Statistical Study On Diabetes Mellitus Type-2 Of Certain Population



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Abstract

This study examines the variables that contribute to the development of type 2 diabetes and compares the survival characteristics of male and female patients using a Cox proportional hazard regression model. In addition to high body weight, high blood pressure, and greater waist measures in males, the data indicate that high cholesterol, low HDL, high glucose, and low haemoglobin levels were important risk factors. The study highlights the significance of lifestyle changes, regular blood pressure, glucose, and cholesterol checks, and early intervention and prevention initiatives in tackling the high prevalence of diabetes. Type 2 diabetes patients' survival was significantly impacted by their weight, blood pressure, and waist size. The study discovered that type 2 diabetes had a higher death rate among female patients. Additionally, waist circumference was found to have a protective impact against problems related to type 2 diabetes, whereas weight and diastolic blood pressure were found to increase the risk. To look at this matter more thoroughly, other survival analysis techniques might be investigated.

Keywords: Cumulative incidence function, Competing risk analysis, Hazard ratio, Proportional Hazard Model, Survival Analysis.

Introduction

"Survival Analysis" refers to a set of statistical techniques used to analyze survival data, where the time until an event occurs is the outcome variable of interest. The term "survival analysis" originated with early research in which death is the event of interest. Although more than one events may be considered in the same analysis, but we will assume that only one event is of designated interest (e.g. death from any of several causes), the statistical problem can be characterized as either a recurrent event or a Competing Risk Problem. Nowadays, survival analysis has a much wider scope. These days, scientists use it to determine how long an illness will last. When will the stock market crash, when will the equipment break down, when will the earthquake occur, and so on.

The Kaplan Meier (K-M) is a non-parametric technique of estimating the survival estimates specially for censored dataset. The K-M assumes that at any time, patients who are censored have the same survival prospects as those who continue to be followed, survival probabilities are the same for the subjects recruited early and late in the study and the event happens at specific time point. Age and the length of the disease are two examples of characteristics that are known to have an impact on survival, but the log rank test is unable to examine (and account for) these impacts. The accuracy with which we can estimate the treatment effect may be increased by accounting for factors that are known to impact survival. Cox's regression approach is used to examine multiple variables simultaneously.

The Cox-PH is a semi parametric method of estimating the hazard rate. There are several

methods available to analyses time to event curves, such as Cox proportional hazards (PH), log-rank and Wilcoxon two sample tests. The Cox model is a regression method for survival data. It provides an estimate of the hazard ratio and its confidence interval. Cox regression considered a 'semi-parametric' procedure because the base line. Hazard function h0(t), does not have to be specified. There are two assumptions about the cox proportional hazard model: the hazard ratio of two people is independent of time, and are valid only for time independent covariates. The Cox-PH model that is a statistical model that is commonly used in survival analysis to estimate the relationship between covariates and time- to- event outcomes.

The Cox proportional hazard model makes two assumptions: (1) Survival curves for different strata must have hazard functions that are proportional over the time t. (2) The relationship between the log hazard and each covariate is linear. Cox regression model, which considers the effect of censored observation, is one of the most applicative and used model in survival analysis to evaluate the effects of the covariates.

Proportional hazard (PH), requires a constant hazard ratio over time, is the assumption of Cox regression model. Using extended Cox regression model provides the test of including a time dependent covariate to assess the PH assumption or an alternative model in case of nonproportional hazards. The Stratified Cox Model is a modification of the Cox proportional hazard (PH) model that allows for control by 'Stratification' of a predictor that does not satisfy the PH assumption. Predictors that are assumed to satisfy the PH assumption are included in

the model, whereas the predictor being stratified is not included.

Literature review

Willems et.al: (Prevalence of coronary heart disease risk factors among rural blacks: A community-based study. Southern Medical Journal 90:814-820; 1997) have analyzed some data from central Virginia for African Americans population prevalence of coronary Heart Disease (CHD) remains the most common cause of death from this study determination of the prevalence of CHD risk factors among a population based on sample of 403 rural black in Virginia. In this analysis community-based screening evaluations included the determination of exercise and smoking habits, blood pressure, height, weight, total and high-density lipoprotein (HDL), cholesterol, and glycosylated hemoglobin. These authors assessed the prevalence of smoking (32.5% of men, 20.0% of women), high cholesterol (16.6% of men, 18.9% of women) and sedentary lifestyle (37.5% of men, 66.7% of women) were like prevalence reported for other black populations. However, the prevalence of diabetes (13.6% of men, 15.6% of women), hypertension (30.9% of men, 43.1% of women) were higher than one those reported elsewhere. Increased body mass index was significantly associated with higher prevalence of hypertension, diabetes, and low HDL cholesterol. With the help of above analysis, it can be concluded that innovative methods needed to decrease the high-risk factor prevalence among this population.

