Determinants of Stroke Mortality through Survival Models: The case of Mettu Karl Referral hospital, Mettu, Ethiopia

Dereje Gebeyehu Ababu (derejegebe@gmail.com)
Mettu University

Azmeraw Misganaw Getahun
Mettu University

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Abstract

Introduction: Every year worldwide between five to six million deaths are associated with stroke; on average, one stroke-related death occurs every four min. In Ethiopia, stroke is a frequent cause of mortality and morbidity from non-communicable diseases. Therefore, this study was aimed to determine factors associated to stroke mortality through survival models in Mettu Carl Referral Hospital.

Methods: This study was conducted from September 1, 2014 to April 1, 2017, and encompassed 202 stroke patients at Mettu Carl Referral Hospital. The Cox Semi-parametric regression and parametric PH Weibull, Exponential, Log-logistic and log-normal models were used for analyzing survival analysis of stroke patients using R software.

Results: A totals of 202 stroke patients were included in the study and among those patients 72.8% and 27.2% were censored and died respectively. According the result of Weibull proportional hazard model, gender of patients (HR=1.5052200, p-value<0.0000207), hypertension (HR= 0.7135953, p-value<0.000737), and baseline complication (HR=0.7246955, p-value<0.00229), had significant effect on survival of the stroke patient.

Conclusion: The estimated survival and hazard rate of stroke patients under gender of patients, baseline complication and hypertension had significant difference with p-values less than 0.05. Finally, the findings of this study implied that Hypertension, sex of the patients, and baseline complication were major factors related to survival time of stroke patients. The researcher recommends that the people should aware on the burden of those risk factors and well informed about the disease.

Introduction

A stroke is caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. This cuts off the supply of oxygen and nutrients, causing damage to the brain tissue [41]. Stroke, although a preventable chronic disease, is the second-highest cause of mortality around the world. Every year worldwide between five to six million deaths are associated with stroke; on average, one stroke-related death occurs every 4 min. Besides the high mortality rate, the high morbidity rate accounts for approximately 50% of survivors being debilitated. Annually, the burden of stroke is estimated to cost about 63 billion dollars globally both in direct and indirect costs [15].

Globally, stroke is the second leading cause of death above the age of 60 years and about 16 million new cases of stroke and 62 million stroke survivors were estimated in 2005, with deaths from stroke accounting for 9.7% of all global deaths, and this is expected to increase to over 23 million new stroke cases and 7.8 million stroke deaths by 2030 in the absence of significant global public health response [36].

In Africa the impact of stroke is increasing due to a rising prevalence of hypertension associated with a very poor level of awareness and control. African countries are undergoing an epidemiological transition

driven by socio-demographic and lifestyle changes [32]. The burden of non-communicable diseases (NCD), including cardiovascular risk factors is increasing. Consequently, the incidence of stroke, a cardinal complication of cardiovascular risk factors, appears to be rising in Africa [30].

In Ethiopia, hypertension was the most important risk factor identified in 1990. However ,during that time ,computed tomography(CT) scan was not available to differentiate stroke sub-types and the modern approach in treating patients with strokes requires early CT scan as it is imperative to diagnose whether the stroke is ischemic or hemorrhagic [26].

Therefore, chronic diseases become major global public health problems, mainly, in developing countries. However, there is limited evidence on the magnitude and factors of stroke in Ethiopia using Survival models, particularly, in Mettu Carl Referral Hospital, which is the aim of this study. Findings of this study were important evidence to the studied hospital and Oromia Regional Health Bureau to know the burden of stroke and determinant factors, and plan appropriate preventive methods against stroke.

Methodology

Study Area

This study was conducted in Mettu Karl referral hospital. This study was conducted from 1st September 2014 to 1st April 2017 in Mettu Karl hospital.

Study design and population

Retrospectives data were gathered from a total number of 202 stroke disease patients diagnosed with stroke case patients in the medical and surgical wards from 1st September 2014 to 1st April 2017 in MCRH.

