SYSTEMATIC REVIEW

Early detection of HCC in patients with cirrhosis using AI; a Systematic Review

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Abstract

Introduction: Hepatocellular carcinoma constitutes for approximately 75% of primary cancers of liver. Around 80-90% of patients with HCC have cirrhosis at the time of diagnosis. Use of AI has recently gained significance in the field of hepatology, especially for the detection of HCC, owing to its increasing incidence and specific radiological features which have been established for its diagnostic criteria.

Objective: A systematic review was performed to evaluate the current literature for early diagnosis of hepatocellular carcinoma in cirrhotic patients.

Methods: Systematic review was conducted using PRISMA guidelines and the relevant studies were narrated in detail with assessment of quality for each paper.

Results: This systematic review displays the significance of AI in early detection and prognosis of HCC with the pressing need for further exploration in this field.

Conclusion: AI can have a significant role in early diagnosis of HCC in cirrhotic patients

Keywords: Carcinoma, Hepatocellular, Liver Neoplasms, Gastroenterology, Liver Cirrhosis, Prognosis, cirrhosis, radiological features.

DOI: https://doi.org/10.47391/JPMA.AKU-9S-05

Introduction

Hepatocellular carcinoma (HCC) constitutes for approximately 75% of primary cancers of liver.[1] Worldwide, it is the sixth most common cancer and is the 3rd leading cause of cancer-related deaths.[2] The five- year survival rate for HCC is 18%. Chronic hepatitis, including Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infection, is a well-established risk factor for development of HCC. While genomic viral integration is common with HBV associated HCC, most HCC cases are still found to develop in a background to cirrhosis and around 80-90% of patients with HCC have cirrhosis at the time of diagnosis which is due the chronic inflammation and oxidative stress leading to hepatocellular necrosis, regeneration and mutagenesis.[3-4]

Currently, all guidelines suggest regular ultrasound screening for HCC in cirrhotic patients. The sensitivity of ultrasound in detecting HCC is reported to be 40-80%. However, it is influenced by obesity and the severity of liver disease. Moreover, detecting very small lesions is difficult and remains unsatisfactory on ultrasound.[5] In case of high suspicion, other modalities such as triphasic CT scan or liver-specific MRI is done to detect HCC. The diagnostic efficacy of MRI to detect small lesions is higher than CT scan[6]. These radiological assessments and tumour markers, such as alpha-fetoprotein (AFP), have been standardized as diagnostic parameters for HCC.

The term Artificial Intelligence (AI) was first described in 1956 by John McCarthy. Since then, it has evolved into systems that simulate human behaviour, speeding up the process of diagnosis and management in medicine with greater precision to improve healthcare.[7] AI incorporates algorithms into systems, including machine learning (ML) and deep learning (DL) models. ML is a sub-type of AI that learns recurring patterns and relationships to predict outcomes and uses pre-processing techniques for problem-solving. ML has further advanced into DL, which consists of complex deep neural network architecture which is based on human neural pathways[8]. Due to its ability to analyse multifaceted associations and interactions in large datasets, its implications have been attributed to be super-human, providing accurate results and mitigating the risk of bias and drift in results[9]. Most ML models are evaluated by performance metrics, such as the area under the curve (AUC), which denotes the ability of the model to discriminate between cases and non-cases. C-index is also used alternatively to quantify the performance of models.

Use of AI has recently gained significance in the field of hepatology, especially for the detection of HCC, owing to its increasing incidence and specific radiological features which have been established for its diagnostic criteria. Clinical data, including demographics, laboratory parameters, and tumour markers, are widely incorporated

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into AI-based models for the detection of HCC. B. Schmauch formulated an algorithm that simultaneously detected focal liver lesions (FLL) and characterized them into benign or malignant lesions using DL.[10] Le-Hang Guo used contrast-enhanced ultrasound (CEUS) and proposed a framework to identify FLL using deep canonical correlation analysis (DCCA) and multiple kernel learning (MKL).[11] Various studies have used CT and MRI-based models reporting 91.67-100% accuracy for the detection of HCC.[12]

Through this systematic review, we aim to review recent studies that describe predictive, AI-based models for early diagnosis of HCC in patients with cirrhosis. This may help in further exploring this most recent, evolving technology and its role in identifying patients at risk of developing HCC earlier and may prove beneficial in the longer run in the prognosis of HCC patients.

