

Machine Learning-Powered 28-Day Mortality Prediction Model Following Hospitalization with Acute Decompensation of Liver Cirrhosis

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Abstract

Background: Chronic liver disease and cirrhosis are persistent global health threats, ranking among the top causes of death. Despite medical advancements, their mortality rates have remained stagnant for decades. Existing scoring systems like Child–Turcotte–Pugh (CTP) and Mayo End-Stage Liver Disease (MELD) have limitations, prompting the exploration of more accurate predictive methods using artificial intelligence (AI) and machine learning (ML).

Methods: we included data of 173 patients admitted with acute decompensated liver cirrhosis. The dataset underwent preprocessing to handle missing values and standardize continuous features. Traditional machine learning and deep learning algorithms were applied to build a 28-day mortality prediction model.

Results: We developed and evaluated multiple models for 28-day mortality prediction. Among traditional machine learning algorithms, Logistic Regression outperformed, achieving an accuracy of 82.9%, precision of 55.6%, recall of 71.4%, and an F1-score of 0.625. Naive Bayes and Random Forest models also performed well, with accuracy and precision at 82.9% and 54.5%, respectively. The deep learning models (Multilayer ANN, RNN, and LSTM) exhibited mixed results, with the Multilayer ANN achieving an accuracy of 74.3% but lower precision and recall. The feature importance analysis identified key contributors, including ICU admission (importance: 0.112), mechanical ventilation (importance: 0.095), and mean arterial pressure (importance: 0.073).

Conclusion: Our study demonstrates the potential of machine learning in predicting 28-day mortality following hospitalization with acute decompensation of liver cirrhosis. Logistic Regression, Naive Bayes, and Random Forest models proved effective, while deep learning models exhibited variable performance. These models can serve as valuable tools for risk stratification and timely intervention. Implementing these models in clinical practice has the potential to improve patient outcomes and resource allocation.

Keywords: Liver cirrhosis; Mortality prediction; Machine learning; Artificial intelligence; Logistic Regression; Risk stratification

Introduction

Chronic liver disease and cirrhosis remain major health concerns, consistently being among the top causes of death worldwide.¹ Despite significant progress in medical treatments, the mortality rate associated with liver diseases has not shown a significant improvement over the past three decades.² To reduce mortality in patients with chronic liver disease and cirrhosis, liver transplantation is a potential solution.^{3,4} However, it is crucial to

consider early transplantation options and discuss the associated risks and benefits early on presentation with evidence of decompensation. This is essential because the window between the patient's death and the intervention may be limited. Failing to address these factors promptly may render intensive care unit (ICU) care futile in treating these individuals.^{5,6} Therefore, it is necessary to establish a rational basis for discontinuing ICU care based on futility. Various scores, including Child–Turcotte–Pugh (CTP) and Mayo End-Stage Liver Disease (MELD), have been developed to assess prognosis and guide treatment -including liver transplantation- prioritization.⁷ Findings suggest the Chronic Liver Failure Consortium—Acute-on-Chronic Liver Failure (CLIF-C ACLF) score might outperform both CTP and MELD in predicting short and medium-term mortalities in a range of patient scenarios.^{8,9} While these scores offer valuable information, they lack accuracy as they group patients with different levels of disease severity into the same risk categories. Also, there are no prognostic models that offer personalized estimates of the risk of liver-related death for individuals with alcohol-associated cirrhosis.¹⁰ In addition to factors included in traditional prognostic scores, there are several factors, including acute kidney injury, plasma ammonia level, sarcopenia, and increased platelet aggregation, that were found to be associated with increased short-term mortality.^{11,12}

Utilizing advanced statistical tools and machine learning techniques can enhance prediction accuracy compared to traditional statistical methods by capturing higher-dimensional and potentially nonlinear effects of variables. This involves the incorporation of a larger set of variables in the analysis.¹³ Artificial intelligence (AI) is an expanding domain within computer science, widely embraced in various sectors such as e-commerce, media, and finance. Although adopting AI, particularly machine learning (ML), has been slow in the health sciences, it is now gaining attention. Machine learning involves training models through mathematical functions or rule sets, yielding precise classification and prediction outputs. Deep learning, a subset of ML, employs deep neural networks (DNNs) to analyse data through multiple layers of interconnected artificial neurons, mimicking the structure of the cerebral cortex. Notably, machine learning stands out from classical statistics by its ability to effectively model intricate non-linear relationships.¹⁴

