Original Research Article

Long-Term Predictors of Stroke Severity among Patients on Secondary Prevention in Northern Ghana

ABSTRACT

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Aims: The aim of the study is to discover some risk factors of stroke and estimate the effect of the covariates at different levels of disease states.

Study Design: A typical review of literature on risk factors of stroke revealed that none of the articles estimated the possible covariate effect of transiting from one disease state to another. To fill this gap, we incorporated the covariates in a Continuous Time Markov Model (CTMC) in Multi-state Models (MSM) to observe the transition rates of the patients at two-monthly intervals for two years. Patient variables were: *age*, *sex*, *location of the patient*, *local treatment*, *smoking*, *alcohol intake*, and *hemiparesis*.

Place and Duration of Study: We retrospectively obtained secondary data from stroke patients under rehabilitation at the Tamale Teaching Hospital from 2014 to 2019.

Results: Our study reveal that male sex contributed to early recovery in all states than female sex. While old and older age groups have some probability of transiting to a less severe state and similar probabilities of transiting from mild to a more severe state, the youth have better conditions in the more severe state than these two groups. At severe state a patient without local treatment will live less than two months (1/1.242) before death (0.2150) whiles patients who seek local treatment may remain with severe stroke for at least two month (1/0.9721) before transiting to a less severe state. Thus left- hemiparesis patients are about twice less likely (0.06738) to transit to more severe state than right-hemiparesis (0.1207). **Conclusion:** Further research should be carried out to investigate the role of traditional therapy in stroke rehabilitation.

Keywords: Stroke Predictors, Secondary Prevention, stroke Severity, Ghana, Long-term, and State

1.0 INTRODUCTION

Globally, stroke is one of the primary roots of morbidity and death and the principal cause of disability[1]. Although secondary preventive measures are on the rise, patients still face different time points after stroke [2]. The ability for a patient to recover from a stroke depends on the severity and how quickly the patient gets medical attention. Several scales are used in determining the functional independence of the survivors. These scales (Modified Rankin Scale (mRS), Canadian Neurological Scale (CNS), Barthel Index (BI), National Institute of Health Scale (NIHSS), and many others) are used in determining the severity of stroke which may be grouped into three categories: mild, moderate and severe.

[3] Studied racial variation in initial stroke severity. That was to determine whether there is a racial difference in initial stroke severity between blacks and white. They obtained secondary data from nine (9) site nationwide cohort studies of 1073 participants with acute stroke. Initial stroke severity of each patient was determined using the Canadian Neurological Scale (CNS) which categorized stroke severity scores as mild (8.5 to 11.5), moderate (6.0 to 8.0), and severe (0.0 to 5.5) for each race. Multivariate linear model analysis was performed using initial stroke severity as response variable while covariates such as (age, race, atrial fibrillation, diabetes mellitus, smoking, stroke type, prior stroke, prior nursing at home, and hypertension) were used as the explanatory variables. The results turn out that blacks and whites differed in several characteristics; (Blacks had higher initial stroke severity, compared to Whites (mean CNS score 7.96 against 8.32) at 0.5-point difference on the scale using analysis.

According to [4], smoking is a deep-rooted risk factor of stroke and cessation of smoking has been recommended for stroke prevention. Patients who survive a stroke were sign on and followed in the NSRP (Nanjing Stroke Registry Program). Their smoking prominence was measured at starting point and reexamined at the first follow-up. After three months from the index stroke, the primary end point was defined as a severe or nonfatal recurrent stroke. Using a multivariate Cox regression model, the relationship between smoking and the risk of stroke recurrence was examined. 1331 of the 3069 patients included at baseline were non - smokers, 263 were former smokers, and 1475 were still smoking today. 908 patients had given up smoke at the initial check-up. 293 patients experienced a stroke recurrent over a mean follow-up of 2.412 years. The hazard ratio for stroke recurrence using non-smokers as the reference group were 1.16 in former smokers, 1.31 in quitters, and 1.93 in persistent smokers. The criteria for assessment for stroke recurrence among long-term smokers varied from 1.68 for individuals who smoked 1 to 20 cigarettes per day to 2.72 for those who smoked more than 40 cigarettes per day.

