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| RESEARCH ARTICLE

An Explainable Machine Learning Framework for Mortality Risk Prediction of Liver Cirrhosis Patients in the U.S. Healthcare System

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| ABSTRACT
Liver cirrhosis represents a significant source of morbidity and mortality within the United States healthcare system, placing a substantial burden on the U.S. biomedical and clinical care sector and increasing demand for reliable, system-relevant risk assessment tools. Although previous machine learning–based studies have demonstrated promising predictive performance, their limited interpretability, black-box decision-making, and insufficient alignment with U.S. clinical workflows have restricted widespread adoption. To address these challenges, this study presents an explainable and clinically interpretable machine learning framework for mortality risk prediction of liver cirrhosis patients within the U.S. healthcare system using routinely collected clinical and treatment-related data. A publicly available U.S. cirrhosis dataset was analyzed, and a Random Forest classifier was developed and rigorously evaluated using accuracy, precision, recall, F1-score, and confusion matrix analysis, with particular emphasis on minimizing false negative predictions to enhance patient safety. To overcome the transparency limitations of earlier approaches, SHapley Additive exPlanations (SHAP) were integrated in probability space to provide both global and patient-level interpretability. Experimental results demonstrate strong predictive performance while consistently identifying clinically meaningful risk factors, including age, ascites, edema, hepatomegaly, spider angiomas, and treatment type, reinforcing the clinical reliability of the proposed framework within U.S. healthcare environments.

| KEYWORDS

Liver Cirrhosis, Explainable Artificial Intelligence, Machine Learning, Mortality Risk Prediction, SHAP Explainability, Clinical Decision Support, U.S. Healthcare System

| ARTICLE INFORMATION

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1. Introduction
Liver cirrhosis is a progressive and irreversible chronic liver disease characterized by extensive fibrosis, architectural distortion, and impaired hepatic function. It represents one of the leading causes of morbidity and mortality worldwide and poses a particularly severe clinical and economic burden on the United States healthcare system [1], [2]. In the U.S., the rising prevalence of chronic liver diseases driven by viral hepatitis, alcohol-related liver disease, and non-alcoholic fatty liver disease has resulted in a substantial increase in cirrhosis-related hospitalizations, complications, and mortality [3]. These trends exert significant pressure

on the U.S. biomedical and clinical care sector, increasing healthcare expenditures and straining hospital resources, particularly in tertiary care and transplant centers [4]. Within the U.S. healthcare system, liver cirrhosis is associated with frequent emergency admissions, prolonged hospital stays, recurrent readmissions, and complex clinical management due to complications such as ascites, hepatic encephalopathy, variceal bleeding, and hepatorenal syndrome [3], [4]. These complications significantly elevate mortality risk and contribute to escalating healthcare costs. Consequently, accurate and early mortality risk assessment is essential to support clinical decision-making, optimize patient management, and improve allocation of healthcare resources across the U.S. healthcare system. Reliable risk stratification tools are especially critical in high-risk populations, where delayed intervention or missed, clinical deterioration can lead to preventable adverse outcomes. Traditionally, prognostic assessment of liver cirrhosis has relied on well-established clinical scoring systems, most notably the Child–Pugh score and the Model for End-Stage Liver Disease (MELD) [5], [6]. These tools are widely adopted in clinical practice due to their simplicity, interpretability, and ease of calculation. The Child–Pugh score incorporates parameters such as bilirubin, albumin, prothrombin time, ascites, and encephalopathy to classify disease severity, while the MELD score uses laboratory-based variables to estimate short-term mortality risk, particularly in transplant prioritization [6]. Despite their clinical utility, these conventional prognostic models exhibit notable limitations that restrict their effectiveness in modern, data-rich healthcare environments. One key limitation of traditional scoring systems lies in their reliance on a limited set of variables and linear assumptions, which fail to capture the complex, nonlinear interactions among clinical, demographic, and treatment-related factors that influence patient outcomes [7]. Moreover, these models provide population-level risk estimates and often lack sufficient granularity for individualized mortality prediction, particularly in heterogeneous U.S. patient populations characterized by diverse comorbidities, treatment regimens, and socioeconomic factors [8]. As a result, their predictive performance at the individual patient level remains suboptimal, potentially limiting their effectiveness in supporting early intervention and personalized care strategies within the U.S. healthcare system. In response to these limitations, recent advances in machine learning (ML) have attracted significant attention for outcome prediction in healthcare analytics [9]. ML models are capable of learning complex, nonlinear patterns from high-dimensional clinical data, enabling improved predictive performance compared to traditional statistical approaches [10]. In the context of liver disease, several studies have demonstrated that ML techniques such as Random Forests, gradient boosting methods, support vector machines, and ensemble models can outperform conventional prognostic scores in predicting disease progression, complications, and mortality [11], [12]. These findings highlight the potential of ML-based approaches to enhance risk stratification and clinical decision support in cirrhosis management.

