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Review

Current status and prospects of artificial intelligence in liver cancer management

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ABSTRACT

Liver cancer is an extremely heterogeneous malignant tumor characterized by high morbidity and mortality rates. Despite significant advancements in cancer care, the outcomes of liver cancer patients remain poor. Artificial intelligence (AI) is a major discipline in computer science that attempts to simulate human intelligence using machines or systems. Owing to the availability of multidimensional databases and recent algorithmic advancements, AI offers tremendous potential to overcome current obstacles in oncology research and practice. There is a growing body of evidence suggesting that AI models enable pathologists to diagnose liver cancer more accurately, customize personalized therapies, and predict cancer prognosis. Therefore, the increasing adoption of AI is expected to improve healthcare accuracy and patients' quality of life. However, only a few AI models are currently authorized for clinical use. This review outlines recent developments in research on the biomedical application of AI technology in liver cancer and discusses both the potential hurdles and future implications of employing AI for clinical cancer management, thereby providing insights for further research. Overall, the clinical implementation of AI technology is anticipated to induce a paradigm shift in medical oncology, leading to significant improvements in patient outcomes.

1. Introduction

Liver cancer is one of the most common fatal malignancies across the globe, accounting for more than 700,000 deaths annually.[1] Based on the origins of malignant tumor cells, primary liver cancers can be divided into hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (iCCA).[2] Notably, the former is responsible for over 80% of all primary liver cancer cases.[3] Moreover, tumors originating from other tissues, including breast, lung, and stomach, may migrate to the liver.[2] In particular, the majority of secondary liver cancers are derived from colorectal cancer (CRC). Over the past decades, research on liver cancer has proceeded rapidly, achieving significant progress in its pathogenesis, diagnosis, grading, and intervention.[4] However, the clinical management of liver cancer patients remains complicated, requiring a collaborative multidisciplinary team comprising hepatologists, liver surgeons, medical oncologists, and radiologists.[5] Currently, several therapeutic approaches—liver resection, transplantation, and chemoembolization—have been established as standard curative treatments for liver cancer.[6,7] However, despite refinements in technologies and new devices, there have been no significant improvements in treatment outcomes for liver cancer patients. Their mortality can be considerably reduced if the tumor is detected early and treated properly.

The integration of artificial intelligence (AI) technology into cancer medicine is emerging as a powerful approach to overcoming many obstacles due to which medical experts fail to control and treat cancers in a clinical setting.[8] Notably, AI systems simulate human cognitive functions, such as problem solving and decision making, by analyzing data, identifying patterns, and comprehending natural language.[9] The technical architecture of AI mainly comprises four modules: human–computer interaction, image recognition, machine learning, and natural language processing.[10,11] Among these, machine learning, a specialized branch of AI, exploits statistical technologies to construct intelligent frameworks (Figure 1).[12] The key algorithms involved in machine learning include artificial neural network (ANN), deep learning (DL), decision tree, and enhancement algorithm.[13] In recent years, AI has received considerable attention owing to its exemplary performance in computer vision (e.g., object recognition and image classification).[14] Furthermore, AI is rapidly accelerating many aspects of cancer research and practice, such as automatic detection, classification, and segmentation of cancer.[15] AI-based techniques have demonstrated clinical value with regard to various aspects of liver cancer,

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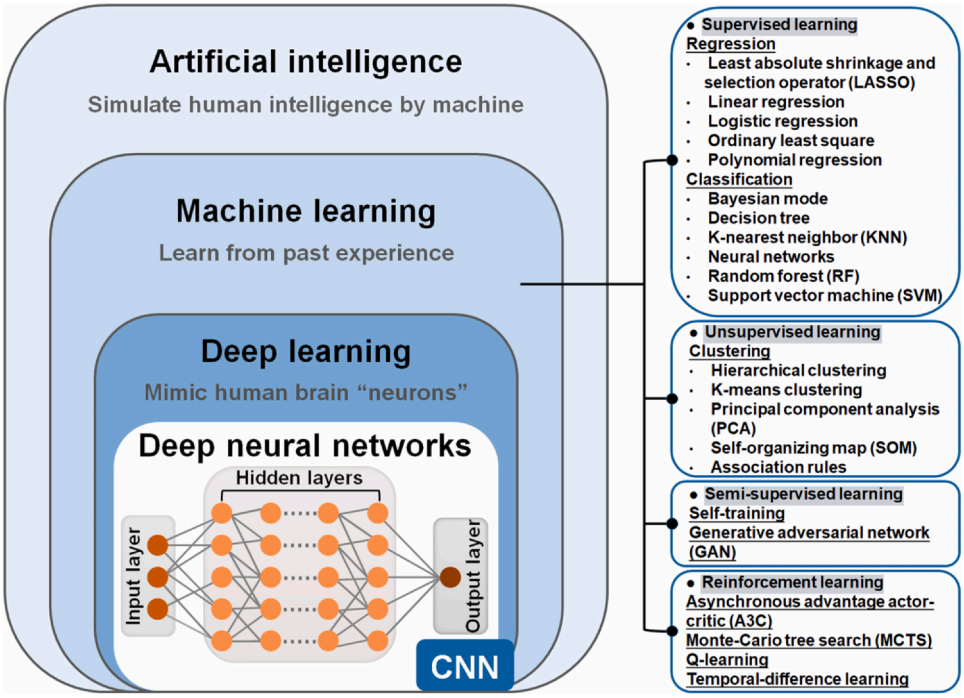


Figure 1. Schematic representation of the relationship among artificial intelligence, machine learning, deep learning, and commonly used algorithms. Abbreviation: 1. CNN: convolutional neural network.

such as identification, early diagnosis, treatment decision-making, and prognostic prediction.

In this study, we provide comprehensive updates on the biomedical application of AI in liver cancer. We discuss the problems and impediments currently being encountered in employing AI technology to treat clinical cancer, as well as possible solutions and future directions. It is established that the increasing integration of AI in medical settings, along with advancements in therapeutic options, is expected to accelerate the realization of personalized care for a wide range of cancers.

2. Recent advances in AI-driven liver cancer treatment

2.1. Role of AI techniques in liver cancer screening and diagnosis

Several studies have investigated the potential of computational intelligence as an assistive tool for the early diagnosis of liver cancer (Table 1), with AI tools demonstrating the ability to screen and identify key characteristics of the disease. For instance, the parametric empirical Bayes algorithm is a computationally straightforward method that employs longitudinal biomarker observations for detection with fewer speculations than other longitudinal screening algorithms.[36] The parametric empirical Bayes algorithm detected variations in patients' data that signal asymptomatic liver cancer.[16] It defined patient-specific thresholds for increased individual-level sensitivity to serum biomarkers des-γ-carboxy prothrombin and α-fetoprotein (AFP), thereby improving early HCC detection. Furthermore, the HCC Early Detection Screening algorithm, accounting for patients' age, AFP, AFP alteration rate, alanine aminotransferase, and platelet number, identified HCC patients 6 months before their diagnosis with 51.20% sensitivity, which was superior to the sensitivity (46.02%) attained using the serum AFP test.[17] These findings imply that AI algorithms offer promising opportunities for realizing the goal of automatic cancer detection.

AI shows great promise as a tool for liver cancer diagnosis through the use of machine learning-based algorithms to analyze massive data for efficient and precise detection (Figure 2). Based on different types of learning, machine learning techniques can be categorized into reinforcement learning, semi-supervised learning, supervised learning, and unsupervised learning (Figure 1).[37] Reportedly, a supervised-learning framework based on hierarchical community detection and AI successfully identified two sets of potential biomarkers that distinguished HCC patients from healthy controls, achieving an accuracy of more than 90%.[18] However, since preexisting chronic illnesses likely influence patient participation in liver cancer screening, rapid and accurate cancer diagnosis remains a challenge. In this regard, AI systems can assist clinicians in discriminating liver cancer from other diseases. SMART-HCC score, a machine learning-based tool developed to predict and stratify the risk of HCC in patients with chronic liver diseases, outperformed existing HCC risk scores.[19] Furthermore, logistic regression is a supervised machine-learning algorithm used to execute prediction and classification tasks. A multiple logistic regression model incorporating clinical and contrast-enhanced image features was developed for the early detection of small HCCs, resulting in the diagnosis of 347 non-HCC and 392 HCC patients.[20] Random forest (RF) is another machine learning algorithm that ensures high accuracy and reliability by adopting a bagging strategy.[38] RF offers the advantages of resolving overfitting, handling non-linear data, and enabling parallel processing. Reportedly, an RF classifier achieved high accuracy (0.762) and a high area under the receiver operating characteristic curve (AUC) value (0.999) in early HCC detection among patients with liver diseases.[21] In addition, an RF-based clinical decision algorithm relying on quantitative imaging features derived from triphasic computed tomography (CT) scans was able to diagnose HCC in cirrhotic patients with visually indeterminate liver nodules.[22] This algorithm attained an AUC of 0.70 and 0.66 for the discovery and validation cohorts, respectively. Meanwhile, mass spectrometry combined with RF permitted the identification of HCC with high accuracy (98.2%), sensitivity (97.4%), and specificity (99%).[23] ANN is one of the most common machine learning algorithms employed to analyze hidden non-linear relationships.[39] An ANN, a neural network that mimics the intricate functions of the human brain, is composed of an input layer, a hidden layer, and an output layer, with interconnections between the nodes in each layer. ANNs have been widely used to diagnose cancer due to their significant information-processing characteristics. For instance, a joint diagnosis model based on RF and ANN demonstrated excellent efficiency in

Table 1
Summary of recent studies exploring the potential of artificial intelligence methods in liver cancer screening and diagnosis.

