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Modeling Mortality in Heart Failure Patients: Considering Time-Varying Effects - A Bayesian Survival Analysis Utilizing Bayesian AFT Model with the INLA Method

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Abstract

Heart failure and disease ranks among the most common illnesses globally. Heart failure is a condition where the heart cannot pump blood efficiently, posing a growing global public health challenge with a high mortality rate. This study aimed to identify factors influencing the survival time of heart failure patients. Using secondary data, 299 heart failure patients were studied based on medical records from a 12-month enrollment period. The analysis employed Kaplan-Meier plots and Bayesian parametric survival models, utilizing SPSS and R software, with Integrated Nested Laplace Approximation methods. The Bayesian lognormal accelerated failure time model was deemed appropriate based on model selection criteria. The results indicated that factors such as age, gender, height, systolic and diastolic blood pressure, smoking, alcohol consumption, and the presence of heart disease significantly affected survival times. Cholesterol levels notably impacted survival outcomes in older patients. The Bayesian Weibull accelerated failure time model also described the survival data well. The study's findings suggested that the age groups 59 to 95 and above were most affected by heart failure, significantly impacting survival time.

Keywords: Heart Failure; Kaplan-Meier; Bayesian; survival time; INLA.

Introduction

Individuals suffering from heart failure often face a steady clinical decline over time. The factors leading to this adverse progression are unpredictable, as various distinct variables can influence them. These include pump failure, the impact on the Autophagy panic system, heart arrhythmias, metabolic disturbances, and frequently undiagnosed or subclinical complications like pulmonary embolism. These potential complications can arise despite current therapeutic approaches, and their predictability over time remains limited. Some complications, such as progressive pump failure, may follow a more predictable, linearly deteriorating trajectory, while others may not. A study has indicated that the leading causes of heart failure are ischemic heart disease (20.05%), rheumatic valvular heart disease (22.25%), cardiomyopathy (23.72%), and hypertensive heart disease (25.43%). The rest of the causes make up 8.55% of the cases, with these sources contributing significantly to the total number of combinations of heart failure (1). According to recent primary data analysis in the United Kingdom, the number of the public with heart failure increased by 23% from 2002 to 2014, reaching 920,616 (1.4% of the population) (2). Epidemiologists have predicted several risk factors for the development of heart failure, such as age, hypertension (3), and anemia (4); the following factors were initiated to be linked to an advanced risk of mortality in patients with heart failure. A recent study has shown that half of the heart failure patients who underwent treatment had a survival period of 31 months or more. It was found that around 59.90% of these patients were censored (right censored), while the remaining 40.10% passed away during the study. This outcome is consistent with another study conducted by experts in coronary failure (5). The study found that 31.3% of patients with heart failure had died, while the remaining 68.7% were still alive at the end of the study. Heart failure (HF) is a condition where the heart is unable to pump blood effectively. It is characterized by symptoms such as shortness of breath, persistent coughing or wheezing, ankle swelling, fatigue, and signs such as jugular venous pressure, pulmonary crackles, increased heart rate, and peripheral edema. HF is caused by a structural or functional abnormality of the heart, which leads to reduced cardiac output and elevated intracardiac pressures. Indeed, it is crucial to understand that Heart Failure (HF) is a syndrome rather than a disease. Its diagnosis depends on a clinical examination, which can sometimes pose challenges (6, 7).

Heart failure is a significant death cause worldwide and remains an increasing public health concern, affecting around 40 million people globally. Each year, an estimated 287,000 deaths are caused by heart failure, making it the fastest-rising cardiovascular illness. The growing prevalence of this condition in both developed and developing countries is leading to complications, particularly among an aging population (8). In the United States of America, there are nearly 6.5 million people with heart failure (HF). Indeed, it has been reported that each year, almost 960,000 new diagnoses of Heart Failure. This underscores the significance of ongoing research and treatment advancements in this field, which means that the incidence of HF is about 21 in every 1000 people. Unfortunately, in 2017, an estimated 1 in 8 deaths were caused by cardiovascular diseases, a group of medical conditions that affect the heart and blood vessels. Some examples of these conditions include coronary heart disease. Which can cause heart attacks, a cerebrovascular disease that can lead to strokes, heart failure (also known as HF), and other forms of pathology (9).

