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Life Expectancy Exploration of Heart Failure Patients Presenting with Diabetes

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Abstract
Background: Diabetes is a condition marked by high blood sugar levels, that could lead to complications in organs such as the kidneys, liver, and heart. Previous research has identified diabetes as a primary risk factor for congestive heart failure (CHF), a condition where stiffened heart muscles hinder oxygenated blood circulation. Despite its severity, few studies have examined CHF prognosis in diabetic patients. This study aimed to provide survival estimates and provide their comparisons among predictors, assess mortality risks based on specific variables, and reveal patient outcome patterns. *Methods*: We analyzed data from a 2015 study at Faisalabad Institute of Cardiology and Allied Hospital (FICAH), Pakistan, focusing on diabetic patients with Class III or IV heart failure and left ventricular systolic dysfunction. Kaplan-Meier estimates provided survival rates, log-rank tests compared survival across variables, Cox regression models estimated hazard ratios, and cluster analysis grouped patients by characteristics and survival rates. *Results*: The study examined 125 diabetic heart failure patients. Of these, 40 (32%) were censored and the remaining 85 (68%) died. The total follow-up period was 278 days, on the 120th day, 0.752 [95% CI = 0.678 to 0.883] of the patients survived after initial diagnosis. Cox regression showed a decrement of 60% in the risk of death for females compared to males and identified age (HR = 1.065, p= 0.0006), smoking (HR = 2.228, p= 0.0669) and hypertension (HR = 1.663, p= 0.1639) as major mortality risk factors. Cluster analysis revealed the risk factors associated with middle aged and the older patients. *Conclusion*: The overall prognosis of heart failure patients with diabetes was poor, with high mortality rates, implying effective treatment and management.

Keywords: Diabetes mellitus (DM); Heart failure (HF); Prognosis; Survival rate; Proportional hazard model

Introduction

Diabetes and Heart Failure (HF) are two interconnected conditions that have a profound impact on each other's progression and outcome. The coexistence of diabetes and heart failure creates a vicious cycle where each condition worsens each other, diabetes damages the heart and blood vessels increasing heart failure, while heart failure exacerbates diabetes by promoting insulin resistance and hyperglycemia [1]. In patients with congestive heart failure

(CHF), diabetes is associated with a worse prognosis including mortality, and the presence of diabetes in CHF patients is linked with a higher risk of cardiovascular events such as stroke [2].

Heart failure is a serious healthcare problem not only for patients and their families but also for society, as it contributes significantly to the enormous costs associated with the care of affected individuals. Nearly 6.5 million people in Europe, 5 million people in the United States (US), and 2.4 million people in Japan suffer from heart failure [3]. Also, diabetes is a serious and costly public health problem in the US affecting more than 16 million people [4]. Previous research conducted by Kennel et al. pinpointed diabetes as the major cause of congestive heart failure (CHF) [5], as diabetic heart failure becomes a major concern for public health and individuals with this condition. The prognosis of heart failure is poor with reported survival estimates of 50% and 10% at 5 and 10 years respectively [6]. Also, approximately 75% of diabetics die from vascular complications leading to heart failure [7].

The cost of medical treatment for diabetes and heart failure is alarming in our world today, due to this, more investigation is done concerning this medical condition. For instance, in Ireland, the average cost of hospital admission for heart failure is IR 2146 pounds [8] and the total estimated cost of diagnosed diabetes in 2017 is $327 billion, including $237 billion in direct medical costs and $90 billion in reduced productivity[9].

Although there have been a lot of studies on diabetes and heart failure, few studies have focused on how diabetes affects the survival in HF patients, therefore this study seeks to understand the prognosis of heart failure patients with diabetes. Specifically, we aimed to provide the survival estimates and provide comparisons among certain patients' characteristics, to determine the relationship between some patient characteristics and the risk of death from HF among diabetic patients, and to identify patterns of patient outcomes based on their survival rates and characteristics.