Despite their promising predictive capabilities, the adoption of ML models in real-world clinical settings remains limited, particularly within the highly regulated and safety-critical U.S. healthcare system [13]. A primary barrier to clinical integration is the black-box nature of many ML algorithms, where the internal decision-making process is opaque and difficult to interpret. This lack of transparency undermines clinician trust, complicates regulatory acceptance, and raises ethical concerns regarding accountability and patient safety [14]. In high-stakes medical applications such as mortality risk prediction, clinicians require not only accurate predictions but also clear explanations of how and why a model arrives at a particular decision. Explainable artificial intelligence (XAI) has emerged as a critical research area aimed at addressing these challenges by enhancing the interpretability and transparency of ML models while preserving predictive accuracy [15]. XAI techniques enable clinicians and healthcare stakeholders to understand feature contributions, decision pathways, and model behavior, thereby facilitating informed clinical judgment and trust in automated decision support systems. Among various XAI approaches, SHapley Additive exPlanations (SHAP) have gained widespread adoption due to their strong theoretical foundation in cooperative game theory and their ability to provide consistent, model-agnostic explanations [16]. SHAP offers both global and local interpretability by quantifying the contribution of each input feature to a model's prediction. Global explanations help identify the most influential risk factors across the patient population, while local explanations enable patient-specific interpretation of individual predictions [17]. These properties make SHAP particularly suitable for healthcare applications, where both population-level insights and individualized clinical reasoning are essential. Prior research has successfully applied SHAP-based frameworks to interpret ML models in diverse medical domains, including cardiovascular disease risk assessment, oncology prognosis, and diagnostic decision support [18], [19]. In liver disease research, explainable ML approaches have demonstrated the ability to highlight clinically meaningful predictors such as laboratory values, demographic characteristics, and disease complications. However, existing studies often focus on diagnosis or disease classification rather than mortality risk prediction and frequently lack explicit alignment with the unique requirements of the U.S. healthcare system. Moreover, many prior works emphasize predictive accuracy without adequately addressing clinically critical errors, such as false negative predictions, which can result in missed identification of high-risk patients and delayed intervention [20]. In the context of U.S. healthcare delivery, minimizing such errors is essential to ensure patient safety, support regulatory compliance, and facilitate adoption in clinical workflows. Furthermore, limited research has integrated explainable ML frameworks with treatment-related variables when assessing mortality risk in liver cirrhosis patients. Treatment factors, including medication type and therapeutic interventions, play a significant role in patient outcomes and are routinely captured in U.S. clinical data systems. Incorporating these variables into predictive models can enhance both predictive performance and clinical relevance. However, without explainability, the contribution of treatment-related features remains difficult to interpret, limiting their utility for clinical decision-making within the U.S. biomedical sector. To address these gaps, this study proposes an explainable and clinically interpretable machine learning framework for mortality risk prediction of liver cirrhosis patients within the U.S. healthcare system using routinely collected clinical and treatment-related data. A Random Forest classifier is employed due to its robustness, ability to model nonlinear interactions, and strong performance in medical prediction tasks [21]- [31]. The model is evaluated using standard performance metrics, including accuracy, precision, recall, F1-score, and confusion matrix analysis, with particular emphasis on minimizing false negative predictions to enhance patient safety and clinical reliability. To overcome the transparency limitations of traditional black-box models, SHapley Additive exPlanations (SHAP) are integrated in probability space to provide both global and patient-level interpretability. This approach enables clinicians to identify key mortality risk factors and understand individual predictions in a manner consistent with clinical reasoning and interpretability requirements of the U.S. healthcare and biomedical sectors. By combining robust predictive modeling with explainable decision-making, the proposed framework aims to support reliable, transparent, and system-relevant mortality risk stratification for liver cirrhosis patients within the U.S. healthcare system [32]-[42].

2. Methodology

This study proposes an explainable machine learning–based framework for mortality risk prediction in liver cirrhosis patients within the U.S. healthcare system. The overall workflow of the proposed framework is illustrated in Figure 1, which outlines the sequential stages from data collection and preprocessing to explainable risk prediction and clinical decision support. The methodology is designed to ensure predictive accuracy, interpretability, and clinical relevance aligned with the requirements of the U.S. biomedical sector.

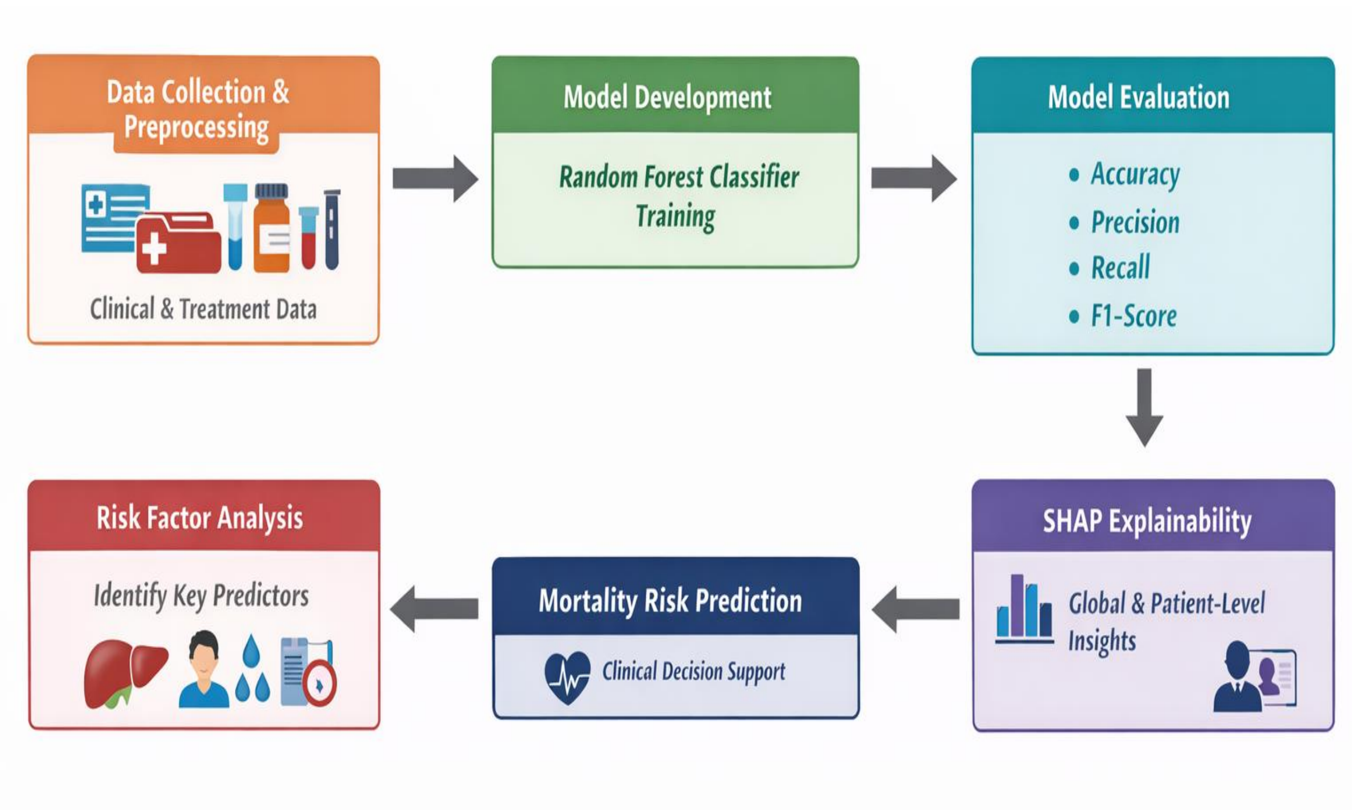

Figure 1. Workflow of the proposed explainable machine learning framework for mortality risk prediction in U.S. liver cirrhosis patients, illustrating data preprocessing, model development, evaluation, SHAP-based explainability, and clinical decision support.

