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Expected the Survival Life Time for heart Patients by using Cox regression model

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Abstract
Cox regression model is one of the models can be used in analyzing survival data and we can detect relationship between the explanatory variables and their survival time, so the cox regression is semi parametric model that consist two parts, the first part is nonparametric ($\lambda 0(t)$) and other is parametric part ($e(\beta \acute{z}$)) where ($\acute{\beta}$) is the vector of unknown parameters, ($\underline{z}$) is the vector of explanatory variable. The data which used in this study is type one of censoring was taken from heart center with *left-censored* data, testing distribution of survival time by using goodness of test and we find the distribution of survival time is unknown. Selecting cox regression model as the best model to analysis data by checking the assumption Cox regression model once graphically by using **Kaplan–Meier estimator** to estimating the survival function from lifetime data of patients, We estimated the parameters by using (partial likelihood) method and test the model parameter by using (Wald) test which shown that only two parameters (?) are effect on survival time.

Keywords: Heart Patients, Cox regression model,

1. Introduction

Survival analysis is a branch of statistics which deals with analysis of time to events, such as death in biological organisms and failure in mechanical systems. This topic is called reliability theory or reliability analysis in engineering, and duration analysis or duration modeling in economics or event history analysis in sociology. Survival analysis attempts to analysis the proportion of a population which will survive past a certain time. The Cox regression model (Cox, 1972) is the most popular method in regression analysis for censored survival data. However, due to the very high dimensional space of the predictors, the standard maximum Cox partial likelihood method cannot be applied directly to obtain the parameter estimates. To deal with the problem of co linearity, the most popular approach is to use the penalized partial likelihood which was proposed by Tibshirani (1995) and is called the least absolute shrinkage and selection operator (Lasso) estimation. In the case of biological survival, death is unambiguous, but for mechanical reliability, failure may not be well-defined, for there may well be mechanical systems in which failure is partial, a matter of degree, or not otherwise localized in time. Even in biological problems, some events (for example, heart attack or other organ failure). More generally, survival analysis involves the modeling of time to event data; in this context, death or failure is considered an "event" in the survival analysis literature traditionally only a single event occurs for each subject, after which the organism or mechanism is dead or broken. The study of recurring events is relevant in systems reliability, and in many areas of social sciences and medical research. The survival function, also known as a survivor function or reliability function, is a property of any random variable that maps a set of events, usually associated with mortality or failure of some system, the term survival function is used in a broader range of applications, including human mortality.

2. Definition

Let (T) be a continuous random variable with cumulative distribution function F(t) on the interval $(0,\infty)$. Its survival function is:

$$\mathbf{S(t) = Pr(T > t) = \int_t^{\infty} f(u)du = 1 - F(t)}$$

Properties

Every survival function S(t) is monotonically decreasing, i.e. S(u) ≤ S(t) for all $u > t$.

The time, t = 0, represents some origin, typically the beginning of a study or the start of operation of some system. S(0) is commonly unity but can be less to represent the probability that the system fails immediately upon operation.

3. Lifetime distribution function and event density:

The lifetime distribution function, conventionally denoted *F*, is defined as the complement of the survival function,

$$F(t) = \Pr(T \leq t) = 1 - S(t).$$

If (F) is differentiable then the derivative, which is the density function of the lifetime distribution, is conventionally denoted (f),

$$f(t) = F'(t) = \frac{d}{dt}F(t).$$

The function (*f*) is sometimes called the event density; it is the rate of death or failure events per unit time.