Methods

After registration at PROSPERO (International prospective register of systematic review) with ID no. CRD42024512816, a systematic review was carried out by following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines[13] (Fig.1) to describe predictive AI-based models for early diagnosis of HCC in cirrhotic patients.

Search Strategy

PubMed, Scopus and Cochrane database were searched from commencement to July 2023 using a combination of keywords including HCC OR liver cancer AND AI OR deep learning AND cirrhosis. The review by authors was done in December 2023. The keywords were modified according to each database as follows:

PubMed

("artificial intelligence"[MeSH Terms] OR ("artificial"[All Fields] AND "intelligence"[All Fields]) OR "artificial intelligence"[All Fields] OR ("machine learning"[MeSH Terms] OR ("machine"[All Fields] AND "learning"[All Fields]) OR "machine learning"[All Fields])) AND ("cirrhosis" [All Fields]) AND ("carcinoma, hepatocellular"[MeSH Terms] OR ("carcinoma"[All Fields] AND "hepatocellular"[All Fields]) OR "hepatocellular carcinoma"[All Fields] OR ("hepatocellular"[All Fields] AND "carcinomas"[All Fields]) OR "hepatocellular carcinomas"[All Fields] OR "HCC"[All Fields] OR ("liver neoplasms"[MeSH Terms] OR ("liver"[All Fields] AND "neoplasms"[All Fields]) OR "liver neoplasms"[All Fields] OR ("liver"[All Fields] AND "cancer"[All Fields]) OR "liver cancer"[All Fields]))
Results: 256

Scopus

TITLE-ABS-KEY (artificial AND intelligence) OR TITLE-ABS-KEY (machine AND learning) AND TITLE-ABS-KEY (hepatocellular AND carcinomas) OR TITLE-ABS-KEY (HCC) OR TITLE-ABS-KEY (liver AND cancer) AND TITLE-ABS-KEY (Cirrhosis))
Results: 576

Cochrane

Cochrane ((Artificial Intelligence) OR (Machine Learning)) AND ((Hepatocellular Carcinomas) OR (HCC) OR (Liver Cancer) AND (Cirrhosis))
Results: 11

The results were included from the time of commencement to July 2023. The references for selected articles and review articles were additionally studied manually to identify relevant articles.

Inclusion and exclusion criteria

Only original, published articles describing the use of AI in diagnosis of HCC in cirrhosis were included. Diagnostic modalities including patient demographics, biochemical, serological parameters and radiological tests were included. Review articles and case reports and articles which only described diagnosis of HCC without cirrhosis, treatment models and surveillance were excluded.

Study selection and Data extraction

Initial search was carried out and duplicate studies were removed. Two authors independently evaluated study titles and abstracts and those which didn't meet the inclusion criteria were excluded. Full text articles were then reviewed for inclusion and data extraction. Discrepancies were amended after mutual discussion. All data was then analysed and reported.

Results

Search Results

The Initial search identified 843 papers; 256 from PubMed, 576 from Scopus and 11 from Cochrane. After excluding duplication, 670 article titles were analyzed and only those relevant to AI, HCC and cirrhosis were included for review of abstracts 21 full texts were reviewed after which 8 articles were included in our study (Fig. 1).

Quality assessment: Quality assessment for selected studies was done using the NHLBI quality assessment tool for observational cohort and cross-sectional studies[14]. The assessment for individual studies is tabulated in Table 1.

