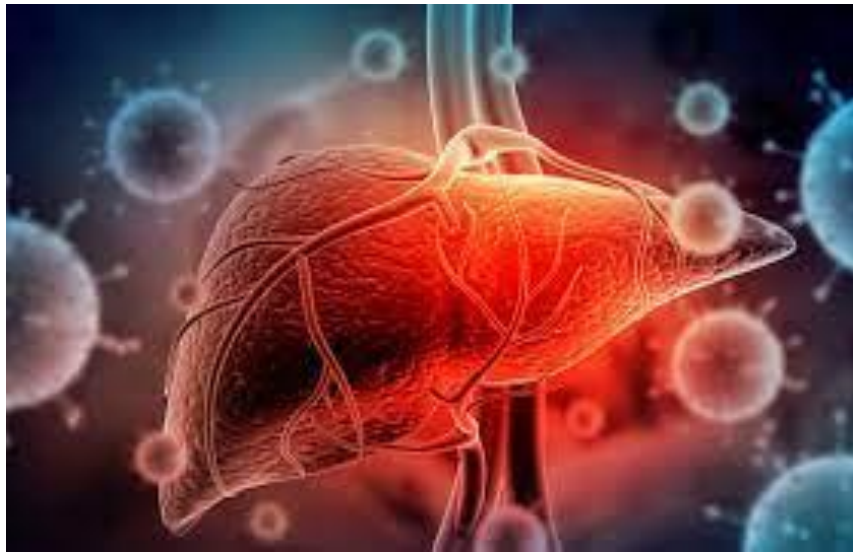




Ben-Gurion University of the Negev

Department of Industrial Engineering and Management

Liver Cirrhosis Stage Prediction



Final Project – Machine Learning and Data Mining
(364-2-5091)

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Date: 26.02.25

Code available at: <https://github.com/Yarden231/Liver-Cirrhosis-Stage-Prediction>



Date: 26.02.25

Abstract

This research project investigates the application of machine learning techniques to predict cirrhosis disease stages using a comprehensive dataset from the Mayo Clinic's primary biliary cirrhosis (PBC) study conducted from 1974 to 1984. The dataset comprises clinical parameters and biomarkers from 418 patients, with 20 variables including both categorical and numerical data points.

Our methodology encompasses extensive data preprocessing, including handling missing values, feature transformation, and addressing class imbalance. We implemented and compared multiple machine learning algorithms, including Random Forest, XGBoost, CatBoost, LightGBM, Artificial Neural Networks, and ensemble voting methods.

Results demonstrate that Random Forest outperformed other models with 72.3% accuracy and an F1-score of 0.722, exhibiting particular strength in identifying advanced cirrhosis stages (77% F1-score for Stage 3). Feature importance analysis revealed that blood lipid indicators (triglycerides and cholesterol) and copper concentration were the strongest predictors, surpassing conventional liver function markers such as bilirubin and SGOT.

This study confirms the potential of machine learning in enhancing cirrhosis diagnosis by improving early detection capabilities, identifying key risk factors, and supporting personalized treatment decisions. Altogether, we acknowledge certain limitation impacting model performance as the relatively small dataset size constrained our ability to achieve higher accuracy rates, particularly for early-stage cirrhosis detection.



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1. Business Understanding

The liver, our largest internal organ, performs critical functions including detoxification, metabolism, and protein synthesis (Asrani et al., 2019). Cirrhosis represents the leading cause of liver-related mortality, ranking 12th among causes of death in the United States (Sumeet et al., 2013). This chronic condition is characterized by progressive replacement of healthy liver tissue with fibrotic scarring, compromising organ function and potentially leading to portal hypertension, hepatic failure, ascites, jaundice, and encephalopathy (D'Amico et al., 2006). The primary causes include chronic alcohol consumption, viral hepatitis (B and C), and non-alcoholic fatty liver disease, with regional variations in prevalence (Singal et al., 2020). Typically, cirrhosis develops insidiously, with patients often remaining asymptomatic during early stages (Smith et al., 2019). The disease progresses from compensated cirrhosis, where liver function remains relatively preserved despite scarring, to decompensated cirrhosis, marked by significant complications and hepatic failure. Early diagnosis is therefore crucial but challenging due to this asymptomatic early phase. In recent years, machine learning has emerged as a promising diagnostic tool, offering superior accuracy over conventional methods while enabling disease trajectory prediction (Zhai et al., 2024). However, clinical implementation faces significant challenges due to patient heterogeneity and complex pathophysiology, highlighting the need for more sophisticated models (Zhang et al., 2021). In response to these challenges, this project employs machine learning to predict cirrhosis and accurately identify its stages, addressing a significant global healthcare need. By analyzing key parameters to improve prediction accuracy across the four distinct stages of cirrhosis, the goal is to enhance patient outcomes and transform the approach to managing this serious condition.

2. Data Understanding

2.1 Data

Data source: Our study is based on the Cirrhosis Prediction Dataset collected between 1974 and 1984 during the Mayo Clinic study on primary biliary Cirrhosis (PBC). The data is available from the UC Irvine Machine Learning Repository ([Link](#)).