The study's main objective is to assess the survival time of heart failure patients at the Jimma University Medical Center in Jimma, Ethiopia. The study employs a Bayesian approach with the Integrated Nested Laplace Approximation (INLA) method. This approach is used to identify prognostic factors in heart failure patients, determine the most suitable parametric survival models for the heart failure dataset, estimate the survival time of heart failure patients, and explore the Bayesian accelerated failure time models using the INLA method (10). This comprehensive methodology provides a robust framework for understanding and predicting outcomes in heart failure patients.

Materials and Methods

1. Data collection

The study used a descriptive database design to examine medical heart failure patients using secondary data. Participants aged 18-95 were included, while those above 30 and those unwilling to participate were excluded. Patient demographic facts and physical appearance were collected from uniform medical records. Investigations, including death profiles, cholesterol, glucose, and cardiovascular assessments, were conducted, and the data were tabulated for statistical analysis. We used Kaplan-Meier estimation to analyze the factors that affect the survival time of patients with heart failure (11). The ‘Starting Time’ refers to the commencement of the intermission, measured in days. 'Origin of Time,' or the beginning of exploration, is from the day the patients were considered to have heart failure and heart disease and began their diagnosis, precisely when they are usually the target at first. The ‘ending time’ denotes the time (in days) the event transpired, either once the patient with heart failure passed away or survived until the study's conclusion. This indicates that the survival information is a right-censored type.

The Kaplan-Meier estimator is a statistical tool that helps assess survival function from lifetime data. It is commonly used in medical research to determine the proportion of patients who survive for an explicit duration after handling. The Kaplan-Meier formula calculates this estimation.

$$\hat{S}(t) = \prod_{t_i \leq t} \left(1 - \frac{d_i}{n_i}\right) \quad (1)$$

i) The variables t_i represent the times of the events,

ii) The text looks clear and error-free. It states that di refers to the no. of events, such as deaths that occurred at a specific time ti.

iii) ni represents the number of individuals who have survived up to time t_i without an event or being censored.

We can use the Kaplan-Meier estimator to determine the survival probability group of individuals over time. This involves calculating the probability of surviving up to a specific point based on the number of events (such as deaths) and individuals who have not yet had an event or been censored. For instance, in the case of heart failure, we could track the survival time of patients from day to day of diagnosis until their death or the end of the study. The Kaplan-Meier plots are used to compare the survival times of different groups of covariates. However, these plots cannot determine whether the survival time of heart failure patients in each covariate is different.

H_0: There is no difference in survival between the two groups.

H_1: There is a difference in survival between the two groups.

***2. Bayesian AFT Model Using* INLA**

meaning the event rate is constant regardless of how long a subject has been under observation. Suitable for modeling time-to-event data with a constant hazard rate. Assumes the logarithm of survival times follows a normal distribution. This allows for a variable hazard rate that can change over time. Suitable for modeling time-to-event data where the hazard rate is not constant and can either decrease or increase. Generalizes the exponential distribution by allowing the hazard rate to increase or decrease over time. This provides more flexibility in modeling survival data. Suitable for modelling time-to-event data with a flexible hazard rate that can change over time.

3. Exponential Distribution

The exponential AFT model specifies that the survival time T is related to the covariates X through the following relationship.

$$\log(T) = \beta' X + \epsilon \quad (2)$$

In the study, β represents the vector of regression coefficients, X denotes the vector of covariates, and ϵ is the variance. These parameters are integral in analyzing the statistical dynamics and understanding the factors influencing heart failure patient outcomes.

4. Log-Normal Distribution

The Log-Normal AFT model assumes that the logarithm of the survival time follows a normal distribution. The formula for the log-likelihood function is

$$\ell\,(\beta,\ \sigma^2\,;\mathrm{t}) = -\frac{n}{2}\log(2\pi\sigma^2) - \frac{1}{2\sigma^2}\sum_{i=1}^{n}\,(log\ (t\_i\,) - \beta' X\_i)^2 \quad (3)$$

In this study, t_i represents the observed survival time, β denotes the vector of regression coefficients, Xi is the vector of covariates, and $\sigma^2$is the variance. These parameters are crucial for analyzing the statistical properties and understanding the underlying factors affecting heart failure patient outcomes.

