Semi-Parametric and Accelerated Failure Time Survival Models for Heart Failure Prediction

Hussin Ragb\textsuperscript{1}, Radhavaram Sriram Akhil\textsuperscript{1}, and Meghana Cheetakonduru\textsuperscript{1}

\textsuperscript{1}Christian Brothers University

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Hussin Ragb, Radhavaram Sriram Akhil, Meghana Cheetakonduru

1Christian Brothers University, Memphis, TN. {hragb@cbu.edu }
2Christian Brothers University, Memphis, TN. { snadhava@cbu.edu }
3Christian Brothers University, Memphis, TN. { mcheetak@cbu.edu }

ABSTRACT

Heart failure is a leading cause of death among Diabetic and Obese patients globally, contributing to 8.5% of all heart disease deaths and potentially 36% of cardiovascular disease deaths. Early detection is crucial for timely intervention, reducing symptoms, lowering hospitalizations, and improving patient outcomes through personalized management. This paper presents the use of Semi-Parametric and Accelerated Failure Time survival models (AFT) on Heart failure prediction. Cox Proportional Hazard model from the family of Semi-Parametric survival models and Weibull’s Accelerated Failure Time models from the family of Accelerated Failure Time models have been compared and contrasted. The Cox proportional hazard allows for the examination of covariate effects on the hazard function, making it a widely used survival model. Weibull AFT model follows a parametric approach, directly estimating the distribution of the survival time. Medical records data of close to 299 patients, who had heart failure, collected during their clinical follow-up period is used for building and evaluating the model. The final evaluation of model performance was conducted, focusing on their capacity to predict the probability of patient survival beyond 250 days from the clinical visit. Among the Cox proportional hazard model and Weibull’s AFT model, the Weibull’s AFT model demonstrated superior performance compared to the Cox model. Remarkably, Weibull’s model exhibited consistently exceptional performance in both train and test validations.

Keywords: Semi-Parametric and Accelerated Failure Time survival models, Cox Proportional Hazard model, Heart Failure Prediction, Weibull AFT model.

1 Introduction

Heart failure, a pervasive and often devastating condition, remains a prominent contributor to mortality rates worldwide, particularly within the diabetic and obese patient populations. Despite advancements in medical science and technology, its prevalence continues to escalate, posing a significant public health concern. In the United States alone, as reported by the Heart Failure Society of America [3], approximately 6.5 million individuals aged 20 and above grapple with the burdens of heart failure. This ailment holds substantial sway in cardiovascular-related deaths, accounting for a noteworthy 8.5% of all fatalities attributable to heart disease and potentially contributing to 36% of the overall mortality associated with cardiovascular diseases.

The ramifications of heart failure extend far beyond mere statistics. Timely detection emerges as a cornerstone for proactive intervention and improved prognosis. Early identification not only enables the implementation of lifestyle adjustments but also plays a pivotal role in symptom management and enhancing the overall quality of life for affected individuals. Moreover, this proactive stance serves to diminish the frequency of hospitalizations and concurrently mitigates the financial burdens associated with prolonged medical care. By embracing personalized management strategies rooted in early detection, healthcare providers can steer patients towards
better outcomes, fostering awareness, and facilitating targeted interventions aimed at addressing underlying causes and risk factors.

Amidst the arsenal of predictive analytics tools, various classification and regression techniques have been employed for the anticipation of heart failure onset. However, we contend that the adoption of Survival models represents a paradigm shift, offering nuanced insights that traditional methods may overlook. Unlike conventional approaches, survival models furnish Hazard or Survival rates for each feature, furnishing clinicians with invaluable insights to tailor treatment strategies to individual patient profiles effectively. Within the ambit of our ongoing project, we endeavor to harness the predictive power of both Semi-Parametric [1] and Accelerated Failure Time (AFT) survival models [2].

Specifically, our undertaking involves the development, evaluation, and comparative analysis of two prominent methodologies: The Cox Proportional Hazard model [2] (Semi-Parametric) and the Weibull AFT [3] (Parametric) models for heart failure prediction. By meticulously crafting and fine-tuning these models, we aim to deliver a robust predictive framework that can be seamlessly integrated into a user-friendly web application developed using Python Streamlit. This holistic approach not only underscores the critical importance of early detection in the management of heart failure but also highlights the transformative potential of innovative modeling techniques in advancing predictive analytics within the realm of cardiovascular health.