Characteristics: The dataset contains 418 records, each representing a patient's biological information. It consists of 19 explanatory variables capturing various biological indicators and one target variable indicating disease stage. This structure enables analysis of the relationship between biological markers and disease progression.

2.2 Variables

Table 1 measurement units and interval of each feature in the dataset

Variable	Meaning	Type	Units	Range
ID	Identifier of the patient	Numeric (Integer)	-	[1, 418]
N_Days	Number of days between registration and the earlier of death, transplantation, or study analysis time in 1986	Numeric (Integer)	Days	[41, 4795]
Status	Status of the patient	Categorical	-	{C - censored, D - death CL - censored due to liver tx}
Drug	Type of drug	Categorical	-	{D-penicillamine, Placebo}
Age	Age in days	Numeric (Integer)	Years	[9598, 28650]
Sex	Gender of the patient	Categorical	-	{M - male, F - female}
Ascites	Presence of ascites	Categorical	-	{N - No, Y - Yes}
Hepatomegaly	Presence of hepatomegaly	Categorical	-	{N - No, Y - Yes}

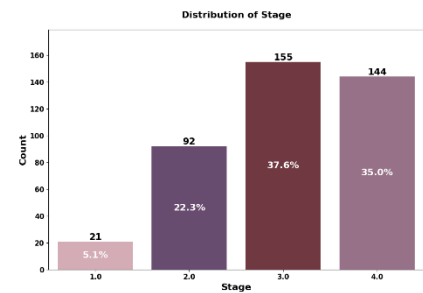


Variable	Meaning	Type	Units	Range
Spiders	Presence of spiders	Categorical	-	{N - No, Y - Yes}
Edema	Presence of edema	Categorical	-	{N - No edema and no diuretics, S - Edema without diuretics or resolved with diuretics, Y - Edema despite diuretics}
Bilirubin	Serum bilirubin in	Numeric (Continuous)	[mg/dl]	[0.3, 28]
Cholesterol	Serum cholesterol in	Numeric (Integer)	[mg/dl]	[120, 1775]
Albumin	Albumin in	Numeric (Continuous)	[mg/dl]	[1.96, 4.64]
Copper	Urine copper in	Numeric (Integer)	[ug/day]	[4, 588]
Alk_Phos	Alkaline phosphatase in	Numeric (Continuous)	[U/liter]	[289, 13862.4]
SGOT	SGOT in	Numeric (Continuous)	[U/ml]	[26.35, 475.25]
Triglycerides	Triglycerides in	Numeric (Integer)	[mg/dl]	[33, 598]
Platelets	Platelets per cubic	Numeric (Integer)	[ml/1000]	[9, 18]
Prothrombin	Prothrombin time in sec	Numeric (Continuous)	[sec]	[62, 721]
Stage (Target)	Histologic stage of disease	Categorical	-	{1, 2, 3, or 4}

Distributions of Continuous Features (Appendix A)

Statistical description of the categorical variables (Appendix B)

The **target variable, Stage**, is a categorical variable representing the histological stage of liver cirrhosis (values 1-4). Our objective is to train a predictive model to classify this variable accurately in the test set. The dataset is imbalanced, with uneven distribution of observations across the four classes.

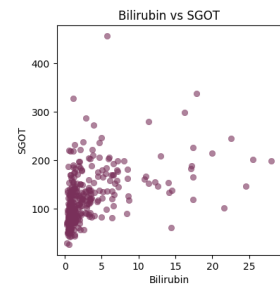


Relationships between variables

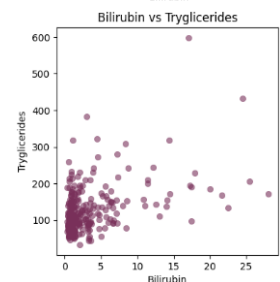
Pearson correlation - **Bilirubin** showed strong positive correlations with **Copper (0.46)**, **Cholesterol (0.40)**, **Triglycerides (0.44)**, and **SGOT (0.44)**, indicating links between bilirubin, liver dysfunction, and lipid metabolism. Conversely, **Bilirubin** correlates negatively with **Albumin (-0.31)**, reflecting decreased protein synthesis in liver dysfunction. **Copper** correlates negatively with **N_Days (-0.36)**, suggesting elevated copper is associated with shorter survival times. **Albumin** correlates positively with **N_Days (0.43)**, confirming its value as a prognostic marker for longer survival (Appendix C).

Selected scatter plots between variables (highest correlations – above |0.4|)

Bilirubin vs SGOT: Higher bilirubin levels corresponded with increased SGOT values, highlighting both as important markers of liver injury - bilirubin indicating impaired waste clearance while SGOT reflecting hepatocyte damage, with their correlation demonstrating the liver dysfunction characteristic of cirrhosis.