Materials and Methods

Data Source and Study Design

The data used in this research was secondary and was obtained from previous research conducted by Davide et. al [10]. Data from their research were extracted from the Faisalabad Institute of Cardiology and at the Allied Hospital in Faisalabad (Punjab, Pakistan) from April 2015 to December 2015, their study contained diabetic patients with congestive heart failure (CHF) specifically those diagnosed with Class III or IV heart failure and left ventricular systolic dysfunction. Non-diabetic patients were excluded from our study. Disease was diagnosed by cardiac echo notes written by physicians and information related to risk factors was taken from blood reports. The type of diabetes (Type I or Type II) among the participants was not specified in the dataset, which may be a limitation. They aimed at applying several machine learning classification models to predict the survival of heart failure patients, and also rank the features corresponding to the most important risk factors of heart failure patients. Their study's dataset included demographic and medical records. The dataset included information on time until death making it suitable to address our research's objectives. In this study, we specifically concentrated on heart failure patients with diabetes. Our study was based on the fact that diabetes and heart failure are interconnected medical conditions and the condition of one worsens the other. As such, patients presenting with both conditions need to know the risks associated and seek medical advice.

Variables

Within the dataset, we used the 'time' variable, which represented the patient's follow-up time, and the 'status' variable, which determined whether the patient was censored (survived) or not censored (died) at the end of the study. Follow-up time, used in this study, is the duration (days) in which the patient is tracked until the event of interest (death) occurs.

Additionally, our dataset involved demographic and health-related information, including the patients age, sex, smoking status, anemic status, high blood pressure, ejection fraction, creatinine phosphokinase, sodium creatinine, serum sodium, and platelet levels. Smoking status, anemia, and high blood pressure were grouped as categorical variables represented as "absent" and "present". Also, sex was grouped as "women" and "men". Numerical

variables were time, creatinine phosphokinase, ejection fraction, serum sodium, serum creatinine, and platelet levels.

Statistical Analysis

Descriptive like frequencies and percentages were used to illustrate and describe categorical data. Quantitative data were described using the mean, median and mode. Survival times were calculated from when patients first joined the study. Kaplan-Meier estimates were used to calculate survival probabilities, and Log-rank tests were used to compare survival rates across different groups.

The Cox Proportional Hazard (PH) model was utilized to estimate hazard ratios for the following variables: HBP, age, serum creatinine, serum sodium, CP, ejection fraction, sex(females), anemia, smoking status and platelets, to determine their relationship with the hazard of dying from HF as a diabetic patient. Cluster analysis examined survival patterns among patients based on their survival durations and predictor variables like smoking status, anemia, age, and high blood pressure. A significance level of 0.05 was maintained throughout the study. Statistical analyzes were conducted using R statistical software (version 4.3.2) and the packages used to carry out these analyzes were tidyverse, survival, ggsurvfit, survminer, cluster and factoextra.

Results

Patient's Characteristics

Our study sample consisted of 125 diabetic heart failure patients, most males (Table 1). Ejection fraction showed a significant association with death status (p-value= 0.006).

Table 1. Frequency distribution of participant characteristics

Variables	Death Status Group		P-value
	Dead (%), n=40	**Alive (%), n=85**	
Sex, male	20 (50)	50 (58.82)	0.354
Presence of anemia	18 (45)	35 (41.18)	0.687
High blood pressure	17 (42.5)	2630.59)	0.191
Smokers, yes	12 (30)	18 (21.18)	0.281
Ejection Fraction (EF)			0.006
≤30	20 (50)	18 (21.18)	
30 < EF ≤ 45	12 (30)	51 (60)	
>45	8 (20)	16 (18.82)	
Age, years			0.079
40-55	10(25)	35(41.18)	
>55	30(75)	50(58.82)	
Summary statistics of participant			
	Mean	**Median**	**Minimum**	**Maximum**
Age (Years)	59.42	60.00	40.00	94.00
Time to-follow-up (Days)	133.3	120.0	0.0	278.0

Right censoring is assumed in this study.

Comorbidity profiles included anemia and high blood pressure. For anemic status, non-anemic cohorts comprised 72 (57.6%) individuals, while anemic cohorts comprised 53 (42.4%) individuals. This emphasizes that non-anemic cohorts have better clinical outcomes, like fewer hospitalizations and improved functional capacity than anemic patients. Also, non-high blood pressure cohorts consisted of 82 (65%) patients while high blood pressure cohorts included 43 (34.4%) patients (Table 1). This signifies that a greater proportion of patients have a

well-controlled blood pressure and healthier lifestyle.

Survival Estimates and Log-rank Tests

Researchers estimated survival probabilities of diabetic heart failure patients at different points using Kaplan-Meier estimates (Figure 1) and (Table 2).

