

## REVIEW

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# Advancing Diagnostic Accuracy in Liver Cancer: A Systematic Review of Artificial Intelligence Applications in Hepatocellular Carcinoma and Cholangiocarcinoma Detection Using Abdominal CT Imaging

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## Abstract

**Objective:** This study aimed to systematically evaluate the diagnostic performance of artificial intelligence (AI) in differentiating hepatocellular carcinoma (HCC) from cholangiocarcinoma (CCA) using abdominal CT and MRI, with an emphasis on its clinical implications for liver cancer management. **Methods:** Following the PRISMA guidelines, we conducted a comprehensive literature search across five major databases (PubMed, Web of Science, ScienceDirect, Scopus, and Google Scholar) from 2000 to May 6, 2025. Eligible studies included original research that applied AI for the diagnosis of HCC or CCA. Data were extracted on study design, population characteristics, imaging modality, AI methodology, diagnostic performance (sensitivity, specificity, accuracy, AUC), validation strategies, and risk of bias, which was assessed using QUADAS-2. **Results:** A total of 44 studies met the inclusion criteria. Most were retrospective, while only a few prospective designs provided real-time validation. CT and MRI were the dominant imaging modalities, with MRI showing superior sensitivity for small lesions, while CT was more effective for large tumors and vascular involvement. Convolutional neural networks (CNNs) were the most frequently used model architectures, although more advanced deep learning and hybrid radiomic-clinical models were also reported. Diagnostic performance was consistently strong: sensitivity and specificity ranged from 75% to 100%, overall accuracy from 73% to 96%, and AUC values from 0.74 to 0.99. Studies incorporating multi-modal imaging (CT+MRI) or radiomic-genomic features achieved the highest diagnostic performance, with accuracy and specificity exceeding 90–95%. Subgroup analyses revealed that tumor size, location, microvascular invasion, and patient demographics influenced AI model performance. Risk of bias was generally low-to-moderate, with limitations related to retrospective data and limited external validation. **Conclusion:** AI models, particularly CNN- and radiomics-based, show accuracy comparable to radiologists in distinguishing HCC from CCA. Multi-modal integration and feature fusion hold the greatest promise for improving workflows. Large-scale, multi-center validation is needed to confirm their utility and enable adoption in liver cancer care.

**Keywords:** Radiomics- deep learning- multi-modal imaging- clinical decision support- precision oncology

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## Introduction

Diagnostic imaging is an essential tool for the non-invasive detection and characterization of diseases, particularly liver malignancies. The accurate differentiation of liver cancers, such as hepatocellular carcinoma (HCC)

and cholangiocarcinoma (CCA), remains a significant challenge, often requiring the expertise of highly trained radiologists. However, interpretation variability exists, especially among less experienced or newly certified radiologists, which can lead to diagnostic delays and inconsistencies [1]. To address these challenges, artificial

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intelligence (AI) has emerged as a transformative force in medical imaging, offering the potential to enhance diagnostic accuracy and efficiency. By mimicking human cognitive functions, such as reasoning and decision-making, AI enables machines to autonomously process complex data with minimal human oversight [2]. The adoption of AI in healthcare is rapidly accelerating, with advances in computing power and large-scale data analytics driving improvements in diagnostic workflows and treatment planning [3]. AI applications are now being extended beyond hospitals to support community-level health services, including public health data collection and disease surveillance.

Globally, liver cancer is the sixth most commonly diagnosed cancer and the third leading cause of cancer-related mortality, accounting for approximately 905,000 new cases and 830,000 deaths annually [4]. HCC constitutes about 75–85% of primary liver cancers, while CCA represents 10–15% [5]. The burden is particularly pronounced in Southeast Asia, including Thailand, Laos, and Cambodia, where CCA prevalence is among the highest worldwide, largely driven by liver fluke infection and chronic biliary inflammation [6, 7]. These epidemiological disparities underscore the pressing need for precise, accessible diagnostic tools tailored to both global and regional contexts.

Liver cancer diagnosis, which requires specialized radiologic expertise, stands to greatly benefit from AI advancements. Deep learning models, in particular, have demonstrated superior performance in the classification, detection, and characterization of liver lesions in imaging studies [8]. Several reports have indicated that AI systems can achieve diagnostic accuracies comparable to, or even exceeding, those of experienced radiologists, especially in identifying HCC and CCA using computed tomography (CT) and magnetic resonance imaging (MRI) [9, 10]. AI has shown remarkable capabilities in analyzing complex imaging data, such as multiphasic CT [11], and has outperformed conventional imaging techniques in certain contexts, such as mass spectrometry-based automated liver cancer diagnosis [12]. Furthermore, AI models are increasingly being used in radiomic analysis to predict the aggressiveness and treatment response of liver tumors [13].

Nevertheless, important challenges remain. Data heterogeneity, algorithm generalizability, and integration into real-world workflows limit translation into daily practice. Moreover, previous reviews have often been descriptive, with limited pooled statistical analyses and without structured risk-of-bias assessments such as QUADAS-2. Few studies have addressed practical considerations such as interpretability, cost-effectiveness, and workflow implementation. These gaps highlight the need for more comprehensive evidence synthesis.

In light of these advancements and unmet needs, our research team undertook a systematic review to comprehensively evaluate the role of AI in the imaging-based diagnosis of hepatocellular carcinoma and cholangiocarcinoma. By incorporating pooled sensitivity, specificity, and AUC analyses, assessing study quality using QUADAS-2, and presenting visual

comparative charts, this study aims to provide a robust overview of AI's diagnostic potential. Additionally, we examine the predictive factors incorporated in AI models for liver lesion classification and discuss their practical implications for clinical adoption. Ultimately, the goal of this review is to inform future AI development and enhance its clinical utility in diagnosing liver cancers, thereby contributing to improved disease prevention and control strategies [14–16].

## Materials and Methods

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [10]. A comprehensive literature search was conducted on May 6, 2025, across five major electronic databases PubMed, Web of Science, ScienceDirect, Scopus, and Google Scholar chosen for their broad coverage of biomedical and technical research. The search period was set from 2000 to 2025, reflecting the rise of AI applications in medical imaging during this timeframe.