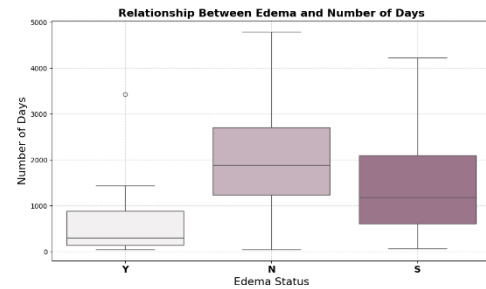
Albumin vs N_Days: Higher albumin levels correlated with longer survival times, reflecting albumin's role as a liver-produced protein and marker of hepatic function. Low levels indicate advanced liver disease and compromised protein synthesis, confirming albumin's value as a prognostic indicator (Appendix D).



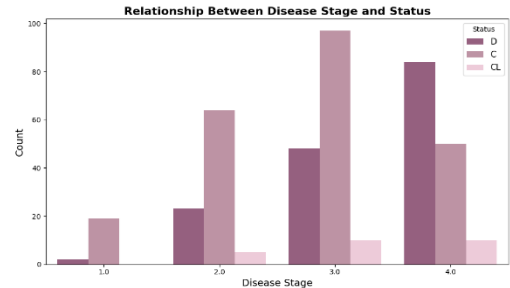


Selected relationships between variables

Edema and N Days - Patients with Edema (Y) had fewer days, indicating more severe disease or shorter survival. Those without Edema (N) or with diuretic-responsive Edema (S) showed wider day ranges and higher median values. This suggests patients with severe Edema experienced worse health outcomes, while those without Edema or responding to treatment survived longer.



Stage and Status - As the disease stage progressed (Stages 3 and 4), the death rate (D) increased significantly while the proportion of patients alive (C) decreased. Additionally, liver transplants (CL) were slightly more common in advanced stages, reflecting the need for urgent medical intervention or the severity of complications in late-stage disease.



Target with features - As disease progressed, liver function indicators (Bilirubin, Copper, Alkaline Phosphatase) significantly increased, while health and clotting markers (Albumin, Platelets, Prothrombin) deteriorated. Advanced stages (3 and 4) showed clear escalation in liver dysfunction markers, highlighting disease's systemic impact. The decline in Albumin, Prothrombin, and Platelets revealed physiological changes in later stages. Some variables like Triglycerides showed subtle changes across stages, while others like N_Days and Bilirubin displayed stark contrasts, emphasizing their diagnostic value. The correlation between advanced stages and older age highlighted the need for early diagnosis in older demographics (**Appendix E**).

3. Data Preparation

Irrelevant feature removal - Removed the ID column, as it was not analytically relevant.

Duplicate records - We have defined a duplicate record as a record whose fields are identical to another. Accordingly, no duplicates were found

Missing values - Missing values were noted in several features.

We grouped these features based on the proportion of missing data:

Significant Missing Data ($\geq 25\%$): Features like Tryglicerides, Cholesterol, Copper, Drug, Ascites, Hepatomegaly, Spiders, SGOT, and Alk_Phos had over 25% of their values missing.

Feature	Missing Count	Missing Percentage
Tryglicerides	136	32.54
Cholesterol	134	32.06
Copper	108	25.84
Drug	106	25.36
Ascites	106	25.36
Hepatomegaly	106	25.36
Spiders	106	25.36
SGOT	106	25.36
Alk_Phos	106	25.36
Platelets	11	2.63
Stage	6	1.44
Prothrombin	2	0.48

Drug: Imputed as "non-participant" for 106 patients not in the clinical trial (according to the dataset source) to reflect this distinction.

Other features: Imputed using median values of respective target groups.

Minimal Missing Data ($< 3\%$): Platelets, Stage, and Prothrombin.

Stage (target variable) - 6 samples with missing values removed to avoid introducing noise.

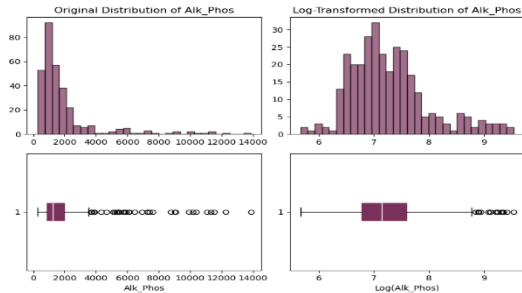
Platelets and Prothrombin - Imputed using median values of respective target groups. Note: using the median as imputing is robust to outliers and better represents the central tendency for skewed data.



Data proportion - During EDA, we observed an imbalance in the distribution of samples across the Cirrhosis stages. Specifically, Stages 1 and 2 had significantly fewer samples than the other stages. The smaller sample sizes in these stages could hinder statistical analysis and model training robustness, leading to biased outcomes or unstable predictions. To address this imbalance and ensure a more reliable and interpretable analysis, we merged Stages 1 and 2 into a single category.

Dataset size - Given the dataset's limited size (412), we avoid resorting to down sampling, which could result in data loss, or up sampling, which may introduce bias.

