

Artificial Intelligence in the Management of Hepatocellular Carcinoma

Subjects: Surgery

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Artificial Intelligence (AI) can be a useful tool in the management of disease processes such as hepatocellular carcinoma (HCC) as treatment decisions are often complex and multifaceted. AI applications in medicine are expanding with the ongoing advances in AI including more sophisticated machine learning and deep learning processes.

Keywords: artificial intelligence ; machine learning ; deep learning ; radiomics ; hepatocellular carcinoma

1. Introduction

Primary liver cancer is the sixth most commonly diagnosed cancer worldwide and hepatocellular carcinoma (HCC) accounts for over 80% of newly diagnosed cases ^[1]. Due to the lack of early diagnostic markers, absence of specific symptoms in early disease, and inadequate screening programs in most countries, nearly two out of every three patients diagnosed with HCC have intermediate or advanced disease upon diagnosis ^{[2][3]}. Unfortunately, these patients often have a poor prognosis as their disease may not be amenable to curative interventions, such as surgical resection, liver transplantation, or ablation, and, until recently, effective systemic options were limited. As a result, HCC is the fourth most common cause of cancer-related death worldwide with a relative five-year survival rate of 18% ^{[4][5]}. However, the recent inclusion of immunotherapy into the HCC treatment paradigm and the expansion of downstaging/bridging protocols to liver transplantation have improved overall survival and established a new standard of care for patients with HCC ^{[6][7]}. In addition to surgical and systemic therapeutic options, a number of liver-directed therapies (e.g., bland transarterial embolization (TAE), transarterial chemoembolization (TACE), radioembolization (RE)) are available depending on the extent of cirrhosis and the stage of the disease ^[8]. With the expanding therapeutic armamentarium for patients with HCC, novel tools are needed to effectively stratify patients to maximize therapeutic benefit.

Artificial intelligence (AI) has recently emerged as a viable clinical tool with growing utility in the management of HCC. Broadly, AI is a subdivision of data science which describes the theory and development of computer systems that perform tasks requiring human-level intelligence such as visual perception or decision making. AI was originally conceptualized in the 1950s by the mathematician Alan Turing and the field has greatly expanded since its original conception. As technology continues to evolve, new AI techniques have been developed to address more complex and sophisticated problems. Machine learning and deep learning are two such subfields of AI (**Figure 1**).

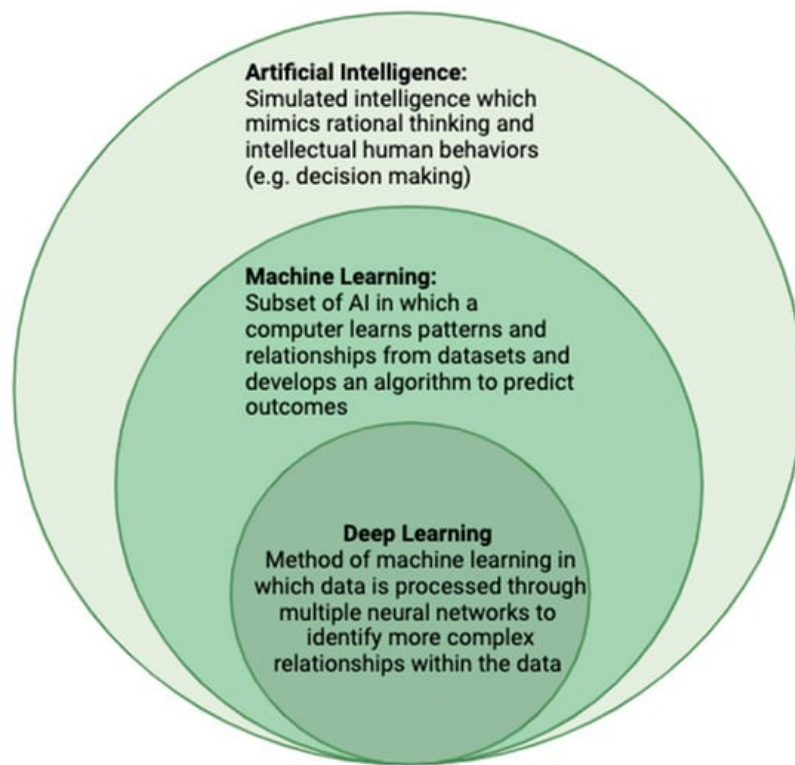


Figure 1. The Relationship between artificial intelligence, machine learning, and deep learning.