### Search Strategy

The search employed a combination of predefined keywords relevant to AI applications in liver cancer diagnosis, using Boolean operators to maximize comprehensiveness. The final search query included:

- (“focal liver lesions” OR “FLLs” OR “hepatic focal lesions” OR “liver tumor” OR “hepatic tumor”)
- AND (“artificial intelligence” OR “machine learning” OR “neural networks” OR “deep learning” OR “automated diagnosis” OR “computed tomography” OR “CT” OR “magnetic resonance imaging” OR “MRI” OR “computer-aided diagnosis” OR “automated CT” OR “automated MRI”)

Key terms such as “Artificial Intelligence,” “Cholangiocarcinoma,” “Hepatocellular Carcinoma,” and “Liver Cancer” were incorporated to refine the search and ensure inclusion of the most relevant studies.

### Eligibility Criteria

Studies were included if they met all of the following criteria:

- Publication period: Published between 2000 and 2025, with 2000 chosen to reflect the emergence and growth of AI applications in medical imaging.
- Study focus: Specifically investigated AI applications for the detection or diagnosis of hepatocellular carcinoma (HCC), cholangiocarcinoma (CCA), or liver cancer.
- Study type: Original research articles with full-text availability.
- Language: Written in English, acknowledging the potential for language bias.
- Methodological rigor: Studies were required to be methodologically sound and provide complete datasets, including sufficient data to assess AI diagnostic performance metrics (e.g., sensitivity, specificity, accuracy, and AUC).

*Studies were excluded if they met any of the following conditions*

- Publication period: Published outside the specified date range (2000–2025).
- Duplicates: Duplicate records identified across multiple databases.
- Study type: Reviews, case reports, conference abstracts or proceedings, letters, or editorials.
- Study focus: Investigations of cancers other than HCC or CCA, or studies including mixed cancer populations without separate analyses for HCC or CCA.
- Data availability: Studies lacking full-text access or providing incomplete, unclear, or insufficient data for extraction and evaluation of AI diagnostic performance.

#### Study Selection

The initial database search retrieved a total of 245 articles: 133 from PubMed, 65 from Scopus, 40 from ScienceDirect, and 7 from Google Scholar. After removing duplicates and applying the eligibility criteria, 236 articles remained. Title and abstract screening identified 183 potentially relevant studies, and subsequent full-text assessment resulted in 44 studies that met all inclusion criteria. The selection process is summarized in a PRISMA flow diagram (Figure 1).

#### Data Extraction and Synthesis

Data were independently extracted by three reviewers using a standardized form to ensure consistency and minimize bias. Extracted variables included:

- Author names and year of publication

- Study location and population characteristics
- Sample size and study design
- Imaging modalities employed (CT, MRI)
- AI methodologies applied (deep learning, machine learning, hybrid approaches)
- Diagnostic performance metrics (sensitivity, specificity, accuracy, AUC)
- Validation strategies (e.g., k-fold cross-validation, external datasets)
- Risk of bias assessment using the QUADAS-2 tool, evaluating patient selection, index test, reference standard, and flow and timing.

Extracted data were organized into structured tables to facilitate comparisons. AI techniques were evaluated for diagnostic capabilities in differentiating HCC and CCA [6, 8, 11].

#### Quality Assessment

The methodological quality of the included studies was evaluated using the QUADAS-2 tool, which assesses risk of bias across four domains: patient selection, index test, reference standard, and flow/timing. For this review, additional emphasis was placed on:

- Relevance and appropriateness of the AI model for liver cancer diagnosis.
- Adequacy of sample size to ensure statistical reliability.
- Clarity and transparency of the AI methodology, including data preprocessing, feature extraction, and training-validation strategies.
- Accuracy, completeness, and reporting transparency