Handling Outliers - Outliers can profoundly impact statistical analyses, particularly in datasets with wide value ranges. Variables such as Bilirubin, Alkaline Phosphatase (Alk_Phos), and SGOT exhibited extreme values that significantly deviated from the primary distribution, distorting central tendency and dispersion measures. We retained these values as they may reflect essential medical conditions for classification. To mitigate their effects, we employed logarithmic transformation to reduce the statistical influence of extreme values while preserving their integrity and relationships within the data.



Data Representation - Categorical Features Encoding (Appendix G)

One-hot encoding - multi-class categorical features (Status, Drug, Edema) were One-Hot encoded to create binary columns for each category (dummy variables). This ensures the model treats each category as distinct without implying ordinal relationships.

Label Encoding - Binary categorical variables labels were encoded into 0 and 1. The binary features we encoded including all dummy variables produced by one-hot encoding and originally binary features (Sex, Ascites, Hepatomegaly, Spiders).

Feature Selection - Multicollinearity Detection via VIF - We employed Variance Inflation Factor analysis to identify multicollinearity among features. Using the standard threshold of $VIF \geq 10$, we identified that Prothrombin, Albumin, and Age exhibited high multicollinearity, which corresponded with patterns observed in our correlation matrix. Consequently, these features were removed from the dataset.

Scaling - Both Normalization and Min-Max - The implementation of feature scaling techniques was necessitated primarily by the inclusion of Artificial Neural Networks in our modeling approach. **Normalization (Standardization)**: Transformed features to have a mean of 0 and standard deviation of 1. **Min-Max Scaling**: Rescaled features to the 0-1 range while preserving relative data relationships.

$$X' = \frac{X - \mu}{\sigma}$$

$$X' = \frac{X - X_{min}}{X_{max} - X_{min}}$$

4. Modeling

We conducted hyperparameter tuning for each model using Optuna, an efficient optimization framework that dynamically explores parameter space while pruning suboptimal trials early. We selected Optuna to maximize F1 scores in our multi-class classification task due to its effectiveness with imbalanced data and its ability to deliver optimal results efficiently.

Random Forest - The Random Forest algorithm is an ensemble learning method that reduces overfitting by incorporating random sampling and variable selection while constructing individual decision trees.



Aggregating predictions from multiple trees improves accuracy and generalization, making it effective for our classification task. We tuned parameters including Criterion, N estimators, Max depth, Max features and Minimum samples split.

	Criterion	N estimators	Max depth	Max features	Minimum samples split
Default RF	<u>gini</u>	100	None	<u>sqrt</u>	2
Tuned RF	<u>gini</u>	464	31	<u>sqrt</u>	10

ANN - An artificial neural network (ANN) is a computational model inspired by biological neural networks in the human brain. It consists of interconnected layers: an input layer for receiving features, hidden layers for processing data, and an output layer for generating predictions. Neurons learn by adjusting weights during training, enabling the network to make accurate predictions. ANNs excel at capturing complex, non-linear patterns, making them theoretically suitable for our multi-class classification of liver cirrhosis stages. However, we anticipated limited performance due to our relatively small dataset size (412 samples), as ANNs typically require substantial training data to achieve optimal results. We tuned parameters including Hidden layers size, Activation, Solver, Alpha and Learning Rate.

	Hidden Layers	Activation	Solver	Alpha	Learning Rate	Max iterations
Default ANN	(64,)	<u>ReLU</u>	<u>adam</u>	0.0001	constant	200
Tuned ANN	(128, 64)	Logistic	<u>adam</u>	0.0014	adaptive	249

XGBoost - Extreme Gradient Boosting is a tree-based algorithm designed for classification tasks. We selected it for its ability to handle complex datasets and deliver high performance. XGBoost constructs multiple decision trees sequentially, with each tree correcting errors from the previous one. We initially trained the model with default parameters, then performed hyperparameter optimization using Grid Search. The parameters we tuned are: Number of Estimators, Maximum Depth, Learning rate, Subsample and Column Subsampling.

	Number of Estimators	Maximum Depth	Learning Rate	Subsample	Column Subsampling
Default XGBoost	100	6	0.1	1.0	1.0
Tuned XGBoost	66	10	0.007	0.849	0.658

Light GBM - LightGBM is built on the gradient boosting framework and uses two key techniques: gradient-based one-sided sampling (GOSS) and exclusive feature Bundle (EFB). GOSS allows LightGBM to train each tree with only a small fraction of the dataset, while EFB handles high-dimensional sparse features efficiently. The parameters we tuned are: Boosting Type, Learning Rate, Max depth, Subsample and Min gain to split.

	Boosting Type	Learning Rate	Max depth	Subsample	Min child samples
Default Light GBM	<u>gbdt</u>	0.1	-1	1	20
Tuned Light GBM	<u>goss</u>	0.064	2	0.915	29

CatBoost - CatBoost is built on the gradient boosting framework, combining multiple weak learners to create a predictive model. It implements this using decision trees with two key innovations: ordered boosting and efficient handling of categorical features. The parameters we tuned are: Bootstrap type, Min data in leaf, Grow policy, Random strength and Learning rate.

	l2 leaf regularization	Bootstrap type	Min data in leaf	Grow policy	Random strength	Learning rate
Default CatBoost	3.0	---	1	Symmetric	1	0.1
Tuned CatBoost	9.349	Bayesian	10	<u>Depthwise</u>	7.812	0.044



Voting - Voting Classifier is an ensemble method that combines predictions from multiple models to potentially achieve higher performance than any individual classifier. We implemented this approach after tuning all individual models to leverage their optimized configurations. Our voting implementation incorporates: **Voting Type** - Set to "soft" to utilize probability predictions, **Weights** - Assigned proportionally based on each model's performance, **Estimators** - Selected best performing optimized classifiers as base models.