4- Hazard function and cumulative hazard function:

The hazard function, denoted (λ), is defined as the event rate at time (t) Conditional on survival until time (t) or later (that is, T ≥ t),

$$\lambda\,(t) = \text{Lim}_{\,dt\to 0}\ \frac{\Pr(t\leq T<t+dt\backslash T\geq t)}{dt} = \frac{f(t)}{S(t)} = -\frac{\acute{S}\,(t)}{S(t)}$$

The hazard function must be non-negative, λ(t) ≥ 0, and its integral over [0, ∞] must be infinite, but is not otherwise constrained; it may be increasing or decreasing, non-monotonic, or discontinuous, also hazard function can alternatively be represented in terms of the cumulative hazard function, conventionally denoted (Λ):

$$\Lambda(t) = -\log S(t)$$

So transposing signs and exponentiation or differentiating (with the chain rule)

$$S(t) = \exp(-\Lambda(t))$$

$$\frac{d}{dt}\Lambda(t) = -\frac{S'(t)}{S(t)} = \lambda(t).$$

The name "cumulative hazard function" is derived from the fact that

$$\Lambda(t) = \int_0^t \lambda(u)\,du$$

Which is the "accumulation" of the hazard over time?

From the definition of (Λ(t)), we see that it increases without bound as (t) tends to infinity (assuming that S(t) tends to zero). This implies that (λ(t)) must not decrease too quickly, since, by definition, the cumulative hazard has to diverge. For example, (exp(t)) is not the hazard function of any survival distribution, because its integral converges to (1).

4. Types of data

4.1 Complete data: that is meaning the values of each sample unit is observed or known.

4.2 Censored data: that is mean a form of death dates of a subject are known, in which case the lifetime is known.

If it is known only that the date of death is after some date, this is called right censoring. Right censoring will occur for those subjects whose birth date is known but who are still alive when they are lost to follow- up or when the study ends.

If a subject's lifetime is known to be less than certain duration, the lifetime is said to be left-censored. It may also happen that subjects with a lifetime less than some threshold may not be observed at all: this is called truncation. We generally encounter right-censored data. Left-censored data can occur when a person's survival time becomes incomplete on the left side of the follow-up period for the person. As an example, we may follow up a patient for any infectious disorder from the time of his or her being tested positive for the infection. We may never know the exact time of exposure to the infectious agent.

5. Multiple Regression model

A Multiple Regression model is a model with a multiple explanatory variables and we can represent as the follows:

$\underline{Y} = \acute{\beta}\, Z + \underline{e}$

Where Y is the response variable, ($\acute{\beta}$) is the vector of unknown parameters, (Z) is a non-singular matrix of explanatory variables, so the Properties of multiple regression model it is important to make sure that the underlying assumptions hold. Plotting residuals versus the (Z) values and other residual diagnostics are useful to check the normality of data.

5.1 Proportional Hazards Models

These models an important model which usually associated with mortality or failure of some system, so we can find a combined model with survival time and hazard function as follows:

$\lambda(t; z) = \lambda_0(t) \exp(\acute{\beta}\, \underline{Z})$ … (1)

Where λ(t, $\underline{z}$) is an arbitrary hazard rate function at time (t) for an individual with covariates ($\underline{Z}$), λ0(t) is an arbitrary unspecified base- line hazard function for continuous (t), $\acute{\beta}$ is the regression coefficients, The density function,

S(*t*) is: $S(t; \underline{Z}) = (t; \underline{z})S(t; \underline{Z}) = \exp(-\int_0 \lambda_0(u)\exp(\acute{\beta}\, \underline{Z})du)$ … (2)

The regression coefficients $\acute{\beta}$ may be estimated with assumptions made about the hazard function then one would maximize the likelihood functions and would consider contributions made to the hazard rate by censored data.There are some Proportional hazards models for survival data as follows:

5.2 Exponential regression model

In this model assume that (survival time) have exponential distribution with (pdf):

$$f(t \backslash \underline{z})= \frac{1}{\lambda \underline{z}} \exp(\frac{-t}{\lambda \underline{z}}), t > 0 \quad \ldots(3)$$

Where (λz) is aconstsnt hazard function with

$\lambda \underline{z} = E(t \backslash \underline{z}) = \exp(\acute{\beta}\ \underline{z})$ which depend on regression parameters (β) and explanatory variables ($\underline{z}$).