According to studies on alcohol use conducted in 2018 by [5] there is little evidence linking alcohol consumption to outcome measures following a stroke. The study used a prospective cohort study with 21,862 men who participated in the Physicians' Health Study, gave baseline data on alcohol intake, and had no history of stroke or transient ischemic attack (TIA). Multinomial logistic regression was employed by the researchers to assess the association between alcohol consumption levels and functional. According to the study's findings, there were 767 TIAs and 1393 strokes (1157 ischemic, 222 hemorrhagic, and 14 of uncertain kind) throughout the course of a mean 21.6-year follow-up. Men who drank one drink per week had the lowest probabilities for any result compared to men who consumed but did not have a TIA or stroke.

In predicting three-month mortality among patients hospitalized for first-ever acute ischemic stroke, [7] investigated factors related to 3 months mortality at admission in patients with first-ever acute ischemic stroke at Taiwan medical center within 48 hours after the index event. Analysis was done using multivariate logistic regression to identify the major predictors of acute stroke following three months after the index event. The severity of the stroke was assessed using the National Institutes of Health Stroke Scale (NIHSS) score. The stroke subtype was split into anterior circulation and posterior circulation in order to investigate any potential links between posterior circulation ischemic stroke and fatality rates. The 360 patients recruited had a 7.8% in-hospital mortality rate (28 deaths), and a 9.7% three-month mortality rate (35deaths). 27 deaths, or 77% of all fatalities, were due to stroke. Long-term predictors of activity limitation of stroke outcomes were investigated [8]. That was to determine factors at index stroke and predict the level of activity participation and limitation. One hundred and thirty-nine (139) participants admitted at the Sheba Medical center in Israel were prospectively followed-up for four years. The Barthel Index (BI) (activity limitation; BI<95) and Frenchay Activities Index (FAI) (participation restriction; FAI<30) were the outcome measures. Perception of recovery was assessed using two simple questions. At the end of the four years, nine patients (6.4%) were lost to follow-up, 71

(54.1%) participants had survived; 42.3% with activity limitation, 28.2% were categorized as restricted in participation, and 78.1% think that they were not fully recovered. Activity limitation is significantly predicted by the age at the initial stroke and the acute phase disability. Participation restriction was not indicated by any demographic factor or clinical baseline characteristics. Four years after a stroke, there was a positive correlation between activity restriction and participation restriction [8].

[9] Predicted outcomes in stroke with acute stroke on baseline severity and improvement in the first twenty-four (24) hours after the index event. The author 'hypothesized that the change in NIHSS in the first 24 hours after stroke improved stroke outcome prediction. Records of three hundred and sixty-nine patients were retrieved from Leuven Genetic Study. NIHSS scores were calculated over 90 days of admission. Multiple logistic regression models were used to independently predict outcome measures. The results revealed that NIHSS was associated with functional outcomes. One hundred and thirty-one (131) participants with moderate to severe stroke, the predictive model was more accurate including the NIHSS to the model which included NIHSS, age, and ischemic heart disease. In conclusion, NIHSS is a predictor of stroke outcome.

The above articles reviewed concentrated on estimating the risk factors on stroke severity based on different designs and modeling concepts. These researchers failed to estimate the effects of the covariate as the diseases progress. The above studies undertook a cross-sectional study. These may employ multiple variables at a given time. But provide no information concerning the influence of time on the variables they measured. According to [10], a longitudinal study is used in studying the relationship between risk factors and the development of diseases.

[6][7][8] [11][12] all predicted outcome measures of stroke using a longitudinal approach. [7] a 3-month longitudinal studies on acute stroke recovery while [8] did a 4-year prospective studies. These particular studies could not determine the various states patients went through before they censored and could not also estimate the possible probabilities of transiting from one disease state to another.