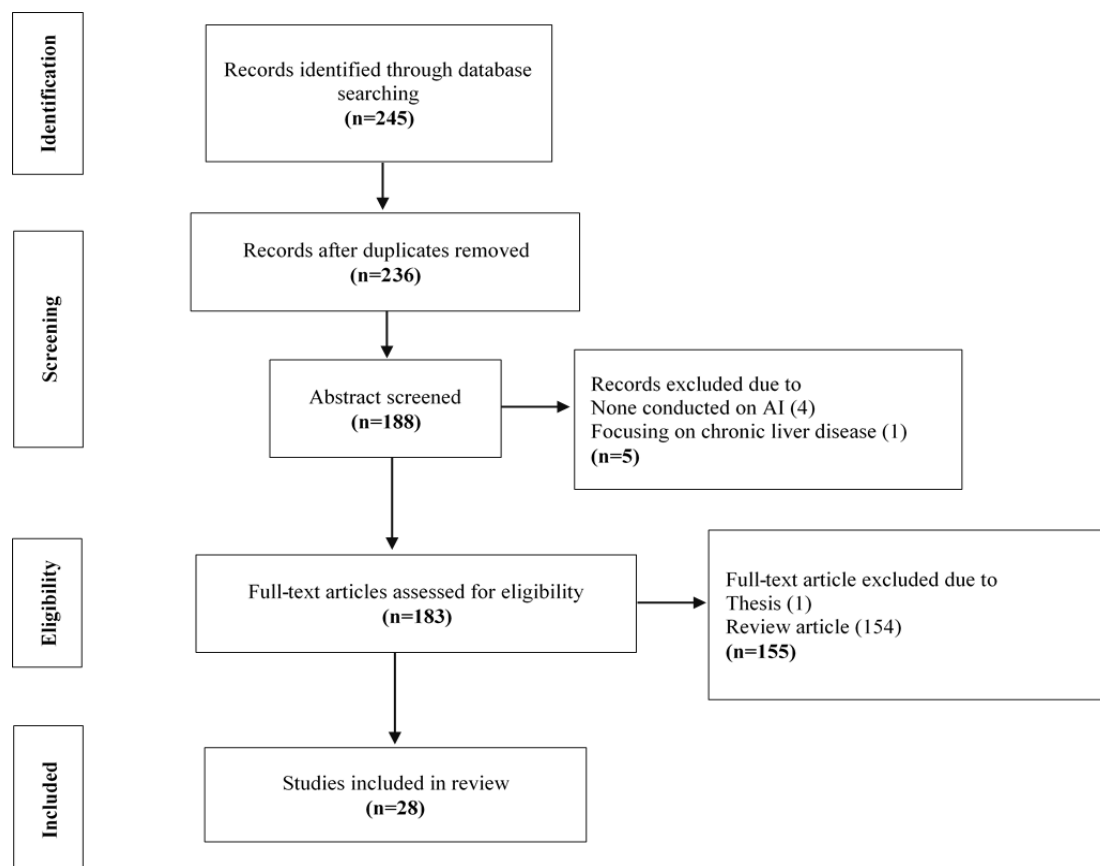


Figure 1. PRISMA Flow Diagram of the Study Selection Process

of diagnostic metrics.

Further considerations included the imaging modalities applied (CT and MRI) and the potential impact of language bias, as only English-language publications were included.

### *Results Interpretation*

Extracted data were synthesized thematically and analyzed according to diagnostic performance, processing efficiency, specificity, and AI model architecture. Studies consistently demonstrated that AI models achieved diagnostic accuracy comparable to, and in some cases exceeding, that of experienced radiologists. Reported accuracy rates in differentiating HCC from CCA frequently approached or exceeded 90%, with sensitivities and specificities in the 80–95% range [8, 11]. Performance was further enhanced in studies integrating multimodal imaging or radiomic–genomic fusion approaches.

This rigorous methodology ensured a transparent and high-quality systematic review, providing critical insights into technological trends, clinical applicability, and the practical utility of AI-driven liver cancer diagnosis.

## **Results**

### *Study Characteristics and Imaging Modalities*

A total of 44 studies were included in this systematic review, all focusing on the application of artificial intelligence (AI) in liver cancer, particularly differentiating hepatocellular carcinoma (HCC) from intrahepatic cholangiocarcinoma (ICC) or other liver malignancies (Table 1). The studies varied in design, sample size, and imaging modality but consistently evaluated AI-based approaches particularly deep learning and radiomics models for improving diagnostic accuracy.

### *Retrospective vs. Prospective Designs*

Most studies adopted a retrospective design, leveraging pre-existing datasets to train and test AI models. Prospective studies were less common but provided opportunities for real-time patient data collection and external validation, enhancing clinical applicability.

### *Imaging Modalities*

Contrast-enhanced CT and MRI were the most frequently utilized imaging modalities. CT provided detailed assessment of tumor vascularity, essential for differentiating HCC from ICC. MRI offered superior soft-tissue contrast, particularly when employing dynamic contrast-enhanced (DCE) and diffusion-weighted imaging (DWI) sequences. A limited number of studies explored hybrid modalities such as PET/CT, whereas ultrasound was rarely applied and demonstrated comparatively lower diagnostic yield.

### *AI Models and Approaches*

- **Model Architectures:** Convolutional Neural Networks (CNNs) were predominant, capitalizing on automated feature extraction from raw imaging data. More advanced architectures, including Residual Networks (ResNets) and Fully Convolutional Networks (FCNs), were applied

for improved segmentation and classification. In select studies, Recurrent Neural Networks (RNNs) and Long Short-Term Memory (LSTM) models were incorporated for analyzing temporal imaging sequences.

- **Input Modalities and Data Types:** Most models were trained on CT or MRI datasets, with some integrating advanced MRI sequences. Studies combining radiomic features (e.g., texture, shape, and intensity metrics) with deep learning demonstrated superior performance. Multi-modal approaches integrating CT and MRI achieved the highest accuracy by leveraging complementary anatomical and functional information.

### *Diagnostic Accuracy and Performance Metrics*

AI models reported sensitivity and specificity between 75–100%, with overall accuracy ranging from 73% to 96%. The area under the curve (AUC) consistently fell between 0.74 and 0.99, indicating strong diagnostic capability. Models integrating multi-modal imaging or radiomic–clinical features often outperformed single-modality approaches.

Figure 2 illustrates the reported AUC ranges across studies. The majority clustered between 0.75 and 0.90, with a subset achieving near-perfect performance (AUC >0.95).

Figure 3 summarizes the diagnostic performance across imaging modalities. MRI and CT demonstrated the highest mean AUC values, particularly when integrated with radiomic or clinical features. Hybrid approaches (multi-modal fusion) consistently outperformed single-modality models, whereas clinical-only datasets yielded lower performance (AUC ~0.70).

### *Subgroup and Stratified Analyses*

Tumor characteristics (size, location, microvascular invasion) and patient demographics influenced diagnostic performance. MRI-based models showed higher sensitivity for small lesions, whereas CT-based models were more effective for large tumors or vascular involvement. Multi-modal integration consistently enhanced performance.

### *Risk of Bias*

Most studies were rated as having low-to-moderate risk of bias using QUADAS-2, with limitations primarily due to retrospective designs and limited external validation. Independent validation cohorts were relatively few, affecting generalizability.

### *Key Takeaways*

1. AI models, particularly CNN-based and radiomics–integrated approaches, achieved high diagnostic accuracy, frequently matching or exceeding experienced radiologists.