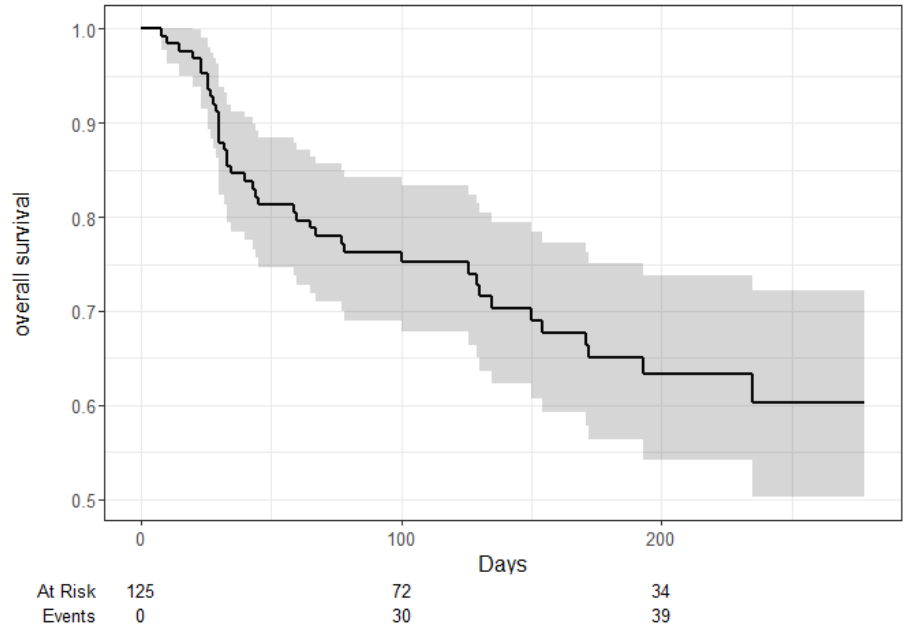

Figure 1. Kaplan-Meier curve for diabetic patients with heart failure

Table 2. Survival estimates for patients

Days (Months)	Survival Probabilities	95% Confidence Interval
0 (0)	0.992	[0.977 to 1.000]
30 (1)	0.879	[0.832 to 0.938]
60 (2)	0.796	[0.728 to 0.871]
90 (3)	0.762	[0.690 to 0.842]
120 (4)	0.752	[0.678 to 0.833]
150 (5)	0.690	[0.607 to 0.784]
180 (6)	0.650	[0.563 to 0.751]
210 (7)	0.633	[0.542 to 0.738]
278 (9.3)	0.602	[0.503 to 0.722]

The probabilities associated to log-rank test by categorical variables based on their survival probabilities are reported in Table 3.

Table 3. Summary of log-rank test

Variables	P-value
High blood pressure	0.001
Anemia	0.6
Smoking	0.002
Sex	0.04

Cox-Proportional Hazard Model

In the Cox PH model for diabetic heart failure patients in Figure 2 and Table 4, smokers had a significantly higher risk of death compared to those who do not smoke, high blood pressure (HBP) showed a relatively high risk of death, females had a lower risk of death on diabetic heart failure patients (constituting to a 60% decrease in

the risk of death) (Figure 2, Table 4). Creatinine phosphokinase (p-value=0.0905) and blood platelets (p-value=0.8303) were not significantly associated with death, hence no effect on mortality.