In machine learning, computer systems learn and adapt by using algorithms and statistical models to draw inferences from patterns present in data [8]. Unlike traditional statistical programming where the data and algorithms are provided and the output is produced, machine learning systems are provided the data and then independently “develop” an algorithm to process the data. Algorithm accuracy improves overtime as the system “learns” from additional data/output cycles. Two common learning methods are supervised and unsupervised learning. In supervised learning, the computer system is provided human-labeled datasets including desired inputs and outputs. The operator knows the desired output; the algorithm “learns” from the observations to identify patterns in the data and make predictions. Examples of supervised learning include classification, regression, and forecasting. In contrast, unsupervised machine learning systems do not receive output information. The system identifies associations and relationships to group the data in a more organized way without an “answer key”. Clustering and dimension reduction are two examples of unsupervised learning [9].

The datasets used to develop machine learning models are typically divided into training, validation, and testing datasets. Once an algorithm has been developed from a training dataset, it is further optimized and tuned with a validation set. Upon completion of the training phase, its performance will be evaluated with a test dataset comprising new data which the system has not yet encountered. Ideally, the algorithm will have a similar predictive power with the test dataset as with the one it was trained through, implying generalizability of the model. It is important to note the generalizability of an algorithm is largely based upon the characteristics of its training and the validation dataset. Any biases present within the dataset, such as homogeneity due to sampling error, will become inherent to the model. This will ultimately lead to decreased generalizability and a poorer predictive performance of the model [9].

Deep learning is a subset of machine learning and more closely mimics human intelligence. The system is built upon artificial neural networks that are modeled on the biologic neural networks of the brain [10]. Deep learning models have the ability to process more complex data, such as images, text or sounds, and are the basis of complex models such as speech recognition or large-scale image analysis. This method of AI processes data through multiple neural layers, progressively extracting higher-level features to produce a complete learned result. These networks can comprise millions of neural layers each of which receives data from the previous layer, transforms the data, and sends them to connected neurons in succeeding layers (**Figure 2**). Each of these connections has a different weighted value based upon which characteristics are most important and predictive in achieving an accurate output. These networks of neurons—in addition to the initial input and final output layers—are known as hidden layers. One major limitation of deep learning methods is that it is not always understood how the model has reached the final output, a phenomenon known as the “black box” of deep learning. It is often unclear how the model has transformed the data to reach the output. Furthermore, data are processed in such a granular fashion and through countless amounts of hidden neural layers that these connections are often not comprehensible or meaningful to the human brain [11]. Another major limitation of deep learning is that these models require sizable training datasets in order to extrapolate meaningful relationships within the data. This can be a

deterrent to developing functional models for entities with few observations as is frequently the case when evaluating rare diseases [12].

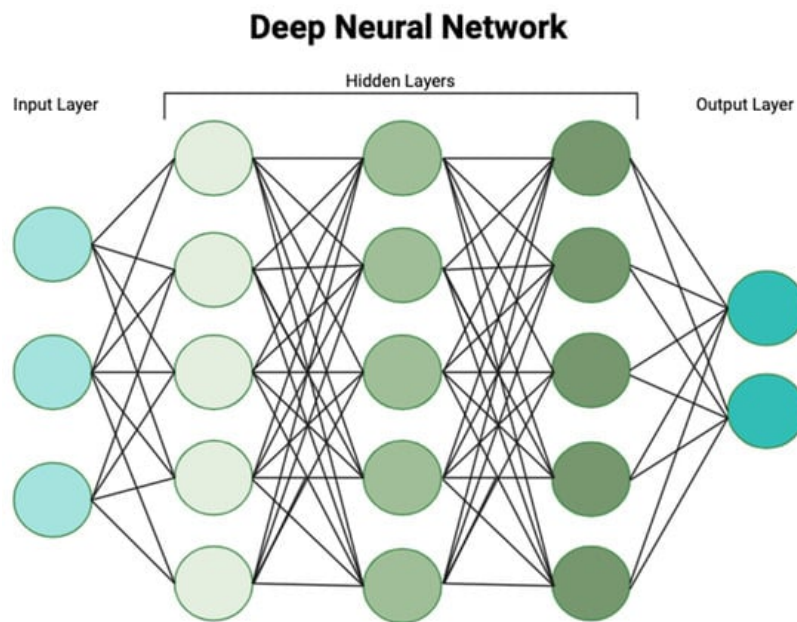


Figure 2. Deep learning processes and transforms data through multiple artificial neural networks to generate a predictive algorithm based on complex patterns within the data.