Given the fact that patients with cirrhosis represent a complex, multidimensional system for prognosis prediction, emerging research suggests artificial intelligence and machine learning, might provide superior mortality predictions in cirrhosis.^{15,16} Yet, existing studies have been limited in scope, highlighting that there is a need for more comprehensive investigations on short-term mortality prediction using modern techniques.^{17,18}

Previous artificial intelligence and machine learning focused on 90 days mortality prediction.^{5,15,17} The objective of this study is to develop a 28-day mortality prediction model using machine learning and artificial intelligence.

Methods

A retrospective study was performed at Sultan Qaboos University Hospital in Oman, a leading multi-specialty and training healthcare institution.^{19,20} The study included all adult patients hospitalized from January 2015 to December 2021, diagnosed with acute decompensation of liver cirrhosis. In case of multiple hospitalizations, the first admission with acute decompensation was taken as the index admission. Comprehensive data was extracted from patients' electronic health records. This included demographic details, admission diagnosis, pertinent comorbidities, cirrhosis aetiology, hospital stay duration, intensive care requirements, and relevant laboratory results. Detailed methods were described previously.² A total of 173 patients were included in the study.

The outcome of interest was 28-day all-cause mortality during the follow-up period. This was ascertained by reviewing the electronic health records of patients or through phone follow-up calls if deemed necessary.

Before proceeding with model development, the dataset was refined. Missing values in binary features were imputed using with the mode, while continuous features had their missing values imputed using the median. To ensure uniformity in range, continuous features were scaled using the MinMaxScaler

Four general machine learning algorithms, namely Decision Tree, Random Forest, Logistic Regression and Naive Bayes, were employed to develop the models. These algorithms were chosen for their ability to handle both continuous and binary features and their capability to capture complex relationships within the data.²¹ Additionally, a deep learning algorithm including Multilayer ANNs, long Short-Term Memory (LSTM), recurrent Neural Network (RNN), was implemented to leverage the power of neural networks in capturing non-linear

dependencies in the data.²² For each algorithm, the dataset was split into training and testing sets using a 80:20 ratio.

To compare the performance of the models, various metrics were calculated, including accuracy, precision, recall, and F1-Score. Accuracy measures the overall correctness of predictions, while precision quantifies the proportion of correctly predicted positive cases. Recall measures the sensitivity of the model in identifying positive cases, and F1-Score combines precision and recall into a single metric. The metrics were calculated for each model and reported. To provide a visual representation of the performance, bar plots were generated for accuracy, precision, recall, and F1-Score, with each bar representing the performance of a given model.²²

Categorical variables were expressed in numerical values and percentages, while continuous variables were presented as means for normally distributed data or as medians with interquartile range (IQR) for non-normally distributed data. To compare continuous variables between the two groups, the student's t-test was employed for normally distributed variables, and the Wilcoxon rank-sum test was utilized for non-normally distributed variables. The chi-squared test was applied to assess the relationship between categorical variables. Statistical significance was established at a two-sided p-value below 0.05. All statistical analyses were conducted using the Stata v. 18.0 software package (StataCorp LLC, College Station, TX, USA).

For models development, and models evaluation we used Anaconda distribution, including Python programming language and various libraries.

The study was approved by the Medical Research Ethics Committee of the College of Medicine and Health Sciences of Sultan Qaboos University (SQU EC/349/2021 MREC #2375).

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Results

A total of 173 patients were admitted with acute decompensated liver disease during the study period. The demographic, clinical, laboratory findings, and factors associated with 28 days mortality are reported in Table 1.

Table 1: Patients characteristics, and relevant clinical and laboratory findings.