Cancer type	Method	Data used for analysis	Results	Reference
HCC	Parametric empirical Bayes	Longitudinal biomarkers	Improve cancer early detection with an AUC of 0.87	16
HCC	HCC Early Detection Screening algorithm	Clinicopathological data	Improve cancer early detection with a sensitivity of 51.20% and a specificity of 90.00%	17
HCC	Machine learning	Microarray data	Discriminate between healthy and cancerous samples with an accuracy exceeding 80%	18
HCC	Machine learning	Clinicopathological data	Efficiently stratify cancer risk with an AUC exceeding 0.89 in validation cohorts	19
HCC	Logistic regression	CT images	Accurately detect small tumors with AUCs of 0.79 and 0.75	20
HCC	Random forest	Clinical data	Improve cancer identification and classification with an accuracy of 76.2% and an AUC of 0.999	21
HCC	Random forest	CT images	Efficiently stratify cancer risk with AUCs of 0.70 and 0.66 in discovery and validation cohorts	22
HCC	Support vector machine; random forest	Mass spectrometry data	Screen cancer tissues with an accuracy exceeding 94%	23
HCC	Random forest; artificial neural network	Gene expression data	Efficiently distinguish cancer patients from non-cancerous individuals with high sensitivity (≥76.5%) and specificity (≥72.2%)	24
HCC	Neural network system	Clinical data	Diagnose early-stage cancer with a sensitivity of 85.3% and a specificity of 85.1%	25
HCC	Neural network system	MRI images	Efficiently identify cancer cases approximately six months prior to diagnosis with an accuracy of 89%	26
HCC	Support vector machine	Clinical data	Facilitate early cancer detection with an accuracy of 85.28% and an AUC of 0.914	27
HCC	Support vector machine	Clinical data	Show good performance in cancer identification with an AUC of 0.86, a sensitivity of 76.6%, and a specificity of 80.5%	28
HCA	Machine learning	Ultrasound images	Facilitate cancer detection with a qualitative diagnostic accuracy of 93.6% and a quantitative diagnostic accuracy of 95.9%	29
HCC	Convolutional neural network	Ultrasound images	Assist in cancer diagnosis with an accuracy of 86.41%, a sensitivity of 96.08%, and a specificity of 76.92%	30
HCC	Convolutional neural network	Electronic health records	Identify early/advanced cancer with high accuracy (92.9%–98.0%), sensitivity (51.9%–83.5%), and specificity (99.0%–99.1%)	31
HCC	Convolutional dense network	CT images	Differentiate cancer from other focal liver lesions with AUCs of 0.862, 0.920, and 0.925 in test sets	32
HCC	Deep learning	Quantitative immunohistochemistry results	Differentiate cancer tissues from cirrhotic tissues with overall accuracies of 56% and 62%	33
HCC	Deep learning	CT images	Efficiently detect cancer with a specificity of 97%	34
HCC	Deep learning	CT images	Achieve high performance in cancer detection with accuracies of 85.3% and 80.5% in internal and external test sets	35

Abbreviations: 1. HCC: hepatocellular carcinoma 2. HCA: hepatocellular adenoma 3. AUC: area under the receiver operating characteristic curve 4. CT: computed tomography 5. MRI: magnetic resonance imaging.

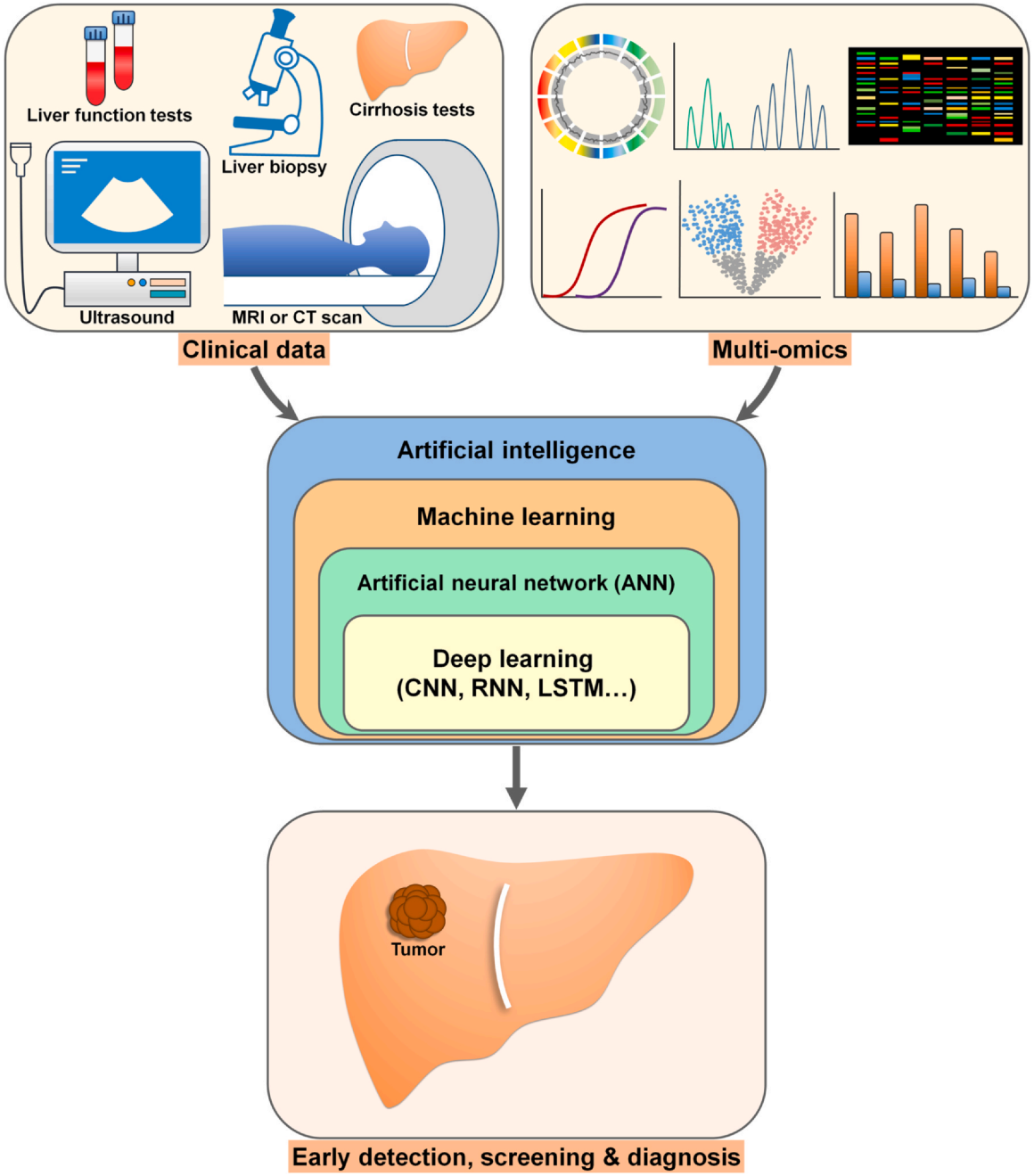


Figure 2. Schematic illustration of artificial intelligence in precise diagnosis of liver cancer. AI improves liver cancer diagnosis by enhancing the analysis of serological/tissue biomarkers and medical imaging. AI also excels at omics data interpretation, facilitating early cancer detection. Abbreviations: 1. MRI: magnetic resonance imaging 2. CT: computed tomography 3. CNN: convolutional neural network 4. RNN: recurrent neural network 5. LSTM: long short-term memory.

differentiating hepatitis B virus (HBV)-related HCC from other non-cancerous individuals with HBV.[24] The model achieved high sensitivities of 88.5%, 90%, 88.5%, and 76.5% for four independent datasets. Furthermore, a neural network system (HCC-Scope) accurately distinguished between non-HCC and HCC nonalcoholic steatohepatitis while maintaining high sensitivity (85.3%) and specificity (85.1%).[25] Another neural network approach is enhancement pattern mapping, which is an imaging system that can detect and quantify lesion signals. The enhancement pattern mapping algorithm identified quantifiable variations between controls and HCC cases in cirrhosis patients, reaching an accuracy of 89%.[26] Meanwhile, a machine learning classification model (support vector machine [SVM]) based on the structural risk minimization principle facilitated early HCC detection in patients with type-2 diabetes with high accuracy (85.28%) and a high AUC value (0.914).[27] Li et al.[28] constructed a predictive model for HCC diagnosis using the SVM method trained with ultrasonic signatures derived from contrast-enhanced ultrasound (CEUS) images and a radiologist's scores. This model was able to differentiate between atypical HCC and focal nodular hyperplasia (FNH), and its performance was comparable to that of radiologists. Machine learning algorithms were also employed to quantitatively analyze apparent microbubble transport parameters visible on CEUS in inflammatory hepatocellular adenoma (HCA).[29] The algorithms efficiently discriminated between FNH and inflammatory HCA lesions, achieving qualitative diagnostic accuracy rates of 93.6% and 95.9%, respectively. Therefore, machine learning-driven systems are capable of reducing the probability of false-positive results while increasing the accuracy and specificity of current detection methods.