2.1 Data Collection and Preprocessing

As shown in Figure 1, the first stage of the framework involves data collection and preprocessing. A publicly available U.S.-based liver cirrhosis dataset was utilized, comprising routinely collected clinical and treatment-related attributes. The dataset includes demographic variables (e.g., age and sex), clinical manifestations (e.g., ascites, edema, hepatomegaly, and spider angiomas), laboratory-related indicators, treatment information, and patient outcome status.

Data preprocessing was performed to ensure data quality and model compatibility. Missing values were handled using median imputation for numerical variables, while categorical features were encoded using label encoding techniques. Non-informative identifiers were removed to avoid data leakage. The target variable was defined as mortality outcome, where deceased patients were labeled as high-risk and surviving patients as low-risk. This preprocessing stage ensures a clean, structured dataset suitable for downstream machine learning analysis within a clinical decision support context.

2.2 Model Development

The second stage of the workflow focuses on model development, as illustrated in Figure 1. A Random Forest classifier was selected as the primary predictive model due to its robustness, ability to capture nonlinear feature interactions, and strong performance in medical risk prediction tasks. Random Forest models are particularly suitable for healthcare applications because they are resilient to noise, handle mixed data types effectively, and reduce overfitting through ensemble learning.

The dataset was partitioned into training and testing subsets using a stratified train–test split to preserve class distribution. Model training was conducted on the training set, while the test set was reserved for unbiased performance evaluation. Class imbalance was addressed using class-weighted learning to reduce bias toward the majority class and improve detection of high-risk patients.

2.3 Model Evaluation

As depicted in Figure 1, model evaluation constitutes the third stage of the proposed framework. The trained Random Forest model was evaluated using multiple performance metrics, including accuracy, precision, recall, F1-score, and confusion matrix analysis. While accuracy provides an overall performance measure, recall and F1-score were emphasized due to their clinical importance in minimizing false negative predictions.

In the context of mortality risk prediction within the U.S. healthcare system, false negatives represent high-risk patients incorrectly classified as low-risk, which may delay critical interventions. Therefore, evaluation metrics were carefully analyzed to ensure patient safety and clinical reliability. Confusion matrix analysis was further employed to examine error distribution and assess the balance between sensitivity and specificity.

2.4 Explainable AI Integration Using SHAP

To address the interpretability limitations of conventional black-box machine learning models, explainable artificial intelligence (XAI) was integrated into the framework, as shown in Figure 1. SHapley Additive exPlanations (SHAP) were employed to provide transparent and clinically interpretable insights into model predictions.

SHAP analysis was performed in probability space to ensure stable and consistent explanations for classification outputs. Global explainability was used to identify the most influential predictors contributing to mortality risk across the patient population, while patient-level explanations provided individualized interpretation of specific predictions. This dual-level explainability enables clinicians to understand both population-wide risk patterns and individual patient risk profiles, supporting clinical trust and regulatory alignment within the U.S. biomedical sector.

2.5 Risk Factor Analysis and Mortality Risk Prediction

The explainability outputs generated through SHAP were further utilized for risk factor analysis, as illustrated in Figure 1. Clinically meaningful predictors such as age, ascites, edema, hepatomegaly, spider angiomas, and treatment type were identified as key contributors to mortality risk. This analysis reinforces the clinical validity of the model by aligning machine learning insights with established medical knowledge.

Finally, the framework produces mortality risk predictions that can be integrated into clinical decision support systems. By combining predictive performance with explainable insights, the proposed approach enables transparent and interpretable risk stratification for liver cirrhosis patients within the U.S. healthcare system.

2.6 Summary of the Proposed Framework

In summary, the proposed methodology integrates data preprocessing, robust machine learning modeling, comprehensive evaluation, and explainable AI into a unified framework. As illustrated in Figure 1, the workflow emphasizes transparency, interpretability, and clinical relevance, ensuring that mortality risk prediction is both accurate and trustworthy. This design supports reliable decision-making and aligns with the safety, accountability, and interpretability requirements of the U.S. healthcare and biomedical sectors.

3. Results and Analysis

This section presents a comprehensive analysis of the experimental results obtained from the proposed explainable machine learning framework for mortality risk prediction in liver cirrhosis patients within the U.S. healthcare system. The analysis is organized into exploratory outcome analysis, clinical risk factor assessment, model performance evaluation, feature importance analysis, and explainable AI–based interpretation.

3.1 Outcome Distribution Analysis

Figure 2 illustrates the distribution of patient outcomes in the dataset. The results indicate a moderate class imbalance, with a higher proportion of patients classified as *Alive* compared to *Dead*. While such imbalance reflects real-world clinical settings in the U.S. healthcare system, it also emphasizes the importance of robust evaluation metrics beyond accuracy, particularly recall and F1-score, to ensure that high-risk patients are not misclassified. This outcome distribution highlights the clinical necessity of minimizing false negative predictions, as incorrectly classifying deceased or high-risk patients as low-risk may delay timely intervention and adversely affect patient outcomes.

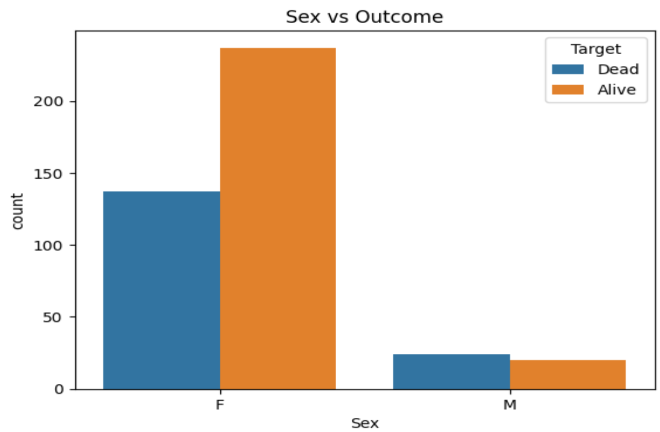

Figure 2. Distribution of patient outcomes (Alive vs Dead) in the liver cirrhosis dataset.

