Study of Mortality Rate of Brain Stroke in Erbil-Kurdistan Region of Iraq in 2016

Lec. Dr. Mahdi Saber Raza
Dep. of Engineering Information System, Erbil Polytechnic University.

دراسة معدل الوفيات لسكتة الدماغ في اربيل / إقليم كردستان العراق لعام 2006

م.د مهدي صابر رضا
الكلية التقنية الهندسية / جامعة اربيل

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Abstract:

This study was carried out in Rizgary Teaching Hospital, Erbil, Iraq from January to December 2016. To measure the prevalence of strokes in the Iraqi Kurdish population, and to identify stroke risk factors. A sample of 73 patients was taken; 39 female and 34 male. The classical Cox-proportional hazard model were used and analyzed to find the mortality and hazard rates, and determine the significant factors. The information about the patients were gathered from official hospital records, includes age, gender, smoking, alcohol drinking, family history and marital status. Cox-regression analysis showed age, smoking and gender had a significant factors on the brain stroke. Based on that we modeled the proportional hazard regression model which shows that the survival function for the female smokers aged 76 at entry is always lower than that for the male smoker aged 66 at entry as long as the other covariates are identical. However, the survival function for the female smokers aged 66 at entry is always lower than that for the male nonsmoker aged 76 at entry.

Keywords: Stroke, Risk Factors, Cox-regression, Proportional Hazard Function, Kurdistan Region, Brain Stroke.

المستخلص:

يعد نموذج السكان في مؤشر النموذج العشوائية (ليزلي) من ابتكارات حديثة بنسبة في الإحصاء والرياضيات، وقد أثبتت أنه مفيد جدا في تجديد النمو السكاني في عام (1945) اكتشف هذا النموذج من قبل (ليزلي) ونطبق هذا النموذج على معدلات الخصوبة ومعدلات البقاء والقاعدة السكانية لنوع معين، وقد تم جمع البيانات من إحصاءات السكان ومستشفى رزكاري في اربيل لمرضى الاضطرابات (البيانات الثانوية) بين عام (2012_2017) وكذلك يمكننا استخدام هذا النموذج في معدل النمو السكاني أيضا. حيث وجد العلماء في جانب دراسة البيئة انه من المفيد تحديد ما إذا كان يمكن للنوع البقاء على قيد الحياة عند إدخاله في بيئة جديدة بالاضافه إلى ذلك، يمكن استخدامه أيضا كنموذج لتحديد عدد السكان ما إذا كان سيزيد أو سينقص خلال فترة زمنية معينة، وبالنسبة للجانب التطبيقي استخدمنا برنامج (spss وeasyfit) كجزء علمي وتطبيقي لهذه الدراسة ومن مفهوم هذه النتيجة المفاجئة إلى حد ما جاء النظر في نموذج ذات الصلة مع وظيفة الكثافة يعتمد على نسبة الجنس الذي يظهر الميزات.

الكلمة الاستدلالية: عمليات العشوائية، تحليل الاضطراب الحاسة والمرونة.

1. Introduction

Stroke is a major health burden in Kurdistan as well as worldwide. In fact stroke occurs when blood supply to the brain is interrupted, starving the brain of nutrients and oxygen. Brain cells begin to die if blood flow is stopped for more than a few seconds. The longer the supply is interrupted, the more likely there is to be permanent and debilitating brain damage. A stroke is a medical emergency that requires urgent treatment (Soman et al., 2016). The way a stroke affects the brain depends on which part of the brain suffers damage, and to what degree. Sitting just above the spinal cord, the brain stem controls your breathing, heartbeat, and blood pressure. It also controls your speech, swallowing, hearing, and eye movements. Impulses sent by other parts of the brain travel through the brain stem on their way to various body parts. We're dependent on brain stem function for survival. A brain stem stroke threatens vital bodily functions, making it a life-threatening condition (Pietrangelo, 2016).