5. Evaluation

We conducted a systematic evaluation of our models using various quality metrics to identify the most suitable one for this problem - producing the best results on the test set. Our approach analyzed accuracy, precision, recall, and F1 scores for a thorough understanding of each model's classification capabilities. We also examined confusion matrices to interpret results across different classes and evaluated confidence intervals (CI) to assess the statistical reliability of our findings.

Random Forest

The tuned Random Forest model achieves 72% accuracy, demonstrating strongest performance for advanced cirrhosis (stage 3) with 0.79 recall and 0.77 F1-score. The model maintains effective detection of early-stage disease while showing slightly reduced sensitivity for intermediate stages, creating an improved balance between early detection and advanced case identification.

Confusion Matrix for RF optuna tuned Classifier				RF tuned Classifier Report:				
True labels					precision	recall	f1-score	support
		1	2	3				
	1	17	3	3	1.0	0.68	0.74	23
	2	6	20	5	2.0	0.74	0.65	31
	3	2	4	23	3.0	0.74	0.79	29
		Predicted labels			accuracy			
					macro avg	0.72	0.73	83
					weighted avg	0.72	0.72	83

XGBoost

The tuned XGBoost model achieved a 71% accuracy, performing best at identifying advanced cirrhosis cases, while showing improved and balanced effectiveness for early and intermediate stages, demonstrating better overall classification capability than the default model.

Confusion Matrix for XGBoost tuned Classifier				Tuned XGBoost Classifier Report:				
True labels					precision	recall	f1-score	support
		1	2	3				
	1	17	3	3	1.0	0.65	0.74	23
	2	7	21	3	2.0	0.70	0.68	31
	3	2	6	21	3.0	0.78	0.72	29
		Predicted labels			accuracy			
					macro avg	0.71	0.71	83
					weighted avg	0.71	0.71	83

ANN

We selected **Min-Max scaling** due to its uniformity, bias prevention, and improved model performance compared to Standard scaling. We also constructed and evaluated the model by adjusting key hyperparameters to optimize performance.

The tuned ANN model with MinMaxScaler achieved 58% accuracy, performing best at identifying advanced cirrhosis cases (precision 0.73) - clinically critical for treatment decisions - while showing weaker performance for early and intermediate stages.



Confusion Matrix for Tuned Model with MinMaxScaler Classifier			ANN tuned with MinMaxScaler Classifier Report:				
				precision	recall	f1-score	support
True labels	1	2	15	0.56	0.65	0.60	23
	2	3	10	0.50	0.55	0.52	31
	3	1	2	0.73	0.55	0.63	29
			accuracy			0.58	83
			macro avg	0.59	0.58	0.58	83
			weighted avg	0.59	0.58	0.58	83

Light GBM

The LightGBM tuned model achieved 67% accuracy with good performance across cirrhosis stages, especially for Stage 1 and Stage 3 cases. Stage 2 showed relatively lower performance, suggesting intermediate stages are more difficult to classify.

Confusion Matrix for LightGBM tuned Classifier			LightGBM tuned Classifier Report:				
				precision	recall	f1-score	support
True labels	1	2	17	0.71	0.74	0.72	23
	2	3	6	0.61	0.61	0.61	31
	3	1	1	0.71	0.69	0.70	29
			accuracy			0.67	83
			macro avg	0.68	0.68	0.68	83
			weighted avg	0.67	0.67	0.67	83

CatBoost

The CatBoost tuned classifier achieved 67% accuracy with good performance across all cirrhosis stages. It performed well for Stage 1 and Stage 3 cases, with Stage 2 showing comparable performance. Most misclassifications occur between adjacent stages, suggesting the model effectively distinguishes between disease progression patterns.

Confusion Matrix for CatBoost tuned Classifier			CatBoost tuned Classifier Report:				
				precision	recall	f1-score	support
True labels	1	2	17	0.71	0.74	0.72	23
	2	3	6	0.59	0.61	0.60	31
	3	1	1	0.74	0.69	0.71	29
			accuracy			0.67	83
			macro avg	0.68	0.68	0.68	83
			weighted avg	0.68	0.67	0.68	83

Voting

The Voting Classifier achieved 68.7% accuracy with excellent performance across all cirrhosis stages. It showed particularly strong results for Stage 1 and Stage 3 cases, with Stage 2 performing adequately. Most misclassifications occur between adjacent stages, demonstrating the model's ability to distinguish different phases of disease progression.