2 Materials and Method

2.1 Dataset

The data for the current research has been extracted from the UCI Machine Learning Repository, an open-source web application hosting dataset for machine learning experimentation purposes. From the UCI Machine Learning Repository, the 'Heart Failure Clinical Records' dataset has been selected for the current experimentation settings. Below is the link to the data source:
https://archive.ics.uci.edu/dataset/519/heart+failure+clinical+records

The dataset contains the medical records of 299 patients who experienced heart failure, and the data were collected during their follow-up period. Each patient profile includes 13 clinical features.

1. **Age**: age of the patient (years)
2. **Anaemia**: decrease of red blood cells or hemoglobin (boolean)
3. **Creatinine phosphokinase** (CPK): level of the CPK enzyme in the blood (mcg/L)
4. **Diabetes**: if the patient has diabetes (boolean)
5. **Ejection fraction**: percentage of blood leaving the heart at each contraction (percentage)
6. **High blood pressure**: if the patient has hypertension (boolean)
7. **Platelets**: platelets in the blood (kiloplatelets/mL)
8. **Sex**: woman or man (binary)
9. **Serum creatinine**: level of serum creatinine in the blood (mg/dL)
10. **Serum sodium**: level of serum sodium in the blood (mEq/L)
11. **Smoking**: if the patient smokes or not (boolean)
12. **Time**: follow-up period (days)
13. **[Target] death event**: if the patient died during the follow-up period (boolean)

2.2 Suggested Approach

Existing online research resources predominantly employ classification models for predicting heart failure events. Notable research papers focus on utilizing machine learning for heart failure prediction. However, our proposal suggests a departure from traditional classification models and advocates for the use of Weibull's Accelerated Failure Time (AFT) model and Cox Proportional Hazard model. These survival models aim to
address the limitations of classification models by providing insights into the time to event and the evolution of outcomes over time in the context of heart failure prediction.

The following are the high-level steps involved in the execution of the current research:

- Performing data exploration
- Performing correlation analysis to understand redundant factors responsible for heart failure events
- Analyzing missing/outlier values in the data and treating them accordingly
- Plotting and analyzing univariate distributions for surviving and non-surviving categories to understand key features useful for survival prediction
- Creating and analyzing partial Kaplan-Meier survival curves for identifying key features influencing heart failure events
- Overlaying partial survival curves and performing log-rank tests to identify significant features contributing to heart failure events
- Developing code for the Weibull AFT model and evaluating its performance in predicting patients' survival post 250 days
- Developing, tuning, and evaluating the Cox Proportional Hazard model in predicting patients' survival post 250 days
- Comparing the performance of the Cox Proportional Hazard model with the Weibull AFT model.

[Refer to Figure 1 below showing the high-level architecture of the proposed heart failure prediction model.]

Figure 1: the proposed heart failure prediction model.

2.2.1 Analyzing Univariate Distributions for Surviving and Non-Surviving Patients

Analyzed univariate distribution for surviving and non-surviving categories to understand key features useful for survival prediction. Following are some key insights:

- Death events are increasing with an increase in age
- Creatinine phosphokinase value is increasing in the event of death
- Ejection fraction is relatively lower for death events
- Platelets, serum sodium counts do not show any difference in death vs survival rate
- Serum creatinine value is increasing in the event of death
- Patients with Anaemia and High BP have a higher tendency to contract heart failure
[Refer to Figure 2 below showing these Univariate distributions across key parameters].

**Figure 2: Univariate Distribution of Surviving and Dying Patients (0 = Surviving Patients, 1 = Patients with Heart Failure).**
2.2.2: Analyzing Partial Kaplan Meier Survival Curves for Heart Failure Patients

Analyzed partial Kaplan Meier survival curves [4], [5] for identifying key features influencing heart failure events. Overlayed partial survival curves and log-rank test for identifying significant features contributing to heart failure events. We observe that Blood Pressure and Gender have a major influence on Heart Failure as log-rank test shows very positive results for these features.