In the Unites State, stroke is considered the third leading cause of death and effective factor for severe disability, more than 140,000 people die each year (American Heart Association, 2009). Predicting the early strokes and treating is significantly related to stroke risks.

Many medical studies and data analyzes have been carried out to categorize effective stroke predictors. Framingham in Wolf, et al., (1991) published a set of risk factors which may related to stroke such as age, including age, systolic blood pressure, the use of anti-hypertensive therapy, diabetes mellitus, smoking, prior cardiovascular disease, a trial fibrillation, and left ventricular hypertrophy by electrocardiogram, creatinine level, time to walk 15 feet, and others (McGinn, et al., 2008).

The risk factors was previously predicted by clinical trials or recorded by medical experts. Depending on cardiovascular health study, Lumley et al.(2002) constructed a 5-year stroke forecast model using a 16 features which was recorded manually from a total of one thousand features. With many features in current medical record it is difficult to manually classify and verify each risk factor. So they used Cox proportional hazard model, which is considered one of the most commonly used statistical research (Bender, 2005). This case was widely studied and has been applied to detect a different diseases including stroke (Ikeda, 2001). None the less, the performance of the original Cox model strongly depends on the quality of the preselected characteristics (Ikeda, 2001).

These risk factors contributed to, and were thought to be responsible for, an estimated 87.8% of the total deaths caused by stroke in Iraq during 2013. Adjust the filters at the top of the visualization to see how which risk factors caused the highest mortality for men and women of different age

groups. The annual mortality rate per 100,000 people from stroke in Iraq has decreased by 16.9% since 1990, an average of 0.7% a year. Although this has been the trend overall, adjust the filters at the top of the visualization to see how the mortality rate for stroke has changed over time for men and women of specific age groups in Iraq. The deadliness of stroke for men in Iraq rises at age 85. Women are died because of strokes at the highest rate at age 70 or more, it recorded 3,060.4 deaths per 100,000 women in 2013, the peak mortality rate for women was higher than that of men, which was 2,471.1 per 100,000 men. For men, the health burden of stroke in Iraq, as measured in years of healthy life lost per 100,000 men, peaks at age 85. Women are harmed at the highest rate from stroke in Iraq at age 70 or more. At 22,214 years of healthy life lost per 100,000 women in 2013, the maximum rate for women was higher than that of men, which was 17,864.3 per 100,000 men (Health Grove, 2017).

Competing the mortality rate of stroke in Iraq with other locations in North Africa and Middle East. Learn how it has changed over time in each location. Interact with the filters to see how the deadliness of stroke varies for specific demographic groups within these locations. In Egypt, Tunisia, Yemen, Syria, Turkey, Libya, Algeria, Iraq, Sudan and Lebanon the mortality rate per 100,000 patients was 104.7, 68.8, 62.6, 60.2, 60.1, 59.3, 57.3, 51.5, 50.9 and 43.1 as the percentage changes during 1990-2013 were -7%, 42%, -4%, -16%, -10%, 36%, 16%, -17%, -16% and -24% respectively (Health Grove, 2017).

Most of these studies also demonstrated that age and strokes strongly and independently correlated with age. The aim of the current study is to identify and verify the most common and significant risk factors for brain strokes factors affecting brain stroke among the Iraqi Kurdish population in Erbil city (see, Al-Shimmery2010).

2. Patients Data and Methods

The data covers the 73 patients, 39 female and 34 male from January 2016 to December 2016 and the data was collected from Rzgary Teaching Hospital in Hawler city-Iraq. The data were analyzed using the SPSS version 22.