DL is a subdiscipline of AI that exploits ANNs to extract patterns and generate predictions from large datasets. The neural network architecture of DL enables more efficient models in addressing intricate computational issues (e.g., large-scale image classification and natural language processing) compared to other machine learning approaches.[14] Moreover, convolutional neural networks (CNNs), a type of DL algorithm widely used in visual recognition tasks, can be applied for cancer detection.[40] For instance, the Xception method was built on CNN architecture.[30] This approach achieved an accuracy of 86.41% in distinguishing between AFP-negative HCC and focal liver lesions (FLLs) in HBV-infected patients. Furthermore, iterated dilated CNNs and a text CNN-based clinical trial matching system were employed to extract medical data from the electronic health record (EHR) system and automatically match patients to clinical trials for early and advanced HCC, exhibiting good performance in a significantly short amount of time.[31] The automatic multiphase convolutional dense network showed comparable diagnostic accuracy with a complete four-phase dynamic contrast-enhanced CT protocol in discriminating HCC from other FLLs.[32] A DL-based prediction model integrating various intensities of transforming growth factor β receptor 2 staining successfully differentiated HCC tissues from cirrhotic tissues with an overall accuracy of 62%.[33] Notably, this biomarker can be integrated into an AI-guided automated imaging analysis pipeline to diagnose HCC from biopsy tissue. A flexible DL-based computer-aided detection algorithm named HPVD analyzed dynamic contrast-enhanced CT scans to reach a specificity of 97% in detecting HCC, which was comparable to the measured physician performance.[34] Therefore, HPVD can be considered a useful tool for opportunistic HCC screening in clinical settings. Meanwhile, Wang et al.[35] built a DL platform called HCCNet trained on CT images of HCC patients that achieved high accuracy in identifying HCC patients, which was comparable to specialized radiologists. Therefore, AI-assisted rapid screening may not only reduce processing time but also prevent misdiagnosis by human negligence.

Overall, AI has the potential to fundamentally change the way liver cancer is detected in the near future. By accounting for the effects of patient-related and disease-specific factors on diagnostic timelines and processes, customized AI systems can be designed to improve the clinical outcomes of cancer patients with preexisting chronic conditions.

2.2. Function of AI in liver cancer classification and grading

2.2.1. Liver cancer classification

Accurate classification of liver cancer enables clinicians to select the optimal treatment regimen for patients. HCC and cholangiocarcinoma (CCA) are two different forms of primary liver cancer that vary in terms of their etiology, histology, and molecular and immunophenotypical characteristics. Notably, the classification of primary liver cancer involves a labor-intensive process. In the context of the histopathological categorization of liver cancers, AI can be considered a potential solution to this diagnostic challenge. For instance, Jang et al.[41] set up a DL model for identifying HCC, CCA, and metastatic CRC using histopathological images. The HCC/other cancer type classifier effectively differentiated HCC from CCA and metastatic CRC, achieving an AUC value of 0.998. Furthermore, an automated machine learning tool, termed the Tree-Based Pipeline Optimization Tool (TPOT), adopted a genetic algorithm to automatically extract and select features, as well as model selection procedures of the radiomics workflow, to improve precision in classification.[42] TPOT efficiently differentiated HCC from iCCA, exhibiting a performance comparable to radiologists.[43] The logistic regression model is another useful tool for the prediction and classification of disease data. As expected, a logistic regression classifier successfully differentiated HCC and iCCA with an AUC of 0.82 and a sensitivity of 73.3%.[44] Furthermore, a weakly supervised learning approach developed to classify primary liver cancers from biopsy samples was able to identify specific morphological characteristics of HCC and iCCA.[45] In addition, it accurately predicted the diagnosis in 97% of HCC cases and 83% of iCCA cases. Meanwhile, an AI pipeline based on a self-supervised feature extractor with an attention-multiple instance learning aggregation model successfully reclassified combined hepatocellular-CCA tumors into pure HCC or iCCA, attaining a sensitivity of 97.9% and a specificity of 97.6%.[46] An AI assistance model STIC based on multiphase contrast-enhanced CT and clinical features achieved an accuracy of 86.2% and an AUC of 0.893 in differentiating between HCC and iCCA.[47] This model demonstrated an accuracy of 72.6% in classifying HCC, iCCA, and metastasis, which was comparable to the diagnostic performance of clinicians' consensus (70.8%). The STIC model assisted clinicians in achieving better diagnostic performance, prompting an average increase of 26.9% in sensitivity and 8.3% in accuracy for iCCA detection. Furthermore, an AI-based liver metastases screening system (ALMSS) conducted automated liver contrast-enhanced CT analysis for the origin prediction of liver metastases (LMs).[48] ALMSS yielded an AUC of 0.917 for distinguishing LMs, HCC, and iCCA, surpassing the AUCs of two radiologists. It achieved an average AUC value of more than 0.80 for predicting six primary origins (breast, intestine, respiratory system, esophagogastric system, pancreatobiliary system, and reproductive system) in two testing sets. AI-powered platforms can therefore be used to discriminate cancer tissue subtypes with high effectiveness and, in turn, help increase diagnostic accuracy in clinical practice.

2.2.2. Liver cancer grading

Liver tumors comprise benign and malignant forms, and the latter can be further categorized into primary liver cancer (originating in the liver) and metastatic liver cancer (disseminating from extrahepatic primary tumors).[49] FLLs are a common finding in liver imaging studies. They include a diversity of benign and malignant tumors (e.g., FNH, HCC, HCA, and LM) with distinct pathogeneses, clinical symptoms, and outcomes.[50,51] However, the identification of benign and malignant forms of FLLs remains a crucial diagnostic challenge because their imaging signs may overlap with those of distinct diseases.[52] Early detection and precise identification of FLLs are essential for effective patient management. Multiple lines of evidence indicate that AI models exhibit good efficacy in identifying FLLs in HCC. For instance, 2D and 3D-densely connected CNNs trained on multi-sequence magnetic resonance imaging (MRI) scans achieved good performance in classifying three FLL types (FNH, HCC, and LM).[52] Likewise, DL methods using 3D CNNs were able to accurately identify the three types of FLLs in HCC.[53] Notably, these AI methods exhibited moderate agreement with expert opinion. In addition, the CNN-based RetinaNet model (100%), which was constructed for the real-time detection of FLLs during ultrasound surveillance for HCC, achieved a higher lesion detection rate than radiologists (69.6%).[54] This implies that AI-based approaches can assist less experienced clinicians in the detection of HCC-indicative features.

Other AI models have demonstrated favorable performance in liver cancer discrimination and segmentation (Figure 3). The Enhanced Swin Transformer Network with Adversarial Propagation, combined with the mask region-based CNN model, achieved an accuracy of 95.62% in the classification of liver cancers from CT images, yielding a better performance than current state-of-the-art models.[55] A CNN-based model for detecting and segmenting HCC lesions using dynamic contrast-enhanced CT was capable of recognizing HCC with 100% sensitivity, with the test set's median Dice score of 0.81 for HCC segmentation between radiologists and the DL model.[56] Moreover, semi-automated single slice and volumetric segmentation CNN models have exhibited good performances with regard to HCC segmentation on MRI.[57] A hybrid deep neural network based on multi-task learning and ensemble learning techniques for HCC segmentation demonstrated state-of-the-art performance on three publicly available datasets, suggesting its possible utility in HCC segmentation in the clinic.[58] Meanwhile, the radiologist-aided deep fusion network model (median Dice similarity coefficient = 0.88) achieved higher accuracy in HCC lesion segmentation compared to a radiologist with moderate experience (median Dice similarity

Table 2
Summary of recent studies exploring the potential of artificial intelligence methods in classifying and segmenting liver cancer.

Potential application	Method	Cancer type	Data used for analysis	Results	Reference
Cancer classification	Deep learning	HCC; CCA	Histopathological images	Facilitate the histopathological classification of liver cancers with an AUC of 1.000	41
Cancer classification	Machine learning	HCC; iCCA	Multiphasic MRI	Differentiate primary liver cancers with an accuracy of 73%–75%	43
Cancer classification	Logistic regression	HCC; iCCA	Contrast-enhanced CT images	Differentiate liver cancers with a sensitivity of 73.3% and a specificity of 85.7%	44
Cancer classification	Weakly supervised learning	HCC; iCCA	Histological images	Identify specific morphological characteristics of two liver cancers with high accuracy	45
Cancer classification	Deep learning	HCC; iCCA	Histopathologic images	Re-classify combined HCC-CCA tumors into pure tumors	46
Cancer classification	Deep learning	HCC; iCCA	Contrast-enhanced CT images; clinical data	Classify liver cancers with an accuracy of 82.6% and an AUC of 0.893	47
Cancer classification	Deep learning	HCC; iCCA	CT images	Efficiently differentiate liver cancers with an AUC of 0.917	48
Cancer classification	Convolutional neural network	HCC	Contrast-enhanced MRI images	Accurately differentiate focal liver lesions with average AUC values of 0.94 and 0.98	52
Cancer classification	Convolutional neural network	HCC	MRI images	Classify focal liver lesions with an AUC of 0.84	53
Cancer classification	Convolutional neural network	HCC	Ultrasound images	Real-time detection of focal liver lesions with an overall detection rate of 89.8%	54
Cancer segmentation	Mask region-based convolutional neural network	HCC	CT images	Classify liver cancers with an accuracy of 95.62%	55
Cancer segmentation	Convolutional neural network	HCC	CT images	Identify cancer with a sensitivity of 100% and a median Dice score of 0.81	56
Cancer segmentation	Convolutional neural network	HCC	MRI images	Achieve a mean Dice similarity coefficient of 0.71 in lesions between 1 cm and 2 cm, 0.85 in lesions between 2 cm and 5 cm, and 0.82 in lesions >5 cm	57
Cancer segmentation	Machine learning	HCC	Whole-slide histopathologic images	Demonstrate state-of-the-art performance, with segmentation accuracies of 76.5%, 79.7%, and 92.3% in three publicly available datasets	58
Cancer segmentation	Deep fusion network	HCC	MRI images	Achieve improved segmentation performance with the median Dice similarity coefficients of 0.72, 0.77, and 0.88	59
Cancer segmentation	Random forest	HCC	MRI images	Differentiate low-grade and high-grade of HCC with an AUC of 0.80 in internal validation and an AUC of 0.70 in external validation	60
Cancer segmentation	Convolutional neural network	HCC	CT images	Show good performance in automatic staging of cancer aggressiveness with an AUC of 0.668	61
Cancer segmentation	Deep learning	HCC	MRI images	Exhibit good performance in LI-RADS classification with an average Dice similarity coefficient of 0.884, a sensitivity of 89.1%, and an accuracy of 88.7%	64
Cancer segmentation	Machine learning	HCC	Contrast-enhanced CT images	Efficiently detect LI-RADS major features with a sensitivity of 67% and a specificity of 91%	65
Cancer classification	Deep learning	HCC	Contrast-enhanced ultrasound images	Achieve a higher specificity (100%) for discriminating malignant from benign tumors than clinicians	66
Cancer classification	Convolutional neural network	HCC	MRI images; clinical data	Perform well in classifying malignancies as liver cancer (AUC = 0.985)	67
Cancer classification	Convolutional neural network	HCC	Ultrasonography images	Show excellent performance in discrimination of benign and malignant tumors with diagnostic accuracies of 86.8%, 91.0%, and 91.1%	68
Cancer classification	Deep neural network	HCC	Whole-slide histopathologic images	Differentiate hepatocellular nodular lesions with an AUC of 0.935	69
Cancer classification	Mask region-based convolutional neural network	HCC	CT images	Automatically detect primary cancers with a sensitivity of 84.8% and a false-positive rate of 4.80 per CT scan	70
Cancer classification	Multivariable logistic regression	HCC	CT images	Predict macrotrabecular-massive subtypes of liver cancer with an AUC of 0.91 and a specificity of 90%	71