AI has a growing presence in medicine; however, ethical considerations and technical constraints initially limited broader adoption and the implementation of AI within the medical field. While many ethical considerations remain, recent advances in AI methodologies have overcome some of the technical constraints. For example, Jiang et al. reported on the superiority of a self-supervised large language model that was trained on unstructured clinical notes from an electronic health record to predict 30-day all-cause readmission, in-hospital mortality, comorbidity indices, lengths of stay, and insurance denial when compared with traditional models [13]. Furthermore, an AI model using deep network automatic segmentation outperformed a clinical model and a radiomic model in discriminating between patients with pancreatic cancer with and without lymph node metastasis [14]. These advances have improved the accuracy and expanded the clinical utility of AI systems in the field of medicine.

2. Screening and Detection

Since many patients diagnosed with HCC have advanced disease and limited therapeutic options, improvements in screening and early detection are necessary to improve outcomes. For example, a review of country-level HCC surveillance programs demonstrated that countries with established and effective HCC surveillance programs detected HCC at significantly earlier stages and had lower overall mortality [15]. Effective programs identify and stratify patients at high-risk of developing HCC and enroll them into regular surveillance protocols such as biannual evaluation with liver ultrasound and liquid tumor markers. Ideally, healthcare professionals intervene prior to the development of irreversible HCC risk factors (i.e., cirrhosis). However, cost/benefit restraints and high false-positive rates limit the utility of screening low-prevalence populations. AI techniques may help us to overcome these limitations (Table 1). In a 2022 study, Blanes-Vidal et al. evaluated asymptomatic patients from a primary care population without a prior diagnosis of liver disease [16]. The authors tested the diagnostic performance of ensemble models, a machine learning approach, to detect liver fibrosis and then compared the performance with standard blood-based scoring systems. The ensemble models included data readily available during a primary care visit. In a subset of 463 patients that received a liver biopsy, the ensemble learning models significantly outperformed standard blood-based indices to detect liver stiffness (>8 kPa) and fibrosis (Kleiner biopsy stage F2 to F4) with AUCs of 0.86–0.94 vs. 0.60–0.76. Furthermore, all the ensemble models had a $\geq 98\%$ negative predictive value. Similarly, other AI models have demonstrated superiority to standard models in predicting the development of HCC [17][18].

Radiomics, a quantitative method to extract features (e.g., shape, intensity, texture) from medical imaging, can significantly improve the diagnostic yield of imaging modalities, especially when combined with other AI techniques such as deep learning. While established criteria exist for the radiologic diagnosis of HCC in high-risk patients (i.e., LI-RADS), the true proportion of patients with LI-RADS 5 lesions (diagnostic of HCC) is unclear. Additionally, this classification system only applies to patients at high risk of HCC (e.g., cirrhosis, HBV infection) [19]. The diagnostic uncertainty of many

newly identified liver lesions may lead to unnecessary serial imaging, invasive procedures (e.g., biopsy), and undue psychological stress on the patient. For these reasons, much energy has been devoted to building radiomic-based models that can accurately detect and diagnose HCC (**Table 1**). Yasaka et al. developed a deep learning model using a convolutional neural network (CNN) to differentiate malignant liver lesions from non-malignant lesions [20]. In this retrospective study, the authors built a CNN using imaging sets from 460 patients who were found to have liver lesions on triple-phase CT. The lesions were classified into five categories as follows: classic HCC (A), malignant tumors other than HCC (B), indeterminate masses and rare benign liver masses (C), hemangiomas (D), or cysts €. The CNN accurately identified malignant lesions with the median AUC of 0.92 for differentiating categories A–B from categories C–E. Furthermore, Mokrane et al. used a radiomic model to improve the diagnostic accuracy of HCC in cirrhotic patients with indeterminate liver nodules [21]. In this multicenter retrospective study, multiphasic CT scans of 178 cirrhotic patients who had undergone the biopsy of indeterminate liver nodules were included. Nearly 14,000 quantitative features were extracted from imaging sets. With machine learning algorithms, a radiomic signature was created and validated to classify these indeterminate liver nodules as HCC or non-HCC. While the LI-RADS scores were similar between the HCC and non-HCC groups, the radiomic signature reached an AUC of 0.70 in the discovery cohort and 0.66 in the validation cohort. AI has also been used to augment the diagnostic capabilities of other imaging modalities including ultrasound and magnetic resonance imaging (MRI) [22][23][24].