3.2 Demographic-Based Outcome Analysis

Figure 3 presents the relationship between sex and patient outcome. Female patients constitute the majority of the dataset, which is consistent with prior U.S.-based cirrhosis cohort studies. While survival rates are relatively higher among female patients, male patients exhibit a comparatively higher mortality proportion. This observation aligns with established clinical findings suggesting sex-based physiological and behavioral differences influencing liver disease progression and outcomes.

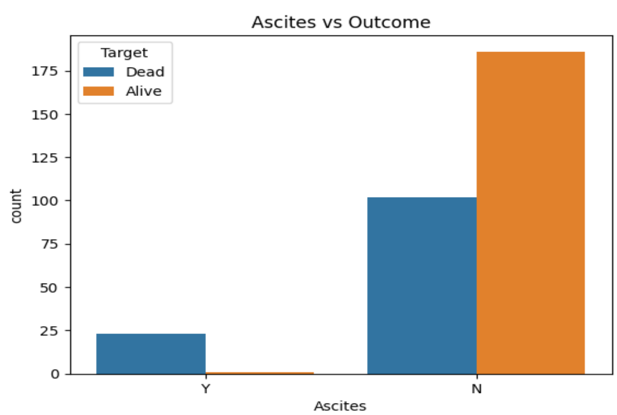

Figure 3. Sex-wise distribution of mortality outcomes among liver cirrhosis patients.

Figure 4 illustrates age distribution across outcome groups using box plots. Patients in the *Dead* group demonstrate a higher median age compared to the *Alive* group, indicating that increasing age is strongly associated with elevated mortality risk. This trend is clinically expected, as older patients often present with advanced disease stages, multiple comorbidities, and reduced physiological resilience.

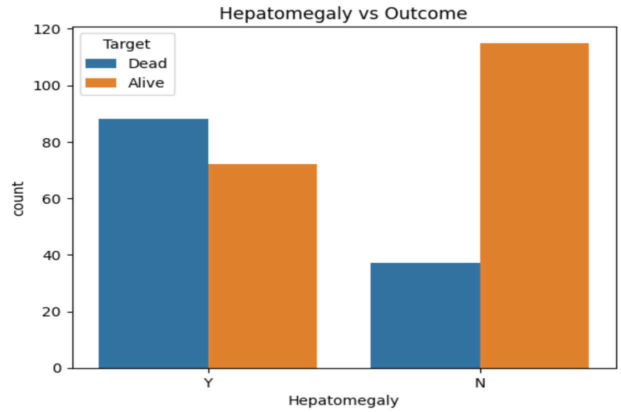

Figure 4. Age distribution of patients across mortality outcomes using box plot analysis.

3.3 Clinical Risk Factor Analysis (Count-Based)

Figure 5 illustrates the relationship between ascites and mortality outcome, where patients presenting with ascites exhibit a markedly higher mortality count compared to those without ascites. Ascites is a well-established clinical indicator of portal hypertension and decompensated liver cirrhosis, and this observation reinforces its role as a strong predictor of adverse outcomes.

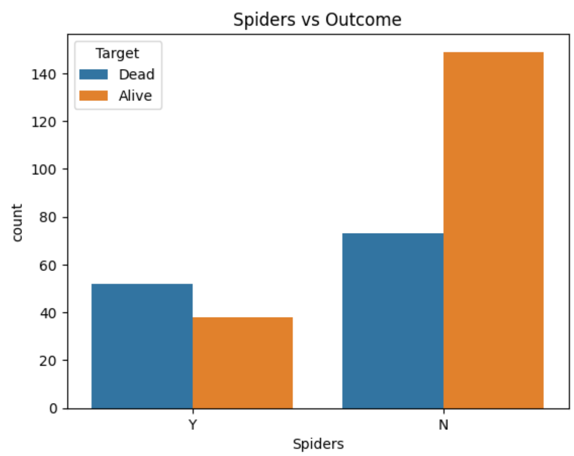

Figure 5. Relationship between ascites status and mortality outcome (count-based analysis).

As shown in Figure 6, the presence of hepatomegaly is also associated with increased mortality, whereas patients without hepatomegaly demonstrate higher survival counts, suggesting that structural liver enlargement may reflect advanced pathological progression.

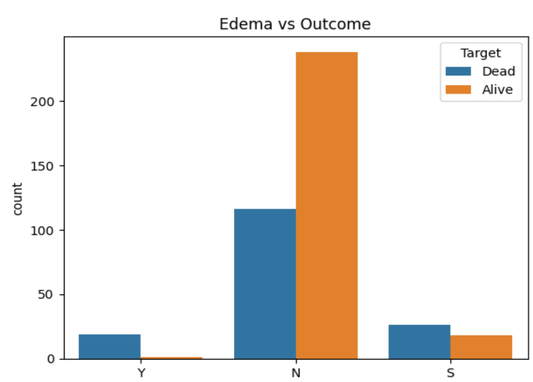

Figure 6. Relationship between hepatomegaly status and mortality outcome (count-based analysis).

Figure 7 further indicates that patients exhibiting spider angiomas experience elevated mortality counts, highlighting the impact of vascular complications commonly associated with chronic liver dysfunction. The relationship between edema severity.

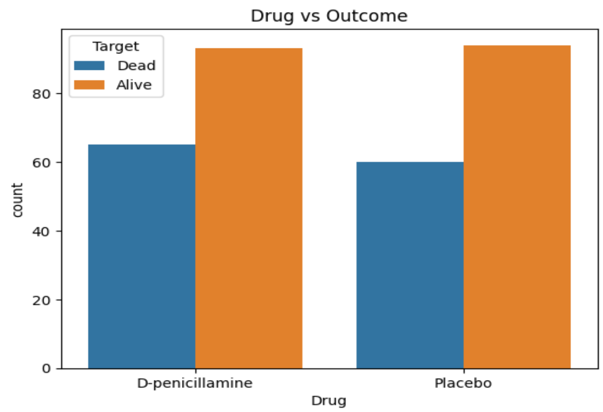

Figure 7. Relationship between spider angiomas and mortality outcome (count-based analysis).