Review of Studies

Out of the eight studies selected, all were retrospective except for two. Only 3 were single-centre studies. All patients were diagnosed with cirrhosis either clinically or

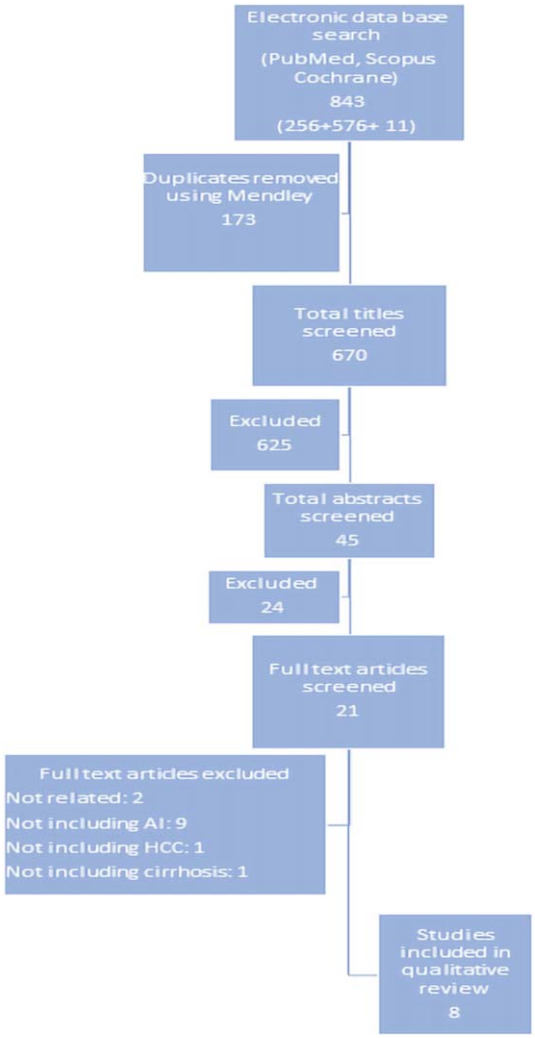

Figure-1: Flow chart for systematic review process.

histologically. HCC was confirmed histologically or by means of international HCC guidelines. Imaging data included ultrasound, CT scan or MRI scan. 5 studies used clinical parameters. [1] study used B-mode ultrasound, and 2 studies used CT scan as a diagnostic modality. HBV infection was the most prevalent group in all studies. Summary of the studies is tabulated in Table 2.

A study conducted at the University of Michigan (UM) enrolled 442 patients with cirrhosis and prospectively followed them for the development of HCC with laboratory investigations, tumour markers and radiological investigations. HCC was identified using the American Association for the Study of Liver Diseases (AASLD) guidelines.[15] A regression model and random forest model were designed and externally validated by the data from Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C) Trial. 41 patients developed HCC. The yearly incidence of HCC was reported as 2.8%. The HALT-C model had a c-statistic of 0.76, while the UM regression model and ML model had a c-statistic of 0.64 and 0.71 respectively.

Loannou et al. [16] formulated and compared 3 models that predicted HCC within 3 years of diagnosis of cirrhosis in HCV-infected patients. The models included (1) Logistic regression (LR) with cross-sectional inputs (cross-sectional LR); (2) LR with longitudinal inputs (longitudinal LR); and (3) Recurrent Neural Networks (RNN) with longitudinal inputs. Variables included 4 baseline variables, including age at diagnosis of cirrhosis, gender, race, and HCV genotype; and 27 longitudinal predictors, namely; establishment of cirrhosis, attainment of sustained virologic response (SVR), and twenty four lab parameters(bilirubin, AST, AST–upper limit of normal (ULN) ratio, ALT, ALT-ULN ratio, alpha fetoprotein(AFP), AFP–ULN ratio, alkaline phosphatase(ALP), ALP–ULN ratio, serum albumin, AST-ALT ratio, fibrosis-4 (FIB-4) score,30 AST-platelet ratio index (APRI), blood urea nitrogen, creatinine, glucose, international normalized ratio, haemoglobin levels, Total leucocyte count, platelets, sodium, potassium, chloride, and total protein). The cross-sectional LR model was created using only the baseline, cross sectional values of each of the predictors approximately before time t (sampled visit immediately after development of cirrhosis), which calculates the linearity of these variables and log odds. Longitudinal LR model, which included the same variables but was specifically created to apprehend longitudinal information available prior to time t: minimum, maximum, minimum of slope, maximum of slope, and total variation. The RNN model used information from both the baseline and the raw longitudinal predictors between 2 consecutive visits. The RNN model resulted in the highest AUC: 0.759. 22.3% of patients developed HCC. The mean age of patients diagnosed with HCC was 58.2 years.