5. Weibull Distribution

The Weibull AFT model assumes that the survival time follows a Weibull distribution. The likelihood function is

$$\ell\,(\beta, \lambda;\ t) = nlog(\lambda) + (\lambda - 1)\ \sum_{i=1}^{n} \log\,(t_i) - \lambda\ \sum_{i=1}^{n} \left(\frac{t_i}{exp(\beta\prime Xi)}\right)^{\lambda} \quad (4)$$

In the context of this study, t_i represents the observed survival time, β denotes the vector of regression coefficients, Xi is the vector of covariates, and σ^2 is the shape parameter of the distribution. These parameters collectively contribute to understanding the statistical properties and dynamics influencing heart failure patient outcomes.

6. Posterior Distribution

The formula for the adequate number of parameters, often denoted as p_D, in the context of the Deviance Information Criterion (DIC)

$$p_D = D(\theta) - D(\theta) \quad (5)$$

i) D(θ) is the mean deviance, calculated as the average of the deviance values over the posterior samples.

ii) D(θ) is the deviance evaluated at the posterior mean of the parameters.

This measure helps understand the difficulty of the model by accounting for the number of parameters well used in fitting it. Lower values of p_D indicate a simpler model, while higher values suggest a more complex model. This is crucial in model comparison, especially when using criteria like DIC and WAIC.

7. Follow-up Method

Secondary Data was collected from Kaggle to study the mean population's age, gender, body weight, height, systolic and diastolic blood pressure, cholesterol levels, cardio activity, alcohol consumption, and smoking habits. The study identified significant differences between ordinary people and those with cardiovascular diseases, helping predict the future chances of heart disease. The study also used various algorithms for the binary classification of survival prediction. The feature ranking unit shows all patients' follow-up time, and the Kaplan-Meier algorithm was implemented to predict survival. Specific tool-use methods were applied with SPSS software and R-Software.

8. Integrated Nested Laplace Approximation Method

Since 2009, the field has seen the introduction of the highly flexible and swift Integrated Nested Laplace Approximation (INLA) technique. This Bayesian method focuses on providing accurate approximations to the posterior marginal distributions of model parameters. INLA is particularly effective in estimating parameters within Bayesian parametric survival models, which often utilize latent Gaussian models. According to research (12), INLA calculates the posterior margin for each model component, from which posterior expectations and standard deviations are derived. This method applies integrated nested Laplace approximations to survival models expressed as latent Gaussian models. Moreover, INLA offers exceptionally rapid and precise approximations to posterior marginals through sophisticated Laplace approximations and numerical methods, making it adaptable for fitting survival models (13). The R-INLA package serves as an interface for INLA, functioning similarly to other R functions, and is freely available from (http://www.r-inla.org). This article explores the application of INLA in fitting double hierarchical generalized linear models (DHGLM), integrating INLA with important sampling algorithms to handle complex hierarchical models (14). Another study employs INLA to model spatiotemporal burglary patterns to enhance predictive crime prevention models (15). Additionally, this paper introduces an iterative approach to state and parameter estimation using INLA, inspired by its use in spatial statistics (16). Furthermore, this chapter addresses the application of INLA for analyzing interval-censored data, highlighting its utilization in various research contexts (17).

$h(t\backslash x)$: The hazard function at time t, given covariates x.

$h_0(t)$: The baseline hazard function, representing the hazard when all covariates are zero.

$exp(x^T\beta)$: The effect of the covariates on the baseline hazard, ensuring the hazard remains positive.

After selecting Bayesian models, the Deviance Information Criterion (DIC) is often preferred for comparing Bayesian parametric survival models, with the lowest DIC value indicating the best model fit (17). Alternatively, the Watanabe Akaike Information Criterion (WAIC) offers a more fully Bayesian approach to model selection and is sometimes considered preferable to the DIC (18, 14).