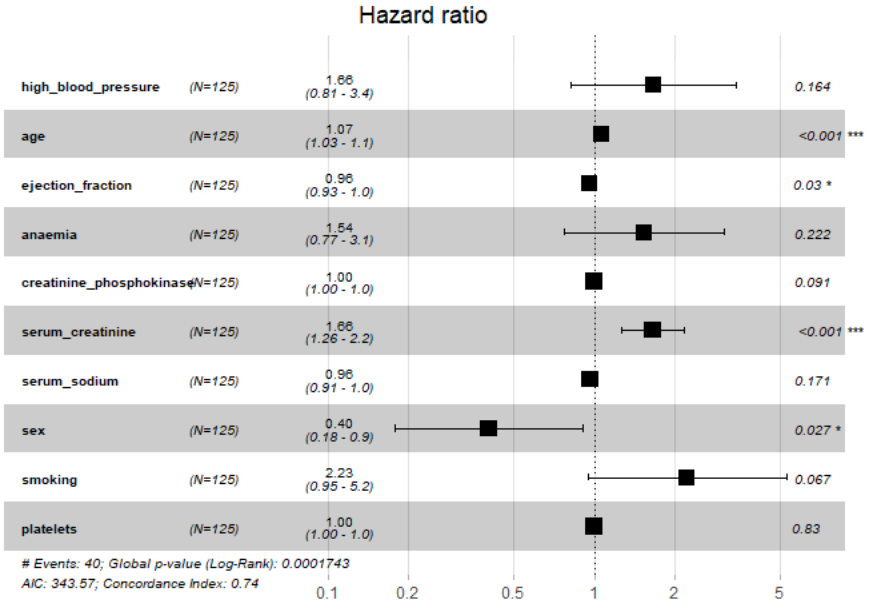

Figure 2. Hazard ratio by variable

Table 4. Cox-Proportional Hazard Model

Variable	Coefficient	Hazard Ratio	P-value
High Blood Pressure, Present	0.5089	1.663	0.1639
Age, years	0.06336	1.065	0.0006
Ejection Fraction	-0.03891	0.9618	0.0305
Anemia, Present	0.4322	1.541	0.2219
Creatinine Phosphokinase	0.000306	1	0.0905
Sodium Creatinine	0.5047	1.656	0.0003
Serum Sodium	-0.03751	0.9632	0.1714
Sex, Female	-0.9109	0.4022	0.0272
Smoking, Smokers	0.8010	2.228	0.0669
Platelets	-0.0000004	1	0.8303

Cluster Analysis

To identify the distinct survival pattern among diabetic heart failure patients, we conducted cluster analysis using the k-means clustering algorithm. The obtained cluster plot revealed two clusters, cluster 1 with more data points than cluster 2. Cluster 1 had a silhouette level of 0.73, which is a good level of cohesion within the cluster plot and cluster 2 had a silhouette level of 0.51, a moderate cohesion but showing a distinct cluster.

Discussion

The main findings from this study were (a) there is a statistically significant difference in the survival of smokers and non-smokers in diabetic heart failure patients, likewise high blood pressure and non-high blood pressure cohorts. This signifies that smoking and high blood pressure constitute as a major risk factor in the survival of these patients. (b) Age, high blood pressure, and smoking had a are significant factors associated with death on diabetic heart failure patients.

In our study, we found that smoking and high blood pressure were associated with a relatively higher hazard rates compared to the other predictor variables, this aligns with previous researches. Researchers have identified hypertension as a major risk factor for heart failure and a common comorbidity in patients with diabetes [12]. In our findings, the hazard ratio of 1.663 implied that HBP is a risk factor for congestive heart failure. The combination of high blood pressure and diabetes increases the risk of damage to the heart, resulting in heart failure [13,14]. Haire et al. [11] and Kathleen et al. [15] found smoking as a primary risk factor for heart diseases and type II diabetes in their respective studies. This aligns greatly with our study's findings, where smoking was significantly associated with increased risk of death from HF. The hazard rate of 2.228 suggest suggest a 122.8% increase in the risk of death for smokers compared to non-smokers, but this increase do not reach the significance level (p-value=0.0669). Kalogeropoulos et al. [16] and Nunez et al. [17] found that creatinine phosphokinase and platelets levels have no effect on mortality of patients with heart failure. We reported similar results (Figure 2), where both clinical indicators had a hazard rate of 1 but the values of confidence intervals indicate an overfitting.

Smokers and non-smokers in our study had different survival rates on heart failure and diabetes. From our log rank test, non-smokers had a better rate of survival compared to smokers. A study by the World Health Federation confirms that, smokers have a significantly lowers rate of survival as compared to non-smokers and the risk of heart failure is 2-4 times higher in smokers than in non-smokers [18]. High blood pressure cohorts and non-high blood pressure cohorts also had a significantly different survival rates, with non-high blood pressure cohorts having the better survival of patients presenting with heart failure and diabetes. Tsimploulis et al. reported that non-hypertensive heart failure patients exhibited a 5-year survival rate of 75%, whereas hypertensive patients had a markedly lower survival rate of 60% [19]. Hypertensive patients are often burdened with comorbidities such as diabetes and chronic kidney disease, which further complicate heart failure management and adversely affect prognosis [20]. For sex, we found that males and females have unequal survival rate of heart failure and diabetes. A recent study by Adams et al., found that there is a gender difference in the survival rate of heart failure, where the female gender lives much longer compared to males and suggesting that men and women have incomparable prognoses [21].