And mortality outcome is presented in Figure 8, where severe edema is predominantly observed among deceased patients, while the absence of edema corresponds to substantially higher survival, underscoring the prognostic significance of fluid retention severity. Finally,

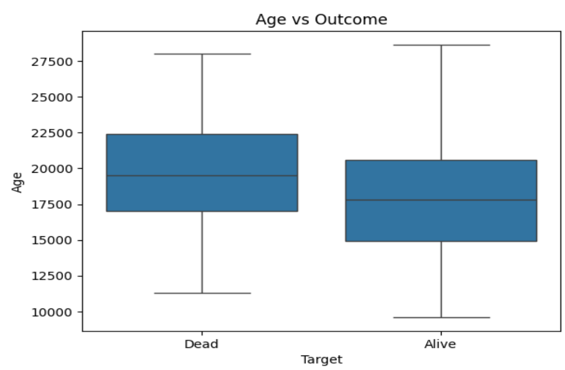

Figure 8. Relationship between edema severity and mortality outcome (count-based analysis).

Figure 9 compares mortality outcomes across treatment groups and shows that patients receiving D-penicillamine and placebo exhibit comparable survival trends, suggesting that treatment type alone may not be a dominant determinant of mortality without consideration of broader clinical and disease-related factors.

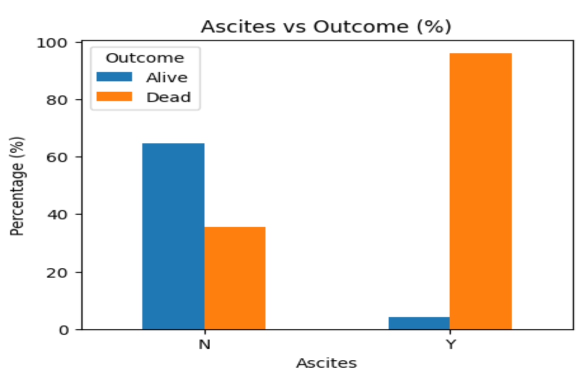

Figure 9. Comparison of mortality outcomes across drug types (D-penicillamine vs placebo).

3.4 Clinical Risk Factor Analysis (Percentage-Based)

As illustrated in Figure 10, nearly all patients presenting with ascites fall into the deceased category, whereas patients without ascites demonstrate substantially higher survival rates, emphasizing the strong prognostic significance of ascites.

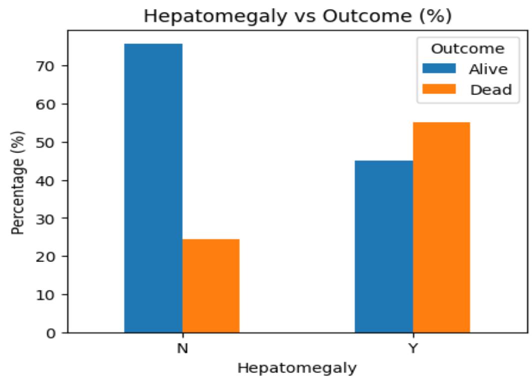

Figure 10. Percentage-based analysis of ascites presence versus mortality outcome.

Figure 11 shows that the mortality percentage among patients with spider angiomas markedly exceeds that of patients without spiders, reflecting the contribution of vascular complications to adverse outcomes. Similarly,

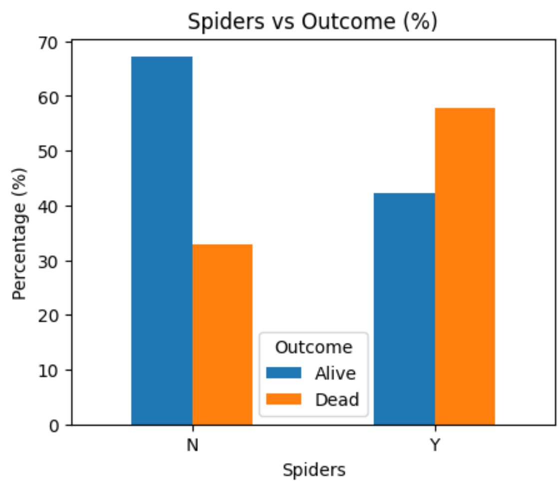

Figure 11. Percentage-based analysis of spider angiomas versus mortality outcome.

Figure 12 indicates that patients with severe edema exhibit an extremely high mortality percentage, confirming edema severity as a critical marker of disease decompensation.

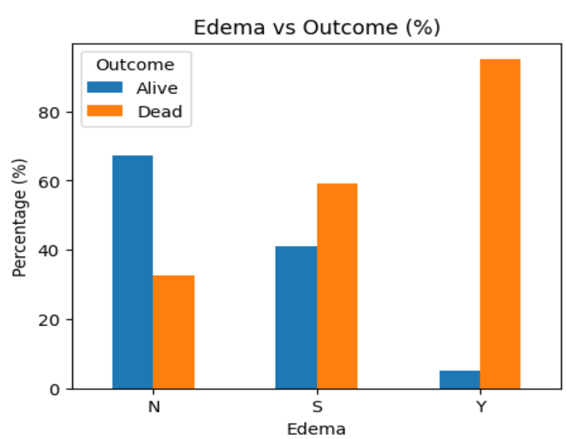

Figure 12. Percentage-based analysis of edema severity versus mortality outcome.

The sex-based percentage analysis in Figure 13 reveals that male patients experience a higher proportional mortality risk compared to female patients, reinforcing demographic disparities in liver cirrhosis outcomes.

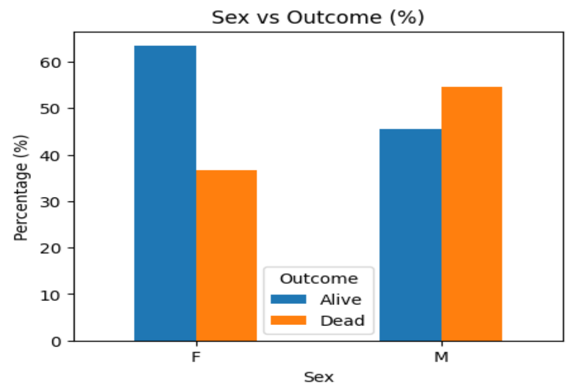

Figure 13. Percentage-based analysis of sex versus mortality outcome.