Variable in the study

The dependent (outcome) variable in this study was the survival time measured (in days) from the date stroke treatment's start until the date of the patient's death or censor. The following are covariate variables in the study. Gender, Age, Hypertension, Cardiac disease, Diabetes mellitus, Stroke type, Baseline complication and Drug type

Method Of Data Analysis

Survival analysis is a collection of statistical procedures for data analysis for which the outcome variable of interest is time until an event occurs. An initial step in the analysis of a set of survival data is to present numerical or graphical summaries of the survival times in a particular group. In summarizing survival data, the two common functions of applied are the survivor function and the hazard function [45].

The Kaplan–Meier estimator is a nonparametric statistic used to estimate the survival function from lifetime data.

The Kaplan Meier estimator of the survivorship function (or survival probability)

S (t) =P (T≥ t) is defined as :-

$\hat{S}(t)=\prod_{t_i \le t} \frac{n_i - d_i}{n_i} = \prod_{t_i \le t} 1 - \frac{d_i}{n_i}$,where $t_1, t_2, \ldots, t_n$ a set of survival time of n independent observations and $t_{(1)} \le t_{(2)} \le \ldots \le t_{(m)}$, $m \le n$ be the m distinct ordered death times.

d_i is the number of individuals who failed (died) at time t_i

n_i is the number of individuals who are at risk of dying at time t_i.

One of the most popular types of regression models used in survival analysis is the Cox proportional hazard model [14]. He proposed a semi-parametric model for the hazard function that allows the addition of covariates, while keeping the baseline hazards unspecified and can only positive values .with this parameterization the Cox hazard function is given by:

$$h(t,x) = h_o(t)exp(\hat{\beta}x)$$

Where ho (t) is the baseline hazard function; $h_0(t)$ is called the baseline hazard function; $x=(x_1,x_2,\ldots,x_p)'$ is the values of the vector of explanatory variables; $\beta' = (\beta_1, \beta_2, \ldots, \beta_p)$ is a vector of regression coefficients. The main assumption of the Cox proportional hazards model is proportional hazards that means that the hazard function of one individual is proportional to the hazard function of the other individual, i.e., the hazard ratio is constant over time.

Results And Discussion

Descriptive Summaries

A total of 295 stroke patients were treated in the hospital during the study period from 1st September 2014 to 1st April 2017. Of total population, this study included 202 stroke patients for whom data for variables of interest are complete. Of all 202 stroke patients 147(72.8%) were censored or not experienced the event and 55(27.2%) are died. Average time duration for all patients was 6.05 with standard deviation of 4.698 and the median and mean survival time of age was 6 and 7.168 days respectively. The mean and median age of stroke patient was 62.56 and 65 days respectively .The mean and median survival time from stroke was found to be 15.596 and 19 days respectively. The mean survival time of male and female were 9.1 days and 5.1 days respectively. The minimum and the maximum survival time observed in the data were 1 days and 24 days respectively. The median survival time of female and male was 3

days and 6 days respectively. Patients with hypertension stayed 4 days of which 72.13% were death. However, patients with no hypertension stayed 9 days on average of which 27.87% were death. Patients with baseline complication stayed 4 days on average of which 67.3 % were death (Table 1).

The Kaplan- Meier Estimate

The estimate for overall Kaplan –Meier survivor function depicted that relatively a large number of the deaths occurred at the earlier days of anti-stroke treatment and the same graph showed the decrement over a follow up period (Figure 1).

Kaplan-Meier Estimates is represented by the survival curves for without hypertension diseases are above those the patients' complications with hypertension. This implied that the patients without hypertension more survival than with hypertension (Figure 2).