Nam et al.[17] included 424 patients with HBV cirrhosis in two tertiary care hospitals. All patients received entecavir and were followed up for 1-6 months. Ultrasound and alpha-fetoprotein were used for HCC surveillance, and HCC was identified either clinically or through biopsy. A DL model was formulated based on age, gender, platelets, serum albumin, serum bilirubin, HBV DNA titre, existence of diabetes, and the duration for which the patient was followed from the first visit. The results were compared with six previous models (platelet count, age, and gender-hepatitis B score [PAGE-B], Chinese University HCC score [CU-HCC], HCC-Risk Estimating Score in CHB patients Under Entecavir [HCC-RESCUE], age, diabetes,

Table-1: Quality assessment of studies. .

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14
Singal et al 2013[15]	✓	✓	?	✓	✗	✓	✓	?	✓	?	✓	?	✓	✓
Loannou et al 2020[16]	✓	✓	?	✓	✓	✓	✓	?	✓	?	✓	?	✓	✓
Nam et al. 2020[17]	✓	✓	?	✓	✗	✓	✓	?	✓	?	✓	?	✓	✓
Audureau et al 2020[18]	✓	✓	✓	✓	✗	✗	✓	✓	✓	✓	✓	?	✓	✓
Kim et al 2021[19]	✓	✓	?	✓	✗	✗	✓	?	✓	?	✓	?	✓	✓
Zhang et al 2022[20]	✓	✓	?	✓	✗	✓	✓	✓	✓	?	✓	?	✓	✓
Mochrane et al. 2019[21]	✓	✓	?	✓	✗	✓	✓	✓	✓	?	✓	?	✓	✓
Yoo et al 2023[22]	✓	✓	?	✓	✗	✓	✓	✓	✓	?	✓	?	✓	✓

Q1. Was the research question or objective in this paper clearly stated?
Q2. Was the study population clearly specified and defined?
Q3. Was the participation rate of eligible persons at least 50%?
Q4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?
Q5. Was a sample size justification, power description, or variance and effect estimates provided?
Q6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?
Q7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?
Q8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?
Q9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
Q10. Was the exposure(s) assessed more than once over time?
Q11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
Q12. Were the outcome assessors blinded to the exposure status of participants?
Q13. Was loss to follow-up after baseline 20% or less?
Q14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

race, cause of cirrhosis, gender, and severity HCC score [ADRESS-HCC], modified PAGE-B score [mPAGE], and Toronto HCC risk index [THRI]). The c-index of the DL based model was 0.782 as compared to the previous studies, whose c-index was <0.6. Furthermore, a cut-off value for probability of 0.5 was established using this model. Patients with scores>0.5 had a higher incidence of HCC.

Audureau et al.[18] included 836 patients with known HCV cirrhosis and followed them semi-annually with lab tests and ultrasounds. Those with a suspicious lesion on ultrasound were further followed with CT or MRI. The primary endpoints of the study were the presence of HCC and the attainment of SVR. The incidence of HCC was recorded in 18.7% (n = 156) of patients. Three machine learning-based models were created, and analysis was characterized on SVR status varied by time: 1) Fine-gray regression models recognized 6 independent factors predicting HCC in patients before SVR (alcohol abuse, genotype 1, elevated AFP and GGT, low platelet count and albuminaemia) and three in patients after SVR (elevated AST, low platelet count and shorter prothrombin time). 2) Single Decision Tree (DT) analysis16 described multiple interactions, and formed 8 patient groups with variable risk of tumour and predicting factors based on SVR achievement. 3) Random Survival Forest (RSF) analysis16 showed that the most important factors predicting HCC were different in SVR and non-SVR patients. In non-SVR patients, no. of platelets, GGT, AFP and albuminemia were identified as most important and in SVR patients, prothrombin time, ALT, age and no. of platelets were identified as predicting factors. Externally validated C-indexes before and after SVR were 0.64 and 0.64 respectively in Fine-Gray, 0.60 and 62 respectively in DT and 0.71 and 0.70 in RSF.