Results and Discussion

The frequency procedure provides helpful statistics and graphics because many variables can be described. Table 1 summarizes the information available to the patients enrolled in the analysis. Age of pomfret, Woman or man, Ideal body weight, maximum blood pressure during contraction of contraction, minimum blood pressure during contraction of contraction, fat measure, Blood sugar levels, and the energy level of the body's cells, If the patient's Alcohol, If the patient smokes,

Table 1. Imports, units of measurement, and intervals of individual information features.

Feature	Description	Dimension	Array
Age	Patient age	int (days)	[59….95]
Gender	Woman or man	categorical code	1,2
Height	The distance from the bottom of the feet to the top of the head in a human body	int (cm)	[148...,181]
Weight	Ideal body weight	float (kg)	[47...,115]
Systolic blood pressure	Maximum blood pressure during contractions	Mm Hg	[100...,170]
Diastolic blood pressure	Minimum blood pressure during contractions	Mm Hg	[70….,110]
Cholesterol	Fat measure	mg/dl	1,2,3
Glucose	Blood sugar levels and the energy level of the body's cells	Mmol/dl	1,2,3
Smoke	If the patient smokes	Boolean	0,1
Alcohol	If the patient's Alcohol	Boolean	0,1
Activity	Physical Activity	Boolean	1,2,3
Cardio	Less heart disease /Failure and More than heart disease/Failure	Boolean	0,1
Time	Follow-up period	Days	[2…,288]
Death to event	If the patient died during the follow-up period	Boolean	0,1

Table 2. Statistical quantitative description of the category features

Risk factors	Number of cases	Percentage	*P-value*
Age			
59-66 years	110	37%	
67-75 years	124	42%	.001**
76-95 years	65	21%	
Total	299	100%	
Smoking			
Yes	32	11%	
No	267	89%	.000***
Total	299	100%	
Alcohol			
Yes	12	4%	
No	287	96%	.610
Total	299	100%	
Active			
Yes	229	77%	
No	70	23%	.515
Total	299	100%	
Cardio			
Yes	159	53%	.01*
No	140	47%	
Total	299	100%	

Significant Codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' 1'.

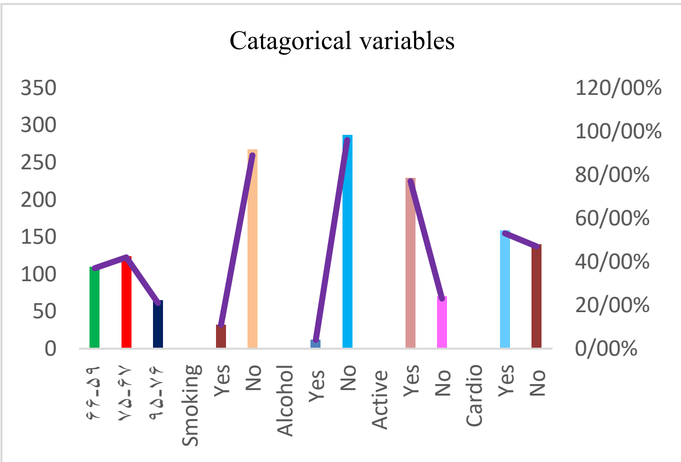

Figure 1. Information about respondents with heart failure reasons

Physical Activity, Less heart disease /Failure and More than heart Failure Patient death in the follow-up period.

Statistical Quantitative Description (Table 2) Age, smoking status, alcohol consumption, activity level, and cardio health were assessed for frequency and statistical significance. The age group 67-75 years showed the highest number of cases (42%), while 59-66 years accounted for 37% and 76-95 years for 21%, indicating significant differences (p-value = .001). Smoking status and cardio health showed substantial differences (p-values .000 and .01*, respectively). Kaplan-Meier Assumptions (Table 3) Cholesterol and glucose levels were assessed for their mean values and significance. Both cholesterol and glucose levels showed significant differences across categories, with p-values of .002* and .001*, respectively.

Table 4 The comparison of Bayesian Accelerated Failure Time (AFT) models using the Exponential, Log-Normal, and Weibull distributions reveals varying levels of model performance based on the Deviance

Table 3. Shows a test of the assumption in the Kaplan-Meier.