Therefore the survival functions as follows:

$$S(t \backslash \underline{z})= \exp\{-(\frac{t}{\exp(\acute{\underline{\beta}}\ \underline{z})})\} \quad \ldots(4)$$

Then the likelihood function is the product of the likelihood of each datum as follows:

$$L(\underline{\beta}, t, \underline{z})= \pi_{i=1}^{n}(\frac{1}{\exp(\acute{\underline{\beta}}\ z_i)}) \exp(\frac{-\bar{t}}{\exp(\acute{\underline{\beta}}\ z_i)}) \quad \ldots(5)$$

5.3 Weibull Regression Model

In this model assume that (survival time) have continuous probability wibull distribution with (pdf):

$$f(t \backslash \underline{z})= \frac{\alpha}{\exp(\acute{\underline{\beta}}\ \underline{z})}(\frac{t}{\exp(\acute{\underline{\beta}}\ \underline{z})})^{\alpha-1} \exp\{\frac{-t}{\exp(\acute{\underline{\beta}}\ \underline{z})}\}^{\alpha}, t > 0, \alpha > 0 \quad \ldots(6)$$

The hazard function of wibulll regression model can take follows formula:

$$\lambda(t \backslash \underline{z}) = \frac{\alpha}{\exp(\acute{\underline{\beta}}\ \underline{z})}(\frac{t}{\exp(\acute{\underline{\beta}}\ \underline{z})})^{\alpha-1} \quad \ldots(7)$$

Then, the survival function has the following formula:

$$S(t \backslash \underline{z})= \exp\{\frac{-t}{\exp(\acute{\underline{\beta}}\ \underline{z})}\}^{\alpha} \quad \ldots(8)$$

So, the likelihood function can take the following:

$$L(\underline{\beta}, t, \underline{z})= \pi_{i=1}^{n}\{\frac{\alpha t^{\alpha-1}}{[\exp(\acute{\underline{\beta}}\ \underline{z})]^{\alpha}} \exp(\frac{t}{\exp(\acute{\underline{\beta}}\ \underline{z})})^{\alpha}\}\{\exp(\frac{t}{\exp(\acute{\underline{\beta}}\ \underline{z})})^{\alpha}\} \quad \ldots(9)$$

6. Cox, Regression Model

This model one of important models published by (D.R. Cox in 1972) and is one of most frequently articles in statistics and medicine**,** which usually associated with mortality or failure of some system, he suggested that model depend on (hazard rate) in time (t), as the follows:

$$\lambda(t; z) = \lambda_0(t) \exp(\acute{\underline{\beta}}\ \underline{Z}) = \lambda_0(t)\exp(\textstyle\sum_{i=1}^{p} \beta_i Z_i) \quad \ldots(10)$$

$\lambda 0(t)$: Initial hazard function when all values of ($\underline{Z} = 0$).
$\acute{B}$: are unknown's regression coefficients.
(Z) : is the *p*-dimensional vector of covariates.

We can write survival function of (10) as follows:

$$S(t; \underline{Z}) = \{S(t)\} \exp(\textstyle\sum p\ \beta\ Z) \quad \ldots(11)$$

Where $\exp(\sum_{i=1}^{p} \beta_i Z_i)$ is the proportional hazard function

But, Cox model is a semi- parametric model with free distribution. So, the estimation problem for (β) is the same under any transform.

Only the rank statistic r (.) can carry information about (β) when $\lambda 0$is completely unknown. It follows that the rank statistic is marginally sufficient to estimate (β). To apply the rank statistic to get inferences about (β), one would use the marginal distribution of the ranks and the marginal likelihood.