Data source and descriptions

This study aims to determine the prevalence of obesity, diabetes, and other cardiovascular risk factors among African Americans in central Virginia. It includes data on 403 respondents out of 1046 subjects who were questioned. Obesity has the strongest correlation with Type 2 diabetes, or adultonset diabetes, according to Dr. John Hong. The waist-to-hip ratio could be a marker of heart disease and diabetes. The two conditions may be related to "Syndrome X"; DM II and hypertension are linked. The individuals who had diabetes screening were the 403 subjects. A glycosolated hemoglobin level of 7.0 indicates a positive diagnosis of diabetes.

Methodology

1. Competing Risk Analysis

Competing risk analysis is a unique kind of survival analysis that seeks to accurately calculate an event's marginal probability when competing occurrences are present. Due to their inability to account for the competing nature of numerous causes of the same event, traditional methods of describing survival processes, such as the Kaplan Meier

product-limit method, sometimes yield inaccurate estimates when examining the marginal probability

for cause-specific occurrences. A workaround for this problem was the Cumulative Incidence Function (CIF), which estimates the marginal likelihood of an event as a function of its overall survival probability and cause-specific probability.

2. Cumulative incidence function

The cumulative incidence function (CIF) allows to estimate the likelihood that an event will occur while accounting for conflicting risks. This makes it possible to calculate the incidence in a population with conflicting decision-making. The cumulative incidence function for the kth cause is defined as follows

$$CIF_k(t) = Pr (T \le t, D = k)$$

where D is a variable denoting the type of event that occurred.

The function $CIF_k(t)$ denotes the probability of experiencing the kth event before time t and before the occurrence of a different type of event. The important property of the CIF is that the sum of the CIF estimates the incidence of each of the individual outcomes consisting of all the competing events.

3. Cox-PH model

The Cox model is expressed by the hazard function denoted by h(t). Briefly, the hazard function can be interpreted as the risk of dying at time t. It can be estimated as follows:

 $h(t) = h_0(t) \times \exp(b_1X_1 + b_2X_2 + ... + b_pX_p)$...(1) where

- t represents the survival time,
- h(t) is the hazard function determined by a set of p covariates $(X_1, X_2, X_3, X_4, ..., X_p)$,
- the coefficients $(b_1, b_2, b_3, \dots b_p)$ measure the impact (i.e., the effect size) of covariates,
- the term $h_0(t)$ is called the baseline hazard. It corresponds to the value of the hazard if all the X_i are equal to zero (the quantity exp (0) equals 1). The 't' in h(t) reminds us that the hazard may vary over time.

The Cox model can be written as a multiple linear regression of the logarithm of the hazard on the variables X_i , with the baseline hazard being an 'intercept' term that varies with time [t].

The quantities $\exp(b_i)$ are called hazard ratios (HR). If the hazard ratio is more than one, or bi is greater than zero, then the length of survival decreases as the eventhazard rises in tandem with the ith covariate value. The conclusion based on hazard ratio (HR) is given as follows

- HR = 1: No effect
- HR < 1: Reduction in the hazard
- HR > 1: Increase in Hazard

Hazard Ratio

The Cox model, in contrast, leaves the baseline hazard function $\alpha(t) = \log h_0(t)$ unspecified:

$$\log h_i(t) = \alpha(t) + b_1 X_{i1} + b_2 X_{i2} + \ldots + b_p X_{ip}$$
 or, again equivalently,

$$h_i(t) = h_0(t) \exp(b_1X_{i1} + b_2X_{i2} + ... +$$

 b_pX_{ip})

Consider two cases such that the corresponding linear predictors is given by

$$\beta_i = b_1 X_{i1} + b_2 X_{i2} + ... + b_p X_{ip}$$

$$\begin{split} \beta_i &= b_1 X_{j1} + b_2 X_{j2} + \ldots + b_p X_{ip} \\ \text{The hazard ratio for these two cases,} \\ \frac{h_i(t)}{h_j(t)} &= \frac{h_0(t) \exp{(\beta_i X_i)}}{h_0(t) \exp{(\beta_j X_j)}} = \exp{(\beta_i - \beta_j)} \end{split}$$

Does not depend on time t. Consequently, the Cox model is a proportional hazards model.