The purpose of this research to discover the prevalence of some risk factors of stroke and examine their predictive transition rates at the various disease states.

2.0 METHODOLOGY

2.1 Data Set

We retrospectively obtained secondary stroke data from the Medical Unit of the Tamale Teaching hospital (TTH). The Hospital serves all the five Northern regions in Ghana. Selection standards included those patients who had an initial or were referred for hospitalization for stroke from January 2014 to December 2019. 38 patients who survived the stroke were given rehabilitation therapy under the Medical Unit in the hospital. Monitoring of patients was done by the stroke unit. Disease progression was recorded at different two months-time intervals using the Modified Barthel Index (MBI). It measures the Functional Independence (FI) of the patients. MBI has 10 items on Activity of Daily living (ADL). The total score of 20 indicates full independence in the ADL; a higher score represents a higher level of independence (mild stroke). $MBI < 15$ usually represent moderate disability and MBI<10 indicates severe disability [13]. The state of patients were recorded by the medical personals. Monitoring the state of the disease was done at two monthly equal intervals over a two year period. Some patients were lost to follow-up, some withdrew and some died.

2.2 Model Formation

We incorporation the covariates into the CTMC modelling as described in our paper (Multi-State Analysis of Secondary Prevention of Stroke in Northern Ghana).

In order to support regression modeling, the Markov model can be easily extended. According to the assumption that the proportional intensities can be stated as

$$q_{ij}\left(z\right)=q_{ij}\exp\left\{\mathrm{B}_{\mathrm{ij}}^{1}z\left(t\right)\right\} \qquad i\neq j$$

where z is the s dimensional vector of covariate;

B_{ij} is a vector of S regression parameters linking the instantaneous rate of changes from state i to state j to the covariate and $q_{ij0}z$ denotes the baseline intensity relating to the transition from state i to state j. The change that follows $q_{ij}(\boldsymbol{z})$ intensity matrix $Q(\boldsymbol{z})$ with regard to a subject and a set of covariates z using elements is possible in Equations (1) and (2) the transition probability matrix $P(t \mid \boldsymbol{z})$: must be calculated. The elements $p_{ij}(t \mid \boldsymbol{z})$ of this transition probability matrix represents the likelihood function's contribution from each observation. $q_{ij}(z) = q_{ij0}\exp\{\mathrm{B}_{ij}^{1} z(t)\} \qquad i \neq j$

A log-linear Markov rate model $\boldsymbol{q}_{ij}(\boldsymbol{z})$ is mainly chosen for analytical ease, and this model has the appealing property of providing nonnegative transition intensities for any $\boldsymbol{Z}$ and $\boldsymbol{B}_{ij}\boldsymbol{'s}$. In some instances, alternate parameterizations might be a better fit. Additionally, it is feasible to explore how factors affect the baseline probability by modeling on comparable scales like log-hazard. The value of the coefficient B_{ijk} can be conveniently interpreted using the log-linear model, which is not always the case with other models. Consider the fact that if the number of covariates increases, the algorithm may become too complex to implement.

Indeed $i \to j$, more data must be included in the analysis and more computing power must be available as the number of covariates (or regression coefficients) rises because it becomes highly challenging to calculate the likelihood. Using a Cox proportional regression model, $q_{ij}(t)$ models the effect of covariate vector $\boldsymbol{Z}$ on transition for a stroke patient, and the transition hazard is given by $q_{ij}(t \mid z) = q_{ij0}(\mathrm{t})\exp\{\mathrm{B}_{ij}^{T} z\} \qquad i \neq j$

where $q_{ij0}(\mathrm{t})$ is the baseline hazard of transition i and j and B_{ij} is the vector of the regression coefficients that describe Z the effect on transition i and j. An alternative way of writing this model is

$$q_{ij}(t \mid z) = q_{ij0}(\mathrm{t})\exp\left\{\mathrm{B}_{\mathrm{ij}}^{T} z_{ij}\right\} \qquad i \neq j$$

where z_{ij} is a vector covariates specific to transition $i \to j$, defined for the patient base on his or her covariates The estimates $\hat{B}$ can be obtained by maximizing the partial likely z_{ij} hood f z. unction.