7. Marginal Likelihood:

Suppose (n) individuals are observed to fail at times (Ti, i= 1,…, n), with corresponding covariates (z1,… , zn). Assume that all failure times are distinct, i.e. no two people (or more) fail or are censored at the same time. The order statistic is defined to be O (t) = [T (1); T(2), …, T(n)] and refers to the T is being ordered increasingly i.e. (T(1) < T(2) < …< T(n)). The rank statistic is defined to be r (t) = [(1), (2)… (n)] and refers to the label attached to the order. To apply the rank statistic to get inferences about (β) one would use the marginal distribution of the ranks and the marginal likelihood. The marginal likelihood is proportional to the probability that the rank vector is observed, i.e.

$$\Pr(r, \beta) = pr\{r = [1, 2, 3 \ldots n] ; \underline{\beta}\} = \int_0^{\infty} \int_{t(1)}^{\infty} \ldots \int_{t(n-1)}^{\infty} \pi_{i=1}^{n} f(t_i, z_{(i)}) dt_n \ldots dt_1$$

and we find : Pr(r, β) =

$$\frac{\exp(\sum_{i=1}^{n} Z_i \beta)}{\pi_{i=1}^{n}\{\sum_{L \in R(t_i)} \exp(Z_L \beta)\}} \quad \ldots(12)$$

Where R(ti) is R(t) = {i: T(i) ≥ t } the risk set at time T(i), that is the group of individuals (i) that are under observation at time (t),

$$\therefore h(T_i) = \exp[-\textstyle\sum_{j=1}^{m_i}(\underline{\acute{\beta}}\ Z_{ij}) \int_0^{t_i} \lambda_0(u) du], i = 1,2,\ldots,k \quad \ldots(13)$$

So, the Probability marginal likelihood is proportional to the probability of the event (14) is:

$$\int_0^{\infty} \int_{t(1)}^{\infty} \ldots \int_{t(k-1)}^{\infty} \pi_{i=1}^{n} f(t_i, z_{(i)}) \lambda(t_i) dt_k \ldots dt_1 .$$

Now, we can find: $\Pr(r, \beta) = \frac{\exp(\sum_{i=1}^{k} Z_i \beta)}{\pi_{i=1}^{k}\{\sum_{L \in R(t_i)} \exp(Z_L \beta)\}}$ …(14)

8. Partial Likelihood

Cox (1975) has shown that this partial log-likelihood can be treated as an ordinary log-likelihood to derive valid (partial) MLEs of (β). Therefore we can estimate hazard ratios and confidence intervals using maximum likelihood techniques. The only difference is that these estimates are based on the partial as opposed to the full likelihood. The partial likelihood is valid when there are no ties in the data set that is no two subjects have the same event time, if there are ties in the data set, the true partial log-likelihood function involves permutations and can be time-consuming to compute. Then, to study (Cox) model which have the following hazard function:

$$\lambda(t \setminus \underline{z}) = \lambda_0(t) \exp(\acute{\underline{\beta}}\, \underline{z}) \text{ with } T_1 < T_2 < \ldots < T_n$$

Survival models can be usefully viewed as ordinary regression models in which the response variable is time. However, computing the likelihood function (needed for fitting parameters or making other kinds of inferences) is complicated by the censoring. So, the likelihood function can take the following:

$$L(\underline{\beta}, \lambda_0(t), t, \underline{z}) = \pi_{i=1}^{n} \{\lambda_0(t_i) \exp(\acute{\underline{\beta}}\, \underline{z})\}^{\delta_i} \exp\{-\int_0^{t_i} \lambda_0(u) \exp(\acute{\underline{\beta}}\, \underline{z}) du\}$$

$$= \pi_{i=1}^{n} \frac{\exp(\acute{\beta} Z_i)}{\{\sum_{L \in R(t_i)} \exp(\acute{\beta} \underline{Z}_L)\}} \sum_{L \in R(t_i)} \lambda_0(t) \exp(\acute{\beta} \underline{Z}_L)\, \pi_{i=1}^{n} S_0(t_i) \exp(\acute{\underline{\beta}}\, \underline{z})$$

…….(15)