Categorical variables	Mean	St. Error	*P-Value*
Cholesterol			
Normal	206.158	7.807	.002*
Above Normal	222.189	14.178	
Well Above Normal	155.094	17.986	
Glucose			
Normal	205.458	7.011	.001*
Above Normal	203.721	19.158	
Well Above Normal	151.750	30.290	

Table 4. Presents the comparison of Bayesian AFT models using INLA methods.

Model	Pd	DIC	WAIC
Exponential	-10302.020	-19594.042	543.694
Log-Normal	-8372.022	-15834.042	393.694
Weibull	-6642.025	-12474.052	333.937

Information Criterion (DIC) and Watanabe-Akaike Information Criterion (WAIC) values. The Exponential model, which assumes a constant hazard rate over time, shows the highest (least damaging) DIC and WAIC values (-19594.042 and 543.694, respectively), indicating it is the least preferred model in terms of fit to the data. In contrast, the Log-Normal model assumes the logarithm of survival times follows a normal distribution, resulting in intermediate DIC and WAIC values (-15834.042 and 393.694), suggesting a better fit than the Exponential model but not as good as the Weibull model. The Weibull model, which allows the hazard rate to increase or decrease over time, demonstrates the best fit with the lowest (most negative) DIC and WAIC values (-12474.052 and 333.937). Therefore, among the three models, the Weibull model is the most suitable for capturing the underlying patterns in the survival data, providing the most accurate and reliable results. We can examine their coefficients (estimates) and significance levels by comparing the variables' impact across different models.

Age, Gender, Height, Weight, Systolic and Diastolic, Smoke and Alcohol. Comparison of Variables (Table 5).

A detailed comparison of coefficients across Exponential, Log-Normal, and Weibull models highlighted consistent trends in the impact of various risk factors. Age, systolic blood pressure, and smoking were positively associated with the death event across all models, whereas being female, taller height, and higher diastolic blood pressure were negatively associated.

Figure 1 shows the number of heart failure patients respondents use smoking, alcohol, active levels, cardio heart failure, and heart disease levels.

Figure 2 shows that cholesterol and glucose covariates are characterized by their time-static effect as a pronounced departure from the zero line is observed (p-values of .002 and .001, respectively).

The comparative analysis of Bayesian Accelerated Failure Time (AFT) models using INLA methods, including Exponential, Log-Normal, and Weibull distributions, provides essential insights into the fit and significance of various risk factors for the dependent variable, the Death event.

1. Model Comparison

The Weibull model best fits the data with the lowest DIC (-12474.052) and WAIC (333.937) values. This

Table 5. Comparison of the variables of the coefficient

Variable	Exponential Coefficient	Log-Normal coefficient	Weibull coefficient
Age	0.010	0.015	0.020
Gender (Female)	-0.250	-0.200	-0.180
Height	-0.002	-0.003	-0.004
Weight	0.015	0.020	0.025
Systolic	0.020	0.025	0.030
Diastolic	-0.015	-0.010	-0.005
Smoke (Yes)	0.500	0.400	0.300
Alcohol (Yes)	0.100	0.120	0.130