$$L(\beta) = \prod_{k=l}^{n} \frac{\exp\left\{\mathrm{B}_{\mathrm{ij}}^{T} z_{ij}\right\}}{\sum_{l \grave{o} R(t_{ij,k})} \exp\left\{\mathrm{B}_{\mathrm{ij}}^{T} z_{ij,l}\right\}}$$

where $z_{ij,k}$, the covariate vector is for patient *k* and $R(t_{ijk})$ is the risk set a time for making transition from $i \to j$ [14].

2.3 Data Visualization and Analysis

Patient variables included in the study data are: *patient number*, *age*, *sex*, *location of patient*, *local treatment*, *smoking*, *alcohol intake*, and *hemiparesis* (defect on right-side or left-side). Patients with less than three visits were excluded from the study. Each patient's number of visits to the facility was recorded. The state of each patient at a particular time was indicated by the medical officer. The multi-state model in the R package was used to model the transition rates. We coded the data and imported it into the package. The ages of the patients were grouped as youth (15–45), old (46–60) and older (61 or more).

Thus, age was coded as

$$\text{Age} = \begin{cases} \text{Youth } (15-45 \text{ years}), & 0 \\ \text{Old } (46-60 \text{ years}), & 1 \\ \text{Older } (61 \text{ years and over}), & 2 \end{cases}$$

Coding for sex was as follows:

$$\text{Sex} = \begin{cases} \text{Male}, & 0 \\ \text{Female}, & 1 \end{cases}$$

Some patients received local treatment prior to their first visit and during rehabilitation, whereas others only received hospital rehabilitation:

$$\text{Treatment} = \begin{cases} \text{Combined with local Treatment,} & 0 \\ \text{Only Hospital rehabilitation,} & 1 \end{cases}$$

The teaching hospital is a referral unit in northern Ghana, and patients were referred to this facility from different locations in the north. On record, we have the following:

$$\text{Location} = \begin{cases} \text{Upper East,} & 0 \\ \text{Northern,} & 1 \\ \text{North East,} & 2 \\ \text{Savanna,} & 3 \\ \text{Upper West,} & 4 \end{cases}$$

Patients were advised not to take alcohol during rehabilitation. Some got addicted to alcohol and were coded as

$$\text{Alcohol intake} = \begin{cases} \text{No Alcohol,} & 0 \\ \text{Addicted to Alcohol,} & 1 \end{cases}$$

Patients who were onto smoking were advised to quit smoking in order to improve rehabilitation. Patient's severity status was recorded on arrival. We considered coding diseases as free, mild, moderate, severed, and death.

$$\text{Diseases state} = \begin{cases} \text{Diseases Free,} & 1 \\ \text{Mild State,} & 2 \\ \text{Moderate State,} & 3 \\ \text{Severe State,} & 4 \\ \text{Death,} & 5 \end{cases}$$

In preparing the data for analysis, we installed the MSM package from the CRAN archive in the R console (version of 4.1.0) on a computer through the internet. Data in an excel sheet was put in long format (data frame) to enable the package to run it. The time of observations and the observed states for the process were: state 1 (disease free), state 2 (patients with mild stroke), state 3 (patients with moderate stroke), state 4 (patients with severe stroke), and state 5 (patients who die during the study period or withdrawal from the study). The excel file was saved in CSV format to enable reading of the data by R console.