Abbreviations: 1. AUC: area under the receiver operating characteristic curve 2. MRI: magnetic resonance imaging 3. CT: computed tomography 4. HCC: hepatocellular carcinoma 5. CCA: cholangiocarcinoma 6. iCCA: intrahepatic CCA 7. LI-RADS: Liver Imaging Reporting and Data System.

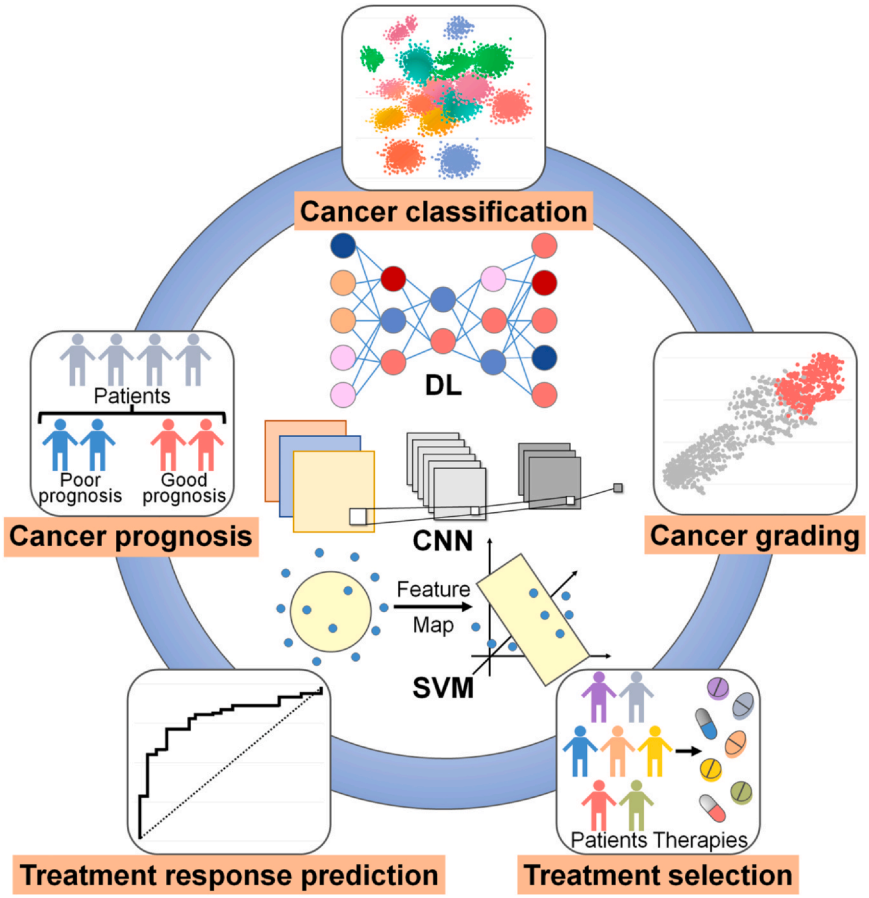


Figure 3. Potential clinical application of AI methods for liver cancer. The continuous advancements of AI technologies may provide new potential to develop powerful computer-assisted approaches that can accurately classify liver cancer, identify low- and high-grade liver cancer, assist in the selection of treatment strategies, predict treatment response and follow patient prognosis. Abbreviations: 1. DL: deep learning 2. CNN: convolutional neural network 3. SVM: support vector machine.

coefficient = 0.83).[59] A hepatobiliary phase radiomics-based machine learning model based on gadoxetic acid-enhanced liver MRI data successfully differentiated between low-grade and high-grade HCCs.[60] Furthermore, an interpretable AI tool (LiSNet) that integrated highly experienced experts' knowledge and deep CNNs accurately graded HCC aggressiveness based on CT imaging, achieving a high AUC (0.668) comparable to that of subspecialists (0.699).[61]

The Liver Imaging Reporting and Data System (LI-RADS) is a standardized classification system for liver observations of patients at risk of developing HCC.[62] Its categories reflect the relative probability of benignity (LR-1 and LR-2) or malignancy (LR-3, LR-4, and LR-5) of a specific observation.[63] An end-to-end DL model that showed high Dice similarity coefficient scores (0.884–0.891) for HCC segmentation achieved good performance in LI-RADS classification using subtraction MRI.[64] It attained accuracies of 72.2%–91.4% and sensitivities of 86.7%–96.6% for three major LI-RADS features: enhancing capsule, nonperipheral washout, and nonrim arterial phase hyperenhancement. Meanwhile, a machine learning-based algorithm showed excellent performance in the assessment of the major features of LI-RADS v2018 and in the stratification of liver observations on CT in patients at risk of HCC.[65] Therefore, this algorithm can potentially assist radiologists by standardizing patients' medical reports according to the latest recommendations.

Moreover, a number of DL algorithms can efficiently differentiate between benign and malignant liver cancers. For instance, a CEUS-based DL system distinguished between benign and malignant HCC with 100% specificity, outperforming two experienced clinicians.[66] Meanwhile, Zhen et al.[67] employed CNNs to construct a DL system for liver cancer classification based on enhanced MRI images, unenhanced MRI images, and clinical data. The CNN combined unenhanced images with clinical information, significantly improving the categorization of liver tumors into HCC, metastatic tumors from other sites, and other primary malignancies. Moreover, the sensitivity and specificity of these integrated models were observed to be comparable to those attained by skilled radiologists. Compared to human experts (63.6%–69.1%), CNN AI models achieved higher accuracy (80.0%–89.1%) in the four-class discrimination of liver tumors into HCC, metastatic liver tumors, liver hemangiomas, and liver cysts.[68] Furthermore, a DL model termed the hepatocellular nodular AI model was able to differentiate between hepatocellular nodular lesions, including well-differentiated HCC, low-grade dysplastic nodules, high-grade dysplastic nodules, FNH, and HCA.[69] The model displayed good performance in the histopathologic diagnosis of hepatocellular nodular lesions, attaining an AUC value of 0.935 in an independent external validation cohort. Notably, the accuracy of this model surpassed that of expert and nonexpert pathologists. Another DL-based automatic model that combined the multichannel integration of multiphase CT scans with automatic liver segmentation demonstrated high sensitivity (84.8%) in identifying primary hepatic malignancies, exhibiting 4.80 false-positives per CT scan in patients at high risk of HCC.[70] Furthermore, a DL-based radiomics model derived from multiparametric dual-energy CT exhibited performances superior to the clinical-radiologic model in identifying aggressive macrotrabecular-massive (MTM) subtype in HCC patients,[71] finding MTM-positive patients to have shorter recurrence-free survival than MTM-negative patients. Accordingly, AI-powered systems can help improve the accuracy and efficiency of the current approaches used for cancer classification and grading. AI techniques in classfying and segmenting liver cancer are summarized in Table 2.

2.3. Significance of AI techniques in liver cancer treatment

2.3.1. Functions of AI in supporting clinical decision-making

AI techniques can potentially revolutionize clinical decision-making processes related to liver cancer, since they can handle vast amounts of multi-omics data. Notably, liver transplantation and surgical resection are considered appropriate treatments for early liver cancer. In this

Table 3
Summary of recent studies exploring the potential of artificial intelligence methods in liver cancer treatment and prognostic prediction.