2. MRI-based models were more sensitive for small lesions, highlighting the importance of imaging modality selection.

3. Multi-modal integration of CT, MRI, and radiomic features enhanced overall diagnostic performance.

4. Widespread clinical adoption requires large-scale, multi-center validation with standardized imaging protocols.

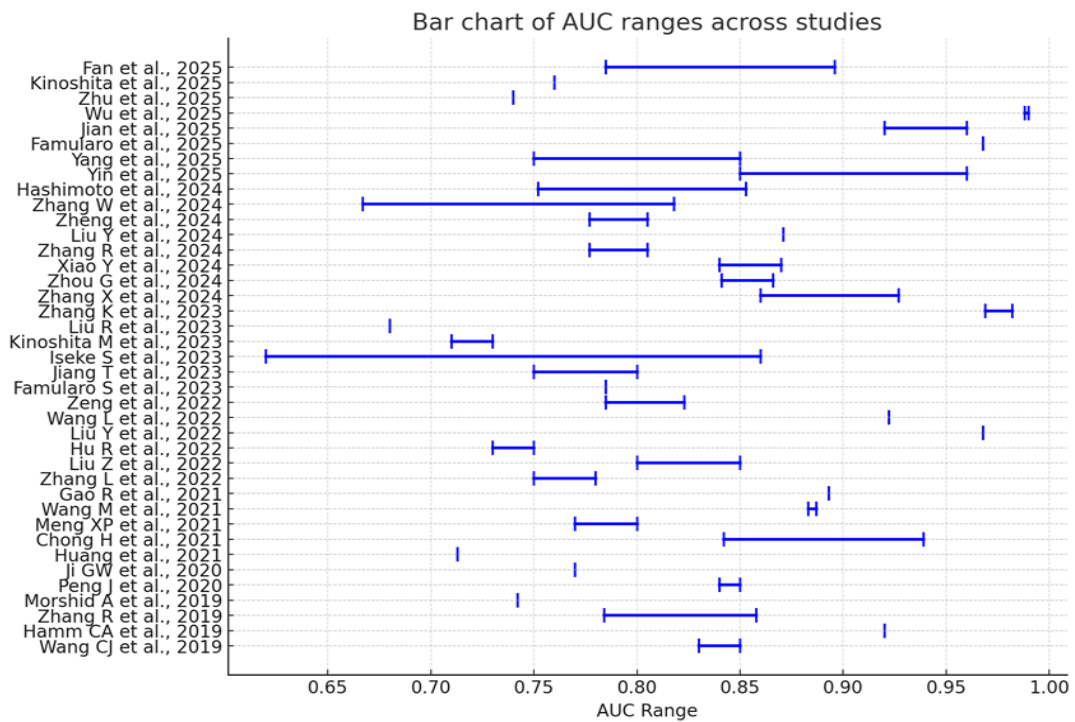


Figure 2. Distribution of Reported AUC Values Across Included Studies

## Discussion

This systematic review provides a comprehensive synthesis of artificial intelligence (AI) applications in liver cancer, particularly in differentiating hepatocellular carcinoma (HCC) from intrahepatic cholangiocarcinoma (ICC) and other liver malignancies. Across 44 included studies, AI models demonstrated strong diagnostic performance, with sensitivity and specificity generally ranging from 75–100%, overall accuracy between

73–96%, and area under the curve (AUC) values spanning 0.74 to 0.99. These findings highlight the rapid evolution of AI tools, which increasingly match or even surpass the performance of expert radiologists in complex diagnostic tasks [2, 5, 6, 12, 17].

### Imaging modalities and diagnostic implications

CT and MRI emerged as the dominant imaging modalities applied in AI studies. CT provided robust assessment of tumor vascularity, which is essential

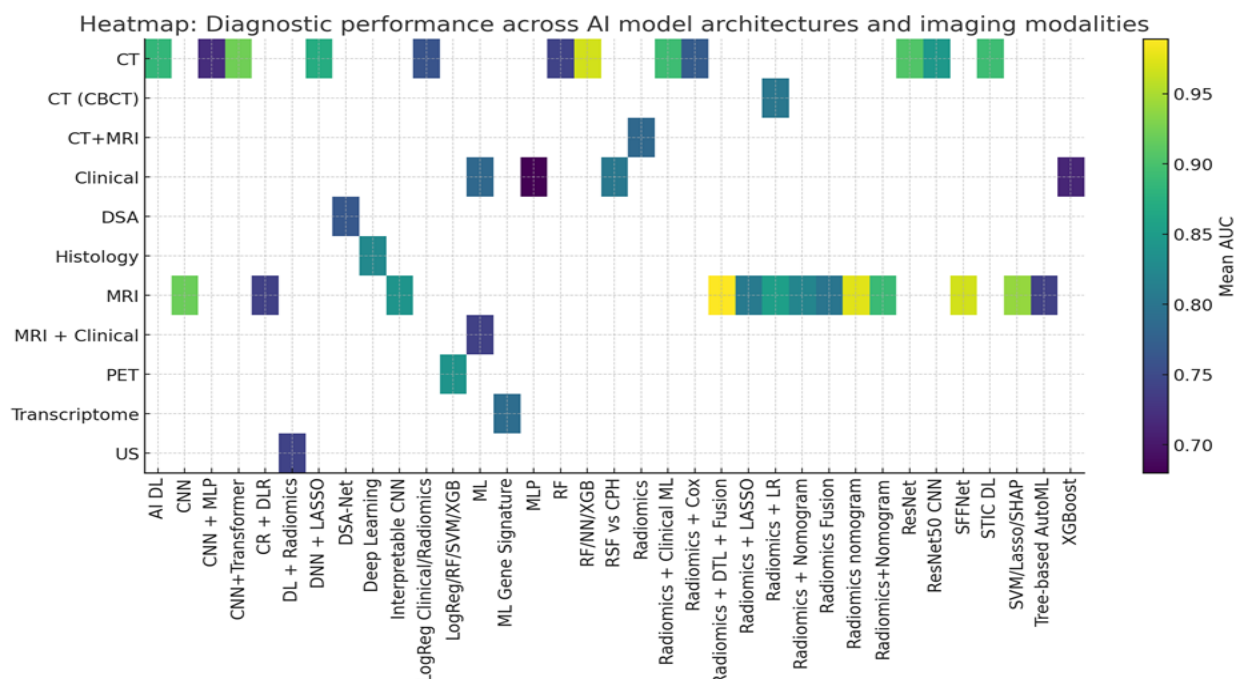


Figure 3. Heatmap Comparing Diagnostic Performance Across AI Model Architectures and Imaging Modalities

Table 1. Summary of Studies Using Artificial Intelligence Models for Differentiating Hepatocellular Carcinoma (HCC) and Intrahepatic Cholangiocarcinoma (ICC)