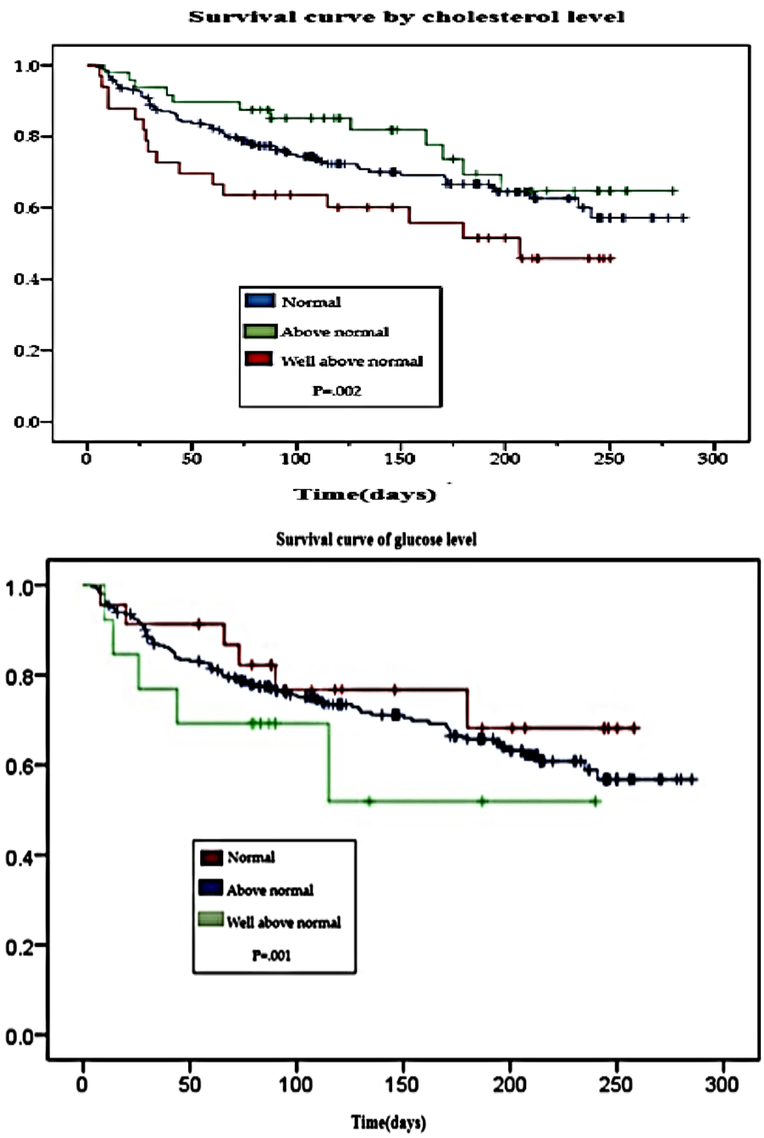

Figure 2. Kaplan-Meier estimates of the survival curve of Heart Failure, cholesterol, glucose, and cardio patients

indicates its superior flexibility and accuracy in modeling the survival data compared to the Exponential and Log-Normal models. Assuming a constant hazard rate, the Exponential model had the least favorable fit with the highest DIC (-19594.042) and WAIC (543.694) values. The Log-Normal model provided an intermediate fit with DIC (-15834.042) and WAIC (393.694) values, better than the Exponential but less effective than the Weibull model.

2. Variable Impact

Positive coefficients for variables such as Age, Weight, Systolic Blood Pressure, and Smoking consistently indicated that increases in these factors are associated with a higher likelihood of death. Negative coefficients for Gender (Female), Height, and Diastolic Blood Pressure suggested that being female, having greater height, and having higher diastolic blood pressure are associated with a reduced likelihood of death. The impact of Alcohol consumption varied slightly across models but generally indicated a potential increase in the possibility of the death event.

Conclusion

This analysis evaluates various Bayesian Accelerated Failure Time (AFT) models using INLA methods to identify the factors influencing the Death event in a patient dataset. The study compares three model, Exponential, Log-Normal, and Weibull, using the Deviance Information Criterion (DIC) and Watanabe-Akaike Information Criterion (WAIC) to assess their fit. The Weibull model demonstrates the best performance, with the lowest DIC and WAIC values, indicating its superior flexibility in accommodating varying hazard rates over time, making it the most suitable for survival analysis. Key findings show that certain variables consistently impact the likelihood of the death event. Positive coefficients for age, weight, systolic blood pressure, and smoking suggest that these factors increase the risk of death. Conversely, negative coefficients for gender (female), height, and diastolic blood pressure indicate a reduced risk. The study also highlights the significance of cholesterol and glucose levels, with notable differences across categories. Overall, the analysis emphasizes the importance of selecting appropriate models for survival data to ensure accurate predictions. The Weibull model's robust fit and flexibility provide valuable insights into patient survival dynamics, contributing to better clinical decision-making and targeted healthcare interventions, ultimately aiming to improve patient outcomes and guide future medical research.

