhanced liver tumors in the arterial phase, particularly in the late arterial phase, with lower enhancement in the portal and/or delayed phases compared to the hepatic parenchyma. Developing fusion models utilizing clinical data mining of CT and/or MRI data for liver cancer has the potential to enhance clinical decision-making processes, such as patient treatment selection, efficacy evaluation, and outcome prediction.<sup>30</sup>

Convolutional Neural Network (CNN), a type of Multilayer Artificial Neural Network (ANN), is proficient in learning complex patterns in deep learning. CNNs have the capability to be incorporated into the examination of extensive imaging datasets utilizing both supervised and unsupervised learning methods. This integration can occur within specific stages of the radiomics workflow, as well as in end-to-end processing, where images are directly transformed into output signals.<sup>31</sup> Through an iterative process, CNNs can enhance their predictive accuracy, thereby improving the diagnostic rate of HCC across various imaging modalities such as ultrasound, CT, MRI, positron emission

tomography (PET), and histology. This advancement in CNN technology can aid in the early clinical diagnosis and treatment of HCC.<sup>7</sup>

## B-Ultrasound

Abdominal B-ultrasound is recommended as the preferred method of screening for space-occupying lesions. Khanh N.Q. Le et al used CNN to diagnose HCC. They concluded that the sensitivity and specificity of CNN on the internal test set were 73.6% (95% CI: 64.3–82.8) and 97.8% (95% CI: 96.7–98.9), respectively, and the external validation set were 81.5% (95% CI: 74.2 – 88.8), 94.4% (95% CI: 92.8 – 96.0).<sup>32</sup> Guo et al introduced an innovative two-stage multi-perspective learning framework for computer-aided diagnosis of liver tumors utilizing contrast-enhanced ultrasound (CEUS). This framework demonstrated accuracy, sensitivity, and specificity rates of 90.4%, 93.6%, and 86.9%, respectively, in distinguishing between benign and malignant liver tumors. These findings offer compelling support for the advancement of artificial intelligence models in the identification of malignant tumors.<sup>33</sup>

## Ct

Dynamic enhanced CT and Magnetic Resonance Imaging (MRI) scans are commonly used imaging modalities for accurately diagnosing liver ultrasound and/or serum AFP screening abnormalities.<sup>30</sup> Gao et al leverage deep CNNs and recurrent neural networks (RNNs) to efficiently extract and combine enhanced CT images and clinical data for patient diagnosis. They introduce a deep learning model with a modular structure consisting of a spatial extractor, time encoder, integration module, and classifier (STIC). The HCC and ICC classification demonstrated an accuracy of 86.2% and an AUC of 0.893 on the test set. In the context of distinguishing malignant liver tumors, the accuracy rate on the test set was 72.6%, aligning closely with the diagnostic proficiency of physicians (70.8%).<sup>34</sup>

## Mri

Magnetic resonance has been fully utilized in imaging omics.<sup>35</sup> Hamm et al utilized a pre-trained CNN to categorize MRI data of 494 lesions from 334 cases, revealing that the AI model exhibited a sensitivity of 90% for HCC diagnosis, surpassing the 60–70% sensitivity range of radiologists. The performance of the pre-trained AI model was notably superior to that of radiologists (82.5% and 96.5%).<sup>33</sup> In a similar vein, Zhen et al employed CNN to construct a DL model for the classification of liver tumors using MR images, integrating clinical data to achieve AUC of 0.985 for HCC diagnosis, with a 95% confidence interval of 0.960–1.000. This outcome demonstrated a high level of agreement (91.9%) with pathology findings.<sup>36</sup> Machine learning and Deep Learning models utilizing data from CT or MRI have demonstrated strong predictive capabilities and have achieved a level of accuracy comparable to that of expert radiologists.

## 18f-Fdg Pet-Ct

Raluca Mititelu et al undertook a thorough review of the literature to assess the effectiveness, precision, and clinical relevance of 18F-FDG PET-CT in the identification and treatment of portal venous tumor thrombosis in patients with HCC, emphasizing the significance of the maximum standardized uptake value as a crucial diagnostic and prognostic indicator. The study concludes that 18F-FDG PET-CT is highly beneficial for identifying recurrence and directing treatment plans, particularly in patients with high-grade HCC, and plays a critical role in distinguishing between malignant and benign portal vein thrombosis.<sup>37</sup>