Log Rank Tests of Each Covariate

The log-rank test indicates that statistically there is a significant difference of survival experience among groups of gender, age, blood pressure (hypertension), and baseline complication. On the other hand, there are statistically no significant difference in survival/death experiencing among groups of the categorical covariates cardiac disease, diabetes mellitus, stroke type and drug type. Accordingly, the mean survival time of male patients' to death had been 9.1 days greater than females 5.1 days with [95% CI [8.04889, 10.3094] (Table 2).

Univariable Analysis of Cox PH regression model

from the outputs in univariable analysis, we can observe that the covariate age of stroke patient (HR=1.011731,P-value= 0.0119),gender of patient (HR=0.4123,P-value=1.58e-06), hypertension (HR=2.5510,P-value=2.4e-06), stroketype(HR= 0.6152, 1.7325, P-value= 0.0140, 0.0961),drug type and baseline complication (HR =3.0710,P-value = 4.84e-08) are significant and hypertension, baseline complication, gender and stroke type are highly significant in the univariable analysis. However, diabetes mellitus and cardiac is not a significant factor for the death time at 25% level of significance (Table 3).

Multivariable analysis of Cox PH Regression Model.

Covariates which become insignificant in the multivariable analysis were removed from the model by using stepwise elimination technique. Accordingly, cardiac disease, and Diabetes mellitus were excluded. In order to decide whether or not a variable is significant, the p-value associated with each Parameter has been estimated and variables that have p-value less than 0.05 cut point or 5% significance level are considered as important variables and hence, are included in the final model (Table 4).

Checking for the Linearity of Continuous Covariates in the Model

For the covariates age the plots show systematic patterns or trends and the resulting smoothed plots are not a straight line. Therefore the plots of martingale residual confirm that age of a patient have no linear

relationship with the survival time (Figure 3).

Checking of Proportional hazard assumption

The test of correlation (rho) is insignificant that indicates proportional hazards assumption is fulfilled. Variables age, gender of patients, Hypertension (blood pressure), base line complication ,drug type and Stroke type are fulfilled the assumption because all the p values are greater than 0.05. In Schoenfeld if the p value is greater than 0.05 it indicates that the Cox proportional hazards assumptions are fulfilled (Table 5).

Diagnosis of the Model: The likelihood ratio and significance of the final Cox PH model

From the likelihood ratio test, it can be seen that the PH model is significant since p-value is less than 5% (Table 6).

PARAMETRIC PH REGRESSION ANALYSIS

The Weibull model appears to be an appropriate PH regression model according to AIC compared with other regression models in multivariate analysis (Table 7).

From the Weibull regression model, after fixing other coefficients, the hazard rate for, male stroke patient 1.4 times than the hazard rate of females patients. The hazard rate of patients with baseline complication was 0.8 times that of patients who had no baseline complications. Finally, the hazard rate of patients who had hypertension was 0.7 times that of patients who had no hypertension. The interpretation of the result from the fitted final Weibull PH model is based on the hazard ratios (Table 8).

Conclusions

The objective of the study was to identify significant risk factors that affect survival of stroke patients who have been under follow-up at Metu Carl Referral Hospital. For determining the risk factors for the survival time of stroke patients, a total of 202 patients were included in the study out of which 40.6% were females and 59.4% were males. Among those patients 27.2% were died and the rest were censored.

The Cox regression analysis showed that the major factors that affect the survival of stroke patients are Hypertension, gender of the patients, and baseline complication were strongly related to mortality and based on the hospital outcome the most common causes of death were hypertension and base line complication. However, there were variables that were significant at univariable stage of analysis but not at multivariate analysis stage. These were stroke type, drug type and age of patients. Moreover, variables that were significant neither at univariable nor multivariable analyses were gender, baseline complication and hypertension. The result of this study also indicated that survival probability of a patient is not statistically different among groups classified by cardiac disease, diabetes mellitus, stroke type, and drug type.

To predict and model the survival time of stroke patients, various parametric regression models were applied. Among which the Weibull regression survival model is better fits to predict the survival time of the disease for the data of stroke patients of Mettu Carl referral hospital than the other parametric models.