	Total number of patients (n = 173)	28- days mortality (n = 36)	No 28- days mortality (n = 137)	p-value
Age	58 ±13.8	62.0±13.7	57.0±13.7	0.05
Male (n)	124(71.7%)	30(83.33%)	94 (68.61%)	0.08
Weight (kg)	69.3 (84-60)	70(60-81.65)	69.2(60.8-85)	0.51
Body Mass Index (BMI)	27.7 (31.8-22.4)	28.1(22.1-30.5)	27.5(22.6-32)	0.44
Comorbidity				
Hypertension	77 (44.51%)	12 (33.33%)	65 (47.45%)	0.13
Diabetes mellitus	75 (43.35%)	14 (38.89%)	61 (44.53%)	0.54
Ischemic heart disease	36 (20.81%)	9 (25.00%)	27 (19.71%)	0.49
Chronic kidney disease (CKD)	20 (11.56%)	5 (13.89%)	15 (10.95%)	0.62
Smoking	30 (17.34%)	10 (27.78%)	20 (14.60%)	0.06
Aetiology of liver cirrhosis				
Alcohol	51 (29.48%)	13 (36.11%)	38 (27.74%)	0.33
Hepatitis B virus (HBV)	46(26.74%)	7 (19.44%)	39 (28.68%)	0.27
Hepatitis C virus (HCV)	48 (27.75%)	13 (36.11%)	35 (25.55%)	0.21
Non- alcoholic fatty liver disease (NAFLD)	24 (13.95%)	5 (14.29%)	19 (13.87%)	1.00
Reason for admission				
Spontaneous bacterial peritonitis (SBP)	15 (8.67%)	4 (11.11%)	11 (8.03%)	0.52
Hepatic encephalopathy	68 (39.31%)	27 (75.00%)	41 (29.93%)	<0.001
Ascites	111 (64.16%)	26 (72.22%)	85 (62.04%)	0.26
Variceal bleeding	85 (49.13%)	12 (33.33%)	73 (53.28%)	0.03
Course of admission				
Intensive care unit (ICU) admission	34 (19.65%)	24 (66.67%)	10 (7.30%)	0.000
Mechanical ventilation	31 (17.92%)	22 (61.11%)	9 (6.57%)	0.000

Length of Hospital Stay days	7(4-12)	10.5 (6.5-23.5)	6 (4-11)	0.0030
Treatment				
Beta blockers	84 (48.55%)	12 (33.33%)	72 (52.55%)	0.040
Diuretics	114 (65.90%)	24 (66.67%)	90 (65.69%)	0.913
Lactulose	134 (77.46%)	34 (94.44%)	100 (72.99%)	0.006
Clinical & haematological and biochemical profile				
FiO2 (%)	0	0.325(0-1)	0	0.0000
Mean arterial pressure (MAP)	71(67-82)	58.5(47-71.5)	72(69-84)	0.0000
Haemoglobin (Hb)	10.2± 2.5	10.3± 2.5	10.2± 2.5	0.8269
Platelets	154.5 (211.5-99.5)	175(112-235)	136(93-205)	0.0857
White cell count	7.2 (10.7-5.1)	9.3(7.15-15.5)	6.8(5-9.1)	0.0004
International normalised ratio (INR)	1.32 (1.5-1.16)	1.46(1.31-1.94)	1.3(1.2-1.5)	0.0012
Prothrombin time (PT)	14.2(12.55-16.45)	15.65(14.4-20.35)	14.0(12.5-15.6)	0.0010
Creatinine (mmol/L)	72(106- 57)	82.5(58-119.5)	71(57-99)	0.1899
Sodium (mmol/L)	135(131-138)	132.5(128.5-137)	135(132-138)	0.1508
Potassium (mmol/L)	4.3(3.9-4.8)	4.7(3.9-5.1)	4.3(3.9-4.7)	0.1009
Alanine Aminotransferase (ALT) IU/l	37(24-70)	51(34-109)	32.5(24-61)	0.0053
Albumin (g/L)	30(25-34)	25(22-31)	31(25- 35)	0.0002
Alkaline Phosphatase (ALP) IU/l	136(100-220)	220(129-392)	125(96- 180)	0.0011
Aspartate Aminotransferase (AST) IU/l	63(42-134)	110(70-232)	55(39-118)	0.0001
Bilirubin (umol/L)	34(17-79)	49 (22-180)	29(15-73)	0.0175
Gamma-Glutamyl Transferase (GGT) IU/l	230(75-481)	258(68-809)	215(75-465)	0.6028
HbA1c	6.4(5-8.4)	5.65(4.7-7.2)	6.4(5.2-8.4)	0.4955
Liver cirrhosis scores				
CTP score	9(7-11)	10(9- 12)	8(7-10)	0.0001
MELD-Na score	18 (13-25)	24(18- 29)	17(12-24)	0.0014
CLIF-C	41(35-48)	52(45-59)	39(33- 44)	0.0000