However, due to the other scanners and reconstruction methods of various manufacturers in different research centers, the final image judgment will be different, so imaging preprocessing is an inevitable operation. Image preprocessing methods include image normalization and reconstruction. By converting the image from the original gray level to the given standard gray level, brightness normalization is carried out to correct the brightness difference between objects. Normalization such as Min-max and z-score are commonly used for preprocessing. The imaging resolution will improve the image quality and eliminate the deviation of any imaging resolution. Second, in situations where data is limited (only a few dozen to 100 cases are available), the high capacity of deep learning models to learn from the data can lead to overfitting, so machine learning models that use more straightforward “features” such as tumor size and shape may be more reliable.<sup>38</sup>

## Preoperative Prediction

Artificial intelligence has the potential to enhance preoperative prognostic predictions for HCC patients, thereby optimizing treatment outcomes. (In predicting pathological types) Ren et al employed a Support Vector Machine (SVM) to develop a preoperative pathological grading model for HCC, enabling non-invasive prediction of HCC pathological grading. The integration of clinical and ultrasound features in the model demonstrated superior performance in the test set, yielding an AUC of 0.874(0.709–0.964).<sup>39</sup> After that, (In the prediction of pathological grade) Ding et al utilized a combination of a clinical model, image omics features, and deep learning model as the foundational framework for their study. They integrated the prediction probabilities derived from these models into a logistic regression model and conducted a multi-model prediction fusion. The resulting fusion model achieved AUC values of 0.89, 0.83, and 0.80 in the training, validation, and test cohorts, respectively. Furthermore, the fusion model was applied to predict HCC pathological grading preoperatively, serving as a noninvasive predictive tool to inform clinical decision-making.<sup>40</sup> (In the prediction of liver cancer immunotherapy) Nakao et al constructed a predictive model utilizing AI and Immune Checkpoint Inhibitors (ICIs) contrast-enhanced CT imaging features to forecast treatment outcomes. The ResNet-18 CNN model was employed, along with 3D t distribution random neighborhood embedding technology for image feature analysis. Ultimately, accurate predictions were made for CT sections of individual patients with HCC treated with ICI targeted drugs, the resulting ResNet-18 model has a PD accuracy of 100% and a recall rate of 100%.<sup>41</sup> (In predicting the survival of HCC patients) Fei et al constructed a nomogram utilizing omics and clinical variables to predict progression-free survival in HCC patients undergoing Radiofrequency Ablation (RFA) or Surgical Resection (SR) therapies. The nomogram achieved a concordance index (C-index) of 0.726 for RFA and 0.741 for SR, thereby enhancing the optimization of treatment strategies for patients with very early or early stage HCC.<sup>42</sup> (In clinical care) The natural language processing model ChatGPT, developed by OpenAI, is currently being utilized in the medical domain. In their study, YeeHuiYeo et al examined the searches conducted by patients and caregivers with HCC on ChatGPT, revealing that the model offered motivational responses to newly diagnosed patients with HCC, thereby promoting proactive approaches in managing their diagnosis and treatment plans. ChatGPT recommended that caregivers promote adherence to treatment strategies, offer emotional support, and prioritize their own physical and mental well-being in order to enhance the quality of care provided to patients.<sup>43</sup>

## Prediction of Portal Vein Tumor Thrombosis

Portal vein tumor thrombosis, the predominant type of macrovascular invasion, is present in approximately 10–40% of individuals diagnosed with HCC.<sup>44</sup> Its occurrence typically signifies accelerated disease advancement and is associated with intrahepatic and extrahepatic metastasis, portal hypertension, hepatocellular jaundice, and refractory ascites. Consequently, the ability to anticipate the development of PVTT in patients and implement timely interventions to postpone or mitigate its effects is imperative. Huang et al conducted a study in which they extracted 48 texture features and developed a prediction model utilizing radiomic features, clinical features, and radiotherapy dosimetry parameters. The researchers utilized a minimum absolute contraction and selection operator regression model to calculate the radiomic score (rad-score), and subsequently created a nomogram incorporating the rad-score, clinical features, and dosimetric parameters. The findings suggest that the image-omics-based nomogram outperforms the clinical nomogram in predicting OS, with a C index of 0.73 (95% CI, 0.67–0.79) and an AUC of 0.71 (95% CI, 0.62–0.79) (Table 1).<sup>45</sup> Cheng et al performed a retrospective analysis in which they extracted 396 image omics features from baseline CT scans, created and verified a CT-based image omics model, and developed a random survival forest model utilizing features with varying importance and minimal depth selection. The study aimed to predict the OS of patients with HCC and PVTT who underwent treatment with Drug-Eluting Beads Transarterial Chemoembolization (DEB-TACE). The image omics model achieved a C-index of 0.759 in the training cohort and 0.730 in the validation cohort. Subsequently, in an effort to enhance predictive accuracy, the team incorporated clinical indicators into the model, yielding a composite model with a C-index of 0.814 for the training cohort and 0.792 for the validation cohort.<sup>46</sup> Wu et al utilized image omics to develop a clinical prediction model for patients with HCC and PVTT who were treated with Stereotactic Radiotherapy (SBRT). The minimum absolute contraction and selection operator regression model was employed to construct the predictive model. Additionally, a multivariate Cox regression risk model was established to assess survival outcomes, and a nomogram was generated to display the imaging and clinical characteristics. The estimated