While the generalizability of screening and diagnostic models derived from AI techniques requires further evaluation, these models offer non-invasive and resource-efficient means to reliably screen and detect HCC in select populations. This technology can be especially useful in low resource centers where specialized liver radiologists may not be readily available to aid in the diagnosis of complex liver lesions. Furthermore, these models may help institutions and governments to more efficiently allocate scarce resources to HCC screening and intervention due to improved risk stratification. For example, using a deep learning recurrent neural network model to generate HCC risk scores, Ioannou et al. found that 80% of HCC cases diagnosed in the subsequent three years occurred in the highest 51% of risk scores [18]. Risk-based screening supported by AI algorithms may increase diagnostic yield, optimize resource utilization, and help us to overcome the suboptimal performance of existing tools [25].

Table 1. Select studies utilizing AI in screening and diagnosis of HCC.

Author, Year	Model Design	Population	AI Methodology	Accuracy
Blanes-Vidal et al. (2022) [16]	Prediction of liver fibrosis using clinical data readily available to primary care physicians	Low-prevalence primary care population	Ensemble learning model	AUC: 0.86–0.94
Ioannou et al. (2020) [18]	Identification of patients at high risk of developing HCC by extracting data from electronic medical records	Patients with known Hepatitis C Virus and cirrhosis	Recurrent neural network	AUROC: 0.759
Yasaka et al. (2018) [20]	Differentiation of liver masses on CT, with categorization into HCC, other liver tumors, hemangiomas, or cysts	Patients who had undergone dynamic contrast-enhanced CT for evaluation of liver lesions	Convolutional neural network	AUROC: 0.92
Mokrane et al. (2020) [21]	Diagnosis of liver nodules as HCC vs. non-HCC based on quantitative features extracted from triphasic CT	Patients with cirrhosis and biopsy-proven indeterminate liver nodules	Machine learning-based radiomic signature	AUROC: 0.66
Schmauch et al. (2019) [22]	Detection and characterization of focal liver lesions as benign- vs. malignant-based on ultrasound characteristics	Patients with known liver nodules	Residual neural network	AUROC: 0.935

3. Prognosis and Treatment

3.1. HCC Prognosis and Risk of Recurrence

Recent multi-omic investigations have advanced the understanding of the carcinogenic mechanisms responsible for HCC, revealing many potential biomarkers [26]. Evaluating these large data sets with AI methods may improve current prognostic ability by identifying more aggressive subtypes and patients at high risk of recurrence (**Table 2**). In an early study using a deep learning framework to integrate multi-omic data in patients with HCC, Chaudhary et al. developed a deep learning model from 360 patients with HCC using RNA sequencing, miRNA sequencing, and methylation data from The Cancer Genome Atlas [27]. The model identified a more aggressive subtype with worse survival characterized through

frequent TP53 mutations; a higher expression of KRT19, EPCAM, and BIRC5; and activated Wnt and Akt signaling pathways. The investigators then validated the model on five external data sets with acceptable results.

In addition to detecting relationships within large multi-omic data sets to improve prognostication, AI techniques can help us identify biomarkers in the preoperative setting typically only identified through pathologic evaluation such as microvascular invasion (MVI) [28]. For example, multiple studies have shown the feasibility of using machine learning algorithms to accurately predict the presence of MVI based on preoperative axial imaging characteristics [29][30][31]. Chong et al. built a radiomic-based nomogram to assess the risk of MVI [32]. This retrospective study analyzed preoperative MRIs from 356 patients with pathologically confirmed solitary HCC less than 5 cm. The nomogram, built by extracting radiomic features from images containing tumors, peritumoral tissue, and non-tumoral liver parenchyma, accurately predicted the risk of MVI as well as recurrence-free survival.