Result

Competing Risk Analysis

The analysis on the basis of risk based on different factors is provided in the form of Figure 1.

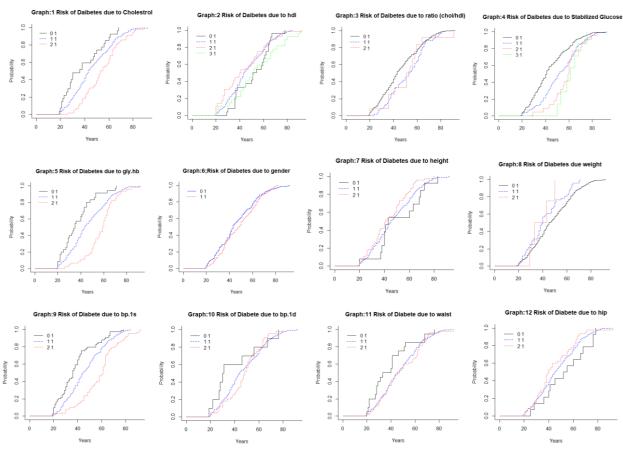


Figure 1: Risk of Diabetes based on different factors

Graph 1 indicates that, with the passage of time, the patients having level 0 (cholesterol less than 150 mg/dL) have more risk of being diabetic in comparison to levels 1 (cholesterol between 150 to 250) and 2 (cholesterol more than 250), and the patients having cholesterol level 2 have minimum risk while graph 2 indicates that the patients having level 2 (HDL between 60 to 80 mg/dL) have more risk of being diabetic in comparison to levels 0 (HDL less than 30), 1 (HDL between 30 to 60), and 3 (HDL more than 80). The patients having HDL level0 have minimum risk.

From the graph, it can be concluded that with the passage of time, the patients having level 0 (Ratio between 2 to 6) have more risk of being diabetic in comparison to levels 1 (Ratio between 6 to 8) and 3 (Ratio more than 8). The patients having Ratio (chol/hdl) level 0 have minimum risk.

It can be observed from the graph, that with the passage of time, the patients having level 0 (stab.glu between 50 to 100 mg/dL) have more risk of being diabetic in comparison to levels 1 (stab.glu between 100 to 200), 2 (stab.glu between 200 to 300), and 3 (stab.glu more than 300). The patients having Stabilized Glucose level 3 have minimum risk.

From the graph, it can be observed that with the passage of time, the patients having level 0 (gly.hb less than 4 mg/dL) have more risk of being diabetic in comparison to levels 1 (gly.hb between 4 to 8) and 2 (gly.hb more than 8). The patients having Glycosolated Hemoglobin level 2 have minimum risk. From the graph, it can be concluded that with the passage of time, the female (level 0) patients have more risk of being diabetic in comparison to male (level 1). The male patients have minimum risk.

It can be observed from the graph, that with the

passage of time, the patients having level 2 (height more than 70 inches) have more risk of being diabetic in comparison to levels 1 (height between 60 to 70) and 0 (height less than 60). The patients having Height level 0 have minimum risk.

From the graph, it can be observed that with the passage of time, the patients having level 2 (weight more than 300 pounds) have more risk of being diabetic in comparison to levels 1 (weight between 220 to 300) and 0 (weight between 100 to 220). The patients having Weight level 0 have minimum risk. From the graph, it can be concluded that with the passage of time, the patients having level 0 (bp.1s between 100 to 120 mmHg) have more risk of being diabetic in comparison to levels 1 (bp.1s between 120 to 160) and 2 (bp.1s more than 160). The patients having First Systolic Blood Pressure level 2 have minimum risk.

From the graph, it can be observed that with the passage of time, the patients having level 0 (bp.1d less than 60 mmHg) have more risk of being diabetic in comparison to levels 1 (bp.1d between 60 to 100) and 0 (bp.1d more than 100). The patients having

First Diastolic Blood Pressure level 2 have minimum risk

From the graph, it can be concluded that with the passage of time, the patients having level 0 (waist less than 30 inches) have more risk of being diabetic in comparison to levels 1 (waist between 30 to 45) and 0 (waist more than 45). The patients having Waist level 0 have minimum risk.