Authors	Country	Study design	Population	Training data	Techniques	Validation methods	Challenges	Reported outcome
Fan et al., 2025 [24]	China	Retrospective	HCC (n=84), MVI-confirmed by histopathology	68Ga-FAP PET radiomics (shape, first-, second-, higher-order features)	Logistic Regression / Random Forest / SVM / XGBoost	Nested test across SUVmax thresholds (30%, 40%, 50%, 60%)	Variation in SUVmax threshold for semi-automatic VOI delineation affecting model performance	AUC = 0.785–0.896; Accuracy = 87.5%; Sn = 100%; Sp = not reported
Kimoshita et al., 2025 [25]	Japan	Retrospective multicenter	HCC (n=533)	CT radiomics + clinical features	Logistic Regression, fused clinical-radiomics model	Training (n=426) / Test (n=107)	Non-standardized CT imaging protocols	AUC: Radiomics 0.76 vs Clinical 0.76; Fused model did not improve performance
Zhu et al., 2025 [26]	China	Retrospective multicenter	HCC (n=304)	Gd-EOB-DTPA MRI radiomics (intratumoral & peritumoral)	Conventional radiomics (CR) + Deep learning radiomics (DLR)	Training (n=216) / Testing (n=88)	Multi-center variability; single vs bi-regional feature extraction	Bi-regional CR-DLR model AUC = 0.740 (testing), Accuracy = 73.9%, Sn = 50%, Sp = 84.5%
Wu et al., 2025 [27]	China	Retrospective multicenter	HCC (n=138), DPHCC (n=122), ICC (n=121)	CE-MRI radiomics	Radiomics, Deep Transfer Learning (DTL), Fusion (vgg19)	Internal (n=244) / External (n=75)	Differentiating DPHCC from HCC & ICC	Fusion model macro-AUC = 0.988–0.990; Accuracy = 0.875–0.935; F1-score = 0.885–0.937
Jian et al., 2025 [28]	China	Retrospective multicenter	Solitary HCC (n=319)	Clinical indicators, MRI, radiomics	SVM, Lasso regression, SHAP interpretation	Internal training/ validation + 2 external validation sets	Integration of heterogeneous multi-center data	Combined model AUC = 0.92–0.96; Improved predictive performance over individual models
Famularo et al., 2025 [29]	Italy	Retrospective multicenter	HCC (n=218)	3-phase CT radiomics (tumoral, peritumoral, healthy liver)	Random Forest, Neural Network, XGBoost	Training (70%) / Test (30%)	Multi-center CT acquisition, high-dimensional data	RF model Accuracy = 96.8%; Sn = 95.2%; Sp = 97.6%
Yang et al., 2025 [30]	China	Retrospective multicenter	HCC (n=320)	DCE-MRI radiomics (intratumoral & peritumoral)	Radiomics, Clinical-radiomics fusion	Internal & external validation	Accurate segmentation and feature extraction from multiple MRI phases	Combined model AUC = 0.75–0.85; Associated with early recurrence & PFS
Yin et al., 2025 [31]	China	Retrospective	Unresectable HCC (n=172)	CT radiomics + clinical features	Deep learning (ResNet) based radiomics	Training/testing/ external validation	Multi-center heterogeneity, combination therapy response prediction	Treatment response AUC = 0.85–0.96; PFS prediction AUC = 0.762–0.874; C-index combination model = 0.75
Mu et al., 2024 [32]	China	Retrospective	HCC ≤5 cm (n=331)	DCE-MRI	ResNet-based deep learning + clinical features	Random split train/ test	Early recurrence prediction; integration of clinical data	Early recurrence prediction; metrics not reported
Alshaghat F et al., 2024 [33]	Saudi Arabia	Retrospective	Liver US images (NAFLD/NAASH)	CNNs (InceptionV3, ResNet50, DenseNet121, EfficientNetB0) + Random Forest	Hybrid deep learning + ML	Cross-validation	Hepatocyte ballooning detection, dual dichotomy classification	Accuracy = 97.4%; AUC = 0.99, Sensitivity = 99% for 'Many' class
Hashimoto K et al., 2024 [34]	Japan	Retrospective	HCC nodules post c-TACE (n=103 in 71 pts)	CBCT lipiodol deposition	Radiomics + logistic regression	Train/test split 7:3	Local tumor recurrence prediction	Clinical-radiomics WS model: AUC train = 0.853, test = 0.752
Zhang W et al., 2024 [35]	China	Retrospective multicenter	HCC (n=576 lesions, 2 centers)	Ultrasound (B-mode, CEUS)	DL and radiomics, ROI enlargement, AFP integration	Cross-center internal/external validation	Cross-institutional robustness, modality comparison	DL AUC = 0.802–0.818 internal, 0.667–0.688 external; Radiomics AUC = 0.749–0.869 internal, 0.646–0.697 external