**Table 1** Research Progress in Prediction of HCC Portal Vein Cancer Thrombus

Author/Trial/Year	Design	Patients	Model	Statistical Approach	Forecast Content	Forecast Effectiveness
Huang et al 2022 <sup>45</sup>	RT	105vs.26	Nomogram based on rad score, clinical features and dosimetric parameters	Multivariate regression analysis	OS after radiotherapy in HCC patients with PVTT	C Index: 0.73 (95% CI, 0.67–0.79), AUC: 0.71 (95% CI, 0.62–0.79)
Cheng et al 2023 <sup>46</sup>	RT	69vs.31	Random survival forest model, image omics model		OS in patients with HCC and PVTT were treated by transarterial chemoembolization with drug-eluted straws	C index: Training cohort: 0.759; Verification queue: 0.730
Cheng et al 2023 <sup>46</sup>	RT	69vs.31	Clinical model, imaging model		OS in patients with HCC and PVTT were treated by transarterial chemoembolization with drug-eluted straws	C index: Training cohort: 0.814; Verification queue: 0.792
Wu et al 2020 <sup>47</sup>	RT	70	Multivariate Cox regression risk model	Multivariate Cox regression analysis	OS in PVTT patients undergoing stereotactic radiotherapy	Experimental group: AUC=0.859 (CI: 0.770–0.948) Comparison group: AUC=0.761 (CI: 0.641–0.881)
Zhang et al 2023 <sup>48</sup>	RT	94	Predictive models integrating clinical and MRI features	Univariate and multivariate Cox regression analysis	OS after surgical resection in PVTT patients undergoing preoperative enhanced MRI	High risk group vs low risk group (11.7vs.25.0 months, p<0.001)
Fu et al 2021 <sup>49</sup>	RT	281vs.85	Optimal model combining clinical/radiological factors and imaging omics features	Multi-task deep learning network	The probability of future large vessel invasion in HCC patients without vascular invasion	Training set AUC: 0.877 Verification set AUC: 0.836 Time to great vessel invasion: Training: hazard ratio [HR] = 0.073, 95% confidence interval [CI]: 0.032 ~ 0.167, p < 0.001, verification: HR = 0.090, 95% CI: 0.022 ~ 0.366, p < 0.001) Overall survival (training: HR = 0.344, 95% CI: 0.246 ~ 0.547, p < 0.001, verification: HR = 0.489, 95% CI: 0.279 ~ 0.859, p = 0.003)
Wei et al 2021 <sup>50</sup>	RT	154vs.72	Integrated clinical-imaging model	Cox regression analysis	The probability of future large vessel invasion in HCC patients without vascular invasion	Training set AUC: 0.986 Verification set AUC: 0.979