CTP, Child-Turcotte-Pugh; MELD-Na, Model For End-Stage Liver Disease-Na; CLIF-C, Chronic Liver Failure Consortium.

Table 2: comparison of performance of various machine learning and deep learning models in predicting 28 days mortality.

Model	Accuracy	Precision	Recall	F1 Score	AUROC
Decision Tree	0.714	0.385	0.714	0.5	0.714
Logistic Regression	0.829	0.556	0.714	0.625	0.786
Naïve Bayes	0.829	0.545	0.857	0.667	0.839
Random Forest	0.829	0.545	0.857	0.667	0.839
Multilayer ANN	0.743	0.375	0.429	0.4	0.625
RNN	0.8	1	0	0	0.648
LSTM	0.8	0	0	0	0.5

Multilayer ANN: Multilayer Artificial Neural Network; LSTM: long Short-Term Memory; RNN: recurrent Neural Network; AUROC: Area Under the Receiver Operating Characteristics curve.

We initially developed our models using four general machine learning algorithms, namely Decision Tree, Random Forest, and Naive Bayes, and Logistic Regression. Additionally, we employed a Multilayer ANNs, long Short-Term Memory (LSTM), recurrent Neural Network (RNN) as a deep learning technique. The models were trained and tested using a dataset containing features related to acute decompensations of chronic liver disease.

The Decision Tree model achieved an accuracy of 71.4%, with a precision of 38.5% and recall of 71.4%. The F1-score for this model was 0.5. The Logistic Regression model showed higher performance, with an accuracy of 82.9%. It achieved a precision of 55.6% and a recall of 71.4%. The F1-score for this model was 0.625. Both the Naive Bayes and Random Forest models demonstrated similar results. They achieved an accuracy of 82.9% and precision of 54.5%. The Naive Bayes model showed a higher recall of 85.7%, resulting in an F1-score of 0.667. The Random Forest model had a recall of 85.7% and an F1-score of 0.667. The Multilayer ANN model achieved an accuracy of 74.3%, with a precision of 37.5% and a recall of 42.9%. The F1-score for this model was 0.4. In contrast, the RNN and LSTM models exhibited lower performance metrics. The RNN model achieved an accuracy of 80%, with a perfect precision of 100%. However, it had a recall of 0 and an F1-score of 0. The LSTM model

also had an accuracy of 80% but performed poorly in terms of precision, recall, and the F1-score, all of which were 0.

Among the traditional machine learning models, the Logistic Regression, Naive Bayes, and Random Forest models showed AUROC values of 0.786, 0.839, and 0.839, respectively, indicating good discrimination capability in predicting mortality. In contrast, the deep learning models had lower AUROC values. The Multilayer ANN model had an AUROC of 0.625, while the RNN and LSTM models achieved AUROC values of 0.648 and 0.5, respectively.

The feature importance analysis using the Random Forest model revealed the top 10 contributing features for mortality prediction in patients with chronic liver disease and cirrhosis following admission with acute decompensation. Among these features, the most influential were ICU admission (importance: 0.112), mechanical ventilation (importance: 0.095), and mean arterial pressure (importance: 0.073). Other significant features included platelet count (importance: 0.063), alkaline phosphatase (importance: 0.056), bilirubin (importance: 0.054), and white blood cell count (importance: 0.048).