Confusion Matrix for Weighted Voting Ensemble Classifier			Voting Classifier Report:				
				precision	recall	f1-score	support
True labels	1	2	17	0.708	0.739	0.723	23
	2	3	6	0.633	0.613	0.623	31
	3	1	1	0.724	0.724	0.724	29
			accuracy			0.687	83
			macro avg	0.689	0.692	0.690	83
			weighted avg	0.686	0.687	0.686	83



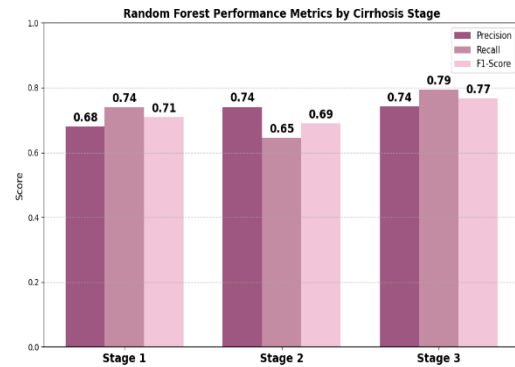
Results and Model Comparison

We evaluated multiple tuned cirrhosis classification algorithms using weighted metrics. F1-score served as our primary criterion due to our dataset's moderate imbalance, with confidence intervals (CI) ensuring that our selection was based on both performance and statistical reliability.

Model	Accuracy	Weighted Precision	Weighted Recall	Weighted F1-Score	CI
Random Forest	0.723	0.724	0.723	0.722	$0.7128 \pm 0.0134 = [0.7027, 0.7229]$
XGBoost	0.711	0.714	0.711	0.711	$0.6991 \pm 0.0190 = [0.6848, 0.7135]$
CatBoost	0.67	0.68	0.67	0.68	$0.6597 \pm 0.0055 = [0.6556, 0.6638]$
ANN	0.578	0.595	0.578	0.581	$0.5787 \pm 0.0176 = [0.5655, 0.5920]$
Light GBM	0.67	0.67	0.67	0.67	$0.6858 \pm 0.0183 = [0.6720, 0.6995]$
Voting	0.687	0.686	0.687	0.686	$0.6749 \pm 0.0105 = [0.6669, 0.6828]$

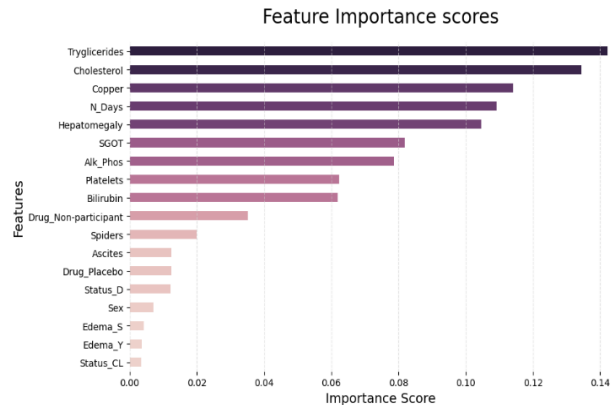
The Chosen Model - Random Forest

Our evaluation identified Random Forest as the optimal model for cirrhosis stage classification, with 0.723 accuracy and 0.722 F1-score. The model's accuracy increases with cirrhosis severity, achieving the highest F1-score (0.77) for Stage 3. This performance ensures patients with advanced cirrhosis requiring immediate intervention are correctly identified, while maintaining balanced overall performance despite relatively lower recall (0.65%) for Stage 2 disease.



Feature Importance Analysis

Triglycerides and Cholesterol emerged as strongest liver disease classification predictors, followed by Copper concentration, treatment duration (N_Days), and Hepatomegaly. Conventional markers like SGOT and Bilirubin showed moderate predictive value, while demographics had minimal impact. This suggests blood lipid panels and copper measurements could enhance liver disease staging efficiency.



Discussion and Conclusions

Model Selection Insights - Ensemble learning algorithms, notably Random Forest, outperformed alternatives for cirrhosis classification (0.72 F1-score), with all models showing higher accuracy for advanced disease stages.

Dataset Limitations - Preserving natural distribution in our limited dataset (412 samples) constrained early-stage classification performance, reflecting a trade-off between data integrity and balanced class performance.

Clinical Applications - Blood lipid indicators as primary predictors suggest potential for metabolic biomarker-focused diagnostic panels over conventional liver function tests, enabling earlier detection of cirrhosis progression.