A surprising observation shows that the survival curve for patients with and without high diabetics is more or less similar and passed the log-rank test marginally (with p=0.04).

[Refer to Figure 3 (a-c) below showing Kaplan Meier Survival Curves for Heart Failure Patients].

![Figure 3(a): Partial Kaplan Meier Survival Curves of Key Features (Anaemia, diabetes, and high blood pressure)](image)

![Figure 3(b): Partial Kaplan Meier Survival Curves of Key Features (sex, smoking, and age)](image)
2.2.3: Correlation Analysis of Key Factors Influencing Heart Failure

Correlation analysis in survival models is essential for identifying relationships between variables impacting the time to an event, enhancing predictive accuracy [10], [11]. It aids in uncovering dependencies crucial for understanding how different factors influence survival outcomes [12], [17]. By assessing correlations, we gain insights into the interplay of variables, allowing for more nuanced and informed model development [13], [14]. We didn't observe any major correlations in the data which is a very good sign for the model developed. [Refer to Figure 4 below showing Pearson and Spearman’s Correlation for Key Features].

Pearson Correlation

![Pearson Correlation](image1.png)

Spearman Correlation

![Spearman Correlation](image2.png)

Figure 3(c): Partial Kaplan Meier Survival Curves of Key Features (creatine phosphokinase, ejection fraction, serum sodium)

Figure 4: Pearson and Spearman’s Correlation for Key Features
2.2.4 Weibull’s AFT Model

Weibull’s Accelerated Failure Time (AFT) [6], [7] model is a survival analysis tool used to predict the time until an event occurs. Unlike hazard-based models, the AFT model directly models the event's time distribution. It assumes a specific distribution, often skewed, and estimates parameters that represent the acceleration or deceleration of time to the event. This model is versatile, accommodating different underlying distributions, such as Weibull, log-logistic, or log-normal. A key advantage is its interpretability, as coefficients directly relate to changes in the event's time. It is extensively used in reliability engineering, medicine, and finance for analyzing time-to-event data.

The AFT model provides valuable insights into the impact of covariates on survival times, aiding in risk assessment and decision-making. Researchers often prefer the AFT model when assumptions about proportional hazards are not met, making it a robust choice in various real-world scenarios.

2.2.5 COX Proportional Survival Model

The Cox Proportional Hazard [8], [9] model is a survival analysis technique widely used to analyze time-to-event data. It operates without assuming a specific survival distribution, making it versatile for diverse datasets. This model estimates the hazard function, representing the instantaneous event risk. It assumes that the effects of covariates on the hazard remain proportional over time, providing a powerful tool for exploring relationships between predictors and survival outcomes. The hazard ratio, a key output, quantifies the relative change in the hazard for a unit change in a covariate [8], [9], [15], [16].

The Cox model is extensively applied in medical research, social sciences, and beyond, offering insights into factors influencing survival without requiring stringent assumptions about the underlying survival times. Its flexibility and interpretability contribute to its popularity in the analysis of complex time-to-event data. [Refer to equation 1 for Cox Proportional Survival Model].

\[
    h(t|X) = h_0(t) \cdot e^{\beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_p X_p}
\]

Where:
- \( h(t|X) \) is the hazard function at time \( t \) given the values of covariates \( X \).
- \( h_0(t) \) is the baseline hazard function, representing the hazard at time \( t \) when all covariates are zero.
- \( \beta_1, \beta_2, \ldots, \beta_p \) are the coefficients associated with covariates \( X_1, X_2, \ldots, X_p \) respectively.

3 Experimental Results

3.1 COX Proportional Survival Model - Results

The Cox Proportional Hazard survival model, trained on 209 patients and tested on 90 patients, demonstrates moderate performance in predicting heart failure events within the upcoming 250 days. In the training set, the model achieves an accuracy of 85.6%, correctly classifying patients' outcomes. The precision and recall metrics are 87.8% and 91.5%, respectively, indicating the model's ability to make accurate positive predictions and identify relevant cases.

