



Diagnosis Hepatitis B Using Machine and Deep Learning: Survey

Gehad Ahmed Soltan Abd-Elaleem^{1,2(✉)}, Fahad Elsheref^{1,2}, Rabab Maher³,
Ahmed Elsayed¹, Doaa S. Elzanfaly¹, and Ahmed Sharaf Eldin^{1,4}

¹ Faculty of Computers and Artificial Intelligence, Helwan University, Helwan, Egypt
eng.gedadahmed2013@yahoo.com

² Faculty of Computers and Artificial Intelligence, Beni Suef University, Beni Suef, Egypt

³ Student's Hospital, Fellow of Tropical Medicine, Cairo University, Cairo, Egypt

⁴ Faculty of Computers and Artificial Intelligence, Sinai University, Sinai, Egypt

Abstract. Machine Learning (ML) improves healthcare systems by helping to reach a proper diagnosis and reducing the diagnosis faults such as severe illness, cancer, inflammatory diseases, other diseases, and pathology. Many studies found that ML-based systems can be better than humans in more critical tasks. The study of liver disease diagnosis is very important, especially the diagnosis of hepatic virus diseases, which are among the most problems facing the liver, particularly Hepatitis B, as this virus is ranked by the World Health Organization (WHO) as the second most dangerous carcinogen in the world, after tobacco. Therefore, it is crucial to identify this harmful virus as soon as possible. As a result, the field of machine learning has focused on the early detection of Liver Hepatitis, particularly virus B. In this paper, we surveyed machine and deep-learning liver disease diagnosis, particularly hepatitis B, and we demonstrated the findings of previous experimental studies and results, as well as the limitations and future work that is suggested in this area.

Keywords: Artificial Intelligence · Hepatitis B · Liver Diseases · Machine Learning · Deep Learning · DL · AI · HBV · HCV · HCC · ML

1 Introduction

The new technology directed it's towards to medical field that is called recently Biomedical fields, the field of artificial intelligence is used widely today in medical diagnosis In all medical specialties; especially the field of machine learning; which reduced the mortality rate and the treatments waste time by more accuracy of classification in diagnosis, patients may need for reviewing consultation of specialists, the developed technology introduced automated detection and diagnosis systems of diseases or illnesses to facilitate the diagnosis for specialists. Humans are prone to error, so it is not surprising that a patient may have over-diagnosis or under-diagnosis. If such problems the patient may receive unnecessary treatment which will be impacting the individual's health and economy.

Machine learning is used in the diagnosis of Hepatitis diseases using various algorithms for the learning machine such as neural networks and Naive Bayes that solved many problems of diagnosis [1].

Among the human body's largest organs is the liver, Therefore, the study in diagnosing diseases of this organ has great importance. Inflammation of the liver which called Hepatitis [2, 3], and [4]. Hepatitis is the most widespread and virulent of liver diseases, as it affects negatively the liver and makes more problems after a long time of inflammation that may appear later after the liver has been damaged especially in viral infections such as viruses B and C.

Epidemiology. In 2019, the World Organization of Health (WHO) reported annual chronic diagnoses of hepatitis B of around 300 million and nearly 820 thousand deaths, a primary cause of this death is cirrhosis, followed by hepatocellular carcinoma [5].

Hepatitis B infection is most common in the African Region of the World Health Organization and the Western Pacific Region, where 81 million and 116 million people, respectively, are chronically infected. There are 60 million infected people in the WHO Eastern Mediterranean Region, 18 million in the WHO South-East Asia Region, 14 million in the WHO European Region, and 5 million in the WHO Americas Region [5].

Hepatitis B is a chronic infection that can be fatal due to serious liver damage [6, 7]. As a result, trustworthy techniques for hepatitis B virus infection diagnosis were developed [8].

In recent years, almost all researchers have used a variety of deep and machine learning techniques, including CNN, RF, Neural Networks, SVM, KNN, Decision Trees, etc., to detect liver diseases.

For all of these reasons, we focused on the work that had already been done in this area. As a result, this paper introduced the diagnosis using machine learning and deep learning Studies, discussions, and limitations. The sections of this paper are organized as follows: Sect. 2 presented the Background of Hepatitis B, Machine and Deep Learning, Sect. 3 introduced the explanation of Machine and Deep Learning in Disease Diagnosis, Sect. 4 is a survey of the machine and deep learning methodologies, algorithms, and techniques for diagnosing liver disease, particularly hepatitis B, Sect. 5 introduced the Discussion and Limitations of Deep and Machine Learning for Diagnosing Liver Disease, and Sect. 6 concluded the paper.

2 Background

2.1 Hepatitis B Definition and Structure

The DNA virus from the Family: Hepadnaviridae Orthohepadna virus, a type of virus that can cause hepatitis B, infects liver cells, and then causes hepatocellular necrosis and inflammation in humans. Figure 1 shows the structure of the hepatitis B virus. According to Fig. 1, there are four layers to hepatitis B. They are as follows.

- An external surface envelope: Its structure consists of a 27 nm core, and an icosahedral nucleocapsid (4 nm).

- The surface layer (or envelope): known as the “surface antigen” or “HBsAg,” is primarily made up of lipids and proteins.
- The basic particles: inner protein shell, or “HBcAg,” contains viral DNA and enzymes used in HBV replication as well as (“DNA polymerase”).
- The HBV nucleocapsid: is closely related to the antigenic major factor known as HBeAg (hepatitis B envelope antigen). Additionally, it appears as a soluble protein in serum.

2.2 Hepatitis B (CHB) Stages

Hepatitis B has consequence phases, which are summarized in Table 1. The following phases are sorted according to the hepatitis case or the sequenced phases of treatment [9], and [10].

Phase 1: Immune Tolerant Phase

‘Immune tolerance phase’ HBV DNA, HBeAg, and HBsAg are all produced during active HBV replication and are detectable in serum. The immune response is confined to the formation of anti-HBc antibodies (first IgM, then IgG), but this does not function to neutralize infection [9], and [10].

Phase 2: HBeAg-Positive CHB (Immune Reactive Phase)

Serum ALT levels are elevated (greater levels indicate a more aggressive reaction and hence more hepatocyte destruction), and chronic active hepatitis is apparent on hepatic ultrasound (USS) or biopsy [9], and [10].

Phase 3: Low Replicative Phase

HBV replication is minimal in patients in the low replicative phase, and HBV DNA levels are low or undetectable. Although HBeAg is negative, HBsAg remains positive [9], and [10].