Potential application	Method	Cancer type	Data used for analysis	Results	Reference
Cancer treatment guidance	Deep learning	HCC	Clinical data	Assess recurrence risk with an accuracy of 82%	72
Cancer treatment guidance	Random forest	HCC	Clinical data	Predict waitlist dropout among liver transplant candidates with liver cancer with a concordance statistic of 0.74	73
Cancer treatment guidance	Deep learning	HCC	Clinical data	Predict the risk of 5-year cancer recurrence post liver transplantation with a concordance statistic of 0.78	74
Cancer treatment guidance	Logistic regression	HCC	Ultrasound images	Predict early cancer recurrence with an AUC of 0.845	75
Cancer treatment guidance	Random survival forest	HCC	Clinical data	Predict early cancer recurrence with a C-index value of 0.747 in external validation cohorts	76
Cancer treatment guidance	Convolutional neural network	HCC	Contrast-enhanced CT images	Predict 3-year recurrence outcomes with an AUC of 0.98 in the training cohorts	77
Cancer treatment guidance	Deep learning	HCC	Contrast-enhanced MRI images	Accurately predict early cancer recurrence with an AUC of 0.909 in the validation set	78
Cancer treatment guidance	Deep learning	HCC	Contrast-enhanced CT images	Predict post-hepatectomy liver failure with an accuracy of 84.15% and an AUC of 0.7927	79
Cancer treatment guidance	Convolutional neural network	HCC	Digital histopathologic images	Predict postsurgical cancer recurrence with concordance indices of 0.724 and 0.683 on the internal and external test cohorts	80
Cancer prognosis	Deep learning	HCC	CT and MRI images	Efficiently predict microvascular invasion	81
Cancer treatment guidance	Deep learning	HCC	CT images	Predict microvascular invasion with an AUC of 0.845	82
Cancer treatment guidance	Convolutional neural network	HCC	CT images	Improve the preoperative prediction of microvascular invasion with an AUC of 0.7839 in the test set	83
Cancer treatment guidance	Deep learning	HCC	CT radiomics	Predict microvascular invasion with an AUC of 0.74 in the validation group	84
Cancer treatment guidance	Deep learning	HCC	MRI images; clinical data	Achieve excellent performance in predicting microvascular invasion	85
Cancer treatment guidance	Deep learning	HCC	CT images	Predict microvascular invasion with an AUC of 0.841	86
Cancer treatment guidance	Deep learning	HCC	Histopathologic images	Identify microvascular invasion with an accuracy of 94.25%	87
Treatment response evaluation	Convolutional neural network	HCC	CT images	Predict patient response to transarterial chemoembolization therapy with accuracies of 82.8% and 85.1% in two validation sets	88
Treatment response evaluation	Deep learning	HCC	Digital subtraction angiography videos	Predict patient response to transarterial chemoembolization therapy with accuracies of 78.2% and 75.1% in internal and external validation cohorts	89
Treatment response evaluation	Deep learning	HCC	Ultrasonographic data	Predict patient response to transarterial chemoembolization therapy with an AUC of 0.93 in the validation cohort	90
Treatment response evaluation	Convolutional neural network	HCC	CT images	Predict the efficacy of immune checkpoint inhibitor treatment, with a precision of 100% for progressive disease	91
Cancer prognosis	Random forest	HCC	Medical data	Identify three prognostic indicators (ALP, AFP, and hemoglobin)	92
Cancer prognosis	Random forest	HCC	Clinical data	Identify prognostic factors (e.g., Milan criteria and albumin levels) with an AUC of 0.96	93
Cancer prognosis	Explainable artificial intelligence	HCC	Clinical data; gene expression data	Discover prognostic factors (e.g., COX7A2L, SSBP3, and TOP3B)	94
Cancer prognosis	Graph structure learning; dynamic network biomarker	HCC	Transcriptome expression data	Identify CCT3 as an independent prognostic factor	95
Cancer prognosis	Multivariate Cox regression model	HCC	Gene expression data	Identify a four-gene signature as a prognostic model that has a high performance with AUCs of 0.780, 0.732, and 0.733 in 1-, 2-, and 3-year survival prediction	96
Cancer prognosis	Machine learning	HCC	Clinical data	Predict 6-, 12-, 24-, 36-, 60-, and 120-month overall survival with mean AUCs of 0.92, 0.81, 0.78, 0.81, 0.82, and 0.66	97
Cancer prognosis	Random forest; neural network approach	HCC	Gene expression data	Accurately predict 5-year overall survival with an AUC of 0.83 in the validation cohort	98
Cancer prognosis	Artificial neural network	HCC	Clinical data	Predict 1-, 3- and 5-year overall survival rates with AUCs of 0.838, 0.833, and 0.843	99
Cancer prognosis	Convolutional neural network	HCC	Clinical, laboratory, and imaging data	Show superiority in predicting patient survival following transarterial chemoembolization therapy	100
Cancer prognosis	Deep residual neural network	HCC	Gene expression data	Effectively classify the 5-year long-term overall survival with an AUC of 0.907	101

(*continued on next page*)

Table 3 (*continued*)

Potential application	Method	Cancer type	Data used for analysis	Results	Reference
Cancer prognosis	Deep learning	HCC	Histopathological data; demographic and clinicopathological characteristics	Predict 1-, 3- and 5-year overall survival after R0 hepatectomy with AUCs of 0.8065, 0.7404, and 0.7944	[102]
Cancer prognosis	Deep learning	HCC	Clinicopathological data	Identify decreased RPA as an independent predictor of cancer-related outcomes (hazard ratio = 2.80, P = 0.001)	[103]
Cancer prognosis	Deep learning	HCC	Contrast-enhanced CT images	Predict overall survival with C-indices of 0.81 and 0.72 for the developing and testing sets	[104]

Abbreviations: 1. HCC: hepatocellular carcinoma 2. AUC: area under the receiver operating characteristic curve 3. C-index: concordance index 4. CT: computed tomography 5. MRI: magnetic resonance imaging 6. ALP: alkaline-phosphatase 7. AFP: α-fetoprotein 8. RPA: reticulin proportionate area.

regard, AI systems can help predict clinical outcomes in liver cancer patients after liver transplantation or surgical resection (Table 3). For instance, a DL model combining clinical data with multiscale histopathologic and radiomic image features achieved high accuracy in assessing recurrence risk among liver transplant recipients with HCC.[72] This model may contribute to expanding the transplantation option to HCC patients with high tumor burdens. Furthermore, an RF model constructed to forecast waitlist dropout among liver transplant candidates with HCC effectively predicted the risk of dropout at 3, 6, and 12 months in the validation set, maintaining a concordance statistic of 0.74.[73] This highlights that machine learning-based methods can help stratify the risk of liver transplant candidates and define their urgency for transplant. Meanwhile, the Time_Radiological-response_Alpha-fetoproteIN_Artificial-Intelligence model achieved higher accuracy (concordance index [C-index] = 0.78) than other commonly used models (e.g., Metroticket 2.0 and the AFP-French model) in assessing the risk of 5-year HCC recurrence after liver transplantation.[74]

Huang et al.[75] integrated clinical data with tumoral and peritumoral ultrasomics models to build a combined logistic regression model for predicting early HCC recurrence following ablation or resection. The combined model (AUC = 0.845) performed better than both the tumoral model (AUC = 0.810) and peritumoral model (AUC = 0.808) in predicting HCC recurrence within 2 years. Furthermore, the random survival forest model outperformed conventional COX proportional hazard (CoxPH) models in predicting early HCC recurrence after curative resection.[76] The clinical and DL-based radiomics model exhibited good performance in predicting 3-year recurrence outcomes of HCC patients based on contrast-enhanced CT, with an AUC of 0.83 in the testing cohort.[77] Therefore, the clinical and DL-based radiomics model can be employed to identify high-risk patients and assist with medical decision-making. A DL nomogram (AUC = 0.909) derived by accounting for gadoxetate disodium MRI, qualitative features, and clinical parameters of HCC patients accurately predicted early tumor recurrence after hepatectomy, exhibiting better performance than a conventional clinical nomogram (AUC = 0.715).[78] An in-house trained liver segmentation model based on preoperative contrast-enhanced CT images achieved satisfactory results in predicting post-hepatectomy liver failure in HCC patients after hemihepatectomy, reaching an accuracy of 84.15% and an AUC value of 0.79.[79] This DL model may be useful for screening high-risk patients requiring alterations in their treatment strategy, since the liver segmentation model is capable of guiding clinicians in delivering precision postoperative care in HCC. Furthermore, a DL-based system named HCC-SurvNet was developed to predict the postsurgical recurrence of HCC directly from digital histopathologic images.[80] HCC-SurvNet achieved better performance than the standard Tumor-Node-Metastasis (TNM) classification system in stratifying patients into low- and high-risk subgroups—a process that could significantly improve the clinical care of HCC patients undergoing surgical tumor resection.

Microvascular invasion (MVI) is an independent risk factor influencing early recurrence and prognosis in HCC patients.[81] Precise preoperative prediction of MVI is crucial for the formulation of personalized treatment strategies and long-term prognosis assessments for HCC patients. In this context, DL models may provide a promising strategy for accurate MVI prediction based on imaging examinations and clinical data. For instance, a DL-based model called ResNet-18 achieved favorable performance in detecting MVI in HCC, attaining an AUC of 0.845.[82] Similarly, a multi-modal domain-adaptive fusion model M-DAFM, on the basis of DL methods, integrated valuable information from multiphase CT images to improve the preoperative predictive performance for MVI.[83] An AI algorithm-based CT radiomics model (AUC = 0.745) exhibited a higher predictive ability for MVI in patients with solitary HCC ≤5 cm compared to image features (AUCs = 0.522 and 0.528).[84] Consequently, this radiomics model may be employed to assist clinicians in selecting suitable treatment. A DL-based cross-

modality unified framework effectively extracted and fused the semantic information in MRI multiphase images and clinical data, thereby enhancing the model's predictive performance for MVI in HCC patients.[85] Another DL classification model based on hybrid features demonstrated good performance in identifying HCC patients using MVI, reaching an accuracy of 85.7% and a sensitivity of 87.5%.[86] Furthermore, a DL-based diagnostic model termed MVI-AIDM achieved an accuracy of 94.25% in MVI detection in an independent external validation cohort.[87] Notably, the MVI-positive detection rate of MVI-AIDM was markedly higher than that of pathologists, which was partially attributed to difficulties in the recognition of micro MVIs using classical pathology.