Table 1. Continued

Authors	Country	Study design	Population	Training data	Techniques	Validation methods	Challenges	Reported outcome
Zheng S et al., 2024 [36]	China	Retrospective	HCC cohorts (TCGA-LIHC, LIRI-JP)	Transcriptome + clinical	ML-based gene signature (HPRGS)	External validation cohorts	Prognosis prediction, treatment guidance	Prognostic 4-gene signature; validated OS prediction; treatment response guidance
Liu Y et al., 2024 [37]	China	Retrospective	HCC undergoing TACE (n=110)	CT-based radiomics	DNN + LASSO + clinical nomogram	Internal validation	Prediction of TACE response	DNN-nomogram: AUC = 0.871; Sens = 0.844; Spec = 0.873
Zhang R et al., 2024 [38]	China	Retrospective	HCC (n=250; 175 train, 75 val)	DCE-MRI	Dynamic radiomics (SR, DR, DSR) + LASSO + logistic regression	External validation	MVI prediction	DSR signature best: AUC train = 0.805, external = 0.777
Xiao Y et al., 2024 [39]	China	Retrospective + prospective	cHCC-CCA (n=143; 82 train, 36 val, 25 test)	MRI	Radiomics + logistic regression	Validation cohort + prospective test	MVI prediction, biological process exploration	Robust MRI-radiomics model for MVI prediction; prognostic and immune process insights
Zhou G et al., 2024 [40]	China	Retrospective	cHCC-CC (n=91)	DCE-MRI	Radiomics + LASSO	Training/validation cohorts	MVI prediction	Radiomics signature: AUC train = 0.866, validation = 0.841
Zhang X et al., 2024 [41]	China	Retrospective	HCC undergoing first DEB-TACE (n=108)	CT + clinical	Radiomics + clinical-radiological + integrated ML	Train/validation split 8:2	Predict objective response	Integrated model AUC train = 0.860, validation = 0.927; Sens/Spec = 0.875/0.833
Zhang K et al., 2023 [42]	China	Retrospective multicenter	HCC (n=260; 140 train, 65 std external, 55 non-std external)	Gd-EOB-DTPA MRI	Radiomics nomogram + radiological predictors	External validation	Preoperative MVI prediction; patient stratification for PA-TACE	Nomogram AUC = 0.982 train, 0.969/0.981 external; identified patients benefiting from PA-TACE
Liu R et al., 2023 [43]	China	Retrospective	HCC post-hepatectomy (n=315)	Clinical + lab data	Machine learning (6 algorithms, MLP best)	10-fold cross-validation	Recurrence risk prediction	MLP AUC = 0.680; SHAP identified top 5 predictive factors; web calculator constructed
Khan RA et al., 2023 [44]	China	Retrospective	Multi-class liver cancer	CT + pathology	Multi-modal deep neural network	Benchmark dataset	Small/imbalanced dataset; 3-class liver cancer classification	Accuracy = 96.06%; AUC = 0.832; integrated pathology + image data improved classification
Kinoshita M et al., 2023 [45]	Japan	Retrospective	Solitary HCC post-hepatectomy (n=543)	Arterial CECT	Deep learning (CNN + MLP)	Train/validation/test split 8:1:1	Early recurrence prediction ( $\leq 2$ years)	AUC test = 0.71, validation = 0.73; high-risk group recurrence 73% vs low-risk 30%
Iseke S et al., 2023 [46]	USA	Retrospective	Early-stage HCC eligible for liver transplant (n=120)	Pretreatment MRI + clinical/lab	ML models (clinical, imaging, combined)	Six time-frame recurrence prediction; Kaplan-Meier	Recurrence prediction pre-treatment	AUCs: clinical 0.60–0.78, imaging 0.71–0.85, combined 0.62–0.86; MRI improved predictive performance
Jiang T et al., 2023 [47]	China	Retrospective	HCC post-resection (n=102)	Multiparametric MRI	Radiomics + LASSO + nomogram	Internal validation	Preoperative peritumoral MVI prediction	Nomogram achieved highest AUC; AFP identified as top clinical predictor
Fanulano S et al., 2023 [48]	Italy	Retrospective registry + external validation	Recurrent HCC post-surgery (n=701)	Clinical registry	Machine learning predictive model	External validation: Italian + Japanese cohorts	Treatment allocation to maximize survival	AUC 78.5% at 5 years; patient-tailored algorithm identified optimal treatment (reoperative hepatectomy/thermoablation, sorafenib, chemembolization)

Table 1. Continued

Authors	Country	Study design	Population	Training data	Techniques	Validation methods	Challenges	Reported outcome
Zeng et al., 2022 [49]	China	Retrospective multicenter	HCC (n=4,758) after curative resection	15 clinical/pathological features (age, gender, labs, tumor characteristics, invasion, cirrhosis)	Random Survival Forests (RSF) vs Cox Proportional Hazard (CPH)	Internal validation + external validation cohort	Need to handle high-dimensional survival data, non-linearity not well captured by CPH	RSF C-index = 0.725–0.762; Time-dependent AUC (2y) = 0.785–0.823; Outperformed ERASL, Korean, AJCC, BCLC, Chinese staging systems; Stratified risk groups ( $p<0.0001$ )
Wang L et al., 2022 [50]	China	Retrospective	HCC (n=138)	CT-based radiomics	Deep learning: MVI-Mind (CNN + transformer)	Test set	End-to-end prediction of MVI	Segmentation mIoU 0.9006; prediction AUC 0.9223; prediction time ~1 min per patient
Liu Y et al., 2022 [51]	China	Retrospective	Mass-forming ICC and HCC	MRI, small datasets	Deep learning: SFNet + Semi-SP preprocessing	Internal	Small dataset, feature extraction and fusion	Accuracy 92.26%, AUC 0.9680; sensitivity 86.21%, specificity 94.70% for MF-ICC/HCC classification
Hu R et al., 2022 [52]	Taiwan	Retrospective	HCC vs ICC	Multiphase MRI	Automated ML: Tree-Based Optimization Tool + genetic programming	Manual vs automated optimization	LR-M subset classification; workflow automation	Accuracy 73–75%; sensitivity 65–75%, specificity 71–79%; performance similar to radiologists
Liu Z et al., 2022 [53]	China	Retrospective multicohort	HCC post-resection or liver transplant (n=1118)	Histological slides, nuclear architecture	Deep learning: U-net + MobileNetV2_HCC_class	Independent validation on LT set and TCGA set	Prognostic prediction for recurrence-free survival	HR 3.44 LT set, HR 2.55 TCGA set; maintained higher discriminatory power than known prognostic factors
Zhang L et al., 2022 [54]	China	Retrospective	Intermediate-stage HCC post-TACE (n=605)	DSA videos	Deep learning: DSA-Net (U-net + ResNet)	Internal + external validation	Real-time TACE response prediction	Dice 0.73–0.75; accuracy 75.1–78.2%; significant difference in PFS between responders/non-responders ( $p=0.002$ )
Gao R et al., 2021 [55]	China	Retrospective	723 patients with HCC, ICC, metastatic liver cancer	Multi-phase CECT + clinical data	Deep learning STIC model (CNN + gated RNN)	Internal & external	Multimodal data integration; limited external validation	Accuracy HCC vs ICC: 86.2%; AUC 0.893; Overall malignant tumor classification accuracy: 72.6%; External test accuracy: 82.9%; Assisted doctors improved accuracy +8.3%, sensitivity +26.9% for ICC
Wang M et al., 2021 [56]	China	Retrospective	7512 patients with HCC	CT images	Deep learning AI system	Internal (385) & external (556)	Heterogeneity of CT data; explainability	Internal AUROC 0.887; External AUROC 0.883; Accuracy ~81%; Sensitivity 78–89%; Comparable to radiologists; Saliency heatmap accuracy 92.1%
Meng XP et al., 2021 [57]	China	Retrospective	402 patients with solitary HCC	CT and MRI	Radiomics RS, R, RR models	Internal validation	Modality comparison; tumor size influence	MRI-based models slightly higher AUC than CT; MRI RS added value for 2–5 cm tumors; Overall performance comparable