Similarly, other groups have identified biomarkers of HCC recurrence using machine learning methods (Table 2) [33]. Yan et al. created a deep learning MR signature derived from imaging characteristics including tumor size, arterial phase enhancement type, capsular appearance, presence of a hypointense halo, intratumoral necrosis, satellite nodules, and peritumoral hypointensity [34]. When combined with clinical factors such as MVI and tumor number, the MR signature predicted early recurrence better than clinical data alone. Another model created by Ji et al. extracted radiomic features from preoperative CT scans to build a radiomic signature that, when integrating clinical data such as MVI, AFP level, and tumor number, accurately predicted the risk of recurrence in patients after resection of early-stage HCC [35]. Improved prognostication and risk stratification with AI techniques may better inform management decisions for patients with HCC.

Table 2. Key studies utilizing AI to predict prognosis and risk of recurrence of HCC.

Author, Year	Model Design	Pertinent Risk Factors	Population	AI Methodology	Accuracy
Chaudhary et al. (2018) [27]	Predictive model for HCC prognosis based on molecular signature and multi-omic data	- TP53 inactivation mutation - EPCAM, KRT1, BIRC5 upregulation	HCC patients within the Genome Cancer Atlas (TCGA)	Deep learning	C-index: 0.68
Liu et al. (2021) [30]	Prediction of MVI preoperatively based on CT imaging characteristics and patient clinical factors	- Radiomic features identified from CT images	Patients with HCC	Residual Neural Network	AUC: 0.845
Chong et al. (2021) [32]	Creation of radiomic-based nomogram to preoperatively predict risk of MVI and recurrence-free survival, based on MRI characteristics and clinical data	- Elevated AFP, total bilirubin - Radiomic values - Peritumoral enhancement - Incomplete or absent capsule enhancement	Patients with solitary HCC smaller than 5cm	Random Forrest	AUC: 0.92

Author, Year	Model Design	Pertinent Risk Factors	Population	AI Methodology	Accuracy
Ji et al. (2020) [35]	Creation of radiomic signature with pre- and post-resection features to predict recurrence for early-stage HCC	- Tumor number - Cirrhosis - Arterial peritumoral enhancement - Tumor necrosis - Satellite lesion - MVI	Patients with HCC that met the Milan Criteria and underwent curative intent resection	Machine learning-based radiomic signature	C-index: 0.77

3.2. Pathologic Assessment

AI techniques have also been applied to evaluate associations between histologic features and outcomes in numerous disease processes, including HCC (**Table 3**) [36][37][38][39]. Using whole-slide imaging, Yamashita et al. developed a deep learning-based system to predict a recurrence-free disease interval after curative-intent hepatectomy in patients with HCC. Their model stratified patients into low-risk and high-risk subgroups and outperformed the standard tumor–node–metastasis (TNM) staging system [40].

Chen et al. built a neural network that was able to assist in the prognostication of HCC based on histologic whole-slide imaging. The model used hematoxylin and eosin slides from a genomic database to train a neural network to classify liver lesions as malignant with 96.0% accuracy and predict lesion histopathological grade with 89.6% accuracy. Furthermore, the model also predicted select gene mutations including CTNNB1, FMN2, TP53, and XFZ4 [41]. AI-based pathology models can also predict the activation of immune signatures in HCC. Zeng et al. used deep learning approaches on whole-slide histologic images and gene expression profiling, derived from the Cancer Genome Atlas Liver Hepatocellular Carcinoma (TCGA-LIHC) public dataset, to develop models that predicted the activation of six key immune signatures that, when overexpressed, correlated with the response to immunotherapy [42]. While prospective validation studies are needed, these data demonstrate the potential utility of AI to select patients who will have a greater response to immunotherapy and may inform adjuvant therapy decisions.

Table 3. Key studies demonstrating the use of AI on whole-slide imaging.