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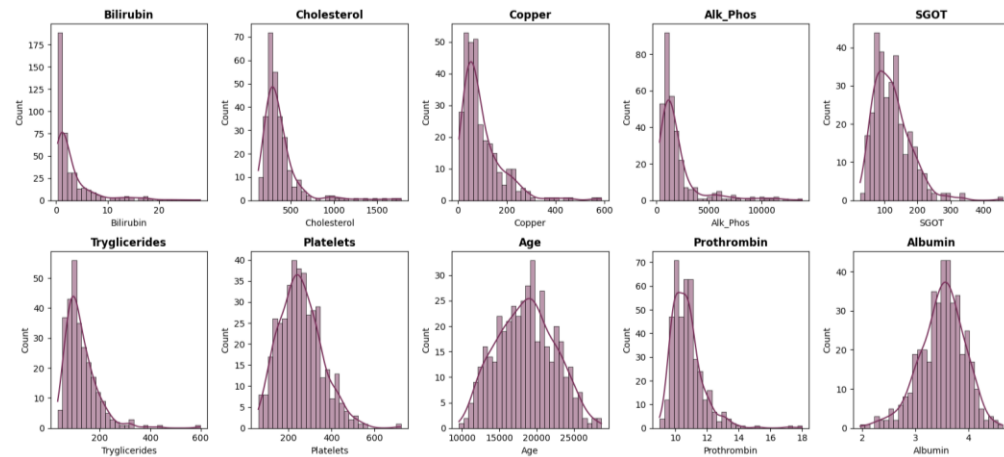
Zhang, Z., Wang, J., Han, W., & Zhao, L. (2021). Using machine learning methods to predict 28-day mortality in patients with hepatic encephalopathy. *BMC Gastroenterology*, 23, 111.



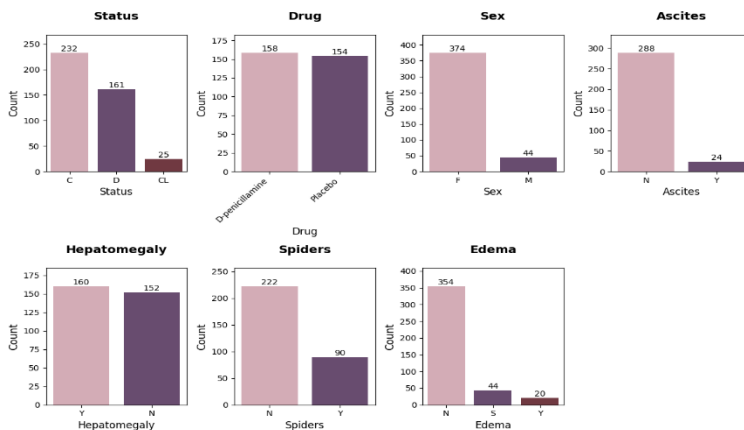
Appendices

Appendix A – Distributions of Continuous Features

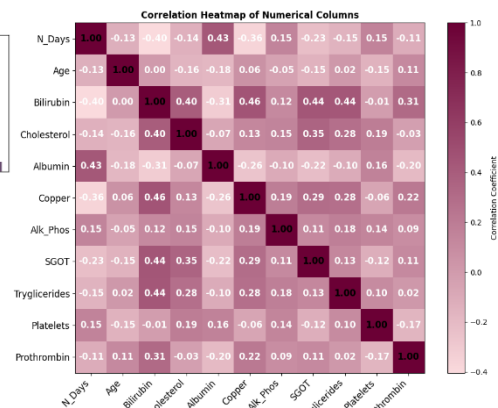
Liver function markers (bilirubin, alkaline phosphatase, SGOT, copper) significantly exceed normal ranges, with elevated cholesterol/triglycerides indicating metabolic abnormalities and borderline albumin suggesting early protein synthesis decline. Mildly prolonged prothrombin times show coagulation impairment, though platelet production remains normal. The middle-aged cohort shows variable disease progression and survival. Right-skewed distributions across biomarkers indicate most patients have moderate disease, with a subset showing severe liver dysfunction affecting multiple systems requiring intensive management.



Appendix B - Statistical description of the categorical variables



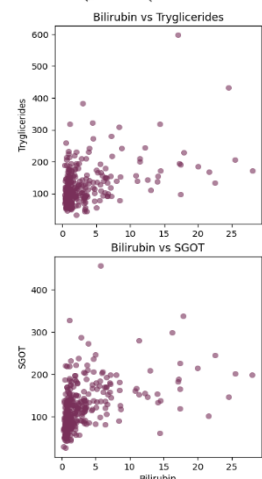
Appendix C - Relationships between variables



Appendix D – Selected scatter plots between variables ($|\text{Correlation}| > 0.4$)

Bilirubin vs Triglycerides: Elevated bilirubin correlated with increased triglycerides despite variability, indicating liver dysfunction disrupts lipid metabolism, linking this liver injury marker to metabolic changes in advanced disease.

Bilirubin vs Copper: Higher bilirubin levels correlated with increased copper despite variability, reflecting liver's diminished copper excretion capacity in advanced diseases like Wilson's or cirrhosis as dysfunction progressed.