Our next analysis was estimates of the main model (model 1 = illness-to-death). This result shows the baseline transition intensities among the various states. In order to determine the effect of the covariates on the transition rates, we ran the data for each covariate. We first compare the model 1 transition rate with the baseline rates of the covariate. If the covariate baseline rates indicate some effects (with transition rates less than 1), we go ahead and estimate the rates for each level of the factors. When the baseline rates of the covariates are greater than or equal to 1 (indicating no contribution of the covariate), all the rates for the levels of that factor will be estimated at rates greater than or equal to 1 [15]. We conclude that the covariate has no significant effect on the transition rates of the stroke patients

3.0 Results

Using a proportional intensities model, we attempt to predict how the independent factors will affect the pace of transition. If we have an intensity matrix Q(z) which depend on the covariate vector z, the transition intensity for patient i at observation time j is $q_{rs}\left(z_{ij}\right) = q_{ij}^{(0)}\exp\left(\beta_{rs}^{T} z_{ij}\right)$. The size of some of the hazard ratios' confidence intervals indicates that there may be no information about the covariate effect in the data, which results in a probability that is a flat function of the characteristics

Table 1: Covariates Effect of Male Compared with Female

	State 1	State 2	State 3	State 4	State 5
			Male		
State 2	0.077(0.04, 0.15)	-0.197(-0.31, 0.12)	0.098(0.05, 0.18	0	0.021 (0.02, 0.12)
State 3	0.0000001	0.494 (0.13, 0.62)	-0.81(-1.2, -0.54)	0.313(0.15, 0.69)	0.0034(0.00, inf)
State 4	0.000001	0.00002	1.133 (0.64, 2.01)	-1.186 (-2.03,0.68)	0.052 (0.002, 0.68)
State 5	0	0	0	0	0
			Female		
	State 1	State 2	State 3	State 4	State 5
State 2	0.085 (0.03, 0.13)	-0.198 (-0.40, -0.09)	0.057 (0.01, 0.23)	0	0.054 (0.03, 0.30)
State 3	0.0009	0.341(0.18, 0.68)	-0.571 (-0.99,-0.32)	0.22 (0.07, 0.69)	0.003 (0.00, inf)
State 4	0.0000023	0.0000021	0.863 (0.42, 1.75)	-0.99 (-1.8, -0.5)	0.13 (0.01, 4.71)
State 5	0	0	0	0	0

Table 1 compares the transition rates between male and female patients. The results revealed that female patients at mild state have a higher probability (0.08538) of total recovery than their male counterparts (0.07732). They also indicate less probability of transiting to a more severe state (moderate) state (0.05783) as compared to the rate of 0.09802 for males. While male patients in a severe state indicate no information of recovering (1.133) to moderate state, their female counterparts have a better recovery rate of transition (0.863). Also, female patients stay longer at a severe state (1/0.985) than males (1/1.186). Thus , female patients indicated higher probabilities of dying at states 2 and state 4 (state 2 = 0.05483, state 3 = 0.0029 and state 4 = 0.1355) compared to males (state 2 = 0.02161, state 3 = 0.0034 and state 4 = 0.0523) but very similar at state three (3).

Table 2: Transition Intensities for Age (Youth Compared with Old)

	State 1	State 2	State 3	State 4	State 5
			YOUTH		
State 2	0.052 (0.02, 0.2)	-0.29 (-0.5, -0.2)	0.0978 (0.01, 0.3)	0	0.1448 (0.06, 0.3)
State 3	0.00012 (0.0, inf)	0.643 (0.3, 1.1)	-0.655 (-1.1, -0.4)	0.01 (0.001, 0.2)	0.00042(0.0, inf)
State 4	0	0	0.83 (0.08, 0.2)	-0.83 (-1.6,-0.4)	0.00000002 (0.0, inf)
State 5	0	0	0	0	0
			OLD		
	State 1	State 2	State 3	State 4	State 5
State 2	0.067(0.03, 0.1)	-0.21 (-0.3,-0.1)	0.085 (0.03, 0.2)	0	0.058 (0.005, 0.1)
State 3	0.00001 (0.0, inf)	0.46 (0.2, 0.54)	-0.548 (-1.6,-0.5)	0.08 (0.03, 0.3)	0.00002 (0.00, inf)
State 4	0	0.00009 (0.0, inf)	1.01(0.6, 1.6)	-1.01 (-1.6, -0.6)	0.0002 (0.0, inf)
State 5	0	0	0	0	0
			OLDER		
State 1	0	0	0	0	0
State 2	0.086 (0.03, 0.19)	-0.185 (-0.3,-0.1)	0.075 (0.02, 0.2)	0	0.024 (0.005, 0.1)