Phase 4: HBeAg-Negative CHB

HBeAg-negative CHB is caused by a form of the HBV virus that is unable to generate HBeAg while still actively replicating. HBeAg-negative CHB can arise after periods of low replicative or HBeAg-positive CHB and is usually at a later stage in disease development [9], and [10].

Phase 5: HBsAg-Negative Phase

The ‘HBsAg-negative phase’ refers to the progression to the elimination of both HBsAg and HBeAg. Although HBV viral replication may continue, it is unlikely to be detected in serum. Once in the HBsAg-negative phase, there is a better result and a lower chance of liver problems, while HBV may reactivate in immunocompromised persons and remains a concern for organ donation [9], and [10].

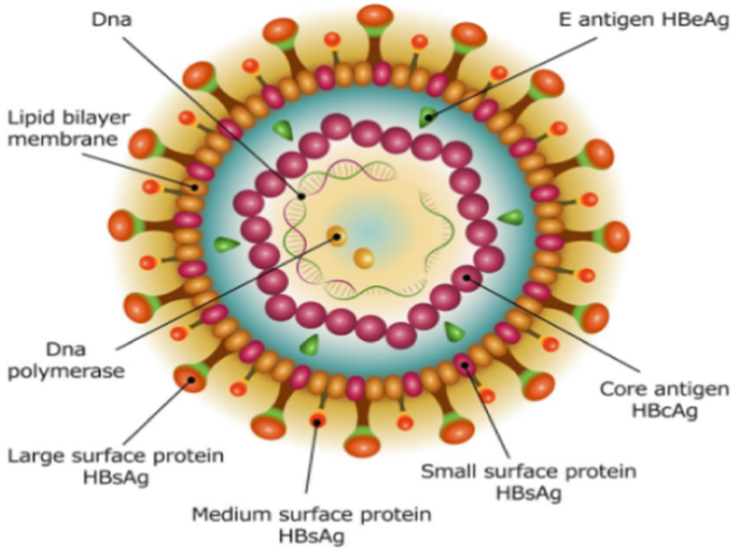


Fig. 1. The structure of Hepatitis B [4]

Table 1. The phases of Hepatitis B

	Acute HBV	Chronic HBV	Cleared HBV	Vaccination
HBcAb IgM	+	-	-	-
HBcAb IgG	+	+	+	-
HBsAg	+	+	-	-
Anti - HBs	-	-	+	+
HBeAg	+	-/+	-	-
Anti - HBe	-	-/+	-/+	-
HBV DNA	High/Low	Low/High	-	-

Stage	ALT	HBeAg	HBV DNA
Immune tolerant	Normal	Positive	High
Immune active	High	Positive/Negative	Low
Immune surveillance	Normal/Slightly raised	Mostly Negative	Low
Immune escape	High	Negative	High

2.3 Machine Learning

We have benefited from machine learning in several ways. Self-driving cars, Google Assistant, weather forecasting, image recognition, language translation, YouTube recommendation, and many other technologies have all benefited from it.

Supervised, unsupervised, and reinforcement learning are the three types of machine learning techniques; the following machine learning techniques and methods are summarized as follows: Linear Regression Methods, KNN Methods, Decision Tree Methods, K-Means Methods, Naive Classifier Methods, and Logistic regression analysis are used for regression, SVM (Support Vector Machine) techniques, Random Forest methods,

Dimensionality Reduction Algorithms, and Gradient boosting algorithms (XG Boost, GBM, Light GBM, and Cat Boost).

The most commonly used machine learning algorithms and approaches for identifying liver disease are SVM, K-Nearest Neighbor, Naive Bayes, and Decision Tree. Scientists and researchers strive to enhance machine learning techniques and procedures to achieve the highest level of categorization accuracy possible. The following is a definition of each method.

- Naive Bayes: This learning algorithm relies on the Bayes theorem and makes strong (naive) assumptions about independence. The metrics derived from training data essentially determine whether an object is related to a specific class.
- SVM (Support Vector Machine): This classifier technique assumes that there is a distinct difference between the data samples. Finding the best hyperplane to maximize the objective's class margin.
- K-Nearest Neighbor: This technique is used to resolve classification and regression issues. It measures all potential probabilities for data instances and then categorizes new ones using metrics for similarity as distance functions.
- Decision Tree: Used to create a training model that may be applied to learning straightforward decision rules produced from ad hoc data to forecast a trustworthy variable class. Trees are mainly composed of arcs and leaves. Each leaf represents a classification class, and each arc displays a feature taken from training data.

Additionally, machine learning finds that it is very beneficial in the fields of biology, health informatics, and medical sciences. Machine learning algorithms are now being taught to recognize cancer simply by examining an image. Such experiments are no longer just hypothetical; they are now a very real possibility. ML may be a good tool for predicting HCC recurrence. To provide a useful tool for the clinical care of HCC patients [11]. Also, ML algorithms seek to describe the strengths and limitations of ML, as well as its potential utility in prognostic prediction, following various HCC treatment regimens [12].

2.4 Deep Learning

Deep Learning (DL): is a machine learning subcategory in which an artificial neural network mimics the brain's ideas to process data, identify patterns, and reach conclusions. The core of the artificial neural network is interconnecting components called perceptron which is a simplified model of a functioning neuron. It has a way for input (of data) and output (of information). There are at least two input layers of a perceptron. In between these two layers, there can be many more layers sandwiched, these sandwiched hidden layers make up a 'deep' neural network. Deep learning is very good at finding a pattern and making predictions from analyzing huge amounts of data which can be incomprehensible to humans. The most crucial component of deep learning, which allows techniques and models to learn from training data and teach themselves, is the convolutional neural network. The procedures and algorithms outlined below are deep learning approaches.

- 1) Neural Network Convolutional
- 2) Long-Term Memory Network
- 3) RNN (Recurrent Neural Network)
- 4) Adversarial Generative Network
- 5) Network with Radial Basis Functions
- 6) Perceptron Multilayer
- 7) Self-Organization Model
- 8) Deep Belief Networks
- 9) Restricted Boltzmann Machine
- 10) Automatic encoders

3 Disease Diagnosis Using Deep Learning and Machine Learning

The medical sector is extremely complicated, particularly when identifying different diseases because many diseases may have symptoms that are similar and might result in an inaccurate diagnosis, and then fault Prescription is prescribed by doctors and may cause death for patients, Therefore, accuracy and clarity in diagnosis are crucial. The machine learning algorithms were based on the accuracy and precision in categorizing things and grouping comparable items in a proper method, as well as scientific equations generated by the machine learning algorithms.