Where $S_0(t) = \exp(-\int_0^t \lambda_0(u) du$

The previous likelihood equations are special cases of (15). Equation (15) can be approximated by:

$$L(\underline{\beta}, t, \underline{z}) = \pi_{i=1}^{n} \frac{\exp(\acute{\underline{\beta}}\, \underline{Z}_i)}{\{\sum_{L \in R(t_i)} \exp(\acute{\underline{\beta}} Z_L)\}}$$

The maximum likelihood estimate of ($\underline{\beta}$) is ($\hat{\underline{\beta}}$) and can be obtained as a solution to the system of the following equations

$$\frac{\partial \log pL\underline{\beta},t,\underline{z})}{\partial \beta_i} = \sum_{i=1}^{k} \{ \underline{Z}_i - \frac{\sum_{L \in R(t_i)} \exp(\acute{\underline{\beta}}\, \underline{Z}_L) \underline{Z}_{Li}}{\sum_{L \in R(t_i)} \exp(\acute{\underline{\beta}}\, \underline{Z}_L)} \}$$

and similarly one can get:

$$\frac{\partial^2 \log pL\underline{\beta},t,\underline{z})}{\partial \underline{\beta}_i\, \partial \underline{\beta}_j} = \sum_{i=1}^{k} \{ \frac{\sum_{L \in R(t_i)} \exp(\acute{\underline{\beta}}\, \underline{Z}_L) \underline{Z}_{Li} \underline{Z}_{Lj}}{\sum_{L \in R(t_i)} \exp(\acute{\underline{\beta}}\, \underline{Z}_L)} - \frac{\sum_{L \in R(t_i)} \exp(\acute{\underline{\beta}}\, \underline{Z}_L) \underline{Z}_{Li}}{\sum_{L \in R(t_i)} \exp(\acute{\underline{\beta}}\, \underline{Z}_L)} * \frac{\sum_{L \in R(t_i)} \exp(\acute{\underline{\beta}}\, \underline{Z}_L) \underline{Z}_{Lj}}{\sum_{L \in R(t_i)} \exp(\acute{\underline{\beta}}\, \underline{Z}_L)} \}$$

…(16)

Where (j = 1, 2, 3 … S)

9. Testing data for goodness:

There many formulas using to testing for goodness data as follows:

9.1 Log Rank Test: The log rank test is a popular test to test the null hypothesis of no difference in survival between two or more independent groups.. Survival curves are estimated for each group, considered separately, using the **Kaplan-Meier method** and compared statistically using the log rank test.

The log rank test compares the observed number of events in each group to what would be expected if the null hypothesis were true (i.e. if the survival curves were identical).

H0: The two survival curves are identical versus

H1: The two survival curves are not identical with (α=0.05). The log rank statistic is approximately distributed as a chi-square test statistic, as follows:

$$X^2 = \sum_{i=1}^{n} \frac{(O_i - E_i)^2}{E_i}$$

……… (17)

9.2 Score test statistic

There are many statistical testing for proportional hazard assumption, one of them is the (Score test statistics) which used to test how effect the covariate vector for proportional hazard in time (t), let the state of unit from life to death can putting in the following model:

$$\lambda(t \setminus \underline{z}) = \lambda_0(t) \exp\{\underline{Z}(\underline{\beta} + \underline{\gamma}t)\} \text{ if } t \in I_t$$

…(18)

For each time with sequencings (I), therefore we can give the test hypothesis as follows:

H0: **γ1**=**γ2**=⋯= **γp**=**0** Versus **H1**: **at least one of them not equal to zero**

With following test statistics: **S = Ú V⁻¹ U**

Where {U} represent the vector of derivatives of log l likelihood under H0 and partial likelihood for vector ($\underline{\beta}$) and

$$(V) = -\{ \frac{\partial^2 \log pL\underline{\beta},t,\underline{z})}{\partial \underline{\beta}_i\, \partial \underline{\beta}_j} \}.$$

…… (19)

So, the score test close to chi- square distribution with (p) degree of freedom

9.3 Wald Test

Another common way to test for the individual hazard ratio is based on Wald test which is testing whether the individual hazard coefficient is zero or not withH0: βj =0.

$$\text{The Wald test:} \quad (W_j) = \{ \frac{\beta_j}{SE(\beta_j)} \}^2$$

…. (20)

10. Experimental Part

10.1 Description data

In this research we use a real data of (Heart Disease Center) in Sulamania - City- Iraq, we have (300) patients with heart disease from (1-1-2015) to (30-5-2015).