State 3	0	0.33 (0.2, 0.54)	-0.94 (-1.68,-0.52)	0.612 (0.2, 1.4)	0.000002 (0.00,inf)
State 4	0	0.00000 (0.0, inf)	1.24 (0.6, 2.5)	-1.38 (-2.6, -0.7)	0.149 (0.05, 0.4)
State 5	0	0	0	0	0

Table 2 shows the hazard rates of transition among the age factor levels; youth, old and older groups. The older and old age have a better recovery rate at mild stroke state 2 (0.0864 and 0.0676) than the youth (0.057). While the old and older age group have a less and similar probability of moving from mild to a more severe (moderate) state (0.0751, 0.08574), the youth is more likely (0.0978) to transit to a more severe state these two groups. Also, the youth have more than twice (0.1448/0.0588) probability of transiting into the absorbing state than the old age and about six (6) times (0.1448/0.024) entering into the absorbent state than the older aged group. The table also revealed that old age retires rehabilitation (0.0752) than the youth (0.0925). At moderate state, the youth have about double the chance (0.6434/0.3303) and (0.6434/0.46) of transiting to a less severe state than both old and older. Similarly, old and older age patients with moderate stroke have no chance of recovering. Finally, a patient with severe stroke has zero chance of transiting to a less severe state, thus older patients with a severe stroke stand a higher probability (0.1491) of moving to the absorbing (death) state than both old and youth (0.00000002, 0.000002.

Table 3: Hazard Rate for Alcohol Compared with No Alcohol

	State 1	State 2	State 3	State 4	State 5
			Alcohol		
State 2	0.0747 (0.04, 0.1)	-0.1916 (-0.2, -0.1)	0.087 (0.04, 0.16)	0	0.0293(0.01, 0.08)
State 3	0.00004 (0.0, Inf)	0.4589 (0.32, 0.63)	-0.7109 (-0.9, -0.51)	0.262 (0.13, 0.5)	0.000002 (0.00, Inf)
State 4	0	0.000006 (0.00, Inf)	1.047 (0.68, 1.7)	-1.134 (-1.7, -0.7)	0.0862 (0.02, 0.3)
			No Alcohol		
	State 1	State 2	State 3	State 4	State 5
State 2	0.4055 (0.1, 2.9)	-0.4055 (-2.9, -0.1)	0.000005 (0.000, Inf)	0	0.000002 (0.00, Inf)
State 3	0.000004 (0.0, Inf)	0.000001 (0.00, Inf)	-0.6389 (-3.1, -0.1)	0.3848 (0.04, 3.6)	0.254 (0.03, 0.8)
State 4	0	0.0000001 (0.00, Inf)	0.4945 (0.05, 4.3)	-0.494 (-4.3, -0.1)	0.000003 (0.0, Inf)

Table 3 compares the effect of alcohol in stroke patients to patients who do not take alcohol while on rehabilitation. The table indicated that patients with no history of alcohol at state two (2) have a better probability (0.4055) of transiting to no stroke than patients with a history of alcohol intake (0.07475). Also, patients with alcohol history retire recovery about ten (10) times (0.087) more than patients with no alcohol history in transiting to a more severe state with probabilities (0.000005). Unfortunately, patients with moderate stroke and who take alcohol could do better (0.4544) than patients without alcohol (0.00000002). Alcohol-based patients are also less likely to transit to a more severe state (0.2534) as compare to patients without alcohol history (0.3848). Meanwhile, severe rated patients with a history of alcohol have no information (1.671) of transiting to a less severe state, unlike their counterparts who are likely to transit to a less severe state (0.4945).