OS [AUC = 0.859 (CI: 0.770 – 0.948)] was superior to clinical features alone [AUC = 0.761 (CI: 0.641 – 0.881)].<sup>47</sup> Zhang et al constructed a prognostic model utilizing clinical data and MRI features to forecast the survival outcomes of HCC patients with PVTT following hepatectomy. They found that MRI, serum albumin (HR, 0.948;  $p = 0.02$ ) and age (HR, 0.978;  $p = 0.04$ ) Total size of the two most extensive tumors (HR, 3.050;  $p < 0.001$ ) and tumor growth subtypes (HR, 1.928;  $p = 0.006$ ) correlated with OS and included a prognostic score, thus the researchers stratified the cohort into high-risk and low-risk categories, determining that individuals in the high-risk group exhibited a significantly shorter OS compared to those in the low-risk group (4.5 months vs 6.1 months,  $p = 0.001$ ).<sup>48</sup> (In terms of predicting macrovascular infiltration) Fu et al conducted a retrospective study involving 366 patients with HCC from five hospitals. They developed a multi-task deep learning network model to forecast future occurrences of macrovascular invasion, integrating it with the most effective model incorporating clinical/radiological factors and imaging omics characteristics. This approach resulted in the highest level of accuracy. The AUC values for the training and validation sets were 0.877 and 0.836, respectively. In each subgroup, the risk ratio [HR] = 0.073, 95% confidence interval [CI]: 0.032 ~ 0.167,  $p < 0.001$ , verification: HR = 0.090, 95% CI: 0.022 ~ 0.366,  $p < 0.001$ ) and overall survival (training: HR = 0.344, 95% CI: 0.246 ~ 0.547,  $p < 0.001$ , verification: HR = 0.489, 95% CI: 0.279 ~ 0.859,  $p = 0.003$ ) were statistically significant.<sup>49</sup> Subsequently, the team developed a final prediction model utilizing the random forest model and employed Cox regression analysis to identify independent risk factors and forecast the timing of MaVI occurrence. The AUC values of the prediction model in the training set and external test set were 0.986 and 0.979, respectively (Table 1).<sup>50</sup> In conclusion, the utilization of PVTT knowledge and advancements in scientific research technology have notably enhanced the precision of prognosticating postoperative survival rates among patients. Nevertheless, further efforts are required to forecast vascular invasion in patients lacking PVTT.

## Limitations, Future, and Expectations

While the utilization of artificial intelligence in predicting PVTT has demonstrated encouraging outcomes, there exist certain constraints. Primarily, the majority of aforementioned studies are retrospective in nature, resulting in relatively small sample sizes that may lead to overfitting and publication bias. Consequently, a high false positive rate may compromise the reliability and applicability of the model. To enhance accuracy and dependability, it is recommended that multi-institutional databases be established and data sets be sourced from diverse geographic regions encompassing various areas, countries, and ethnicities. Furthermore, certain studies exhibit a deficiency in external validation, thereby undermining the credibility of established models and hindering the integration of imaging omics into clinical practice.<sup>45–48</sup>

Additionally, the manual implementation of image segmentation and feature extraction during image omics processing introduces significant subjectivity, potentially influencing the accuracy of the final prediction model. To mitigate this issue, future research should consider utilizing trained automated or semi-automated segmentation techniques for delineating target areas, thereby minimizing errors attributable to subjective factors.<sup>51</sup>

Finally, studies based on AI-based imageromics have provided “black box” models, resulting in a decision-making process that is difficult to understand and understand. Therefore, it is necessary to solve the problem of the “interpretability” of AI image-omics models, which is essential to increase doctors’ trust in these AI-assisted devices. This is also worth further exploration by researchers in the future. For example, Eduardo Pontes Reis et al used an interpretable open-source AI algorithm for automatic abdominal CT contrast phase detection. In internal validation, the classifier’s accuracy was 92.3%, and the average F1 score was 90.7%. During external validation, the algorithm maintained an accuracy of 90.1%, with an average F1 score of 82.6%. Finally, the open source and explainable AI algorithm can accurately detect the contrast phase of abdominal CT scan with high accuracy and verify F1 internally and externally, which confirms the conclusion of its generalization ability,<sup>52</sup> which provides an excellent example for us.

## Conclusion

In Conclusion, significant advancements have been achieved in utilizing AI for diagnostic detection, pre-treatment assessment, and postoperative overall survival prediction in patients with HCC. Nevertheless, there is a paucity of literature on the prediction of macrovascular infiltration, particularly in the context of portal vein cancer thrombus. Utilizing advanced feature extraction techniques in medical imaging to identify imperceptible characteristics, and developing predictive models incorporating clinical, radiological, and imaging omics data, can aid clinicians in making

informed decisions, leading to improved treatment outcomes, reduced post-surgical recurrence rates, and ultimately enhanced survival rates for patients with HCC. We can establish a comprehensive and non-invasive risk prediction model based on the current research status of vascular invasion of liver cancer and the characteristics of HCC to improve the therapeutic effect of PVTT further. It is hypothesized that advancements in AI, particularly in the areas of liver cancer treatment, imaging omics, and deep learning, will lead to significant breakthroughs in predicting and diagnosing PVTT in HCC patients, ultimately resulting in improved clinical outcomes for a larger population of individuals.

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## Disclosure

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