We study the following variables: T: Survival Time

$Z1$: The age of patient in first visit hospital

$Z2$: The gender of patient takes (1 for male and 2 for female)

$Z3$: Location type takes follows: (1) for Towner patient and (2) for out of the town

$Z4$: The Month takes follows: (1) for Jan. (2) for Feb. (3) for Mar. (4) for Apr. (5) for May.

$Z5$: Treatment type takes follows: (1) for Biological Treatment and (2) for Surgery Treatment

$Z6$: State of Censored takes follows: (1) Patient with Censored and (2) Patient exit

After analysis the data of patients in each four month of period study, we get the following results:

Table 1: No. patients, No. of death and No. of censored in each five months

Month	No. patients	No. death	% death	No. of censored	% censored
January	45	18	40.00	27	60.00
February	57	19	33.33	38	66.67
March	73	33	45.21	40	54.79
April	69	26	37.68	43	62.32
May	56	31	55.36	25	44.64
Total	300	127	42.33	173	57.67

Table 2: The age classes in years according to state of survival

Classes of patients	No. death	No. of censored	Total	% censored
Less than 20	0	36	36	20.8
20 – 40	5	22	27	12.7
40- 60	31	57	88	33.0
More than 60	91	58	149	33.5
Total	127	173	300	100.0

Table 3: The class of gender according to state of survival

The gender patients	No. death	No. of censored	Total	% censored
Male	72	99	171	57.2
Female	55	74	129	42.8
Total	127	173	300	100.0

Table (3) showing that the censored of male (%57.2) more than female (%42.8) and the death of male also more than female.

Table 4: Types of diagnosis according to the death patients:

Types of Treatment	No. death	% death
Heart attack	113	89
Heart failure	14	11
Total	127	100.0

Table 5: Types of Geographic location according to the patients and state of survival

Types of Geographic location	No. death	No. of censored	Total	% censored
Towner	75	82	157	47.4
Out of town	52	91	143	52.6
Total	127	173	300	100.0

10.2 Testing and statistical data Analysis

I- Testing data: In this statement we go to test the data of patients before applied cox procedure, we find the following results:

Table 6: The results testing of data patients

Types of distribution	X2 -values	X2 table	d.f.	P- value
Exponential	40.4682	15.51	8	0
weibull	26.7805	16.92	9	0
Lognormal	42.8663	15.51	8	0

According to results of table (6), the data of patients have no specific distribution of survival time.

II- Log Rank Test

Kaplan-Meier method with treatment variable:

Using Kaplan- Meier method to test there is no difference in survival curves between two independent treatments as in following figure:

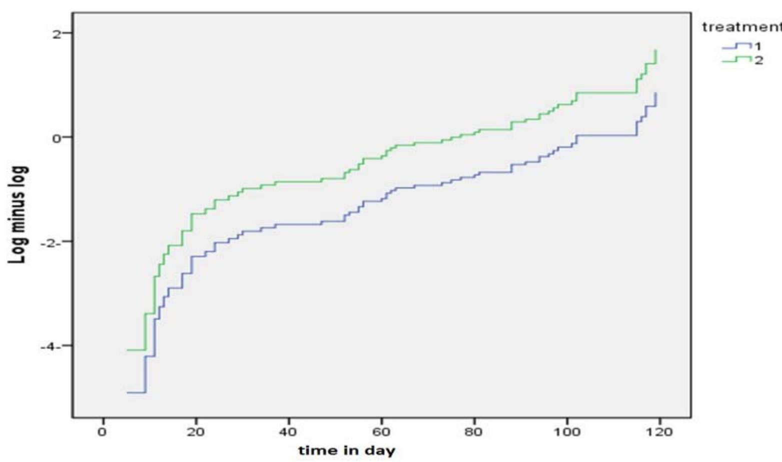

Fig 1: Kaplan-Meier test with treatment variable

III- Statistic Score Test

According to equation (18) for Statistic Score Test under the hypothesis:

H0: $\gamma 1 = \gamma 2 = \cdots = \gamma p = 0$ Versus H1: at least one of them not equal to zero We get the following result:

Table 7: Types of treatment according to the patients and state of survival

Test	Chi-square	d.f.	Table- vale	sign
S- statistic	11.4642	6	12.59	0.0824

Score test showing that model is not significant as same as showing in the Kaplan-Meier test.

10.3 Estimation Cox regression parameters

Table 8: The results of Cox- Regression model estimation

Variables	$\hat{\beta}$	S.E.	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
Age	.045	.006	54.307	1	.000	1.046	1.033	1.058
Sex	-.082	.182	.205	1	.650	.921	.644	1.316
Location	-.428	.186	5.315	1	.021	.652	.453	.938
Month	-.031	.067	.221	1	.638	.969	.850	1.105
Treatment	-.251	.076	10.940	1	.001	.778	.671	.903

Table 9: The results of (Backward method) for select sig. variables

Step No. and Variables in the model		ˆ	S.E.	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
								Lower	Upper
Step 1	Age	.045	.006	54.307	1	.000	1.046	1.033	1.058
	Sex	-.082	.182	.205	1	.650	.921	.644	1.316
	Location	-.428	.186	5.315	1	.021	.652	.453	.938
	Month	-.031	.067	.221	1	.638	.969	.850	1.105
	Treatment	-.251	.076	10.940	1	.001	.778	.671	.903
Step 2	Age	.045	.006	54.168	1	.000	1.046	1.033	1.058
	Location	-.432	.186	5.411	1	.020	.649	.451	.934
	Month	-.030	.067	.198	1	.656	.971	.852	1.106
	Treatment	-.246	.075	10.794	1	.001	.782	.676	.906
Step 3	Age	.045	.006	57.600	1	.000	1.046	1.034	1.058
	Location	-.440	.185	5.689	1	.017	.644	.449	.925
	Treatment	-.243	.075	10.575	1	.001	.784	.677	.908

Table 10: showing that model in step (3) is more significant than others.

Step	-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
		Chi- square	df	Sig.	Chi- square	df	Sig.	Chi-square	df	Sig.
1a	1245.860	69.862	5	.000	87.582	5	.000	87.582	5	.000
2b	1246.066	69.751	4	.000	.206	1	.650	87.376	4	.000
3c	1246.264	69.151	3	.000	.199	1	.656	87.177	3	.000

a. Variable(s) Entered at Step Number 1: Age Sex Location Month Treatments7
b. Variable Removed at Step Number 2: Sex, c. Variable Removed at Step Number 3: Month

After gets proportional Hazard assumption, now we can find the estimation parameters (Z1, Z2, Z3, Z4, Z5) with survival time (T) as in equation (10) ,then we get only three significant variables with Cox model and we select the best model of likelihood ratio statistic as follows:

$$Y = \lambda_0(t)\exp(0.45Z_1 - 0.440Z_3 - 0.243Z_5) \quad \text{and}$$

$$Y = \mathrm{Ln}\frac{\lambda(t/Z_1,Z_2,Z_3,Z_4,Z_5)}{\lambda_0(t)} = 0.45Z_1 - 0.440Z_3 - 0.243Z_5$$