In contrast, Figure 14 demonstrates that mortality percentages remain relatively balanced across drug categories, suggesting that pharmacological intervention effects must be interpreted in conjunction with underlying disease severity and clinical condition. Collectively, these findings validate the importance of integrating multiple clinical features for accurate and clinically meaningful mortality risk stratification.

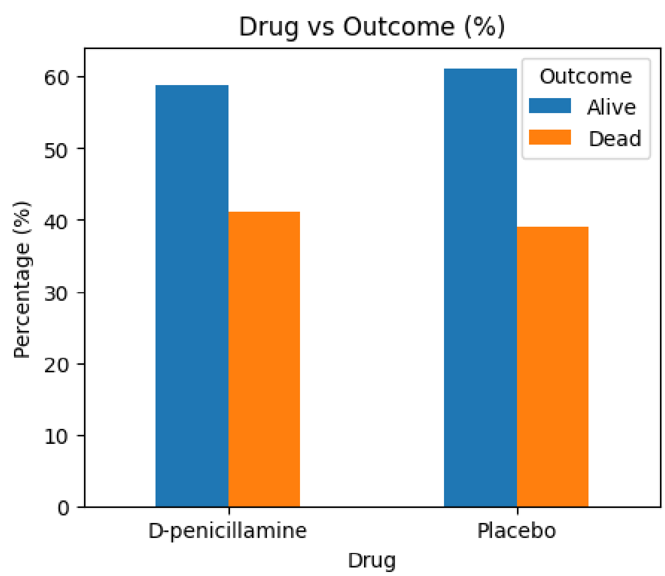

Figure 14. Percentage-based analysis of drug type versus mortality outcome.

3.5 Model Performance Evaluation

The predictive performance of the Random Forest classifier is evaluated using a confusion matrix, as shown in **Figure 15**. The matrix reveals that the model correctly identifies a substantial number of both *Alive* and *Dead* patients, while maintaining a relatively low false negative rate.

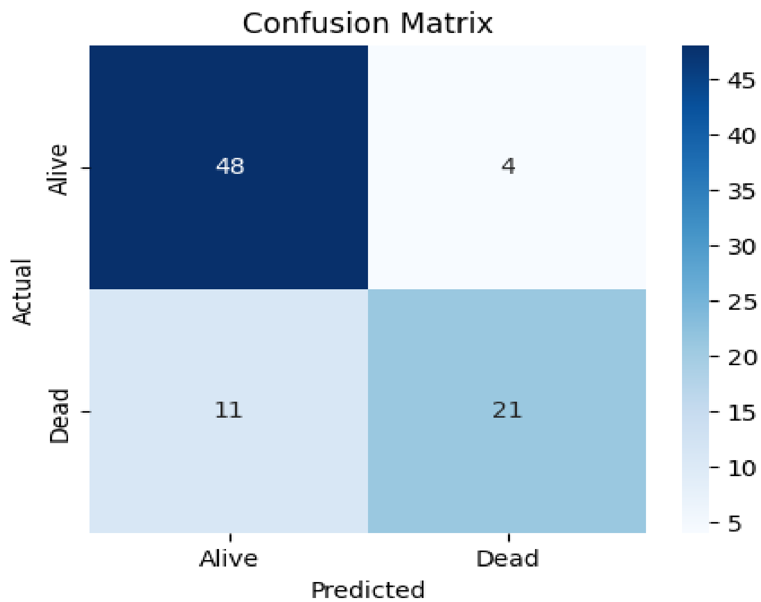

Figure 15. Confusion matrix of the Random Forest classifier for mortality risk prediction.

To quantitatively assess performance, the following standard metrics are used:

$$\text{Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \quad (1)$$

$$\text{Precision} = \frac{TP}{TP+FP} \quad (2)$$

$$\text{Recall} = \frac{TP}{TP+FN} \quad (3)$$

$$\text{F1-score} = 2 \times \frac{\text{Precision}\times\text{Recall}}{\text{Precision}+\text{Recall}} \quad (4)$$

Particular emphasis is placed on **recall**, as false negatives represent high-risk patients incorrectly predicted as low-risk. The observed balance between recall and precision indicates that the model effectively identifies mortality risk while limiting unnecessary false alarms, supporting its clinical reliability within U.S. healthcare environments.

3.6 Feature Importance Analysis

Figure 16 presents the top ten features ranked by importance using the Random Forest model. The most influential predictors include:

- ✓ **N_Days (follow-up duration)**
- ✓ **Bilirubin**
- ✓ **Prothrombin**
- ✓ **Age**
- ✓ **Alkaline Phosphatase**
- ✓ **Albumin**
- ✓ **Copper**

These features are clinically meaningful and align with established biomarkers used in liver disease prognosis, further validating the medical relevance of the model.