2.1 Cox-Proportional Hazard Model

This model is one of the semi-parametric duration model, which are very flexible since the baseline hazard function is nonparametric and eliminates the risk of corrupting the estimated-hazard parameters while the effect of the covariates takes a particular functional form. An important

feature of this formula, which concerns the proportion hazard (PH) assumption is that the baseline hazard is a function of *t* but does not involved the variable *x*'s, where the exponential expression involves the *x*'s but does not involved *t*. the variable *x* are called time-independent *x*'s.
This class of model also called the Cox Proportional Hazards Model (PH) (Cox and Oakes, 2001: Fabsic, et al., 2011). The proportional-hazard model assumes that

$$h_i(t,x) = h_0(t) * \exp(\sum_{j=1}^{p} \beta_j x_j) \quad (1)$$

Where:
$h_i(t)$: denotes the hazard function for life *i* at duration *t*.
$h_0(t)$: denotes the baseline hazard function at duration *t*, but not *x*'s.
x_j: denotes the factors at entry of life *i*.
β_j : is the coefficients of the parameters, $i=1, 2,...,p$, $j=1,2,3,...,k$

In general, the survival time measured from birth to death for an individual. For the conditional hazard definition, let $T \geq 0$ have probability density function $f(t)$ and cumulative distribution function $F(t)$. The survival function $S(t)$ is:

$$P_r(T > t) = S(t) = 1 - F(t) \quad (2)$$

When T is a survival time, $F(t)$ is the probability that a randomly selected subject from the population will die before time *t* and the hazard rate or hazard function $h(t)$ is:

$$h(t) = \frac{f(t)}{1 - F(t)} = \frac{f(t)}{S(t)} \quad (3)$$

To fix ideas consider two sample problem where we have a dummy variable *x* which serves to identify groups one and zero. Then the model is:

$$h_i(t,x) = \begin{cases} h_0(t) & if\ x = 0, \\ h_0(t)e^{\beta} & if\ x = 1. \end{cases} \quad (4)$$

Thus, $h_0(t)$ represents the risk at time *t* in group zero, and $\exp\{\beta\}$ represents the ratio of the risk in group one relative to group zero at any time *t*. If $\beta = 0$ or $e^{\beta} = 1$ then the risk are the same in two groups. If $\beta = 0.6931$ for instance or $e^{\beta} = 2$, then the risk for an individual in group one at any given age is twice the risk of a member of group zero who has the same age (see Crrowder, 2012).

Note that the model separate clearly the effect of time from the effect of the covariates. Taking logs, we find that the proportional hazards model is a sample additive model for the log of the hazard, with

$$\log h_i(t, x_i) = h_0(t) + x_i\beta_i \tag{5}$$

Where $h_0(t) = \log h_0(t)$ is the log of the baseline hazard function. As in all additive models, we assume that the effect of the covariates *x* is the same at all times or ages *t*. The similarity between this expression and a standard analysis of covariance model with parallel lines should not go unnoticed. Returning to Equation 1, we can integrate both sides from 0 to *t* to obtain the cumulative hazards:

$$\int_0^t h_i(t,x)dt = \int_0^t h_0(t) * \exp(\sum_{j=1}^{p} x_j\beta_j)\, dt \tag{6}$$

Which are also proportional. Changing signs and exponentiating we obtain the survivor functions:

$$S_i(t, x_i) = S_0(t)^{\exp(\sum_{j=1}^{p} x_j\beta_j)} \tag{7}$$

Where**:**

$$S_0(t) = \exp\{-\int_0^t h_0(t)dt\} \tag{8}$$

is a baseline survival function. Thus, the effect of the covariate values x_i on the survivor function is to raise it to a power given by the risk $\exp(\sum_{i=1}^{p} x_i\beta_i)$.

In our two group example with a relative risk of e^{β} =2, the probability that a member of group one will be alive at any given age *t* is the square of the probability that a member of group zero would be alive at the same age (Spruance, et al., 2004: Hosmer and Lemeshow, 1999).