Altogether, DL-based methods can judge the occurrence of MVI in liver cancer patients with high accuracy and specificity, hence offering important guidance to clinicians on tailoring care based on individual patients. In summary, the utilization of AI technology in precision cancer therapy is likely to contribute to better treatment outcomes for cancer patients.

2.3.2. Functions of AI in predicting treatment response

AI techniques empower clinical workflows by allowing the full-stack analysis of liver cancer and the precise matching of optimal treatment to cancer patients, effectively contributing to improvement in patients' chances of successful convalescence (Figure 3). In this regard, recent advancements in DL may open up new opportunities for developing computational tools aimed at therapy response prediction. Using the transfer learning capabilities of a residual CNN (ResNet50), Peng et al.[88] developed a DL model to predict responses to transarterial chemoembolization (TACE) therapy among HCC patients. This ResNet50 model achieved accuracies of 85.1% and 82.8% in predicting complete response, partial response, stable disease, and progressive disease. It exhibited high AUCs for predicting objective responses in HCC patients who received TACE therapy. Meanwhile, a DL system ResNet, based on digital subtraction angiography videos, yielded accuracies of 78.2% and 75.1% in predicting treatment response to the first TACE therapy for the internal and external validation cohorts, respectively.[89] Notably, this model classified treated patients into responder and non-responder groups. Non-responders were predicted to have a poorer prognosis than responders, suggesting that responders might benefit more from TACE treatment. Likewise, a DL-based radiomics approach accurately predicted the responses of HCC patients to TACE sessions by quantitatively analyzing CEUS cines.[90] A DL model YOLOv7 using pre-immune checkpoint inhibitors (ICIs) contrast-enhanced CT imaging features to predict the efficacy of ICI treatment in HCC patients achieved high accuracy (98.3%) in classifying ICI-treated patients into three categories: progressive disease, partial response, and stable disease.[91]

These findings indicate that AI models can serve as an innovative tool for screening patients' responses to interventional treatments for liver cancer and for selecting appropriate clinical treatments for liver cancer patients. Therefore, more AI systems should be developed to predict patients' responses to different therapies.

2.4. Status of AI in liver cancer prognosis

Many existing studies on clinical cancer concentrate on predicting patient survival and prognosis, since cancer patients with accurate prognoses can obtain timely and effective medical interventions. Considering the unprecedented accuracy level achieved by AI techniques, researchers are increasingly investigating their application in cancer prognosis. In this regard, AI techniques have successfully identified promising biomarkers for cancer prognosis (Table 3). For instance, an RF classifier that ranked clinical features according to their relevance in predicting patient survival accurately identified blood concentrations of alkaline-phosphatase, AFP, and hemoglobin as prospective prognostic factors for HCC.[92] Another study proposed an RF model that presented high accuracy in identifying prognostic factors for HCC at diagnosis, reaching an AUC value of 0.96.[93] Meanwhile, the explainable AI successfully identified a series of key genetic biomarkers (e.g., COX7A2L, SSBP3, and TOP3B) related to HCC prognosis.[94] A predictive model combining the dimensionality reduction via graph structure learning and dynamic network biomarker approaches also identified several key prognostic factors for HCC, including CCT3, DSTYK, and EIF3E.[95] Notably, these identified molecules might be considered early warning signals for disease progression and deterioration in HCC patients.

AI-assisted models can be adopted to predict patient survival, permitting clinicians to monitor patient progress and modify treatment options in a timely manner. For example, a prognostic model based on an integrated statistical and bioinformatics approach was constructed for overall survival prediction in HCC patients.[96] The model's risk score indicated that it achieved good performance in identifying HCC patients at a high risk of mortality. A gradient boosting machine learning algorithm successfully predicted 6-, 12-, 24-, 36-, 60-, and 120-month overall survival in HCC patients, with mean AUC values ranging from 0.66 to 0.92.[97] Furthermore, a molecular HCC prognostic score system built using the RF machine learning and neural network approaches accurately stratified the overall survival of HCC patients based on the expression pattern of 23 prognosis-related genes, achieving an AUC value of 0.83 in the validation cohort.[98] Moreover, the molecular HCC prognostic score system was closely associated with pathologic tumor and TNM stages in HCC. An ANN model effectively classified HCC patients according to their risks of death.[99] Notably, the model's prediction of 1-, 3-, and 5-year overall survival rates attained higher AUCs compared to the other models, including the Barcelona Clinic Liver Cancer (BCLC), Cancer of the Liver Italian Program, and TNM.

A CNN-based splenic segmentation algorithm displayed superior survival forecasting in HCC patients undergoing TACE compared to 2D spleen size assessments.[100] In particular, this method exhibited high sensitivity in detecting patients at risk of hepatic decompensation. Furthermore, a deep residual neural network model GeneSet-ResNet using CLST and activated $CD4^+$ T cells effectively classified the 5-year long-term overall survival of patients with HBV-related HCC and predicted their response to chemotherapy.[101] Wang et al.[102] constructed a DL platform that incorporated the area of MVI to predict survival outcomes in HCC patients after R0 hepatectomy. This model demonstrated better prognostic prediction than the BCLC staging system and the traditional COX regression analysis. Meanwhile, a vision-guided attention-enhanced network proposed by Liu et al.[81] achieved superior performance in MVI prediction, and therefore could be adopted for prognostic predictions in the future. Furthermore, a cloud-based DL AI platform employed to detect and quantify the reticulin framework in HCC tissues and normal livers found that the relative reticulin proportionate area can be considered an independent predictive factor for HCC-related clinical outcomes, including metastasis risk, disease-free survival, and overall survival.[103] Meanwhile, a DL system FAIS based on whole-liver information, which was constructed to predict the overall survival of HCC patients before surgery,[104] achieved the best performance (C-index = 0.72) among models using clinical and/or tumor-based radiomics features (C-indices = 0.62 and 0.68).

The above observations indicate that the integration of AI technology into cancer prognostic prediction could possibly refine patient management, resulting in better health outcomes. Nonetheless, while previously established models have demonstrated relatively high performance, few have been implemented into clinical practice due to the complexity of individual variations in the prognosis of liver cancer patients. Hence, future research should focus on utilizing large amounts of clinical data to optimize and validate these established models.

Table 4
Summary of clinical trials evaluating the effect and performance of artificial intelligence methods in liver cancer.

Type of study	Cancer type	Number of participants	AI task	Method	Results	Reference
Randomized controlled trial	Primary clear cell carcinoma of the liver, common hepatocellular carcinoma	151	Cancer diagnosis using CT images	Deep learning	Accurately distinguish tumor subtypes with an accuracy of 96.2%	105
Prospective, single-center, randomized study	Hepatocellular carcinoma	68	Cancer diagnosis using CT images	Deep learning	Achieve a cancer detection rate of 70.4%	106
Randomized controlled noninferiority trial	Hepatocellular carcinoma	90	Cancer diagnosis using CT Images	Deep learning	Reduce CT contrast dose by 40% without impairing cancer conspicuity	107
Randomized controlled trial	Small liver cancer	100	Cancer diagnosis using ultrasound images	Deep learning	Efficiently diagnose benign and malignant cancers with an accuracy of 97.23%	108
Single-center prospective randomized controlled study	Hepatocellular carcinoma	504	Cancer diagnosis using ultrasound images	Deep learning	Achieve a high detection rate (66.7%) of focal liver lesions	109
Phase 1/2 clinical study	Hepatocellular carcinoma	127	Chemotherapy response prediction using clinicopathological indicators	Machine learning	Identify drug responders with an accuracy of 67% in the training and an accuracy of 64% in the testing set	110
Phase 3 clinical trial	Hepatocellular carcinoma	542	Chemotherapy toxicity prediction using clinicopathological data	Machine learning	Identify sex, bilirubin, and hemoglobin as important factors in predicting drug-induced adverse effects	111
Randomized controlled trial	Intrahepatic cholangiocarcinoma	536	Tailored treatment planning using clinicopathological indicators	Machine learning	Predict early cancer recurrence with AUCs of 0.904 and 0.779 in the training and testing cohorts	112
Randomized controlled trial	Perihilar cholangiocarcinoma	274	Individualized treatment planning using radiomics	Machine learning	Predict early cancer recurrence with an AUC of 0.883 and an accuracy of 82.6%	113
Randomized controlled trial	Hepatitis B virus-related hepatocellular carcinoma	2,890	Survival prediction using clinicopathological indicators	Machine learning	Predict 1-year overall survival with an AUC of 0.877	114
Randomized controlled trial	Hepatocellular carcinoma	1,136	Survival prediction using clinicopathological data	Machine learning	Show better performance (C-index = 0.6890) in predicting survival than the standard CoxPH model (C-index = 0.669)	115
Randomized controlled trial	Hepatocellular carcinoma	114	Survival prediction using CT images	Deep learning	Show excellent prognostic potential to predict overall survival with a mean C-index of 0.74	116

Abbreviations: 1. CT: computed tomography 2. AUC: area under the receiver operating characteristic curve 3. C-index: concordance index 4. CoxPH: COX proportional hazard.