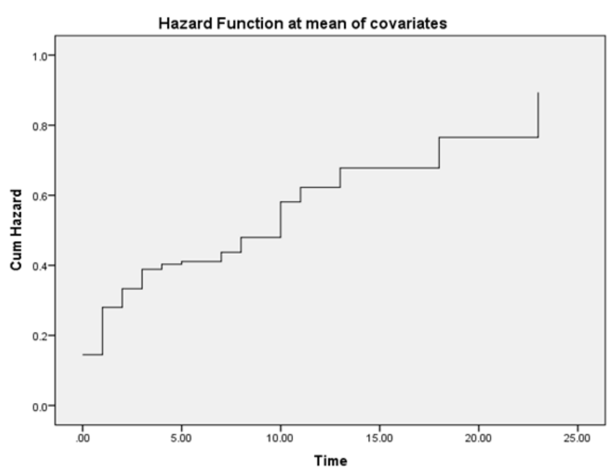

Fig 2: Cumulative hazard function for patients

Table 11: Showing the baseline hazard, Cum. Hazard with decreasing probability of survival for patients.

Time	Baseline Cum Hazard	At mean of covariates		
		Survival	SE	Cum Hazard
.00	.060	.865	.017	.145
1.00	.117	.756	.025	.280
2.00	.139	.717	.028	.333
3.00	.162	.678	.031	.388
4.00	.167	.669	.031	.402
5.00	.171	.664	.032	.410
7.00	.182	.646	.034	.436
8.00	.199	.620	.038	.479
10.00	.242	.559	.049	.581
11.00	.259	.537	.052	.622
13.00	.282	.508	.058	.677
18.00	.317	.467	.064	.762
23.00	.370	.411	.073	.889

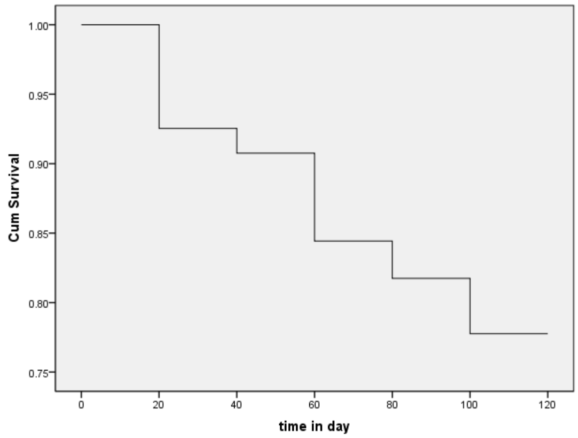

Fig 3: Cumulative survival function for patients.

11. Conclusion

1. We find from data analysis that most ratio of death (%55.36) and (%45.21) in the months of May and March. Also we find most death for patients of age more than (40 years) is (% 96).
2. Most death is the patients of male (% 56.7) and most common disease is (Heart attack) with ratio death is (%89). And most patients are from Towner location with ratio death (%59) from the total death of patients.
3. From the results of Cox- reg. model we have only three sig. variables (Age, Location and Treatment).
4. Most risk at survival time at (0- 23) days with probability survival (0.865 – 0. 411) with cumulative probability of hazard from (0.145) to (0.889) and we find that the risk of death is increasing with time.

12. References

1. Agresti A. Categorical Data Analysis. John Wiley and Sons, New York, 1990.
2. Bender. Generating survival times to simulate cox Proportional hazard models, sander for schung sbereich, 2003; 386:338.
3. Cox DR. partial likelihood, biometric. 1975; 62(2):269-276.
4. Inger person. Essays on the Assumption of Proportional Hazards in Cox Regression" Uppsala University. Sweden, 2002.
5. Izenman AJ, Tran LT. Estimation of the survival function and hazard rate, Journal of stat planning and Inference, 1990; 24:233-247.
6. Long J Scott. Regression Models for categorical and limited dependent variables, Sage publication, Oaks, 1997.
7. Nihal Ata, Tekin Säozer M. cox regression model with Nonprortional hazard applied to lung cancer survival", Hacettepe Journal of Mathematics and Statistics, 2007: 36(2):157-167.
8. Walter A. Shewhart, Samuel S. Wilks. Weibull Models, Johan Wiley & Sons. New York, 2004.