2.1.1 The Hazard Ratio (HR) for the extended Cox model

we now described the formula for the hazard rate that derives from the extended Cox model. the most important feature of this formula is that the proportional hazards assumption is no longer satisfied when using the extended Cox model. The general hazard ratio formula for the Cox model is shown in Equations (9) and (10). This formula describes the rate of hazards at a particular time *t*, and requires the specification of two sets of

predictors at time *t*, These two sets are denoted as $x^*(t)$ and $x(t)$. (Spruance, et al., 2004: Mark, 2009).

$$HR(t) = \frac{h_i(t)}{h_j(t)} \tag{9}$$

$$\frac{h_i(t, x^*(t))}{h_j(t, x(t))} \propto \frac{\exp(\sum_{i=1}^{p} \beta_i x^*{}_i)}{\exp(\sum_{j=1}^{k} \beta_j x_j)} \tag{10}$$

2.2 Statistical Analyses

This paper uses secondary data based on laboratory investigations. These data are supplied by Rizgary Teaching Hospital, Erbil, Iraq for the year 2016. The data was collected from existing databases in terms of the time of death. The data includes the factors affecting the brain stroke which are family history, age, smoking, alcohol, gender and marital status. Data were translated into codes using a specially designed coding sheet, and then converted to computerized database. An expert statistical advice was required and statistical analyses were done using (SPSS) (Statistical Package for Social Science) version 22 computer software. The classical semi-parametric model "Cox-proportional hazard model" were used and analyzed to find the mortality and hazard rates. With the *P*-value less than and equal to 0.05 regarded as statistically significant.

3. Results

To determine an major factors which impact brain stroke among patients in the Rizgary Teaching Hospital, Erbil-Kurdistan Region of Iraq. This is performed by finding the hazard function curve for the selected variables, beginning with the use of Kaplan Meier method and comparison of the variables by using tests including the Mantel-Cox test. The Cox-regression is used to determine the significant variables among the 6 used in the study. Based on the largest p-value, we delete sequentially the variables repeating the process until we get all significant variables with p-value less than 0.05. As shown in Table 1.

Table 1

All variables in the Cox regression model

Variables	*B*	*SE*	*Wald*	*D.f*	*Sig.*	*Exp(B)*	*95.0% CI for Exp(B)*	
							Lower	*Upper*
Age	-.014	.016	.804	1	.370	.986	.955	1.017
Gender	.920	.514	3.212	1	.073	2.510	.918	6.869
Smoking	-1.228	.465	6.980	1	.008	.293	.118	.728
Alcohol	-.305	.457	.445	1	.505	.737	.301	1.806
Family history	.020	.600	.001	1	.973	1.020	.315	3.305
Martial status			2.727	2	.256			
Martial status (1)	-.751	.894	.707	1	.401	.472	.082	2.719
Martial status (2)	-.729	.458	2.533	1	.111	.482	.197	1.184

Applying Cox-regression model gives the results as shown in Table 2. and Table 3.

Table 2

The general Cox-proportional model

Overall (score)			*Change From Previous Step*			*Change From Previous Block*		
Chi-square	*D. f*	*Sig.*	*Chi-square*	*D. f*	*Sig.*	*Chi-square*	*D. f*	*Sig.*
10.084	3	.018	9.260	3	.026	9.260	3	.026

Table 3

Significant variables in the Cox-regression model

Variables	*B*	*SE*	*Wald*	*D.f*	*Sig.*	*Exp(B)*	*95.0% CI for Exp(B)*	
							Lower	*Upper*
Age	-.005	.008	.373	1	.542	.995	.979	1.011
Gender	-.850	.383	4.931	1	.026	.427	.202	.905
Smoking	1.160	.416	7.779	1	.005	3.190	1.412	7.207

Depending on Table 3, we can find the survival function of male smoker aged 66 at entry; *i* relative to that of a female smoker aged 76 at entry; *j* based on the proportional hazards regression model is fitted as:

$$h_i(t,x^*) = h_0(t) * \exp[\, Age\,(x_i - \bar{x}) + Gender\, y_i + Smoking\, z_i\,]$$

Where:
x_i : denotes the age at entry of life *i*.
y_i : is an indicator denoting the gender status of life *i*.