Table 1. Continued

Authors	Country	Study design	Population	Training data	Techniques	Validation methods	Challenges	Reported outcome
Oestmann PM et al., 2021 [58]	Switzerland	Retrospective	118 patients, 150 lesions (HCC and non-HCC)	Multiphasic MRI	3D CNN	Cross-validation (150 runs)	Atypical imaging features; small sample	CNN can classify typical and atypical HCC lesions; proof-of-concept
Chong H et al., 2021 [59]	China	Retrospective	323 HCC patients without macrovascular invasion	Gd-EOB-DTPA MRI	Peritumoral dilation radiomics + nomogram	5-fold cross-validation	Integration of radiomics and clinical features	Training AUC 0.939; Validation AUC 0.842; NRI improvement 35.9–66.1%
Huang et al., 2021 [60]	China	Retrospective multicenter	HCC (n=7,919) after surgical resection	Clinical + pathological features from EHS & MHH	XGBoost (best model vs others)	Internal validation + external validation (Kaplan-Meier stratification)	Time-dependent variation in recurrence risk; heterogeneity across centers	XGBoost c-index = 0.713 (internal); Stratified external cohort into distinct risk groups ( $p < 0.05$ ); Tumor factors drive 0–1y relapse, HBV/smoking drive 3–5y relapse; Risk heat map enabled personalized follow-up
Naem S et al., 2020 [61]	Pakistan	Retrospective	Benign & malignant liver lesions	Fused MR + CT images (1200)	Hybrid-feature extraction; MLP, SVM, RF, J48	10-fold cross-validation	Multimodal fusion; feature selection	MLP accuracy 99% on fused dataset
Ji GW et al., 2020 [62]	China	Retrospective	295 early-stage HCC patients	Contrast-enhanced CT	Radiomics + Cox regression models	External validation (118 patients)	Prediction of recurrence; multi-institutional data	C-index $\geq 0.77$ ; Lower prediction error; Better net benefit than non-radiomics models
Peng J et al., 2020 [63]	China	Retrospective	789 patients (3 centers) with intermediate-stage HCC	CT images	ResNet50 residual CNN	Internal + 2 independent validation cohorts	Prediction of TACE response; heterogeneous cohorts	Training accuracy 84.3%; Validation 85.1% & 82.8%; High AUC for CR, PR, SD, PD
Morshid A et al., 2019 [64]	USA	Retrospective	105 HCC patients	CT quantitative features + clinical data	Random Forest	Internal	Small sample; feature selection	Accuracy 74.2% (features + BCLC) vs 62.9% (BCLC alone)
Zhang R et al., 2019 [65]	China	Retrospective	267 HCC patients	Multimodal MRI	Bi-regional radiomics + nomogram	Internal validation	MVI prediction; tumor heterogeneity	Fusion radiomics AUC 0.784–0.820; Nomogram AUC 0.858; Outperformed clinical model
Hamm CA et al., 2019 [66]	USA	Retrospective	494 hepatic lesions	Multiphasic MRI	CNN-based deep learning	Internal test (60 lesions)	Limited lesion types; small test set	Accuracy 92%; Sn 92%; Sp 98%; HCC Sn 90% vs radiologists 60–70%
Wang CJ et al., 2019 [67]	USA	Retrospective	Same 494 lesions as above	Multiphasic MRI	Interpretable CNN; feature maps & relevance scoring	Internal test (60 lesions)	Explainability; misclassification	PPV 76.5%; Sn 82.9%; Misclassified lesions 12%; Feature maps consistent with predictions

in differentiating HCC from ICC [2, 5]. By contrast, MRI—especially dynamic contrast-enhanced (DCE) and diffusion-weighted imaging (DWI) sequences—proved more sensitive for small lesions and intratumoral heterogeneity [8, 9, 18]. These modality-specific strengths translated into differential diagnostic advantages: MRI-based models were superior in early tumor detection, whereas CT-based models were more effective for evaluating vascular invasion and larger lesions. Hybrid modalities, including PET/CT, and ultrasound-based AI approaches were less common but demonstrated potential when combined with radiomics or machine learning techniques [2, 12]. This suggests that multimodal fusion strategies may represent the most effective approach for maximizing diagnostic accuracy. Importantly, imaging access differs by region. In Southeast Asia, where ICC prevalence is disproportionately high due to liver fluke infection, CT is more widely available than MRI [14–16, 19]. Thus, tailoring AI models to available imaging infrastructure may improve diagnostic equity in resource-limited regions.

#### *AI model architectures and feature integration*

Methodologically, convolutional neural networks (CNNs) were predominant, with newer studies employing residual networks (ResNets), fully convolutional networks (FCNs), and deep transfer learning architectures [7, 13]. These advances improved tumor segmentation and classification, even in atypical imaging presentations [5, 12]. Radiomics capturing quantitative features such as texture, shape, and intensity was widely integrated with clinical data to form fused models [12, 20]. Evidence consistently showed that combined radiomics-clinical models outperformed single-domain approaches. For example, multi-center studies employing clinical, radiomic, and genomic signatures reported significantly enhanced performance in predicting recurrence and microvascular invasion (MVI). Multi-omics frameworks further expanded predictive capability: transcriptomic signatures [21] and hepatitis B virus (HBV)-specific risk biomarkers [22] have been successfully integrated into AI pipelines, demonstrating how computational models can inform both diagnosis and therapeutic stratification. These findings underscore that AI's clinical utility extends beyond image interpretation toward precision hepatology and personalized treatment decision-making [12, 17].