Author, Year	Model Design	Population	AI Methodology	Accuracy
Qu et al. (2022) [36]	Creation of histological score using whole-slide imaging to predict HCC recurrence	Patients with early-stage HCC who had undergone surgical resection in a single institutional dataset and the TCGA dataset	Convolutional neural network	C-index: 0.804
Saillard et al. (2020) [37]	Use of whole-slide imaging to predict risk of HCC recurrence and stratifying it into low- and high-risk subgroups	Patients with HCC who had undergone surgical resection in a single institutional dataset and the TCGA dataset	Convolutional neural network	C-index: 0.72
Yamashita et al. (2021) [40]	Use of whole-slide imaging to formulate a risk score predictive of HCC recurrence	Patients with HCC in the TCGA and Stanford-HCC dataset	Convolutional neural network	C-index: 0.724
Zeng et al. (2022) [42]	Prediction of activation of immune gene signatures based on whole-slide imaging	Patients with HCC who had undergone surgical resection in the TCGA dataset	Clustering-constrained attention multiple instance learning	AUROC: 0.78–0.91

3.3. Locoregional Therapies

AI-based models may help to select patients who are good candidates for locoregional therapies such as radiofrequency ablation (RFA) (**Table 4**). Wu et al. built an artificial neural network based on fifteen clinical variables from HCC patients who had undergone CT-guided RFA [43]. Variables included patient characteristics, tumor size, tumor number, and laboratory values (e.g., AFP). Ultimately, the artificial neural network model predicted one-year disease-free survival with

an AUC of 0.84 and one-year disease-free survival with an AUC of 0.75. Lui et al. created a deep learning radiomic-based model of preoperative contrast-enhanced liver ultrasound images and predicted the response to the first TACE session in patients with HCC [44]. In another study, investigators trained and validated a CNN to automatically assess splenic volume. Patients with higher splenic volumes, as automatically determined by the CNN, had significantly higher risk of hepatic decompensation and lower overall survival after TACE. Conversely, axial and craniocaudal splenic diameter did not correlate with outcomes [45].

3.4. Automatic Methods for Liver and Tumor Segmentation

Automatic liver and tumor segmentation has numerous clinical applications which may aid in the management of HCC such as the preoperative volumetric quantification and assessment of treatment responses to locoregional therapies (Table 4). The use of manual and semi-automatic liver segmentation methods can lead to inconsistencies due to user variability. Furthermore, segmentation is often a slow, labor-intensive process. With advancements in deep learning techniques and CNNs, completely automatic liver segmentation is now feasible [46][47][48]. However, automatic algorithms do have their own limitations including the need for large training datasets to develop accurate algorithms. Automatic tumor segmentation can be even more challenging as tumor characteristics, such as variability in size, variability in location, and indiscrete borders between healthy liver parenchyma and tumors, can decrease the accuracy of models. Regardless, early studies demonstrate that automatic segmentations outperform semi-automatic methods with regard to the accuracy and repeatability of segmentation [49]. Meng et al. used a three-dimensional (3D) dual-path multiscale CNN to build a liver and liver tumor segmentation algorithm based on abdominal CT images. The dual path multiscale 3D network architecture allowed the model to capture large scale global features through one path while capturing more granular local features through the second path. Notably, their algorithm performed best on large tumors [50]. Zheng et al. built a four-dimensional (4D) deep learning model to segment HCC lesions based on dynamic contrast-enhanced MRIs. In an attempt to avoid the “black box” learning that occurs with many automatic segmentation models, the investigators first build a 3D CNN to separately extract imaging features from each individual phase of imaging. From there, these data were fed into a convolutional long short-term memory (C-LSTM) network module in order to extract higher-level features, including temporal information and dynamic features, that varied through the multi-phase imaging. This allows us to use dynamic features that are not only characteristic of HCC but critical to diagnosis, such as arterial phase hyperenhancement and portal venous or delayed-phase washout. Their model achieved a Dice score of 0.825 ± 0.077 for HCC tumor segmentation in an internal test set and 0.786 ± 0.073 in an external set, implying good generalizability of this model [51].