3. Ongoing clinical trials of AI in liver cancer

3.1. Clinical studies assessing the role of AI in liver cancer diagnosis

Most cases of liver cancer are usually diagnosed at an advanced stage when they are unresectable, resulting in poor clinical outcomes for patients. In a clinical setting, liver cancer diagnosis relies heavily on CT and tissue biopsy. However, CT radiomics analysis may lead to misdiagnosis, since CT images of hepatic nodules are quite intricate, while tissue biopsy is invasive. These limitations pose considerable challenges for clinicians. Considering these circumstances, the integration of AI in cancer medicine has emerged as a promising field, with multiple studies suggesting that AI is critical for improving cancer diagnosis (Table 4). In a clinical trial that randomly grouped 109 patients with common HCC and 42 patients with primary clear cell carcinoma of the liver (PCCCL) into a test set and a training validation set, the faster region-based CNN model was able to diagnose PCCCL and common HCC with an accuracy of 96.2%.[105] The AI model increased the accuracy of radiologists and saved time, enabling clinicians to formulate appropriate treatment plans for PCCCL and HCC patients. Furthermore, a DL-based contrast-boosting algorithm working on double-low-dose CT scans enabled an increased contrast-to-noise ratio of the aorta and portal vein without dramatically reducing the HCC detection rate relative to the standard-dose CT in 68 patients at high risk of HCC.[106] In a randomized controlled noninferiority trial involving 90 patients at high risk of HCC, low monoenergetic (50-keV) images reconstructed using DL-based denoising algorithms, characterized by a 40% lower contrast media dose depending on the lean body weight, were able to achieve similar image quality and lesion conspicuity to those generated based on a standard-contrast-dose protocol using model-based iterative reconstruction.[107] In other words, the 50-keV DL-based denoising images generated using the low-contrast-dose protocol exhibited comparable accuracy in identifying HCC compared to the model-based iterative reconstruction images obtained using the standard-contrast-dose protocol. Furthermore, multimodal ultrasound images based on the mask region-based CNN segmentation algorithm were employed to detect small liver cancers.[108] The algorithm effectively conducted ultrasonic image processing. Moreover, this approach achieved high accuracy in the diagnosis of benign and malignant small liver cancers, maintaining sufficient consistency with pathological examination results. Thus, multimodal ultrasound technology may have good clinical application prospects. In a single-center prospective randomized controlled study, the use of a CNN-based AI system significantly increased the FLL detection rate in 260 patients at high risk of HCC during ultrasound examinations conducted by non-expert operators.[109]

These findings imply that AI may be considered a viable instrument for cancer diagnosis, allowing radiologists and oncologists to detect cancer more accurately. The application of AI algorithms will also facilitate the development of more effective treatment modalities. However, AI techniques are currently not applicable in the clinical detection of liver cancer, which means that further research is necessary to promote the bench-to-bedside translation of AI-assisted diagnostic models.

3.2. Clinical studies on the role of AI in evaluating therapeutic effects

The complicated relationship between accurate health measurements and treatment modalities can be efficiently modeled using AI techniques. Along these lines, a combination of machine learning and population pharmacokinetic/pharmacodynamic modeling of tumor growth inhibition was implemented to investigate the relationship between Roblitinib (FGF401) exposure and clinical efficacy in 127 HCC patients.[110] The once-daily administration of 120 mg FGF401 led to a response at 4 and 6 months in 59.4% and 43.8% of high-risk patients and 69.8% and 60.3% of low-risk patients, respectively. Such an approach may pave the way for individualized precision treatment of HCC patients. Furthermore, an RF machine learning tool screened bilirubin, hemoglobin, and sex as important variables in predicting severe hand-food syndrome in 542 HCC patients following sorafenib treatment.[111] This model might facilitate the assessment of personalized risks of developing hand-food syndrome from sorafenib in HCC patients. The RF tool predicted individualized patient risk related to early recurrence after iCCA resection based on clinicopathologic characteristics, achieving an AUC of 0.779 in a testing cohort comprising 160 participants.[112] These results suggest that RF-based predictive tools can be depended upon to provide reliable information on surveillance strategies and customized treatment plans. Furthermore, a radiomics-based multilevel model aimed at quantifying the risk of early recurrence in 274 patients with perihilar CCA, who had undergone contrast-enhanced CT and curative resection, yielded a higher accuracy (82.6%) in predicting early recurrence than conventional staging systems (58.1%–64.1%).[113] These instances indicate that AI systems facilitate continuous therapeutic monitoring and timely treatment adjustments, which lead to better patient outcomes and survival rates.

3.3. Clinical studies on the role of AI in liver cancer prognosis

Diagnosis time, acquired drug resistance, tumor metastasis, and recurrence of liver cancer, as well as other related factors, lead to difficulties in making accurate prognostic judgments. In this context, AI-based models can assist clinicians in predicting the clinical outcomes of liver cancer patients through the analysis of multifactor data acquired from patient records and imaging examinations. For example, an ANN model was employed to predict progression-free survival in 2890 hospitalized patients with HBV-related HCC.[114] It efficiently predicted 1-year progression-free survival and presented better predictive performance than the other models, including the BCLC and TNM. Moreover, the ANN model worked as a convenient risk stratification system, dividing HCC patients into different prognostic subgroups (low-, medium-, and high-risk groups). Meanwhile, three machine learning algorithms (neural network multitask logistic regression, DeepSurv, and random survival forest) exhibited significantly better discrimination performance in forecasting survival in 1136 patients with early HCC compared to the standard CoxPH model.[115] The machine learning-based personalized treatment recommendations achieved higher hazard ratios than CoxPH model recommendations. Moreover, chemotherapy treatment recommendations offered by machine learning models contributed to significantly improved survival. In contrast, no improved survival was observed in patients who received treatments recommended by the CoxPH model. These findings imply that machine learning-based survival models can effectively facilitate the prognostic assessment and treatment of HCC. Furthermore, a clinical Cox-regression model (C-index = 0.71) using CT-based conventional radiomics features and DL CNNs presented better performance in predicting the overall survival of 114 HCC patients compared to conventional radiomics approaches (C-index = 0.66).[116]

Despite these encouraging results, it should be noted that AI prognostic models require extensive high-quality prospective clinical validation, as there are various clinical heterogeneities among cancer patients (e.g., comorbidities, lifestyle factors, and treatment courses and responses) that may affect prognosis and survival. In summary, the successful translation and implementation of state-of-the-art AI technology in clinical practice still faces multiple significant challenges, highlighting the urgent need for more research to foster its utilization in cancer prognosis.

4. Future perspectives

AI has the potential to revolutionize the field of medical oncology by facilitating early cancer detection, accurate identification of cancer subtypes, patient-tailored treatment, and frequent therapeutic monitoring

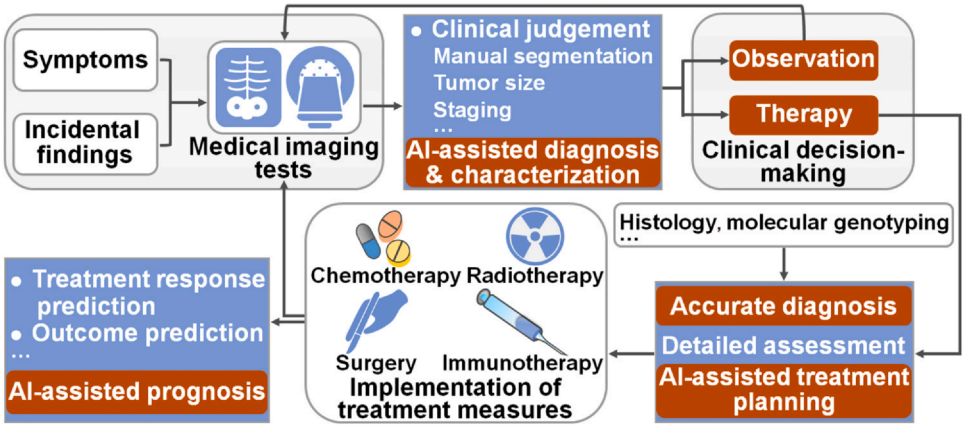


Figure 4. Schematic diagram of potential improved clinical workflow using artificial intelligence in cancer.
Current cancer care involves sequential steps: tumor imaging for detection and staging, clinical assessment for treatment planning, and histopathology/molecular testing for definitive diagnosis. AI enhances this clinical workflow by analyzing clinical data and medical imaging to optimize diagnosis and treatment selection, ultimately improving patient outcomes.

(Figure 4). It holds tremendous promise for advancing several key therapeutic modalities, including interventional therapy, surgical procedures, radiation therapy, and systemic treatment regimens. With regard to interventional therapy, AI can potentially improve a number of aspects, such as treatment planning and patient follow-up. AI can facilitate the automatic segmentation of tumors and treatment areas in interventional procedures, thereby enabling accurate tumor targeting and providing an objective assessment of treatment areas.[117] Effectively, the integration of AI into interventional oncology could lead to improved treatment outcomes and a reduction of postoperative reactions in patients.[118] Additionally, akin to image-guided interventional treatments, AI can help detect the recurrence of lesions, which would lead to a reduction in radiation exposure for both cancer patients and physicians.[119] In surgical practice, AI tools serve to enhance surgical precision, efficiency, intraoperative safety, and therapeutic outcomes.[120] AI also strengthens surgical education by aiding the development of automated skill assessment tools and providing real-time intraoperative feedback.[121] Moreover, AI-driven robotic systems can improve surgical outcomes by minimizing human error, increasing accuracy, and enabling more complex procedures.[122] Such systems will empower physicians to make highly accurate decisions in real time.[123] Furthermore, AI-enabled robots can help automate repetitive tasks (e.g., suturing and tissue dissection), thereby reducing surgeon workload and allowing them to concentrate on more critical aspects of procedures. This, in turn, will result in an overall increase in efficiency and better patient outcomes. AI has transformed radiotherapy by enabling the precise delineation of tumor boundaries, optimizing treatment planning, and allowing real-time adjustments.[124] This has enhanced therapeutic outcomes while reducing damage to healthy tissues. AI has brought about significant advancements in chemotherapy through the prediction of patient responses to various treatment regimens, which has enabled more personalized and effective therapeutic measures.[125] In the context of targeted therapy, AI technology plays a crucial role in identifying molecular targets for tailored treatments.[126] In immunotherapy, AI-driven algorithms can be implemented to aid the selection of ideal candidates for treatment and the prediction of patient responses.[127] In addition, the AI-assisted analysis of high-throughput genetic and imaging data can provide valuable insights for cancer immunotherapy management,[128] thereby contributing to better patient selection, treatment optimization, and personalized prognostic prediction. However, most AI tools are still in the research phase, with only a few adopted in clinical practice, which implies that further research is necessary to evaluate their reliability and clinical utility in cancer treatments (Figure 5).