$$\text{i.e. } y_i = \begin{cases} 1 & if \;\; life \;\; i \;\; is \;\; a \;\; male \\ 0 & if \;\; life \;\; i \;\; is \;\; female \end{cases}$$

z_i: is an indicator denoting the smoking of life *i*.

$$\text{i.e. } z_i = \begin{cases} 1 & if \;\; life \;\; i \;\; is \;\; a \;\; Smo\,\text{ker} \\ 0 & if \;\; life \;\; i \;\; is \;\; non \;\; Smo\,\text{ker} \end{cases}$$

$$\frac{h_i(t,x^*)}{h_j(t,x)} \propto \frac{\exp[-0.005(66-66)+1.160(1)-0.850(1)]}{\exp[-0.005(76-66)+1.160(1)-0.850(0)]}$$

$$\frac{h_i(t,x^*)}{h_j(t,x)} \propto \frac{\exp[0.31]}{\exp[-1.21]} = \exp[-0.8] = 0.4493$$

$$S_i(t,x^*) = [S_j(t,x)]^{0.4493} \Rightarrow S_i(t,x^*) > S_j(t,x) \qquad \text{for all } t > 0.$$

That mean the survival function for the female smoker aged 76 at entry is always lower than that for the male smoker aged 66 at entry as long as the covariates are identical. In the other hand, the result of survival function of female smoker aged 66 at entry relative to that of a male non smoker aged 76 at entry is greater than 1,

$$S_i(t,x^*) = [S_j(t,x)]^{1.5} \Rightarrow S_i(t,x^*) < S_j(t,x) \qquad \text{for all } t > 0.$$

As a result, the survival function for male non smoker aged 76 higher than that for female smoker aged 66.

In order to find the hazard function for age group we divided the age variable into two groups based on their mean. Table 4, shows that from 32 patients how aged less and equal 66 years old 21 of them are dead and 11 patients were censored or left the study. In the meantime, 41 patients how

aged greater than 66 years old 23 of them were died and 18 patients were censored as the previous case they left the study.

Table 4
Significant age variable

Age Code	*Total N*	*N of Events*	*Censored*	
			N	*Percent*
Age <=66	32	21	11	34.4%
Age > 66	41	23	18	43.9%
Overall	73	44	29	39.7%

Table 5
Mantel-Cox test for the age variable

Test	*Age Code*	*Age <=66*		*Age > 66*	
		Chi-Square	*Sig.*	*Chi-Square*	*Sig.*
Mantel-Cox	Age <=66			.473	.492
	Age > 66	.473	.492		

The mantel-Cox test is used to compare inside each variables, in Table 5, the p-value of Chi-Square shows that the relation between patients aged less and equal 66 years old and patients with ages greater than 66 years old are not very strong or the difference between them is big. The hazard function in Figure 1, for the same variable illustrate that the hazard function for both age groups are very close to each other they are fluctuated until 20 days after that from 20 to 35 they are in the same hazard rate then the hazard function for the age group greater 66 years old having higher risk than the other group.