To help clinicians and doctors overcome the constraints, and make wise, and accurate decisions in disease diagnosis, Methodologies of some disease diagnoses using machine learning (ML) algorithms have been recently reviewed [13]. Among these diseases is Liver disease which is the most important in diagnosis because of hidden almost symptoms and the lately almost symptoms that may lead to death. The examples listed below demonstrate how deep learning and machine learning have been applied to liver disease diagnosis and treatment.

3.1 Applying Machine Learning to Identify Liver Problems

In Liver Fibrosis Evaluation and Inflammation, a proprietary ML algorithm developed using a dataset of 2862 different biomarker clinical assessments was used to examine three major stages of liver lesions to detect fatty liver [14], even though other studies that used ML ideas for the detection of liver disease have been presented in a variety of ways [15].

Using Machine Learning in Hepatocellular Cancer

The most prevalent form of chronic liver disease worldwide is liver cirrhosis. The capacity to predict the start of liver cirrhosis disease is essential for effective treatment and the avoidance of grave health consequences. As a consequence, the researchers used machine learning to construct a prediction model to predict liver cirrhosis [16]. Although new machine-learning algorithms yielded accurate risk ratings for hepatocellular cancer in individuals with chronic viral hepatitis (HCC). The HCC ridge score was consistently more accurate than earlier HCC risk assessments. To develop efficient cancer monitoring strategies and reduce cancer-related mortality, new models might be used for electronic medical health systems [17]. Although a very accurate HCC detection model has been

built using individualized biological pathways analyses and machine learning methods. This model's outstanding interpretable performance and transferability make it ideal for customized medicine, assisting physicians in the identification of HCC patients. [18, 19].

3.2 Deep Learning for Liver Disease Prediction

Liver tumors have been divided into seven types using deep learning. The CNN approach performs effectively in separating benign from malignant liver tumors, unenhanced images are utilized (AUC, 0.95; 95% CI, 0.92–0.97 vs. 0.95; 0.92–0.98, $P = 0.66$). New CNN Combining clinical data with unassuming images significantly enhanced the efficacy of diagnosing cancers such as hepatocellular carcinoma [20]. Deep learning algorithms are also being used to forecast the long-term mortality serious risks of liver transplant recipients [21], and finally, a framework of deep learning is demonstrated for automatically predicting liver fibrosis, where the information has been provided by multiple ultrasound images for more accuracy [22].

4 Diagnosis Hepatitis B Using Machine and Deep Learning: Survey

The diagnosis of hepatitis B using machine and deep learning was presented in Sects. 4.1 and 4.2 respectively, to identify liver disorders, particularly hepatitis B, which have been sequenced from the oldest to the most recent order, the two following sections of 4.1, 4.2 summarized the previous studies that have been introduced in this area, and also presented in Table 2 and Table 3 respectively, where Table 2 summarizes studies in machine learning algorithms for hepatitis B diagnosis and Table 3 summarizes studies in deep learning algorithms for hepatitis B diagnosis, each table one and two contain authors and year of the study, techniques, and algorithms used, and finally results of each algorithm.

Table 2. Machine Learning Algorithms for Hepatitis

	Algorithm	Author	Year	Main Enhancements
NN Algorithms	MLP, RBF, CSFNN, C4.5, NB, TAN, BNND, BNNF	OZYILMAZ, L.,	2003	5. Fold cross-validation method outcomes are accuracy (81,3750 (average) 85, 90, 83,60 (max) 87,830 (max) 90,10 (max) 90 (max) 88,760 (max)) Respectively

(continued)

Table 2. (continued)

	Algorithm	Author	Year	Main Enhancements
	BPNN, RBFNN, PNN, GRNN	Panchal, D.,	2011	HBV is Positive IF (anti-VHD = Negative) AND (AgHBe = positive) AND (AgHBs = Positive)
	(MLNN)	Çetin, O.	2015	Classification accuracies for activation were 91.90% to 93.80% through 10-fold cross-validation
	ANFIS	Abtahi, S.,	2020	<ul style="list-style-type: none"> • The rapid, highly accurate estimation capability of the ANFIS observer • After each therapy session, the high ability of ANFIS can observe and predict the trend of safe and inflamed cells • The error rate is negligible. About 0.1% of errors are allowed at their maximum
DT and GB Algorithms	C4.5 Decision Tree	Shankarsowmien, V.,	2016	determining the abnormalities of the patient which resulted in 85.81% accuracy
	(J48), (LMT), (Random Forest), (Random Tree), (REP Tree), (Decision Stump) (Hoeffding Tree)	Nahar, N.,	2018	Classification Accuracy (65.69, 69.47, 69.30, 66.55, 66.13, 70.67, 69.75) Respectively

(continued)

Table 2. (continued)

	Algorithm	Author	Year	Main Enhancements
	GB-based	Wei, R.,	2018	In HBV and HCV cohorts. Consistent improvements compared to FIB-4
	(XG Boost), (RF), (DCT), And (LR))	Tian, X.,	2019	AUC (95% CI) [0.891 (0.889, 0.895), 0.829 (0.824, 0.834), 0.619 (0.614, 0.624), 0.680 (0.677, 0.683)] respectively
	SMOTE (XG Boost, RF, DT), XG Boost, RF, DT And (LR))	Wang, Y.,	2019	Accuracy (0.702, 0.681, 660, 0.711, 0.634, 0.719, 668) respectively
	Enhanced RF	Chen, S.,	2021	(AUC, 0.9660; 95% confidence interval, 0.9220–0.9890) with α -fetoprotein (0.7130; .6320–.7840)
	CART	Jameel, A.,	2022	CART with a sensitivity of 88%, an accuracy of 80%, and a specificity of 52%
	(GBM) algorithm	Kim, H.	2022	During an 8-year follow-up, the minimal-risk group (11.2% of the Korean cohort and 8.8% of the Caucasian cohort) had a risk of HCC of less than 0.5%
Support Vector Machine	A confusion matrix	Alamsyah, A.,	2021	The prediction accuracy for hepatitis was 93.55%

(continued)

Table 2. (continued)