From the graph, it can be observed that with the passage of time, the patients having level 2 (hip more than 50 inches) have more risk of being diabetic in comparison to levels 1 (hip between 35 to 50) and 0 (hip less than 35). The patients having hip level 2 have minimum risk.

Cox PH Model For Male Patient

There are 11 independent variables Chol, glucose, hdl, ratio, glyhb, height, weight, bp.1s, bp.1d, waist, hip. The result of the parameter significance test on the Cox PH hazard regression, which was carried out partially

Table 1: Significant Test

Likelihood Ratio test	Wald test	log-rank test	Degree of freedom	Significance
93.48	89.5	93.44	11	0.00

In Table 1, the Cox regression with proportional hazard model shows a likelihood ratio of 93.48, Wald test value of 89.5, and log-rank value of 93.44 with 11 degrees of freedom. The significance indicates that the alpha value (α = 0.05). The decision to reject H_0 is based on the value of Sig \leq 0.00, which indicates that at least one independent variable has a significant impact on the survival behavior of the Diabetes Mellitus type II male patient based on the data and variables calculated in this analysis. The Cox PH

model is declared suitable for use in assessing the survival of Diabetes Mellitus type II male patients. Based on equation (1) and according to the result analysis in Table 2, the Cox PH model is written as follows:

 $h_i(t) = h_0(t) \exp \{-0.00124X_1 + 0.000047X_2 + 0.02385X_3 + 0.1558X_4 - 0.07754X_5 + 0.05838X_6 + 0.02897X_7 - 0.02695X_8 + 0.3367X_9 -0.2374X_{10} + 0.5967X_{11}\}$

Table 2: Estimated Cox Regression

Variables	Coef	exp (Coef)	SE	Z	Sig.	Decision
Chol	-0.00124	0.9988	0.00393	0.317	0.751108	Accept H ₀
Stab.glu	0.000047	1.000	0.00194	0.025	0.980384	Accept H0
Hdl	0.02385	1.0241	0.01493	1.597	0.110173	AcceptH ₀
Ratio	0.1558	1.1685	0.1560	0.999	0.317989	Accept H ₀
Gly.hb	-0.07754	0.9254	0.0574	-1.349	0.177295	Accept H ₀
Height	0.05838	1.0601	0.0329	1.771	0.076625	Accept H ₀
Weight	0.02897	1.0294	0.00568	5.100	0.0000003	Reject H ₀
Bp.1s	-0.02695	0.9734	0.00636	-4.236	0.000022	Reject H ₀
Bp.1d	0.03367	1.0342	0.00890	3.783	0.000155	Reject H ₀
Waist	-0.2374	0.7887	0.03862	-6.146	0.000	Reject H ₀

Most independent variables generate regression coefficients with positive sign, with only four variables having a negative effect, namely chol, gly.hb, bp.1s, waist in Table 2. According to Table 2, rejecting H_0 suggests that the independent variables have a significant impact on the dependent variable in this analysis, namely, Diabetes mellitus type II male patient survival behaviour. The p-value is used to search for a meaningful impact, i.e., to reject H_0 (significance). Compare the p-value with the standard significance level of 0.05, that is, rejecting H_0 when Sig. < α (0.05).

Table 2 clearly shows that the partial analysis reveals there are four variables that have a statistically significant impact on the survival behaviour of Diabetes mellitus type II male patient with all these variables having significance value less than 0.05. Weight, bp.1s, bp.1d, waist variables to consider. The p-value of these four variables are 0.0000003, 0.000022, 0.000155, 0.00 respectively. These findings suggest that these four variables play an important role in male patient survival. Additionally, other factors have been shown to have no statistically meaningful impact on Diabetes mellitus type II male patient survival characteristic.

Hazard Ratio

The hazard ratio is the risk of failure for one group of individuals separated by the risk of failure for another group. To analysis whether different factor is significant or not in terms of hazard ratio, significant values are provided in Table 3.

Table 3: Hazard Ratio

Variables	Hazard Ratio	Sig.
Weight	1.0601	0.0000003
Bp.1s	0.9734	0.000022
Bp.1d	1.0342	0.000155
Waist	0.7887	0.00

Only the independent variable with a statistically important effect on the survival behaviour of Diabetes mellitus type II male patient is used to measure the hazard ratio. Thus, only four variables were analyzed in terms of their hazard ratios they were used to compare the risk of failure of individual patients for each category of the variable. The failure ratio for each independent variable that has a major contribution to male patients' survival characteristics can be determined from Table 2, as seen in Table 3.