A study done by Kim et al.[19] included 13508 patients from multiple centres with chronic HBV infection and cirrhosis. Patients were grouped into the derivation cohort from 4 hospitals (6,051 patients) and the Korean validation cohort (5,817 patients from fourteen hospitals). 1,640 patients in total, were registered from eleven Western institutions as the Caucasian validation cohort.

Table-2. Summary of reviewed studies.

Ref.	Title	n	Study type	Population	Diagnostic Modality	AI tools	Outcomes
Singal et al2013[15]	Machine Learning Algorithms Outperform Conventional Regression Models in Predicting Development of Hepatocellular Carcinoma	442	Prospective	Cirrhotic patients	Demographics, laboratory parameters	ML	c-index: 0.64-0.71
Loannou et al2020[16]	Assessment of a Deep Learning Model to Predict Hepatocellular Carcinoma in Patients With Hepatitis C Cirrhosis	48151	Retrospective	HCV infection	Demographics, disease characteristic and laboratory parameters	DL	RNN model AUC:0.759
Nam et al.2020[17]	Deep learning model for prediction of hepatocellular carcinoma in patients with HBV-related cirrhosis on antiviral therapy	424	Retrospective	HBV infection	Demographics, disease characteristic and laboratory parameters	DL	c-index: 0.719-0.782
Audureau et al2020[18]	Personalized surveillance for hepatocellular carcinoma in cirrhosis – using machine learning adapted to HCV status	836	Prospective	HCV infection	Demographics, genotype, laboratory parameters	ML	c-index: 0.60-0.71
Kim et al2021[19]	An artificial intelligence model to predict hepatocellular carcinoma risk in Korean and Caucasian patients with chronic hepatitis B	13508	Retrospective	HBV infection	Demographics, disease characteristic and laboratory parameters (PLAN-B)	ML	c-index: 0.79-0.81
Zhang et al2022[20]	Deep Learning for Approaching Hepatocellular Carcinoma Ultrasound Screening Dilemma: Identification AFP Negative Hepatocellular Carcinoma From Focal Liver Lesion Found in High-Risk Patients	407 (209 HCC and 198 FNH)	Retrospective	HBV infectionAFP -ve	B-mode ultrasound	DL	AUC: 0.93
Mochrane et al.2019[21]	Radiomics machine-learning signature for diagnosis of hepatocellular carcinoma in cirrhotic patients with indeterminate liver nodules	178	Retrospective	Cirrhotic patients	Triphasic CT scan	Radiomics	AUC: 0.66-0.70
Yoo et al2023[22]	Prognostic role of computed tomography analysis using deep learning algorithm in patients with chronic hepatitis B viral infection	2169	Retrospective	HBV infection	Contrast enhance CT	DL	Standardized spleen volume predicts HCC. Cut off value: 112.6 mL/m^2

Surveillance was done using ultrasound, alpha-fetoprotein, and CT/MRI in selected cases. The gradient-boosting machine (GBM) algorithm was used to create the prediction model for HCC. [3] models were created, and the superlative model was further tested using a validation test. The final model selected was designated the name PLAN-B which included the presence of cirrhosis, age, no. of platelets, type of antiviral [ETV or TDF], gender, ALT levels, HBV DNA levels, serum levels of albumin and bilirubin, and HBeAg status. The outcomes of this study revealed that the patients of the Korean and derivation cohorts were younger than the Caucasian cohort (mean age, 48.1 and 49.5 years vs. 52.8 years, respectively; p <0.001). The PLAN B model showed a higher discrimination function as compared to the previous models (PAGE-B, modified PAGE-B, REACH-B, and CU-HCC) in Korean (c-index, 0.79 vs. 0.64–0.74; all p <0.05) and Caucasian cohort (c-index, 0.81 vs. 0.57–0.79; all p <0.05 except modified PAGE-B, p = 0.42).