In our cluster analysis, two distinct clusters were attained, clusters 1 and 2. Cluster 1 appears to be significantly larger than cluster 2. This implies that the majority of data points belong to the population represented by cluster 1, while cluster 2 is smaller, potentially an outlier group. Cluster 2 is tightly concentrated and cluster 1 is more dispersed, indicating greater variability within this population, especially along the Dim1 axis. We found that older patients often have high blood pressure and anemia in cluster 1. A study by Thomas et al. [22] and Alpert et al. [23] stated that hypertension and anemia are found in patients who present to the hospital with diabetes and advanced heart failure. This signifies that in cluster 1, older patients have greater risk of dying faster since both HBP and anemia have a very high hazard rate from our cox-proportional model. In cluster 2, we found that middle aged adults have low high blood pressure and frequent habit of smoking. Studies by Rodgers et al. [24] and Joes et al. [25] confirm this, noting that the young and middle-aged adults usually have fewer health issues, better heart function, and more physical resilience to cope with heart failure.

Our research study had several limitations that must be acknowledged. First, the dataset we analyzed contained a relatively small number of patients who had both diabetes and heart failure. This may be because it was difficult to obtain data on patients with both medical conditions. Having a smaller sample size limits how much we can generalize or apply our findings to broader populations. Secondly, our dataset grouped together all heart failure patients who also had diabetes. We did not specify whether the patients had type 1 or type 2 diabetes. Separating and analyzing the two diabetes types may have provided more useful information, since we know there are differences in the risk factors associated with each type. Lastly, because we used an existing dataset collected by others, we had to make some modifications to the original data. This data alteration process may have inadvertently changed or introduced errors into a key variable we used for analysis. As a result, there could be some confounding variables we did not properly account for that may have impacted our results. These limitations mean the results from our study should be interpreted with some caution. Further investigation through additional research may be needed to validate and expand on our findings, especially with a larger sample size that distinguishes diabetes types. Despite the limitations, this study still provides insights into factors impacting outcomes for patients with both diabetes and heart failure.

Conclusions

Our study reveals significant differences in survival probabilities among some predictor variables in patients suffering from diabetic heart failure. Modifiable risk factors like smoking and hypertension emerged as significant predictors of mortality, highlighting the crucial importance of aggressive risk factor modification through lifestyle interventions and optimized medical therapy. Females had a better chance of survival and males had the greater risk of dying from diabetic heart failure. Also, from our findings, we revealed that there are two groups of patients presenting with diabetic heart failure, older and middle-aged adults. Older individuals being at risk of dying early from diabetic heart failure and middle-aged adults relatively surviving for a longer period of time. This signifies that ageing is also a risk factor for diabetic heart failure patients.

These conclusions carry important implications for clinical practices and management of patient's specific characteristics. Notwithstanding the limitations of this study, this research warrants more investigations to shed more light on this medical condition.

List of Abbreviations: CHF – Congestive Heart Failure; HF – Heart Failure; CI – Confidence Interval; HR – Hazard Ratio, EJ – Ejection Fraction, AIC – Akaike Information Criterion

Author Contributions: Roselyn Oforiwaa Acquah critically reviewed the study's proposal. Grace Aba Bart-Plange, Daniel Wiafe Preko; defined the research's aim and experiment design. Prosper Narh; participated in the design of the study and performed statistical analysis. Prosper Narh, Michael Asante Ofosu, Elliot Owusu Addo; coordinated and helped to draft the manuscript. All authors reviewed the results and approved the final version of the manuscript.

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Ethics Statement: The original study containing the dataset analyzed in this manuscript was approved by the Institutional Review Board of Government College University (Faisalabad, Pakistan), and states that the principles of Helsinki Declaration were followed .

Data Availability Statement: The data that supports the findings of this research are available under the Creative Common Attribution 4.0 International License (CC BY 4.0). The dataset is accessible through Kaggle database, which provides unrestricted access and reuse of the data. Researchers are encouraged to explore and use the dataset while adhering to the terms of the creative common license.

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Conflict of Interest: The authors declare that they do not have no conflict of interest.

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