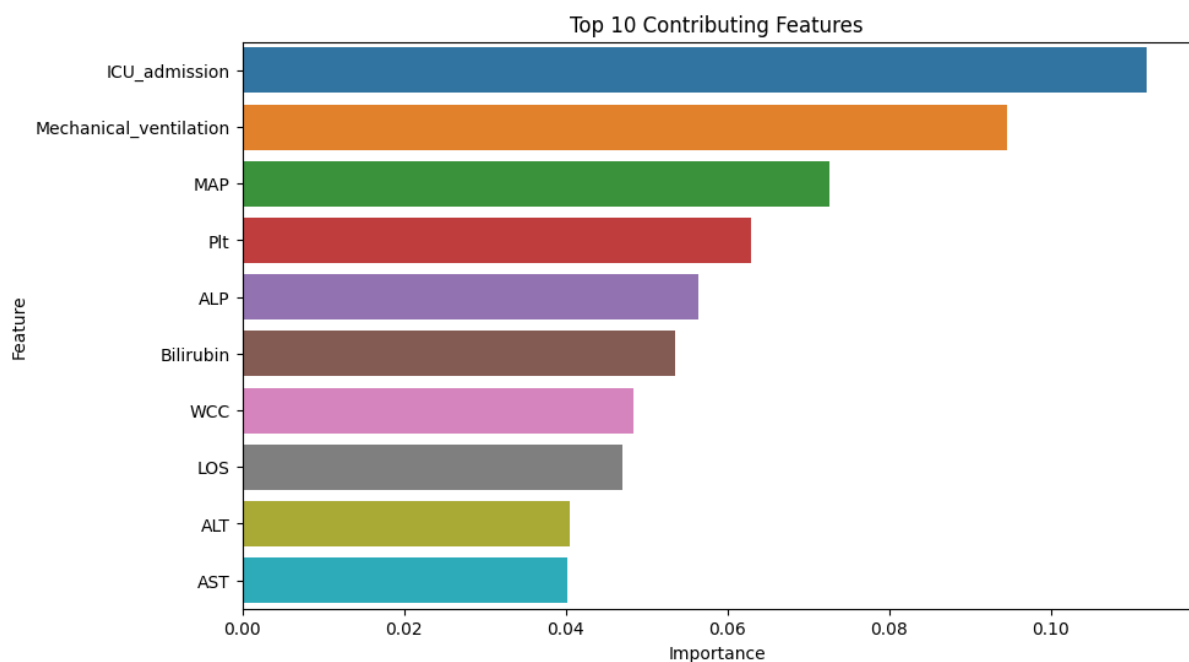


Figure 1: The feature importance analysis using the Random Forest model revealed the top 10 contributing features for mortality prediction.

Discussion

Our study aimed to develop 28 days mortality prediction model for patients with admitted with acute decompensation of liver cirrhosis using machine learning and deep learning techniques. We evaluated the performance of various models, including Decision Tree, Logistic Regression, Naive Bayes, Random Forest, Multilayer Artificial Neural Network (ANN), Recurrent Neural Network (RNN), and Long Short-Term Memory (LSTM), using a dataset that included demographic, clinical, and laboratory features related to chronic liver disease.

The results of our study indicate that the Naive Bayes, and Random Forest models showed the highest performance metrics among the traditional machine learning models. These models achieved high accuracy, precision, recall, and F1-scores, demonstrating their effectiveness in predicting 28 days mortality in patients admitted with acute decompensation of chronic liver disease. Despite its simplicity, Naive Bayes was able to capture relevant patterns in the data and make accurate predictions for mortality.