Zhang et al.[20] in their study, included HBV-infected patients with focal liver lesions and formulated a DL model based on B-mode ultrasound to differentiate between histologically proven HCC and FNH. 407 patients

were recruited for the study, and preoperative B-mode ultrasound was done. The slice of lesion included for analysis the following characteristics: 1) lesions with liver parenchyma background and 2) size between 1 and 10cm. Patients were then divided into model and test cohorts. The model cohort included patients with any stage of HCC/FNH irrespective of AFP level, and an internal validation was established arbitrarily at 4:1 ratio for development of model. The test cohort consisted of patients with positive HBV and negative alpha-fetoprotein and were tested for external validation. The DL model designed was named Xception, which was grounded on a conventional neural network and compared with previously designed models, namely Mobile Net, Resnet50, DenseNet121, and InceptionV3, in terms of diagnostic accuracy. 209 and 198 HCC and FNH cases were identified. The model cohort showed AUCs of 100%, 100%, 100%, 100%, and 96.00% for Xception, Mobile Net, Resnet50, DenseNet121, and InceptionV3, respectively. In the test cohort, AUC of 0.94, 0.89, 0.86, 0.84, and 0.78 was detected for Xception, MobileNet, Resnet50, DenseNet121, and InceptionV3, respectively. The Xception model, based on DL, showed an overall AUC of 93.68%.

A study by Mokrane et al.[21] included 178 cirrhotic patients from 27 institutes with histologically-proven HCC. Patients were randomly assigned into two groups; 1) the discovery cohort which consisted of two sets. 106 patients including 85 HCC and 21 non-HCC patients in the training set and calibration set of 36 patients in which 30 had HCC and 6 were non-HCC 2). The external validation cohort which included 36 patients out of which 23 had HCC and rest were non-HCC. Two radiologists independently assessed the LI-RADS features of all patients. Imaging features were pulled out at each phase from segmented liver lesions including: non-contrast (NC), arterial (A), and portovenous (V). Dual phase (delta) features were demarcated from changes between the features of images pulled out from two different phases (A-NC, V-A, V-NC). 3 approaches for assessing this change were tested: (1) standardized subtraction (delta 1), (2) direct subtraction (delta 2), and (3) relative subtraction (delta 3). In the training set, a small set of radiomics features was selected, and 3 controlled ML classification algorithms, K-nearest neighbor (KNN), support vector machine (SVM), and RF, were applied to create candidate models. AUC was computed to assess the models. K-Fold cross-validation was used for validation of the models with k = 20. The DeLong method19 determined the significance of the model association. A two-sample t-test was used for the evaluation of the distribution of features in HCC and non-HCC groups. In the calibration set, the candidate model with the highest AUC was chosen as the ultimate model and designated the radiomics signature. Most patients were male (87.7%). Alcoholic intoxication (60%) was the most common cause of cirrhosis. No substantial dissimilarity between HCC and non-HCC nodules features including size or density was identified. LR-4 class was reported most (56.2% in all cases) in the two groups. In the discovery cohort, the preliminary model was designated as the superlative prediction model and used the dual-phase change analysis between arterial and portal venous phases (Delta2V-A: type 2 direct subtraction of delta-phase features, and KNN algorithm and had an AUC of 0.81 (95%CI 0.65, 0.91; sensitivity = 0.81 and specificity = 0.72). The calibration of the preliminary model using calibration set achieved an AUC of 0.74. In the validation cohort, the classifier performance of Delta VA_DWT1_LL_Variance-2D had an AUC of 0.66 (95%CI 0.64–0.84). The sensitivity of the model was 0.70, while the specificity was 0.54. Most false positives were cholangiocarcinomas (13.6%). A simplified radiomics model was created, which identified high-risk patients for HCC.