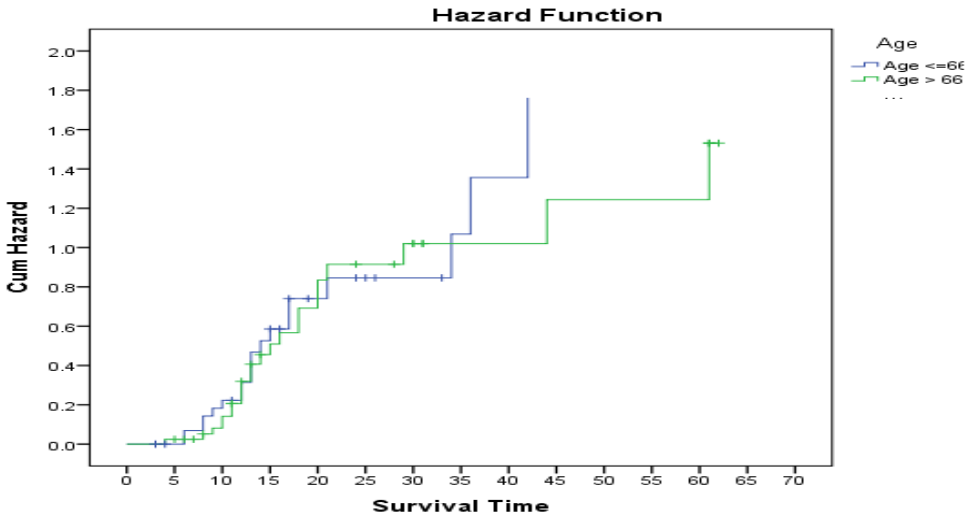

Figure 1

Hazard function curves for the age variable

To calculate the hazard function for smoking variable. Table 6, shows that from 31 patients how are not smoking 13 of them are dead and 18 patients were censored or left the study. While, 42 patients how are smoking 31 of them were died and 11 patients were censored as the previous case they left the study.

Table 6

Significant smoking variable

Smoking	*Total N*	*N of Events*	*Censored*	
			N	*Percent*
No	31	13	18	58.1%
Yes	42	31	11	26.2%
Overall	73	44	29	39.7%

Table 7, illustrates the Mantel-Cox test for the smoking variable. The results show that the relationship between its individuals; the smokers and non smokers is very strong. The hazard function in Figure 2, for the same variable illustrate that the hazard function for nonsmokers are higher than the smokers, the nonsmokers have better opportunity to live longer than smokers.

Table 7

Mantel-Cox test for the smoking variable

Test	*Smoking*		*No*		*Yes*	
			Chi-Square	*Sig.*	*Chi-Square*	*Sig.*
Mantel-Cox	No				3.695	.05
	Yes		3.695	.05		

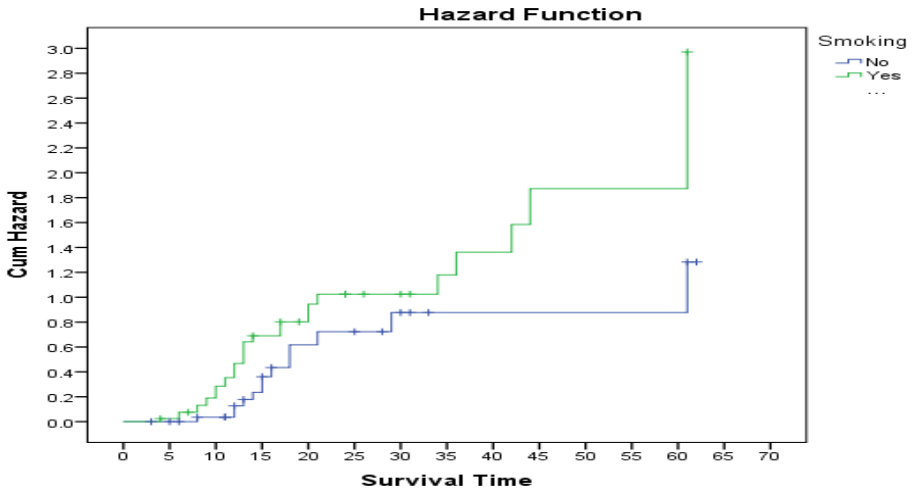

Figure 2

Hazard Function curves for the smoking variable

The hazard function for gender variable. Table 8, shows that from 39 female patients 23 of them are dead and 16 patients were censored or left the study. While, 21 male patients were died and 13 patients were censored or left the study.

Table 8

Significant gender variable

Gender	*Total N*	*N of Events*	*Censored*	
			N	*Percent*
Female	39	23	16	41.0%
Male	34	21	13	38.2%
Overall	73	44	29	39.7%

Table 9, states the results of the Mantel-Cox test for the last significant variable in the study, which is the gender. It shows that the difference between individuals where not very strong. The hazard function in Figure 3, for the same variable illustrate that the hazard function for males until 12 days are higher than that for the females. After 12 days the hazard function for the female will rise until day 60. Then in day 62 the male curve will start to rise again.