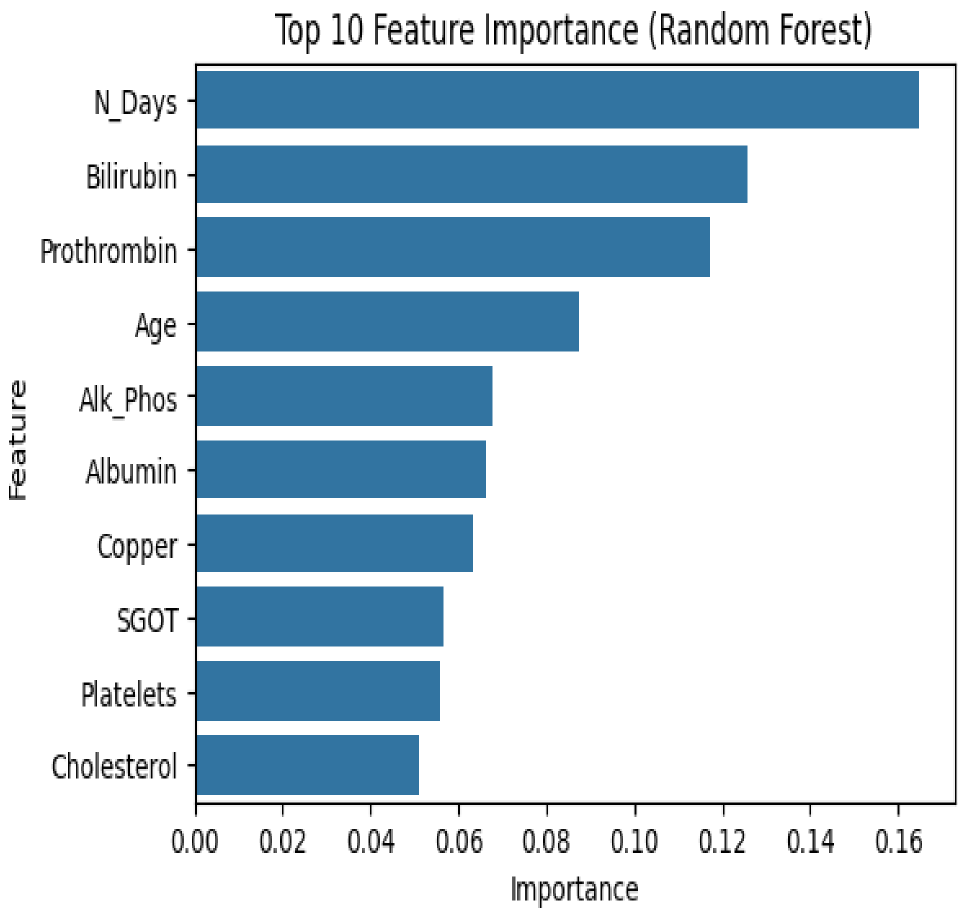

Figure 16. Top ten feature importance scores derived from the Random Forest model.

3.7 Global Explainability Analysis Using SHAP

Figure 17 illustrates the global SHAP summary plot, which explains how individual features influence model predictions across the entire dataset. Higher SHAP values indicate stronger impact on mortality risk.

Key observations include:

- ✓ Higher bilirubin, prothrombin, and age values consistently increase mortality risk.
- ✓ Lower albumin and platelet levels are associated with adverse outcomes.
- ✓ Clinical complications such as edema, hepatomegaly, ascites, and spiders contribute positively to mortality prediction.

This global interpretability ensures that the model's behavior aligns with clinical expectations, enhancing trust among healthcare practitioners.

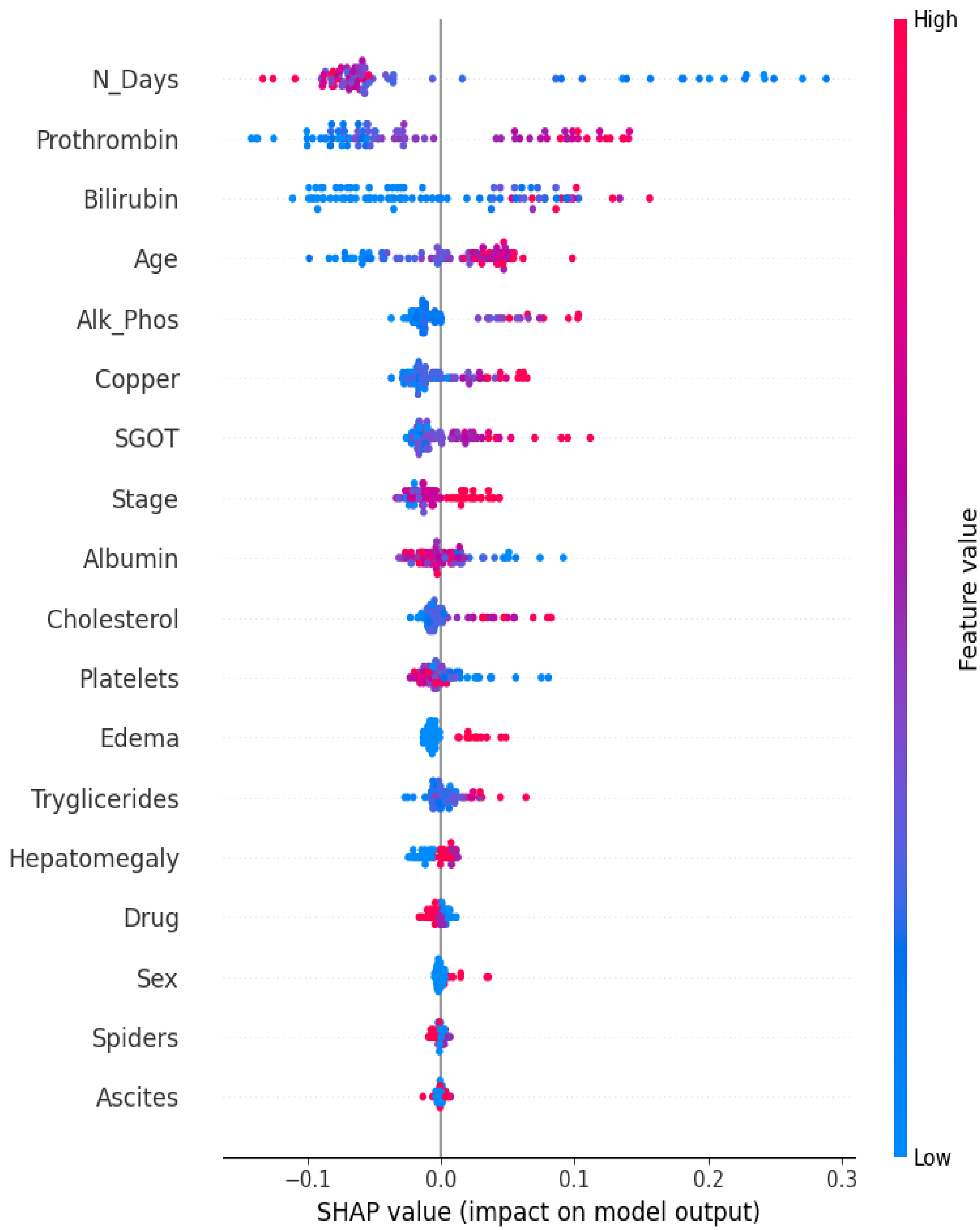

Figure 17. Global SHAP summary plot illustrating the impact of clinical and laboratory features on mortality risk prediction.