Algorithm	Author	Year	Main Enhancements
SHAP	Obaido, G.,	2022	92% accuracy, 91% specificity, and 93% sensitivity, respectively. Meanwhile, both the decision tree and the SVM achieved 73% balanced accuracy

Table 3. Deep Learning Algorithms for Hepatitis

Algorithm	Author	Year	Main Enhancements
(SOM)	Uttreshwar, Gh. SH.,	2008	HBV is Positive If(AgHBs = Positive) and (anti-VHC = Negative) and (anti-VHD = Negative) and (AgHBe = Positive)
(DLRE)	Wang, K.,	2018	DLRE AUCs are 0.970 of F4 (95% CI 0.940 - 0.990), 0.980 of \geq F3 (95% CI 0.960 - 1.000), and 0.850 (95% CI 0.810 - 0.890) of \geq F2, which outperformed all other methods except 2D-SWE in \geq F2
Pre-Trained Alex Net-CNN	Yu, Y.,	2018	Accurately and automatically score the stages of liver cirrhosis
(DLS) and LR	Choi, KJ.,	2018	AUROC For (F2–4), (F3–4), and (F4) are (0.960, 0.970, and 0.950), respectively, and an Accuracy of 79.40% (707 of 891)
DCNN Model	Yasaka K,	2018	The FDL score was related to the stage of fibrosis (correlation coefficient is 0.630; P, .001). The ROC curve of (F4, F3, and F2) are (0.840, 0.840, and 0.850), respectively

(continued)

Table 3. (continued)

Algorithm	Author	Year	Main Enhancements
SOM, ANFIS, DT	Nilashi, M.,	2019	Accuracy are K-NN = 71.410%, SVM = 81.170%, NN = 78.310%, ANFIS = 79.670%, NIPALS-SOM-ANFIS = 93.060%, PCA-LSSVM = 95.00%, PCA-AIRS = 94.120%, LFDA SVM = 96.770%, RES-ELM = 100%
(MLFFDNN)	Murty, S.,	2019	71.0%, 97%, 92%, 75.0%, 83%, and 98% for Nave Bayes, C4.5, AD Tree, SVM, RBF, and MLFFDNN, respectively
TL-ResNet101 model	Ali, S.,	2020	Accuracy, sensitivity, and AUC of 99.70%, 100%, and 98.70%, respectively, and compared with PCA-SVM and PCA-LDA and showed an increase in accuracy of more than 7.0%
HBSRS with DL Model	Guo, Z.,	2020	Accuracy GRU-MCNN SVM LDA KNN MLP CNN, 0.9680 ± 0.0060 0.9040 ± 0.0300 0.8150 ± 0.0940 0.7810 ± 0.0320 0.9350 ± 0.0070 0.9460 ± 0.0020 Precision is 0.9600 ± 0.0130 0.9420 ± 0.0220 0.8090 ± 0.1260 0.8710 ± 0.0310 0.9400 ± 0.0140 0.9400 ± 0.0090 Sensitivity is 0.9800 ± 0.0080 0.8390 ± 0.0630 0.8240 ± 0.0830 0.6460 ± 0.0750 0.9400 ± 0.0070 0.9590 ± 0.0030 Specificity is 0.9550 ± 0.0110 0.9610 ± 0.0380 0.8130 ± 0.0750 0.9250 ± 0.0540 0.9300 ± 0.0230 0.9310 ± 0.0070 AUC is 0.9500 ± 0.0100 0.9180 ± 0.0410 0.8090 ± 0.0530 0.8040 ± 0.0210 0.9250 ± 0.0130 0.9190 ± 0.0140

(continued)

Table 3. (continued)

Algorithm	Author	Year	Main Enhancements
Deep NN	Nam, J. Y.,	2020	cohort (PAGE-B [c-index 0.5700; 95% CI 0.5140–0.6260], CU-HCC [c-index 0.5480; 95% CI 0.4910–0.6040], HCC-RESCUE [c-index 0.5770; 95% CI 0.520–0.6320], ADDRESS-HCC [c-index 0.5510; 95% CI 0.4950–0.6070
CNN	Wu, C.,	2021	The deep HBV With an AUROC of 0.9430 and an AUPR of 0.9310 after adding genomic features, the model significantly improved
METAVIR method	Zhu, Z.,	2021	the accuracy, sensitivity, specificity, precision, F1, MCC, and FMI were $88.13\% \pm 1.47\%$, $81.45\% \pm 3.69\%$, $91.12\% \pm 1.72\%$, $80.49\% \pm 2.94\%$, $80.90\% \pm 2.39\%$, $72.36\% \pm 3.39\%$, and $80.94\% \pm 2.37\%$, respectively
Combined Mueller matrix	Pham, T.,	2022	As a consequence, five separate deep learning models—Xception, VGG16, VGG19, ResNet 50, and ResNet 150—take M22 and M33 as their inputs. The best classification accuracy (94.5%) is demonstrated to be achieved using the VGG19 model with element M22 as the input

4.1 Hepatitis B Using Machine Learning Algorithms

The following models and techniques of machine learning algorithms have been implemented for diagnosing hepatitis B, sorted from the oldest to the most recent, and grouped according to the unified machine learning techniques and summarized in Table 2.

Neural Network

In [23] A hybrid network has been applied successfully for the detection of hepatitis, it was introduced with the Results after standard feed-forward, and hybrid networks were both tested and proved that the hybrid network is more advanced than the feed-forward network (OZYILMAZ, L., 2003) [23]. Also in [24] The Hepatitis B virus has been

detected using the generalized neural network, which provided more effective results for determining whether the patient has Hepatitis B or not (Panchal, D., October 2011) [24].

Another form of NN algorithms is the approximations of the sigmoid function that have been applied as an activation function, This technique of hepatitis disease classification introduced an accuracy from 91.90% to 93.80% via ten-cross-validation using 10 folds that consist of a neural network with multiple layers and sigmoid activation functions, which are used to determine hepatitis disease (Çetin, O., 2015) [25].

The Adaptive Neuro Fuzzy Integrated System (ANFIS) approach is implemented in [26] to generate a controller for the drug's dosage that is based on the number of viruses combined; the ANFIS system's superiority is reducing the required number of input variables to quantify the proper dosage; The ANFIS performs well in tracking the desired reducing virus replication (Abtahi, S., 2020) [26].