Table 9

Mantel-Cox test for the gender variable

Test	*Gender*	*Female*		*Male*	
		Chi-Square	*Sig.*	*Chi-Square*	*Sig.*
Mantel-Cox	*Female*			*.172*	*.678*
	Male	.172	.678		

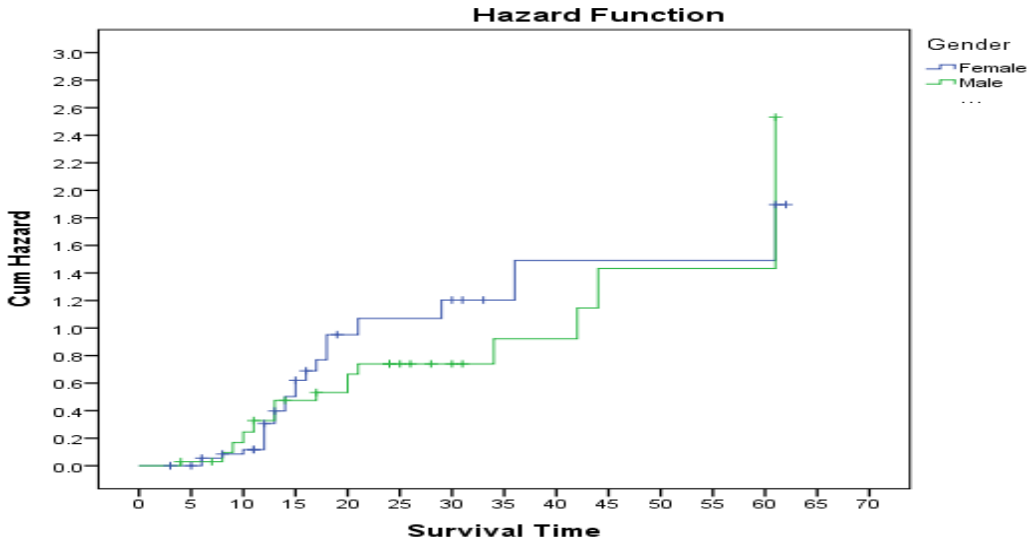

Figure 3

Hazard function curves for the smoking variable

4. Discussion and Conclusions

We focused on the Cox model, the class of semi-parametric models of PH as tools to analyze survival time data. Using the Cox model offers more flexibility than parametric alternatives and, especially, the baseline hazard function does not require any direct estimation,(i.e. the distribution of survival time is not necessary). Although the relative risk assumption of is vital that must be met for logical results and has not always been achieved. Depending on our case study, incidence of brain stroke for the year 2016 in the Rizgary Teaching Hospital, Erbil - Kurdistan Region of Iraq. The result shows that ages, smoking and gender were the main factors affecting brain stroke. There is a strong relationship among smokers and nonsmokers as the p-value for Mental Cox is les s than and equal to 0.05. In general the mortality rate for smokers are more than for nonsmokers. Furthermore, the survival function for male smoker aged 66 is higher than that for female smoker aged 76. In the meantime, for the females smoker aged 66 is lower than for male nonsmoker aged 76. This is due to the physical structure for the men is more than for the women. Moreover, Tables 4, 6and 8 shows that out of 32 patients 34.4% of were encored, aged less and equal to 66 years old. While, 43.9% patients aged greater than 66 years old from 41 patients. out of 31 non smokers patients 58.1% were censored and out of 42 smokers 26.2% patients were censored. For the last significant factor gender, 41.0% of censored patients were female, while 39.7% were male out of 39 and 34 patients, respectively. Lastly, we recommended that we

can apply this model to the difference cancer especially the time is continues including the time of the death or survival, on the other hand reliability (machine) also we could to apply on it. The most important is relation with real life data for the rate mortality.

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