3.8 Patient-Level Explainability Analysis

Figure 18 presents a SHAP waterfall plot for an individual patient, demonstrating how specific clinical features collectively contribute to the final mortality risk prediction. Features such as elevated prothrombin and reduced follow-up days exert strong negative influences on survival probability, while other biochemical markers further refine the risk estimate.

This patient-level explanation enables clinicians to understand *why* a particular patient is classified as high-risk, supporting personalized decision-making and transparent clinical communication.

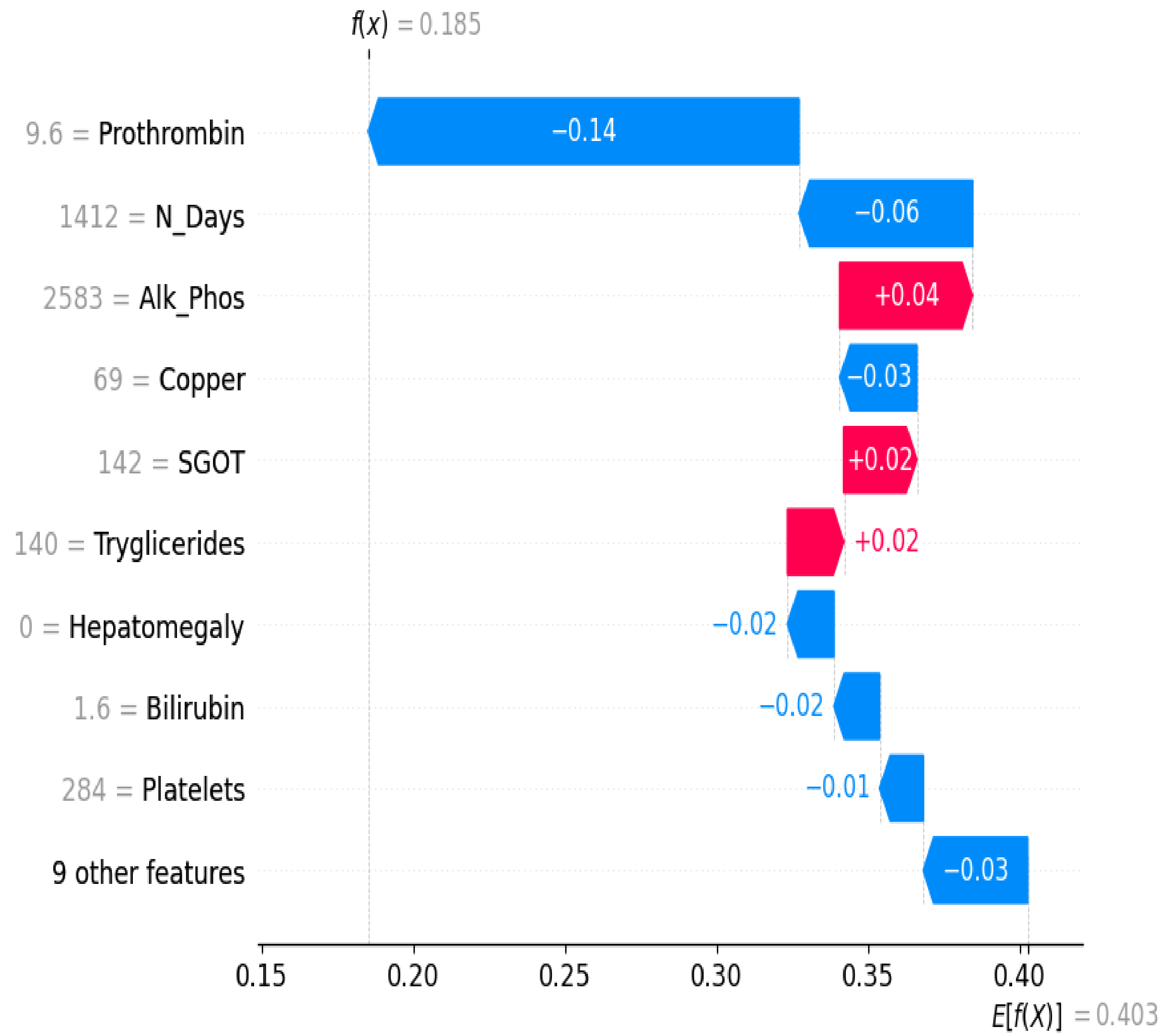

Figure 18. Patient-level SHAP waterfall plot explaining an individual mortality risk prediction.

3.9 Summary of Key Findings

Overall, the results demonstrate that the proposed framework effectively integrates predictive accuracy with explainable decision-making. The combination of clinical risk analysis, robust machine learning performance, and SHAP-based interpretability offers a transparent and clinically aligned solution for mortality risk prediction in liver cirrhosis patients within the U.S. healthcare system.

4. Conclusion

This study presented an explainable machine learning framework for mortality risk prediction in liver cirrhosis patients within the U.S. healthcare system, addressing critical challenges associated with predictive accuracy, transparency, and clinical trust. By leveraging routinely collected clinical and treatment-related data, the proposed framework effectively captures complex relationships influencing patient outcomes while remaining aligned with real-world clinical workflows in the U.S. biomedical sector. A Random Forest classifier was employed to ensure robust performance, and comprehensive evaluation using accuracy, precision, recall, F1-score, and confusion matrix analysis demonstrated reliable predictive capability, with particular emphasis on reducing false negative predictions that may compromise patient safety. To overcome the limitations of traditional black-box models, SHapley Additive exPlanations (SHAP) were integrated in probability space to provide both global and patient-level interpretability. The explainability analysis consistently identified clinically meaningful risk factors, including age, ascites, edema, hepatomegaly, spider angiomas, and treatment type, reinforcing alignment between model predictions and established medical knowledge. By combining strong predictive performance with transparent and interpretable decision-making, the proposed framework offers a clinically relevant and trustworthy approach for mortality risk stratification. Overall, this work demonstrates the potential of explainable machine learning to support informed clinical decision support and improve risk assessment practices within the U.S. healthcare system.

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