Decision Tree

The decision tree method is used for liver disease prediction where it constructs all possibilities of the disease's liver. The tree was built using the C4.5 algorithm, which used 19 features to diagnose liver diseases. These 19 attributes determined the abnormal results of the patient with 85.8% accuracy, Also To identify the early stages of liver disease, the author used classification tree algorithms (Shankar sowmien, V., Jun-Jul 2016) [27].

Different outcomes are produced via accuracy, precision, mean absolute error, kappa statistics, recall, and runtime; these study's findings, which evaluated and contrasted the performance of the methodologies utilized, showed that Decision Stump performed better than other algorithms (Nahar, N., Mar 2018) [28].

The author Used a random forest (RF) model, which takes into account (10 features) in [22], and illustrated the highest result for prediction accuracy both Cross-validation and independent validation resulted in accuracy, and AUC is 0.90, and 0.96, respectively, regardless of HBV genotypes or sequential depth. Moreover, HCC risk scores obtained from the RF model (confidence interval, 0.922–0.989 AUC, 0.96; 95%) performed better results in fetoprotein (0.713; 0.632–0.784) for categorizing HCC and CHB patients (Chen, S., June 2021) [29].

The prognosis of hepatitis disease classification is introduced by using the J48 decision tree algorithm. Where J48 predicted effective results with the highest classification rate and gives a better understanding regarding performance parameters as compared to CART with a sensitivity of 88%, an accuracy of 80%, and a specificity of 52% that will aid physicians (Jameel, A., 2022) [30].

Gradient Boosting

The study in [31] aimed to compare logistic regression (LR), decision tree (DCT), random forest (RF), and extreme gradient boosting (XGBoost), which are four well-known machine learning algorithms by regressing (HBsAg seroclearance), which is a substantial achievement for disease outcome of liver diseases during CHB treatment. The findings show that machine learning algorithms, specifically XGBoost, can predict exactly (HBsAg seroclearance) (Tian, X., Jun 2019) [31].

The author used machine learning for HBV and HCV-related hepatic fibrosis detection, he used gradient boosting (GB) to outperform other methods in addition to FIB-4 scores in the discovery data. The GB is based on the same parameters as FIB-4, and the GB prediction system produced consistent enhancements compared to FIB-4 in HCV and HBV cohorts with required values in different etiological groups (Wei, R., Sep 2018) [32].

Another study used Gradient Boosting to improve and validate models for recognizing communities at great risk that must be examined for hepatitis B surface antigen (HBsAg). The data were preprocessed using the borderline-synthetic minority oversampling technique (SMOTE), and four predictive models, including the extreme gradient boosting (X-GBoost), random forest (RF), decision tree (DT), and logistic regression (LR) algorithms, were developed in [33] (Wang, Y., December 2019)[33].

The GBM has the best predictive power for HCC risk in Korean and Caucasian patients with CHB and treated with entecavir or tenofovir. This model was used to develop and validate an artificial intelligence-based HCC risk prediction (Kim, H., February 2022) [34].

Support Vector Machine

A confusion matrix is used to assess classification performance. The prediction accuracy for hepatitis was 93.55%. This result outperforms the results of support vector machine classification without the use of principal component analysis (Alamsyah, A., 2021) [35].

The predictions of machine learning models employed for hepatitis B diagnosis were explained and shown using Shapley Additive exPlanations (SHAP), a game-based theoretical method. The SHAP values revealed that bilirubin is the most important factor causing a greater death rate is bilirubin. As a result, elderly individuals with high bilirubin levels have a higher risk of passing away. The findings of this study can help medical professionals by providing an explanation of how machine learning models for health-related issues work (Obaido, G., 2022) [36].

4.2 Hepatitis B Using Deep Learning Algorithms

A self-organization map (SOM) is used to predict HBV accuracy; it's an efficacious tool for predicting normal hepatitis B based on lab results because it generates quicker and more accurate hepatitis prediction. (Uttreshwar, Gh. SH., 2008) [37].

The author improved the prognosis of chronic hepatitis B using Radiomics of shear wave elastography, by developing Deep Learn Radiomics elastography (DLRE), which outperforms two-dimensional shear wave elastography (2D-SWE) in terms of overall advancements in the prediction of the different stages of hepatic fibrosis (Wang, K., May 2018) [38].

Another deep learning study has been enhanced, that the author used deep learning for scoring liver fibrosis stages automatically, He evaluated several deep learning-based algorithms and machine learning algorithms and demonstrated that the pre-trained CNN's Alex Net-CNN by makes use of deep learning-based algorithms could automatically score stages of liver fibrosis with better accuracy comparable to non-linear MLR,

Conventional ANN (CNN), feature ranking-based RF algorithms, and linear SVM. (Yu, Y., Oct 2018) [39].

Another form of the deep learning algorithm is regression analysis which is implemented by using CT techniques and patient characteristics on the DLS staging accuracy in the liver, the author's objective was to validate and enhance a deep learning system (DLS) for trying to stage Fibrosis of the liver (Choi, KJ., Dec 2018) [40].

DCNN model has been used for more efficient results and differentiates between the stages of liver fibrosis and the fibrosis score [FDL score]; which was produced using the technique of deep learning (Yasaka K, April 2018) [41].

The author proposed employing ensemble learning to create an advanced, accurate way of diagnosing hepatitis, he used Iterative Non-linear using Partial Least Squares to reduce data dimensionality, Clustering using the Self-Organizing Map technique, and Ensembles of Neuro-Fuzzy Inference Systems to predict the diagnosis of hepatitis disease; decision tree algorithms were also applied to select the most important attributes of the experimental input data. He implemented the technique to the test on a real dataset and compared the results to the most recent study results of previous research. The method of [34] outperforms ANFIS, K-Nearest Neighbors (KNN), the Neural Network (NN), and the Support Vector Machine (SVM) (Nilashi, M., Feb 2019) [42].

A Deep Neural Network with Multiple Layers of Feed Forward (MLFFDNN) has been tuned to make more accurate prognostications concerning liver disease by trying to fit the appropriate number of hidden nodes and layers, and a function for dropping out after hiding each layer to remove overfitting, learning rate loss functions, activation functions, and bias should all be reduced to a minimum rate. (Murty, S., July 2019) [43].