In this case, the risk of developing complications associated with type 2 diabetes. A hazard ratio greater than 1 indicates an increased risk, while a hazard ratio less than 1 indicates a decreased risk The hazard ratio for weight is 1.0601, which suggests that for every unit increase in weight, the risk of complications associated with type 2 diabetes increases by approximately 6%. The hazard ratio for systolic blood pressure (Bp.1s) is 0.9734, which

indicates that for every unit increase in systolic blood pressure, the risk of complications associated with type 2 diabetes decreases by approximately 3%.

The hazard ratio for diastolic blood pressure (Bp.1d) is 1.0342, which suggests that for every unit increase in diastolic blood pressure, the risk of complications associated with type 2 diabetes increases by approximately 3%. Finally, the hazard ratio for waist circumference is 0.7887, which indicates that for every unit increase in waist circumference, the risk of complications associated with type 2 diabetes decreases by approximately 21%.

For female patients

There are 11 independent variables: Chol, glucose, hdl, ratio, glyhb, height, weight, bp.1s, bp.1d, waist, hip. The result of the parameter significance test on the Cox PH hazard regression, which was carried out partially, is shown in Table 4.

Table 4: Significant Test

Likelihood Ratio test	Wald test	log-rank test	Degree of freedom	Significance
134	104.5	110.8	11	0.0

Table 4, the Cox regression with proportional hazard model shows a likelihood ratio of 93.48, Wald test value of 89.5, and log-rank value of 93.44 with 11

degrees of freedom. The significance indicates that the alpha value (α = 0.05). The decision to reject H₀ is based on the value of Sig \leq 0.00, which indicates that

at least one independent variable has a significant impact on the survival behavior of the Diabetes Mellitus type II male patient based on the data and variables calculated in this analysis. The Cox PH model is declared suitable for use in assessing the survival of Diabetes Mellitus type II male patients. Based on equation (1) and according to the result

Based on equation (1) and according to the result analysis in Table 5, the Cox PH model is written as follows:

Most independent variables generate regression coefficients with negative sign, with only three variables having a positive effect, namely height, weight, and bp.1d in Table 5. According to Table 5, rejecting H_0 suggests that the independent variables have a significant impact on the dependent variable

in this analysis, namely, Diabetes mellitus type II male patient survival. The p-value is used to search for a meaningful impact, i.e., to reject H₀ (significance). Compare the p-value with the standard significance level of 0.05, that is, rejecting H_0 when Sig. $< \alpha$ (0.05). Table 5 clearly shows that the partial analysis reveals there are five variables that have a statistically significant impact on the survival of Diabetes mellitus type II female patients, with all these variables having a significance value less than 0.05. Chol, weight, bp.1s, bp.1d, and waist variables are to be considered. The p-value of these four variables is 0.03274, 0.02498, 0.00, 0.00008, and 0.00806, respectively. These findings suggest that these five variables play an important role in female patient survival. Additionally, other factors have been shown to have no statistically meaningful impact on Diabetes mellitus type II male patient survival.

Table 5: Estimated Cox Regression

Variables	Coef	exp (Coef	SE	Z	Sig.	Decision
Chol	-0.00124	0.9988	0.00393	0.317	0.751108	Accept H ₀
Stab.glu	-0.003893	0.996114	0.002496	-1.560	0.11883	Accept H ₀
Hdl	-0.009968	0.990082	0.009794	-1.018	0.30882	Accept H ₀
Ratio	-0.011973	0.988098	0.009794	-1.018	0.30882	Accept H ₀
Gly.hb	-0.025825	0.974506	0.055056	-0.469	0.63902	Accept H ₀
Height	0.042618	1.043539	0.028067	1.518	0.12890	Accept H ₀
Weight	0.013971	1.014069	0.006232	2.242	0.02498	Reject H ₀
Bp.1s	-0.031466	0.969024	0.004682	-6.720	1.81e-11	Reject H ₀
Bp.1d	0.027759	1.028147	0.007052	3.936	8.27e-05	Reject H ₀
Waist	-0.069423	0.932932	0.026202	-2.650	0.00806	Reject H ₀
Hip	-0.026194	0.974146	0.039994	-0.655	0.51250	Accept H ₀

Most independent variables generate regression coefficients with negative sign, with only three variables having a positive effect, namely height, weight, and bp.1d in Table 2. According to Table 5, rejecting H_0 suggests that the independent variables have a significant impact on the dependent variable in this analysis, namely, Diabetes mellitus type II male patient survival. The p-value is used to search for a meaningful impact, i.e., to reject H_0 (significance). Compare the p-value with the standard significance level of 0.05, that is, rejecting H_0 when Sig. < α (0.05).