3.5. Surgical Complications

Many HCC patients have some level of hepatic dysfunction upon presentation, increasing the risk of post-hepatectomy liver failure (PHLF). PHLF remains the most frequent cause of postoperative mortality in patients following hepatectomy, highlighting the importance of identifying patients at high risk of PHLF prior to resection to more effectively select patients for adjuncts such as portal vein embolization. Wang et al. constructed a machine learning clinical model using laboratory values, tumor characteristics, and surgical variables (e.g., surgical approach, extent of resection, intraoperative blood loss) to predict the risk of PHLF. The model outperformed traditional models such as MELD, Child-Turcotte-Pugh, or albumin-bilirubin grade when predicting PHLF [52]. AI-derived algorithms have successfully predicted other surgical complications. Laino et al. predicted the risk of a postoperative bile leak following hepatectomy using a combined clinical–radiomic model in 378 patients with a preoperative CT. Radiomic data was extracted from a virtual liver biopsy obtained from a 2 cm cylinder of non-tumoral liver parenchyma on the portal phase of preoperative CT. Their combined model (AUC 0.74) outperformed a model using clinical data alone (AUC 0.61) to predict the risk of a bile leak [53].

Table 4. Key studies demonstrating the use of AI in management of HCC.

Author, Year	Model Design	Population	AI Methodology	Accuracy
Wu et al. (2017) [42]	Prediction of disease-free survival after radiofrequency ablation based on clinical variables	Patients who underwent CT-guided radiofrequency ablation	Artificial neural network	AUC: 0.75–0.84
Liu et al. (2020) [44]	Prediction of response to first TACE session using contrast-enhanced liver ultrasound	Patients who underwent ultrasound within one week of TACE for HCC	Radiomic-based deep learning	AUC: 0.81–0.93
Meng et al. (2020) [50]	Automatic liver parenchyma and liver tumor segmentation from CT images	Multi-institutional liver tumor segmentation (LiTS) dataset	Dual path multiscale convolutional neural network	Dice: 0.689–0.965

Author, Year	Model Design	Population	AI Methodology	Accuracy
Zheng et al. (2022) ^[51]	Automatic segmentation of HCC lesions based on dynamic MRI	Patients with HCC who underwent dynamic contrast-enhanced MRI	Convolutional neural network and recurrence neural network	Dice: 0.825
Wang et al. (2022) ^[52]	Prediction of post-hepatectomy liver failure based on clinical characteristics and surgical variables	Patients with HCC who underwent hepatectomy	Light gradient boosting machine learning	AUC: 0.822–0.944

4. Intraoperative Use of Artificial Intelligence

A thorough understanding of the vascular and biliary anatomy from adequate multiphasic abdominal imaging is necessary to perform a safe hepatectomy and minimize complications. Three-dimensional liver reconstruction technology may improve perioperative outcomes in patients undergoing a major hepatectomy by further elucidating spatial relationships between the tumor and critical vascular and biliary structures. A meta-analysis evaluating the efficacy and safety of 3D-reconstruction liver models in patients undergoing a major hepatectomy showed shorter operative times, less intraoperative blood loss, fewer hepatic inflow occlusion events, shorter hospital stays, and fewer postoperative complications when using such technology ^[54]. Deep learning algorithms can help us to automate the reconstruction of 3D liver models with reliable accuracy and detail ^[55].

As an adjunct to intraoperative liver ultrasound (IOUS), machine learning algorithms may help us to overcome some limitations of traditional ultrasounds and improve the accuracy of identifying liver lesions intraoperatively. Barash et al. trained a CNN on intraoperative ultrasound imaging to detect liver lesions. The algorithm achieved an AUC of 80.2% and an overall classification accuracy of 74.6% ^[56]. Furthermore, Takamoto et al. used real-time virtual sonography (RVS), an AI-assisted platform that merges preoperative CT images with real-time IOUS, to enhance IOUS with the identification of small intrahepatic lesions ^[57]. The median liver lesion size was 6.0 mm and RVS significantly improved surgeon confidence in lesion identification. Importantly, of the 17 lesions undetectable using fundamental IOUS, 14 were identified through RVS and ultimately treated.

However, despite the successful applications of AI technology during liver surgery, several challenges remain. This is especially true of 3D overlays, which are difficult to use during hepatectomy. The mobilization of the liver and the deformation of the parenchyma during hepatectomy make real-time overlays onto tissues more challenging and less accurate. This is in comparison with other surgical disciplines such as neurosurgery, where the target—in this case the brain—is rigid and fixed, allowing for an easy overlay of 3D reconstructions. Preliminary studies demonstrate the feasibility of a physics-based elastic augmented reality model that can provide a real-time 3D overlay during hepatectomy, allowing for the deformation and mobilization of the tissue; however, further quality improvement needs to occur prior to meaningful use during hepatectomy ^[58].

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