The AUROC values further confirmed the discriminatory ability of these models, with values ranging from 0.786 to 0.839. The Naive Bayes model, although simpler in its assumption of feature independence, delivered competitive results. It showed a balanced trade-off between precision and recall, similar to the Decision Tree

model. It is worth noting that the AUROC values for predicting 28-day mortality using the Naive Bayes and Random Forest models were comparable to the AUROC values for CLIFC and superior to those for CTP and MELD-Na within the same cohort of patients, as previously reported.²

In a prior study, the prediction of 90-day mortality was examined through the utilization of three AI models: logistic regression (LR), kernel support vector machine (SVM), and random forest classifiers (RFC). This study included a cohort of 2,170 patients and yielded a modest AUROC score of 0.67 for the prediction of 90-day mortality.²³

In contrast, the deep learning models, including the Multilayer ANN, RNN, and LSTM, showed lower performance metrics. The Multilayer ANN model achieved moderate performance, while the RNN and LSTM models showed poor performance, with recall and F1-scores of 0 for predicting mortality. A study involving 34,575 cirrhosis patients aimed to predict mortality using laboratory tests and diagnoses. Deep learning models, including deep neural networks (DNN), outperformed the traditional MELD score in predicting mortality at various time frames (90, 180, and 365 days).¹⁷

The superior performance of traditional machine learning models like logistic regression in comparison to deep learning models such as Multilayer ANN, RNN, and LSTM -in our cohort-can be attributed to several factors. Firstly, with a small sample size of 173, traditional machine learning models are often more efficient in processing and extracting meaningful patterns from the data.²⁴ Deep learning models, on the other hand, require a larger amount of data to capture the complexity of the problem adequately. Additionally, traditional machine learning models have a simpler architecture and fewer hyperparameters to tune, making them less prone to overfitting in small datasets.²⁵

Furthermore, our feature importance analysis revealed the top 10 contributing features for mortality prediction in patients with chronic liver disease and cirrhosis. Among these features, ICU admission was found to be the most influential, followed by mechanical ventilation and mean arterial pressure. Other significant features included platelet count, alkaline phosphatase, bilirubin, and white blood cell count. Similarity previous AI and ML models identified alkaline phosphatase, alanine aminotransferase, and haemoglobin as top informative features besides MELD-Na variables in predicting mortality in patients with liver cirrhosis.¹⁷

These findings suggest that clinical indicators of disease severity and organ dysfunction play a crucial role in mortality prediction in this patient population. These findings provides additional factors associated with short term poor outcomes not highlighted in traditional prognostic score (i.e MELD, CLIF C),^{9,26} which empowers clinicians to make well-informed decisions regarding care prioritization, including the consideration of liver transplantation or a re-evaluation of the appropriateness of certain treatments, all of which have the potential to significantly impact patient outcomes.

Our study contributes to the growing body of literature on mortality prediction in patients with chronic liver disease and cirrhosis using machine learning and deep learning techniques. The results highlight the potential of traditional machine learning models, such as Logistic Regression, Naive Bayes, and Random Forest, in accurate mortality prediction in this population. These models leverage a combination of clinical and laboratory features to provide valuable insights for healthcare providers in identifying patients at higher risk of mortality.

However, it is important to note the limitations of our study. Firstly, our analysis was based on a relatively small dataset, which may impact the generalizability of the results. Future studies with larger and more diverse datasets are warranted to validate the performance of these models. Additionally, external validation of the developed models using independent cohorts would provide further evidence of their usefulness in clinical practice. Furthermore, our study focused on predicting mortality within a 28-day period, and longer-term predictions were not explored. Future research could extend the prediction horizons to encompass different time frames and evaluate the performance of the models accordingly.

Conclusion:

This study demonstrates the potential of machine learning and deep learning techniques in predicting 28 days mortality in patients admitted with acute decompensation of chronic liver disease. The Logistic Regression, Naive Bayes, and Random Forest models showed favourable performance metrics, indicating their utility in mortality prediction. However, further validation in larger cohorts and external datasets is necessary to establish the

robustness and generalizability of these models. The identification of key features, such as ICU admission, mechanical ventilation, and mean arterial pressure, highlights the importance of disease severity indicators in mortality prediction. Implementing these models in clinical practice may enhance risk stratification and aid in timely intervention for patients with chronic liver disease and cirrhosis.

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