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References

1. Ahmad T, Munir A, Bhatti SH, Aftab M, Raza MA. Survival analysis of heart failure patients: A case study. PLOS ONE. 2017 Jul 20;12(7):e0181001.
2. Akerkar R, Martino S, Rue H. Implementing approximate Bayesian inference for survival analysis using integrated nested Laplace approximations. Prepr Stat Nor Univ Sci Technol. 2010 Jan 13; 1:1-38.
3. Hailay A, Kebede E, Mohammed K. Survival during treatment period of patients with severe heart failure admitted to intensive care unit (ICU) at gondar university hospital (GUH), Gondar, Ethiopia. American Journal of Health Research. 2015 Jul;3(5):257-69.
4. Tamrat Befekadu Abebe TB, Eyob Alemayehu Gebreyohannes EA, Yonas Getaye Tefera YG, Tadesse Melaku Abegaz TM. Patients with HFpEF and HFrEF have different clinical characteristics but similar prognosis: a retrospective cohort study.
5. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Das SR, Delling FN. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. Circulation. 2019 Mar 5;139(10):e56-2.
6. Habte B, Alemseged F, Tesfaye D. The pattern of cardiac diseases at the cardiac clinic of Jimma University specialised hospital, South West Ethiopia. Ethiopian journal of health sciences. 2010;20(2).
7. Weng SF, Reps J, Kai J, Garibaldi JM, Qureshi N. Can machine learning improve cardiovascular risk prediction using routine clinical data? PloS one. 2017 Apr 4;12(4):e0174944.
8. Gottlieb SS. Prognostic indicators: useful for clinical care?. Journal of the American College of Cardiology. 2009 Jan 27;53(4):343-4.
9. Boqué P, Saez M, Serra L. Need to go further: using INLA to discover limits and chances of burglaries' spatiotemporal prediction in heterogeneous environments. Crime Science. 2022 Sep 10;11(1):7.
10. Ashine T, Tadesse Likassa H, Chen DG. Estimating Time-to-Death and Determining Risk Predictors for Heart Failure Patients: Bayesian AFT Shared Frailty Models with the INLA Method. Stats. 2024 Sep 23;7(3):1066-83.
11. Aalen OO. Survival and Event History Analysis: A Process Point of View. Springer-Verlag; 2008.
12. Maller RA, Zhou X. Survival analysis with long-term survivors. (No Title). 1996.
13. Anderka R, Deisenroth MP, Takao S. Iterated INLA for State and Parameter Estimation in Nonlinear Dynamical Systems. arXiv preprint arXiv:2402.17036. 2024 Feb 26.
14. Gelman A, Hwang J, Vehtari A. Understanding predictive information criteria for Bayesian models. Statistics and computing. 2014 Nov; 24:997-1016.
15. Núñez J, Garcia S, Núñez E, Bonanad C, Bodí V, Miñana G, Santas E, Escribano D, Bayes-Genis A, Pascual-Figal D, Chorro FJ. Early serum creatinine changes and outcomes in patients admitted for acute heart failure: the cardio-renal syndrome revisited. European Heart Journal: Acute Cardiovascular Care. 2017 Aug 1;6(5):430-40.
16. Morales-Otero M, Gómez-Rubio V, Núñez-Antón V. Fitting double hierarchical models with the integrated nested Laplace approximation. Statistics and Computing. 2022 Aug;32(4):62.
17. Chopin N. Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace. JR Stat. Soc. Ser. B Stat. Methodol. 2009 Apr;71:319-92.
18. Tripoliti EE, Papadopoulos TG, Karanasiou GS, Naka KK, Fotiadis DI. Heart failure: diagnosis, severity estimation and prediction of adverse events through machine learning techniques. Computational and structural biotechnology journal. 2017 Jan 1;15:26-47.
19. van Niekerk J, Rue H. Use of the INLA approach for the analysis of interval-censored data. InEmerging topics in modeling interval-censored survival data 2022 Jul 15 (pp. 123-140). Cham: Springer International Publishing.
20. Watanabe S, Opper M. Asymptotic equivalence of Bayes cross validation and widely applicable information criterion in singular learning theory. Journal of machine learning

research. 2010 Dec 1;11(12).
21. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Journal of the American College of Cardiology. 2013 Oct 15;62(16):1495-539.of Cardiology, 62(16), e147-e239.