#### *Diagnostic accuracy and subgroup performance*

The pooled diagnostic performance across studies was encouraging, with most models achieving AUCs between 0.75 and 0.90, and several exceeding 0.95. MRI-based models offered superior sensitivity for small lesions [9, 18], whereas CT-based approaches proved advantageous for evaluating macrovascular invasion and resectability [2, 5]. Multi-modal fusion consistently outperformed single-modality approaches [12, 18]. Subgroup analyses revealed that tumor characteristics (size, location, vascular involvement) and patient demographics influenced AI model performance. For instance, younger patient cohorts and smaller tumor subsets were more accurately assessed with MRI-based approaches, while CT was more reliable

for large and vascularly complex lesions. Such stratified analyses indicate that modality selection should be tailored not only to tumor biology but also to patient demographics.

#### *Sources of bias and methodological limitations*

Despite promising findings, several methodological limitations warrant attention. The majority of studies were retrospective, relying on pre-existing datasets [1, 5]. Prospective and multicenter validation studies remain scarce, which limits generalizability. Imaging heterogeneity arising from differences in acquisition protocols, scanner hardware, and contrast administration posed additional barriers to reproducibility. These concerns highlight the need for harmonization of radiomic features and standardized imaging protocols [20]. High-dimensional data and relatively small sample sizes also raise risks of overfitting, while class imbalance in datasets may distort model performance [4, 13]. Another critical challenge is explainability: many deep learning models function as “black boxes,” making clinical adoption more difficult in high-stakes decision-making contexts [4, 13].

#### *Clinical implications and public health perspectives*

AI tools have the potential to substantially impact hepatology practice. Integration into clinical workflows could reduce inter-observer variability, enhance diagnostic efficiency, and provide decision support [10, 12, 18]. Comparative analyses suggest that AI systems often complement rather than replace radiologists, improving detection and classification when used in tandem [2, 5, 10]. Beyond diagnosis, AI has shown value in predicting recurrence, treatment response, and MVI, with implications for surgical planning, transplant eligibility, and allocation of therapies such as TACE and immunotherapy [9, 23]. These prognostic utilities are particularly important in high-burden regions, where liver cancer outcomes remain poor and resources are constrained [14–16, 19]. Cost-effectiveness analyses and implementation studies will be critical in bridging the gap between technical performance and real-world utility [4].

#### *Future directions*

To advance clinical adoption, future research should prioritize large-scale, prospective, multicenter studies with external validation [1, 20]. Standardization of imaging acquisition and radiomic feature extraction is urgently needed to ensure reproducibility across institutions [20]. Multi-omics integration linking imaging, clinical, and genomic features represents a frontier for precision hepatology [21, 22]. Development of explainable AI systems will be essential to enhance clinician trust and regulatory approval [4, 13]. Moreover, AI should be designed for seamless integration into existing radiology and oncology workflows, with attention to user interface, interpretability, and clinical decision support. Finally, consideration of public health perspectives particularly in high-burden regions such as Asia—will be vital to ensuring that AI technologies address global disparities in liver cancer care [14–16, 19].

In conclusion, AI has demonstrated substantial promise

in differentiating HCC from ICC, with performance metrics frequently rivaling expert radiologists. While challenges remain in terms of reproducibility, standardization, and clinical translation, ongoing advancements in multi-modal integration, multi-omics approaches, and explainable AI systems point toward a future where AI can play a central role in precision hepatology and global liver cancer control.

## Author Contribution Statement

All authors contributed equally in this study.

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### Declarations

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### Ethics approval

Ethical clearance for this study was obtained from the ethics committee of Suranaree University of Technology, under the auspices of protocol number EC63-41.

### Conflict of interest

No conflict of interest.

### Abbreviations

ACA – Adenocarcinoma  
MRI – Magnetic resonance imaging  
AI – Artificial intelligence  
MS – mass spectrometry  
ANN – Artificial neural network  
MVI – Microvascular invasion  
AUC – Receiver operating curve or area under the curve  
NN – Neural network  
AW – Advanced workstation  
OARs – Organ-at-risk  
AutoML – Automated machine learning model  
PESI – Probe Electrospray Ionization  
CBCT- cone-beam computed tomography  
PET – Positron Emission Tomography  
CCA – Cholangiocarcinoma  
ResNet – Residual Net  
CGP – Comprehensive genomic profile  
RF – Random Forest  
cHCC-CCA – Combine hepatocellular carcinoma cholangiocarcinoma  
SBRT – Stereotactic body radiation therapy  
CNN – Convolutional neural networks

SCC – Squamous cell carcinoma  
CT – Computer tomography  
Semi-SP – Semi-segmented preprocessing  
CUP – Cancer of unknown primary  
SFFNet – strided feature fusion residual network  
1D-CNN – 1D convolutional neural network  
Sp – Specitivity  
1D-Inception – 1D Inception convolutional neural network  
Sn – Sensitivity  
3D VR – Three-dimensional volume rendering  
SPECT – Single Photon Emission Computed  
18F-FDG PET/CT – 18F-fluorodeoxyglucose positron emission tomography/computed tomography  
SVM – Support vector machine  
HB – Hepatobiliary  
TARE – Transarterial radioembolization  
HBV – Hepatitis B virus  
TCGA – The Cancer Genome Atlas project  
HCC – Hepatocellular carcinoma  
TPOT – Tree-Based Pipeline Optimization Tool  
MIP – Maximum intensity projection  
ICCA – Intrahepatic cholangiocarcinoma  
UDC – Undifferentiated carcinoma  
ICGC – International Cancer Genome Consortium  
VAE – Variational autoencoder  
KNN – K-nearest neighbor  
VCAR – Volume computer assisted reading  
MF-ICC – Mass-forming intrahepatic cholangiocarcinoma  
WSI – Whole-slide image  
ML – Machine learning  
<sup>90</sup>Y – Yttrium 9

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