A novel diagnostic technique for HBV diagnosis has been introduced by using the concept of transfer learning and deep neural networks with Images of Raman spectroscopy. The suggested technique was generated by implementing pre-trained neural networks with convolutions ResNet101 was trained on an actual HBV-infected blood plasma samples dataset that used transfer learning, and TL-ResNet101 was evaluated and achieved results with (100%, 99.70%, 98.70%, and 99.25%) classification sensitivity, accuracy, AUC, and specificity respectively were obtained. The recommended TL-ResNet101 method exceeded conventional methods like PCA-LDA and PCA-SVM with more than a 7% improvement in accuracy. The developed TL-ResNet101 model has high performance that has the potential to be used for HBV diagnosis (Ali, S., 2020) [44].

A newer method for detecting the Infection of the hepatitis B virus using human blood serum Raman spectroscopy in conjunction with a model of deep learning has been introduced, the principal component method was used to decrease the dimensionality of the data. The features of multiple scales were then prepared and fused using a multiscale fusion convolution operation. Time series features were extracted using a gated recurrent unit network and then the output was classified using a soft-max (Guo, Z., March 2020) [45].

The author developed deep learning architecture and introduced the SSAE algorithm for the diagnosis of three focal liver diseases in addition to the normal liver. The Unsupervised SSAE architecture can obtain high-level image features of input pixels. These characteristics enable the classifier to efficiently diagnose lesions from patient images.

In classification performance, the experimental findings showed that the softmax and SSAE classifier outperformed the KNN, Naive Bayes, and multi-SVM. (Hassan, T.M., Jan 2017) [46].

In [47], a new deep learning model for predicting HCC risk was presented; in patients with HBV- cirrhosis taking effective anti-viral, this model performed noticeably better than earlier models at predicting the risk of HCC [47] (Nam, J. Y., 2020).

The author introduced Deep HBV which predicts Sites for HBV integration that were discovered by automatically finding local genomic attributes. The Deep HBV model's efficiency improved after integrating genomic capabilities, the results of this study are 0.9430 for AUROC and 0.9310 for AUPR. Furthermore, the author used a convolution neural network to reinforce the transcription factors binding sites of proteins [48] (Wu, C., 2021).

For the automatic classification of liver fibrosis in chronic hepatitis B, the author proposed a 5-layer deep convolution neural network structure. There were three convolution layers and two fully connected layers in the 5-layer deep convolution neural network structure, and each convolution layer was connected with a pooling layer. 123 ADC images with Magnetic Resonance were collected, and it achieved more effective results (Zhu, Z., 2021) [49].

The detection of the hepatitis B (HB) virus using a combined Mueller matrix imaging technique and deep learning method, the Mueller matrix imaging polarimetry is applied to obtain 4×4 Mueller matrix images of 138 HBsAg-containing (positive) serum samples and 136 HBsAg-free (negative) serum samples. The kernel estimation density results show that, of the 16 Mueller matrix elements, elements M22 and M33 provide the best discriminatory power between the positive and negative samples (Pham, T., July 2022) [50].

The authors correctly highlight the accuracy of DL models for predicting severe fibrosis in CHB patients when compared to existing standards. We challenge them to assist us to take this knowledge to the next level. How can such models assist enhance patient care, how will they be used in real-time, and how will they help categorize patients at the bedside to avoid disease progression and change the natural history of CHB? (Verma, N., 2022) [51].

5 Discussion and Limitations (Future Work)

Hopefully, the ANFIS system will be able to work with scatter information (drug dosage) to only be used in diagnostic and therapeutic therapy as a treatment, assisting in how many drugs patients should be injected every day or every week. Doctors can also count the number of normal and inflamed cells after each drug injection. Non-incremental learning was also used to learn classification techniques in the ANFIS system. Furthermore, the developed ANFIS system does not support incremental learning and requires precomputing all of the training data to build the prediction models. It is proposed that the ANFIS system be designed to incrementally update the trained models as new data becomes available, making memory more efficient and accurate in memory requirements.

Hepatitis B will be diagnosed using diverse data samples from various sick people. The results of the experiments with diverse data will introduce good results using both neural networks and logical methodologies in the recognition of the hepatitis B Stage.

The advanced TL-ResNet101 model was contrasted to the most recent methods of (PCA – SVM) and (PCA – LDA), and it accomplished improvement in accuracy of 5.71% and 7.21%, respectively. The outcomes of the supervised classification suggest that it has to be used for low-cost clinical HBV diagnosis and treatment. This system can be expanded in the future to recognize other diseases.

The classification accuracy is low using MLP in some cases. MLP already does not provide relatively similar achievement for a single run as random weight initialization in training RBF, which presents good results. However, CSFNN has height accuracy for hepatitis diagnostic tests. For these results using a combination of RBF and MLP called hybrid network CSFNN is more reliable for the diagnosis than one only.

Classification accuracy obtained in some previously proposed models is 98%. In the future, it will try to improve accuracy even greater by using boosting methodologies and trying to deal with data sets with imbalances.

In the future, larger HBV cohorts may be used to train and learn machine learning models. It may be used to rebuild existing clinical scoring systems and could be implemented for different indicators in different disease cohorts.

In the future, deep learning-based algorithms will use irrelevant or weak image sources using a transfer learning approach to address the requirement of large datasets.

Although the method of using Raman spectroscopy tended to detect hepatitis B, it will believe that applicable to other spectroscopies and diseases by fine-tuning the proposed model, it may achieve this very efficiently.

Future research might focus on how to better combine the information from video and indicator images and how to fully encode the information from ultrasound video rather than just select frames.

Deep HBV, powerful deep learning for predicting HBV integration sites, was the first attempt to use CNNs for HBV integration prediction. Deep HBV's attention mechanism could be used to validate the genomic preference for HBV integration and provide a more comprehensive understanding of the mechanism underlying HBV-related cancer.

The future work of most papers is to expand research on the above algorithm and to bring the efficient discovery of emerging patterns.

6 Conclusion

In this paper we surveyed machine and deep-learning-based liver disease diagnosis focusing on hepatitis B, and we presented the findings and results of the last and earlier experimental studies, as well as the drawbacks and recommended future research in this field, and a summary of all studies has been provided in Tables 2 and 3, which verify the experimental results, authors, models, and years of the studies.