Nonetheless, while oncologic AI has gained tremendous success at the bench, several challenges have yet to be addressed to warrant its clinical translation. The primary barrier to the development and application of oncologic AI systems is data limitation, both in quantity and quality.[129] Existing AI models are primarily derived from public databases, which ensure their validity. However, this raises the possibility of certain sampling biases. In particular, related studies with small sample

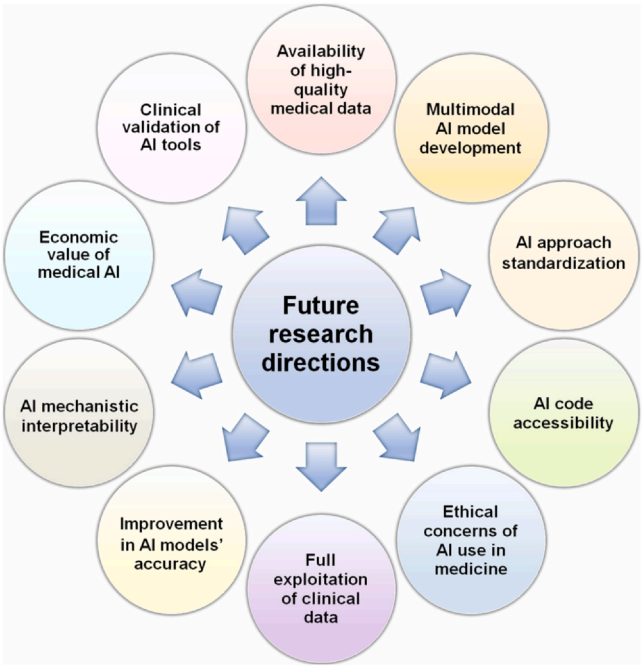


Figure 5. Future research directions for AI technology in oncology.

sizes tend to cause measurement errors.[130] Therefore, the development of large-scale open-access databases is required to enhance the availability of high-quality medical data, which will help maximize the power of AI models. Moreover, since minority groups are commonly underrepresented in clinical studies, this may result in biased results. Adequate clinical data on minorities will enable the comprehensive assessment of patient diversity and aid in the development of more accurate AI algorithms. It is well known that a useful AI model requires a massive amount of well-documented data for training, validation, and testing. This implies that the actions of AI models in real-world settings will differ dramatically if the distribution of their testing and training data vary. Thus, it is imperative to evaluate the clinical validity of AI models using various external validation sets. Furthermore, training AI models using only one type of medical images is not appropriate for the diagnosis and prognosis of cancer in clinical practice. To address this, further research in this area should be oriented toward accounting for multimodal features based on medical images and multi-omics. As knowledge of cancer biology and practice continues to expand, clinical cancer trials and associated datasets are expected to evolve constantly and become more integrated, comprehensive, and easily accessible over time, thereby setting the stage for weaving AI models into real-world cancer care.

For successful AI development, AI approaches are required to be methodologically rigorous, reproducible, and transparent. Intra-individual differences, image acquisition techniques, multi-machine reproducibility, and test-retest repeatability are key impediments to the reproducibility of these approaches.[19] To address the challenge of reproducibility, only repeatable characteristics should be retained for model construction, and the external validation of AI models are encouraged. In addition, standardization of AI approaches, such as image acquisition, processing, segmentation, and feature extraction, can potentially increase the reproducibility of AI models. Code sharing for AI models is another concern that affects its broad application in oncology. Currently, the sharing of well-annotated codes for constructing intricate AI models has yet to be widely adopted. The accessibility of codes and their itemized specifications will pave the way for further evaluation of the clinical utility of AI models. Moreover, before AI platforms can be employed as practical decision-making tools, a variety of ethical issues need to be addressed, including confirmation of the responsibility for erroneous AI decisions, assessment of public recognition of AI systems, as well as data privacy and security concerns.[131] Given this context, more AI ethics studies and public education initiatives are essential. Although machine learning-based solutions and big data have garnered widespread popularity in recent years, only a few studies have investigated the impact of AI on current cancer practices,[132] which warrants further research. At the same time, it should be noted that overdependence on computational automation and the complete abandonment of common sense should be avoided.

With current AI models focusing on imaging and omics data, the EHRs of cancer patients, which usually include valuable data on clinical history and characteristics, have yet to be adequately exploited. EHRs are largely unstructured and characterized by high levels of inconsistency, noise, and sparseness. Algorithms permitting the visualization of patient data and frameworks that favor the exploitation of EHRs to establish clinical prediction models will not only empower AI technology but also improve precision and confidence in clinical decision-making. However, as AI is characterized by a decision-making process that is predictive, it tends to make inaccurate decisions in certain circumstances. Inherent biases in the data, model misspecifications, and data selection, accuracy, and integrity issues may contribute to uncertainties in AI models. Moreover, the quality of images could affect the use of AI models in radiomics. The implementation of different image acquisition procedures and post-processing tools leads to substantial image heterogeneity. In this context, DL techniques can be employed to improve data quantity and quality via magnification modes, reduce dependence on data annotation via unsupervised learning, and exploit models trained on large volumes of data via transfer learning. Explainable AI and interpretable DL can be employed to reduce the error rate of AI systems and identify the rationale behind their decision-making process. The interpretability of AI models is an additional barrier to their applicability in cancer care. AI models run the risk of overfitting, which necessitates a compromise between accuracy and interpretability. In this regard, techniques such as feature visualization, hidden-state analysis, saliency maps, and variable importance metrics may be implemented to clarify some aspects of the AI prediction rationale.[129] Furthermore, the “black box” feature of DL, which prevents a definite explanation of its decision-making process, can lead to unintended negative consequences in a clinical setting. The involvement of a large number of elements makes it arduous to decipher the details of how DL algorithms analyze data and make clinical decisions. To address this, the interpretability of AI models can be increased by defining how DL algorithms learn from specified data and by elucidating mechanistic insights drawn from AI models. In addition, significant improvements in data visualization tools have broadened the visual understanding of algorithm-based decision-making, which can advance the optimization and clinical applicability of AI models.[133]

The cost-effectiveness of AI in healthcare has been widely studied for its potential to improve diagnosis, streamline screening procedures, and optimize laboratory examinations and surgical appointments. Likewise, AI can be expected to yield cost savings in clinical oncology. Researchers have already observed that the implementation of AI tools can be considered a cost-saving strategy for CRC prevention.[134,135] Another study found that AI can effectively detect melanoma through skin photographs at a lower cost than traditional detection methods.[136] This indicates that AI offers promising solutions for improving cancer care in areas with limited resources.[137] By facilitating the development of cost-effective diagnostic tools, AI can expand access to advanced healthcare technologies, making them available not only in well-resourced hospitals but also in underserved regions. This democratization of access is particularly crucial for low- and middle-income countries, where healthcare resources are usually scarce. In addition, AI holds promise for significantly enhancing treatment outcomes in these areas by ensuring diagnostic accuracy and efficiency. Nonetheless, the potential for cost savings when using AI varies significantly based on use cases and assumed treatment effects after diagnosis.[138] However, existing studies assessing the impact of AI on healthcare are relatively limited and marred by methodological shortcomings. To promote the current state of research in the area, more studies analyzing the cost-effectiveness of AI healthcare applications should be conducted, both in terms of quantity and quality. These analyses should include comprehensive details related to initial investments, ongoing operational costs, and comparisons with alternative technological solutions. A clear understanding of these aspects is crucial for evaluating the financial viability and sustainability of AI implementations as well as determining the value they add over existing methods. Under this context, a comprehensive and clearly segmented cost–benefit analysis can serve as a solid foundation for decision making regarding AI implementation. The economic implications of AI are multifaceted, which is expected to affect not only care providers and insurers but also the pharmaceutical and medical technology industries.[139] Integrating AI into clinical oncology offers various advantages, such as improved diagnostic precision, tailored treatment plans, and therapeutic efficiencies, which can potentially reduce healthcare costs.[140] Cost reduction may be achieved through several other factors, such as the digitalization of healthcare, advancements in healthcare information technology, and the integration of new translational technologies into clinical laboratories. These cost savings may compel the healthcare industry to shift its focus from disease treatment to wellness promotion, which would yield numerous benefits for individuals, the industry, and society as a whole. However, given the lack of studies on the economic implications of AI, detailed economic evaluations of AI-based medical interventions are likely to be crucial for its implementation in clinical practice.

5. Conclusions

The integration of AI in medical oncology, particularly for liver cancer, can significantly alleviate the workload of healthcare professionals and improve the accuracy and efficiency of its diagnosis and treatment. Furthermore, AI can offer real-time, accurate information and optimize medication selection. Although some challenges have yet to be addressed, AI is expected to revolutionize cancer research and care by offering better access to personalized treatment and facilitating improved patient outcomes.

CRediT authorship contribution statement

Man Wang: Writing – original draft, Validation, Supervision, Resources, Methodology, Investigation, Funding acquisition, Conceptualization. **Fei Yu:** Writing – review & editing, Resources, Methodology. **Yuan Zhang:** Writing – review & editing, Validation, Formal analysis.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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