Limitations

This research paper was limited to time from date of first diagnosis until the occurrence of the death or end of the study period for 202 stroke patients in case of Karl Hospital, Ilu Ababor Zone.

List Of Abbreviations

AIC: Akaike's Information Criterion; AIDS: acquired immune deficiency syndrome; BIC: Bayesian Information Criterion; CT: computed tomography; HIV: human immunodeficiency virus; NCD: non-communicable diseases; WHO: World Health Organization

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by Mettu University Research Ethical Committee. As the study was based on retrospective cohort study, informed consent was not needed.

Consent for publication

Not applicable.

Availability of data and materials

If needed, the data in excel format is available for this article.

Competing interests

The authors declare that there is no competing interest.

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There is no fund for this article.

Authors’ contributions

DG and AM designed the research, collect the samples, wrote the paper, analyzed data; DG conducted research and had primary responsibility for final content. All authors read and approved the final manuscript.

Corresponding author

Correspondence to Dereje Gebeyehu Ababu

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Tables

Due to technical limitations the Tables are available as a download in the Supplementary Files.

Figures

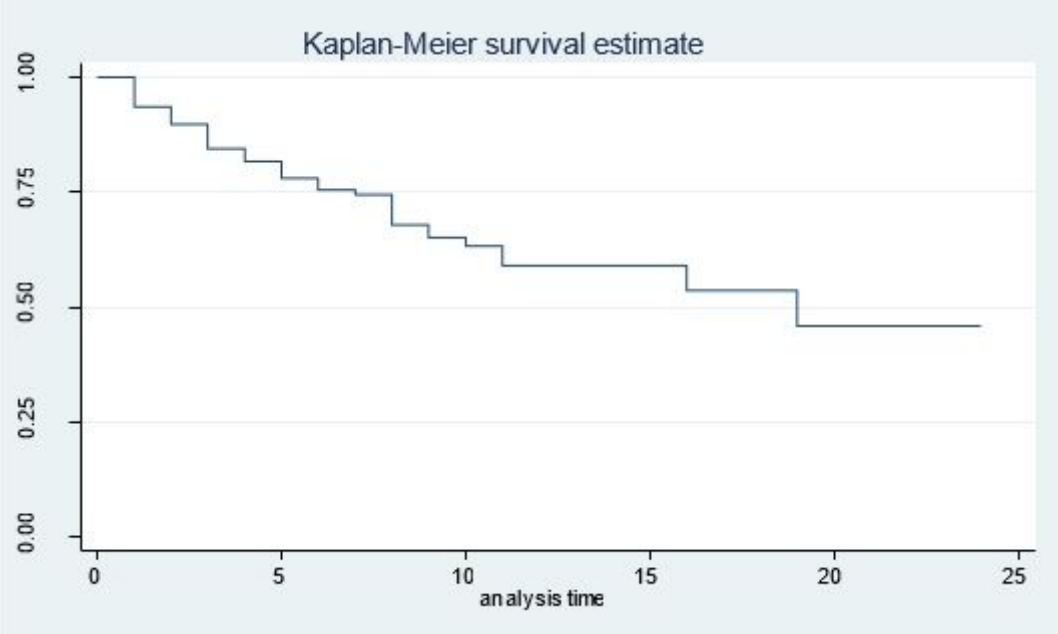

Figure 1

Overall Kaplan-Meier survivor function

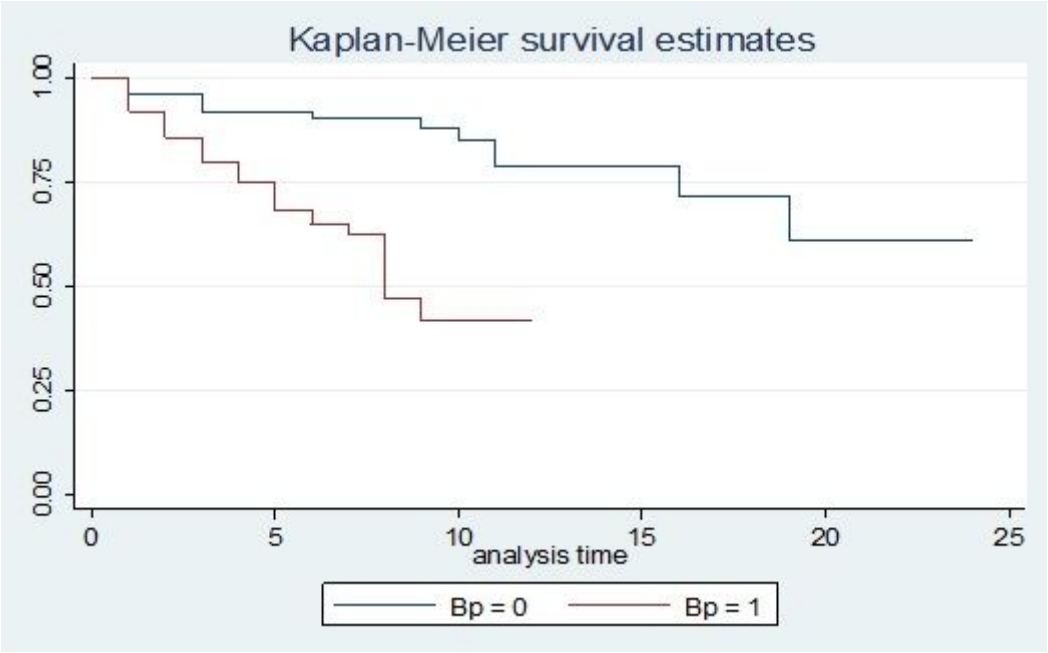

Figure 2

K- M plot survivals Time-to death by hypertension of stroke patients

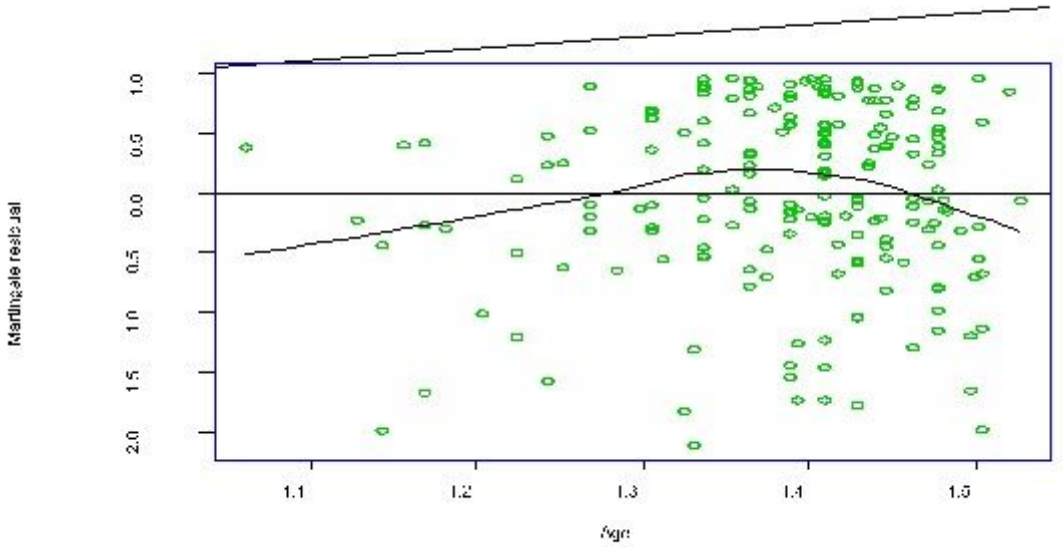

Figure 3

Plots of the Martingale Residuals against the covariate age.

Supplementary Files

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