References

1. Karlik, B.: Hepatitis disease diagnosis using backpropagation and the Naive Bayes classifiers. *J. Sci. Technol.* **1**(1), 49–62 (2011)
2. <https://www.niddk.nih.gov/health-information/liver-disease/viral-hepatitis/hepatitis-b>. Last accessed 22 Dec 2022

3. Frank, H. Netter, M.D.: Atlas of Human Anatomy, 3rd edition, Icon Learning Systems, 2002 ISBN 10: 1929007116 ISBN 13: 9781929007110
4. Young, B., O'Dowd, G., Woodford, Ph.: Wheatear's Functional Histology 4th edn. Churchill Livingstone (2000)
5. <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b>. 27 Jul 2021
6. British Liver Trust: "Fighting liver disease", A professional's guide to Hepatitis B
7. Terrault, N., Lok, A., McMahon, B.: Update on prevention, diagnosis, and treatment of chronic Hepatitis B: AASLD 2018 Hepatitis B guidance. *Hepatology* **67**(4), 1560–1599 (2018)
8. Villar, L., Cruz, H., Barbosa, J.: Update on Hepatitis B and C virus diagnosis. *World J. Virol.* **4**(4), 323–342 (2015). <https://doi.org/10.5501/wjv.v4.i4.323>
9. Aspinall, E.J., Hawkins, G., Fraser, A., Hutchinson, S.J., Goldberg, D.: Hepatitis B prevention, diagnosis, treatment and care: a review. *Occup. Med.* **61**(8), 531–540 (2011). <https://doi.org/10.1093/occmed/kqr136>
10. Liaw, Y.F., Chu, C.M.: Hepatitis B virus infection. *Lancet* **373**(9663), 582–592 (2009). [https://doi.org/10.1016/S0140-6736\(09\)60207-5](https://doi.org/10.1016/S0140-6736(09)60207-5). PMID: 19217993
11. Mega, A., et al.: Supervised machine learning techniques for the prediction of hepatocellular carcinoma recurrence. *J. Surg. Res* **05**(02), 238–251 (2022)
12. Zou, Z.-M., Chang, D.-H., Liu, H., Xiao, Y.-D.: Current updates in machine learning in the prediction of therapeutic outcome of hepatocellular carcinoma: what should we know? *Insights Imaging* **12**(1), 1–13 (2021). <https://doi.org/10.1186/s13244-021-00977-9>
13. Bhavsar, K.A., Singla, J., Al-Otaibi, Y.D., et al.: Medical diagnosis using machine learning: a statistical review. *Comput. Mater. Continua* **67**(1), 107–125 (2021)
14. Aravind, A., Bahirvani, A., Quiambao, R., Gonzalo, T.L.: Machine learning technology for evaluation of liver fibrosis, inflammation activity and steatosis (LIVERFASTM). *J. Intell. Learn. Syst. Appl.* **12**, 31–49 (2020). <https://doi.org/10.4236/jilsa.2020.122003>. <https://www.scirp.org/journal/articles.aspx?journalid=102>
15. Tanwar, N., Rahman, Kh.: Machine learning in liver disease diagnosis: current progress and future opportunities. *IOP Conf. Series: Mater. Sci. Eng.* **1022**, 012029 (2021). <https://doi.org/10.1088/1757899X/1022/1/012029>
16. Jamila, G., Wajiga, G.M., Malgwi, Y.M., Maidabara, A.H.: A diagnostic model for the prediction of liver cirrhosis using machine learning techniques. *Comput. Sci. IT Res. J.* **3**(1), 36–51 (2022). <https://doi.org/10.51594/csitrj.v3i1.296>
17. Wong, G., Hui, V., Tan, Q.: Novel machine learning models outperform risk scores in predicting hepatocellular carcinoma in patients with chronic viral Hepatitis. *JHEP Reports* **4**, 100441 (2022). <https://doi.org/10.1016/j.jhepr.2022.100441>
18. Cheng, B., Zhou, P., Chen, Y.: Machine-learning algorithms based on personalized pathways for a novel predictive model for the diagnosis of hepatocellular carcinoma. *BMC Bioinform.* **23**, 248 (2022). <https://doi.org/10.1186/s12859-022-04805-9>
19. Kawka, M., Dawidziuk, A., Jiao, L.R., Gall, T.M.H.: Artificial intelligence in the detection, characterisation and prediction of hepatocellular carcinoma: a narrative review. *Trans. Gastroenterol. Hepatol.* **7**, 41–41 (2022). <https://doi.org/10.21037/tgh-20-242>
20. Zhen, S., Cheng, M., Cai, X., et al.: Deep learning for accurate diagnosis of liver tumor based on magnetic resonance imaging and clinical data. *Front. Oncol.* **10**, 680 (2020). <https://doi.org/10.3389/fonc.2020.00680>
21. Nitski, O., Azhie, A., Ali Qazi-Arisar, F., et al.: Long-term mortality risk stratification of liver transplant recipients: real-time application of deep learning algorithms on longitudinal data. *The Lancet Dig. Health* **3**(5), e295–e305 (2021). [https://doi.org/10.1016/S2589-7500\(21\)00040-6](https://doi.org/10.1016/S2589-7500(21)00040-6). www.thelancet.com/digital-health
22. Liu, J., Wang, W., Guan, T., Zhao, N., et al: Ultrasound Liver Fibrosis Diagnosis using Multi-indicator guided Deep Neural Networks. arXiv: 2009.04924v1 [eess.IV] 10 Sep 2020