2169 patients with chronic HBV were retrospectively studied by Yoo et al.[22] CT scans of all patients were analysed using convolutional neural networks, and parameters such as liver and spleen volume, fat composition, and skeletal muscle indices were evaluated to identify prognostic factors pertinent to HBV infection. The principal outcome was overall survival (OS). Secondary outcomes included the development of HCC, decompensation, and metabolic outcomes such as diabetes mellitus. Diagnosis of HCC was made either radiologically or histopathological confirmation using trucut biopsy or surgical resection. HCC was identified in 5.7% patients. The multivariate analysis revealed concluded that HCC was significantly associated with standardized spleen volume (P=0.025) as well as with age, gender, serum albumin and no. of platelets. The cut-off value to predict HCC for standardized spleen volume was 112.6 mL/m2. The incidence of HCC development in patients with standardized spleen volume more than 112.6 was 0.8%, 5.1%, and 9.9% at 1, 5, and 10 years, respectively.

Discussion

AI has recently gained immense prominence in clinical diagnosis and prognosis of cirrhosis and HCC owing to machine-based models which may help in reducing the expert-based evaluation and improve early detection of HCC. Previous studies have reported models for predicting HCC in patients with hepatic diseases using different scoring systems, radiological values, and

biochemical parameters, which are then incorporated into AI designs. Though much work is being done, a standardized approach using AI is yet to be established. Most of the data in this regard is scattered, and repetitive studies have been conducted using similar parameters.

We systematically reviewed articles that focused on the early detection of HCC in cirrhotic patients and summarized studies that were based on models evaluating demographical, clinical and radiological parameters related to HCC. For each article, we described the population selected, the modality of AI that was used to formulate a predicting model and explicit results obtained from those models. We further tabulated the key findings of each article for better understanding, which may prove to be helpful in further research. In our systematic review, we thoroughly described 8 articles, 5 of which were based on demographic and lab values, and 3 were based on radiological findings. Most of the studies compared their results with previously designed predictive models. The comparison showed a significant increase in AUC in newer models.

Studies done by Singal, Loannou, Nam and Audureau et al.[15-18] described various variables for prediction. Which included sex, age, race, the genotype of HCV or HBV, biochemical tests including LFTs, electrolytes, glucose, renal function tests, blood profile, coagulation profile and SVR. This systematic review demonstrates that baseline investigations and patient characteristics may help in clinically diagnosing HCC at a very early stage using AI, which may be an economical and efficient way to improve the prognosis of patients with cirrhosis.

Further described studies have shown the use of radiology in detection of HCC at a very early stage and also characterize it from other FLLs. The AI model described by Zhang et al.[18] distinguished HCC by FNH by using B-mode ultrasound regardless of the a-fetoprotein values, which is always a diagnostic challenge. Similarly, Mokrane's model provided a simple radiomics-based model using triphasic CT scans to predict HCC. Further studies are needed to formulate guidelines or predictive scores and incorporate them into surveillance protocols for all cirrhotic patients. This may prove beneficial for decreasing the rising incidence of HCC in cirrhotic patients.

This is a systematic analysis including all types of modalities used to formulate AI-based predictive models for HCC; therefore, a standardized quality/bias assessment tool for the studies could not be developed due to vast spectra of the included studies. Furthermore, meta-analysis couldn't be performed owing to the diversity of one article from the other.

Conclusion

Our study compiles and describes previous work done for early detection of HCC using AI. All of the studies reviewed in this article report promising results in early detection of HCC using AI and has shown improved results when compared to previously designed AI algorithms. Our systematic approach may prove beneficial for the formulation of a standardized methodology for detection of HCC and help in developing a more robust and accurate AI tool for early detection of HCC in cirrhosis.

Disclaimer: None.

Conflict of Interest: None.

Funding Disclosure: None.

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