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Chol, weight, bp.1s, bp.1d, and waist variables are to be considered. The p-value of these four variables is 0.03274, 0.02498, 0.00, 0.00008, and 0.00806, respectively. These findings suggest that these five variables play an important role in female patient survival. Additionally, other factors have been shown to have no statistically meaningful impact on Diabetes mellitus type II male patient survival.

Hazard Ratio

The Table 6 presents five variables, including cholesterol (Chol), weight, systolic blood pressure (Bp.1s), diastolic blood pressure (Bp.1d), and waist circumference. For each variable, the table provides a hazard ratio and a significance level.

In this case, the risk of developing complications associated with type 2 diabetes. A hazard ratio

greater than 1 indicates an increased risk, while a

hazard ratio less than 1 indicates a decreased risk.

Table 6: Hazard Ratio

Variables	Hazard Ratio	Sig
Chol	0.992664	0.03274
Weight	1.0601	0.0000003
Bp.1s	0.9734	0.000022
Bp.1d	1.0342	0.000155
Waist	0.7887	0.00

The hazard ratio for cholesterol (Chol) is 0.992664, which suggests that for every unit increase in cholesterol, the risk of complications associated with type 2 diabetes decreases by approximately 0.7%. The hazard ratio for weight is 1.0601, which suggests that for every unit increase in weight, the risk of complications associated with type 2 diabetes increases by approximately 6%. The hazard ratio for systolic blood pressure (Bp.1s) is 0.9734, which indicates that for every unit increase in systolic blood pressure, the risk of complications associated with type 2 diabetes decreases by approximately 3%. The hazard ratio for diastolic blood pressure (Bp.1d) is 1.0342, which suggests that for every unit increase in diastolic blood pressure, the risk of complications associated with type 2 diabetes increases by approximately 3%. Finally, the hazard ratio for waist circumference is 0.7887, which indicates that for every unit increase in waist circumference, the risk of complications associated with type 2 diabetes decreases by approximately 21%.

Conclusion

From competing risk analysis, it can be observed that individuals with cholesterol levels exceeding 250 mg/dl, HDL levels ranging from 60 to 80 mg/dl, and a cholesterol/HDL ratio of 2 to 6 have the lowest risk of developing diabetes over time. Individuals with stabilized glucose levels over 300 mg/dl, glycosylated hemoglobin levels over 8mg/dl, height less than 70 inches, and weight between 100 to 200 pounds also have a minimal chance of developing diabetes. Furthermore, male patients have a lower likelihood of developing diabetes compared to female patients. The risk of acquiring diabetes is lowest in those whose first systolic blood pressure is greater than 160 mmHg and their first diastolic blood pressure is greater than 100 mmHg. Additionally, individuals with a waist circumference exceeding 45 inches, hip circumference less than 35 inches, and a waist-to-hip ratio greater than 1 have a minimal risk of developing diabetes.

A Cox proportional hazard regression model is used here to examine the survival characteristic of type 2 diabetes patients (male and female) in this study. The results of the analysis indicate that weight, bp.1s, bp.1d, and waist all these factors have a statistically significant impact on the survival behaviour of patients with type 2 diabetes for male patients, and chol, weight, bp.1s, bp.1d, and waist have a significant impact for female patients. Patient's gender seems to have a positive impact on survival behaviour, as female patients have a higher hazard ratio than male patients. This suggests that women are more likely to die than men. The results suggest that weight, diastolic blood pressure, and waist circumference are significant factors that increase or decrease the risk of complications associated with type 2 diabetes. Specifically, for every unit increase in weight or diastolic blood pressure, the risk of complications increases by approximately 6% and 3%, respectively. On the other hand, for every unit increase in waist circumference, the risk of complications decreases by approximately 21%. Additionally, systolic blood pressure was found to have a small but significant protective effect against complications associated with type 2 diabetes, decreasing the risk by approximately 3% per unit increase. Overall, managing weight, blood pressure, and waist circumference may be key in reducing the risk of complications associated with type 2 diabetes. Additionally, other survival analysis approaches may be used.

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