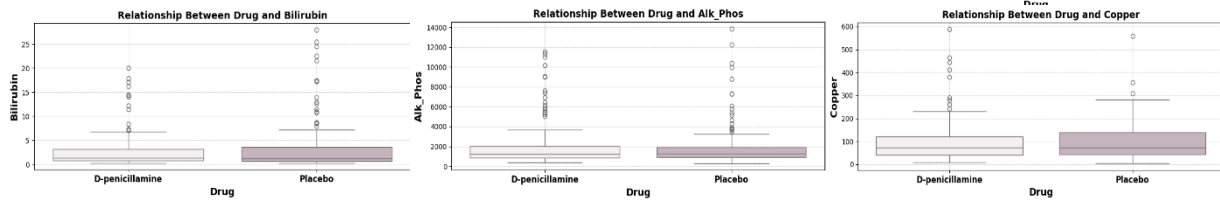




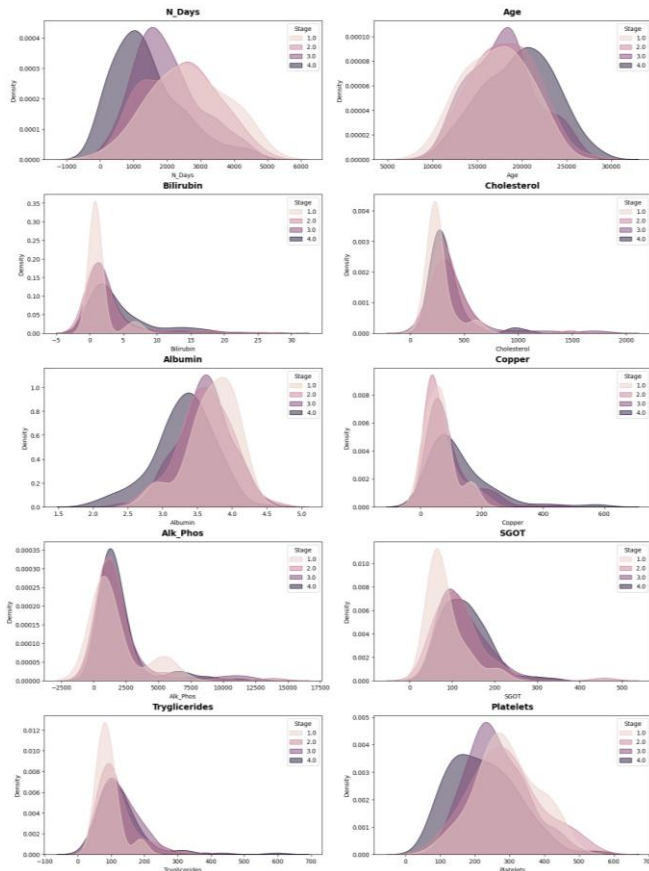
Appendix E - Selected relationships between variables

Age and Stage - Advanced disease stages (3-4) featured older patients than earlier stages (1-2), suggesting association with longer disease duration or gradual organ function decline typical with aging.

Drug and Status - Patient outcomes (alive, transplant, death) were similar between D-penicillamine and placebo groups, indicating no significant impact on survival or transplant rates. While mortality showed no difference, those taking the drug exhibited lower copper, phosphatase, and bilirubin levels.



Appendix F – Distribution of Continuous Features by Stage



Appendix G - Categorical Features Encoding

Feature	VIF	Feature	VIF	Feature	VIF	Feature	VIF
Prothrombin	80.75	Albumin	39.89	Age	14.99	SGOT	7.70
Albumin	64.12	Age	22.53	Platelets	8.77	Platelets	7.48
Age	26.89	Platelets	9.89	SGOT	8.10	Tryglicerides	7.09
Platelets	9.96	SGOT	8.74	Tryglicerides	7.46	Cholesterol	5.85
SGOT	9.01	Tryglicerides	7.69	Cholesterol	5.86	N_Days	4.91
Tryglicerides	7.70	N_Days	7.02	N_Days	5.60	Copper	3.85
N_Days	7.13	Cholesterol	5.90	Copper	3.88	Bilirubin	2.78
Cholesterol	5.90	Copper	3.89	Bilirubin	2.88	Status_D	2.61
Copper	3.89	Bilirubin	2.93	Status_D	2.74	Hepatomegaly	2.39
Bilirubin	2.99	Status_D	2.79	Hepatomegaly	2.51	Alk_Phos	2.34
Status_D	2.79	Hepatomegaly	2.51	Alk_Phos	2.44	Drug_Placebo	1.98
Hepatomegaly	2.54	Alk_Phos	2.45	Edema_Y	1.99	Edema_Y	1.96
Alk_Phos	2.45	Drug_Placebo	2.04	Edema_Y	1.99	Ascites	1.95
Drug_Placebo	2.07	Edema_Y	2.00	Ascites	1.97	Spiders	1.70
Edema_Y	2.04	Ascites	1.98	Drug_Non-participant	1.86	Drug_Non-participant	1.63
Drug_Non-participant	2.03	Drug_Non-participant	1.91	Spiders	1.72	Sex	1.27
Ascites	2.00	Spiders	1.72	Sex	1.29	Edema_S	1.23
Spiders	1.77	Sex	1.29	Edema_S	1.25	Status_CL	1.21
Sex	1.29	Edema_S	1.25	Status_CL	1.23		
Edema_S	1.26	Status_CL	1.24				
Status_CL	1.24						

Figure 1 - all features

Figure 2 - after removing

Figure 3 - after removing Albumin

Figure 4 - after removing Age