On the test set, the model maintains a reasonable level of performance, with an accuracy of 81.1%, precision of 84.5%, and recall of 86.0%. These metrics suggest that the model generalizes adequately to new patient data. The Concordance Index of 0.74 indicates a good ability to rank patients based on their risk of heart failure within the specified time frame. Overall, the model exhibits balanced performance, considering the limited dataset, with potential clinical utility for risk prediction. [Refer to Figure 6 below showing the performance of Weibull’s model on Train and Test datasets].
3.2 Weibull AFT Model - Results

Weibull’s Survival Model, trained on a dataset of 209 patients out of a total of 299, displays promising predictive capabilities for heart failure events. With an accuracy of 88.5% on the training set, the model correctly identifies patients’ outcomes. Precision and recall, at 90.5% and 93.1% respectively, highlight the model’s ability to make accurate positive predictions.

Upon generalization to the test set of patients (remaining 90 out of 299), the model maintains robust performance with an accuracy of 85.6%, precision of 84.5%, and recall of 89.5%. The Concordance Index of 0.74 reinforces the model’s effectiveness in ranking patients based on their risk of heart failure within the upcoming 250 days. The model’s balanced performance, considering the limited training data, underscores its potential clinical utility.  

[Refer to Figure 7 below showing the performance of Weibull’s model on Train and Test datasets]
COX and Weibull’s Model Comparison and Final Model Inferences:

Although the concordance index of both the models (COX and Weibull) is the same, Weibull model outperformed COX model across all the parameters of accuracy, precision, and recall. The test accuracy of the COX model is 68.3% while that of Weibull model is 71.6% (advantage by 3.3%).

Weibull’s AFT model outperformed COX Proportional hazards model in all parameters (Accuracy, Precision, and Recall) and hence selected as the best model.

Model Output Inferences – log (accelerated death rate):

Analysis of the log (accelerated death rate) of the model for patients across various features shows that Gender, Smoking, Serum Sodium, and Ejection Fraction are the factors responsible for the increase in heart failure. The remaining factors (apart from the above four) are inversely proportional to death due to heart failure. The impact from Sex, Smoking, Diabetes, and Anemia has a high CI leading to higher uncertainty. The Exp(coef) represents the hazard ratio, i.e., the Exp(Coef) for Smoking is 1.09, which basically conveys that patients who smoke tend to have a 9% higher chance of dying than patients who do not smoke. [Refer to Figure 8 below, showing the log (accelerated death rate) from the model, illustrating key features influencing survival and death rates].

![Figure 8: log(accelerated death rate) from Model showing key features influencing survival and death rates](image)

Model Output Inferences - Weibull’s Partial Dependency Survival Curves:

Weibull’s Partial Dependency curves provided key information on the behavior of patients' survival across top key features.

- Patients who smoke have a 3% higher chance of dying from heart failure after 250 days from the consultation period.
- Male patients have nearly a 3% higher chance of dying due to heart failure than female patients.

Ejection Fraction plays a critical role in determining heart failure. As ejection fraction decreases, the probability of heart failure increases exponentially. Refer to Figure 9 below, which shows the drastic change in survival curves for patients with different ejection fraction values. Similar to Ejection Fraction, Serum Sodium and Creatinine Phosphokinase values in the body critically influence the chances of heart failure. [Refer to Figure 9 below showing Weibull’s Partial Dependency Survival Curves for Key Features].
4 Conclusion

In the realm of heart failure prediction, traditional classification models have been predominant in online research. However, we advocate for a departure from this approach by proposing the use of Weibull's Accelerated Failure Time (AFT) model and the Cox Proportional Hazard model. Unlike classification models, these survival models offer insights into the time-to-event aspect, addressing the limitations of traditional approaches.

The developed Weibull's AFT model demonstrates robust performance with a 74% concordance index, achieving 88.5% accuracy in the test set and 85.6% in the training set, with a notable recall of 89.5%. Similarly, the Cox Proportional Hazards model performs well, maintaining consistent accuracy and recall.

Comparatively, the Weibull's AFT model outperforms the Cox model across multiple metrics, including accuracy, precision, and recall, with a notable 4.5% advantage in test accuracy. Further analysis identifies factors such as Gender, Smoking, Sodium Serum, and Ejection influencing heart failure risk, with Smoking showing a 9% higher likelihood of death for smokers compared to non-smokers. However, factors like Sex, Smoking, Diabetes, and Anemia exhibit high uncertainty.

References