23. Ozyilmaz, L., Yildirim, T.: Artificial neural networks for diagnosis of Hepatitis disease. In: Proceedings of the International Joint Conference on Neural Networks, vol. 1, pp. 586–589 (2003). <https://doi.org/10.1109/IJCNN.2003.1223422>
24. Panchal, D., Shah, S.: Artificial intelligence based expert system for Hepatitis B diagnosis. *Int. J. Model. Optim.* **1**(4), 362–366 (2011)
25. Çetin, O., Temurtaş, F., Gülgönül, Ş.: An application of multilayer neural network on Hepatitis disease diagnosis using approximations of sigmoid activation function. *Dicle Med. J.* **42**(2), 150–157 (2015). <https://doi.org/10.5798/diclemedj.0921.2015.02.0550>
26. Abtahi, S., Sharifi, M.: Machine Learning Method to Control and Observe for Treatment and Monitoring of Hepatitis B Virus. arXiv. <https://doi.org/10.48550/arXiv.2004.09751> (2020)
27. Shankar Sowmien, V., Sugumaran, V., Karthikeyan, C.P., et al.: Diagnosis of Hepatitis using Decision tree Algorithm. *Int. J. Eng. Technol. (IJET)* **8**(3), 1414–1419 (2016)
28. Nahar, N., Ara, F.: Liver disease prediction by using different decision tree techniques. *Int. J. Data Min. Knowl. Manag. Process* **8**(2), 01–09 (2018)
29. Chen, S., Zhang, Z., Wang, Y., Fang, M., et al.: Using Quasispecies patterns of Hepatitis B virus to predict hepatocellular carcinoma with deep sequencing and machine learning. *J Infect Dis.* **223**(11), 1887–1896 (2021). <https://doi.org/10.1093/infdis/jiaa647>. PMID: 33049037
30. Jameel, A., Bajwa, I., Ponum, M.: Prognosis of Hepatitis Disease Classification using Non-Linear Compound Algorithms. 14 Sep 2022. <https://doi.org/10.21203/rs.3.rs-2022961/v1>
31. Tian, X., Chong, Y., Huang, Y., et al.: Using machine learning algorithms to predict Hepatitis B surface antigen seroclearance. *Comput. Math. Methods Med.* **2019**, 6915850 (2019). <https://doi.org/10.1155/2019/6915850>
32. Wei, R., Wang, J., Wang, X., et al.: Clinical prediction of HBV and HCV-related hepatic fibrosis using machine learning. *EBioMedicine* **35**, 124–132 (2018)
33. Wang, Y., Du, Z., Lawrence, W.R., et al.: Predicting hepatitis B virus infection based on health examination data of community population. *Int. J. Env. Res. Public Health* **16**(23), 4842 (2019)
34. Kim, H., Lampertico, P., Nam, J.: An artificial intelligence model to predict hepatocellular carcinoma risk in Korean and Caucasian patients with chronic Hepatitis B. *J. Hepatol.* **76**(2), 311–318 (2022)
35. Alamsyah, A., Fadila, T.: Increased accuracy of prediction Hepatitis disease using the application of principal component analysis on a support vector machine. *J. Phys.: Conf. Ser.* **1968**(1), 012016 (2021)
36. Obaido, G., et al.: An interpretable machine learning approach for Hepatitis B diagnosis. *Appl. Sci.* **12**(21), 11127 (2022)
37. Uttreshwar, G.S., Ghatol, A.A.: Hepatitis B diagnosis using logical inference and self-organizing map. *J. Comput. Sci.* **4**(12), 1042–1050 (2008)
38. Wang, K., Lu, X., Zhou, H., et al.: Deep learning Radiomics of shear wave elastography significantly improved diagnostic performance for assessing liver fibrosis in chronic Hepatitis B: a prospective multicentre study. *Gut* **68**(4), 729–741 (2019). <https://doi.org/10.1136/gut.jnl-2018-316204>
39. Yu, Y., et al.: Deep learning enables automated scoring of liver fibrosis stages. *Sci. Rep.* **8**(1), 1–10 (2018)
40. Choi, K.J., Jang, J.K., Lee, S.S., et al.: Development and validation of a deep learning system for staging liver fibrosis by using contrast agent-enhanced CT images in the Liver. *Radiology* **289**(3), 688–697 (2018). <https://doi.org/10.1148/radiol.2018180763>. Epub 2018 Sep 4 PMID: 30179104
41. Yasaka, K., Akai, H., Kunimatsu, A., Abe, O., Kiryu, S.: Liver fibrosis: deep convolutional neural network for staging by using gadoxetic acid-enhanced hepatobiliary phase MR images. *Radiology* **287**(1), 146–155 (2018). <https://doi.org/10.1148/radiol.2017171928>. Epub 2017 Dec 14 PMID: 29239710

42. Nilashi, M., Ahmadi, H., Shahmoradi, L., Ibrahim, O., Akbari, E.: A predictive method for Hepatitis disease diagnosis using ensembles of neuro-fuzzy technique. *J. Infect. Public Health* **12**(1), 13–20 (2019). <https://doi.org/10.1016/j.jiph.2018.09.009>
43. Murty, S.V., Kumar, R.K.: Enhanced classifier accuracy in liver disease diagnosis using a novel multi layer feed forward deep neural network. *Int. J. Recent Technol. Eng. (IJRTE)* **8**(2), 1392–1400 (2019). <https://doi.org/10.35940/ijrte.B2047.078219>
44. Ali, S., Hassan, M., Saleem, M., Tahir, S.F.: Deep transfer learning-based Hepatitis B virus diagnosis using spectroscopic images. *Int. J. Imaging Syst. Technol.* **31**(1), 94–105 (2021)
45. Guo, Z., Lv, X., Yu, L., Zhang, Z., Tian, S.: Identification of Hepatitis B using Raman spectroscopy combined with gated recurrent unit and multiscale fusion convolutional neural network. *Spectrosc. Lett.* **53**(4), 277–288 (2020). <https://doi.org/10.1080/00387010.2020.1737944>
46. Hassan, T.M., Elmogy, M., Sallam, E.S.: Diagnosis of focal liver diseases based on deep learning technique for ultrasound images. *Arab. J. Sci. Eng.* **42**(8), 3127–3140 (2017). <https://doi.org/10.1007/s13369-016-2387-9>
47. Nam, J.Y., Sinn, D.H., Bae, J., Jang, E.S., Kim, J.W., Jeong, S.H.: Deep learning model for prediction of hepatocellular carcinoma in patients with HBV-related cirrhosis on antiviral therapy. *JHEP Rep.* **2**(6), 100175 (2020)
48. Wu, C., Guo, X., Li, M., et al.: Deep HBV: a deep learning model to predict Hepatitis B virus (HBV) integration sites. *BMC Ecol Evo* **21**, 138 (2021). <https://doi.org/10.1186/s12862-021-01869-8>
49. Zhu, Z., Lv, D., Zhang, X.: Deep learning in the classification of stage of liver fibrosis in chronic Hepatitis B with magnetic resonance ADC images. *Contrast Media Mol. Imaging* **2021**, 2015780 (2021). <https://doi.org/10.1155/2021/2015780>
50. Pham, T.-T.-H., Nguyen, H.-P., Luu, T.-N.: Combined Mueller matrix imaging and artificial intelligence classification framework for He/patitis B detection. *J. Biomed. Opt.* **27**, 075002 (2022). <https://doi.org/10.1117/1.JBO.27.7.075002>
51. Verma, N., Asrani, S.K.: Deep learning and non-invasive assessment of significant fibrosis: does adding more toppings improve the flavor of prediction? *Hepatol. Int.* **16**, 492–494 (2022). <https://doi.org/10.1007/s12072-022-10329-4>