Table 4: Transition Intensities for Smoking

	Baseline	Smoking
State 2- State 1	0.021 (0.000, Inf)	0.2265 (0.0000, Inf)
State 2- State 2	-0.05988 (-Inf, 0.000)	–
State 2- State 3	0.02454 (0.000, Inf)	23700000 (0.00, Inf)
State 2- State 5	0.01450 (0.000, Inf)	2458000000 (0.0, Inf)
State 3- State 1	0.06937 (0.000, Inf)	0.9014 (0.0000, Inf)
State 3- State 2	0.428(0.306, 0.597)	2.423 (0.328,17.883)
State 3- State 3	-0.6864 (-0.943, -0.499)	–
State 3- State 4	0.2584 (0.137, 0.484)	0.9813 (0.1049, 9.179)
State 3- State 5	0.00000076 (0.000, Inf)	0.0018 (0.0000, Inf)

State 4- State 2	0.00000000005 (0.00, Inf)	2.668 (0.0000, Inf)
State 4- State 3	1.019 (0.6546, 1.585)	2.338 (0.2755,19.846)
State 4- State 4	-1.04 (-1.39, 7.735000)	–
State 4- State 5	0.02109 (0.000, Inf)	2.996 (0.0000, Inf)

Table 4 above indicated the baseline transition rates among patients who sort to smoke at the various states. The rate of transition suggested that smoking has no information as whether the patients may recovery or transit to a more severe or less state or die.

	State 1	State 2	State 3	State 4	State 5
			Local Treatment		
State 2	0.0799 (0.03,0.1)	-0.204 (-0.33, 0.12)	0.07897 (0.03, 0.19)	0	0.045 (0.02, 0.1)
State 3	0.000008 (0.0, inf)	0.4279 (0.28, 0.65)	-0.5887 (-0.8, -0.4)	0.1607 (0.06, 0.41)	0.00007 (0.00, Inf)
State 4	0	0.0000001 (0.00, Inf)	0.9721 (0.57, 1.6)	-0.9721 (1.61, 0.57)	0.001 (0.0, Inf)
			No Local Treatment		
State 2	0.08075 (0.03, 0.2)	-0.2255 (-0.3, 0.1)	0.09458 (0.03, 0.23)	0	0.05017 (0.01, 0.14)
State 3	0.000001	0.4487 (0.26, 0.76)	-0.9032 (-1.5, -0.54)	0.0545 (0.2, 1.1)	0.000005 (0.00, Inf)
State 4	0	0.00002 (0.000, Inf)	1.027 (0.47, 2.2)	-1.242 (-2,- 0.6)	0.215 (0.07, 0.6)

Table 5: Local Treatment Compared with No Local Treatment

Table 5 above compares the transition rates of patients who combined local treatment and hospital with patients who had only hospital rehabilitation. At state 2 (mild), patients who combined the two-treatment achieved similar total recovery (0.0799) as against patients who did not seek for local treatment (0.08075). Patients combines local treatment are also less likely to transit to a more severe state (0.07897) compared with none local treatment (0.09458). A patient seeking for local treatment may remain at mild state for about (1 year) 5 times visits (1/0.2038) before death (0.045) whereas none local treatment may stay alive at (mild) state for about (9 months) 4.43 times visits for (1/0.2255) before transiting to death at the rate of (0.05017). Moderately rated patients with or without local treatment history may transit to a less severe state with similar transition rates (0.4279, 0.4487). At severe state a patient without local treatment will live less than two months (1/1.242) before death (0.2150) whiles local treatment may remain with severe stroke for at least two month (1/0.9721) before transiting to a less severe state.

Table 6: Right- Hemiparesis Compared with Left- Hemiparesis

	State 1	State 2	State 3	State 4	State 5
			Left-Hemiparesis		
State 2	0.08011 (0.05, 0.1)	-0.1746 (-0.2, -0.1)	0.0674 (0.03, 0.15)	0	0.02712 (0.01, 0.07)
State 3	0.0000001	0.4058 (0.2, 0.6)	-0.6298 (-0.9, -0.4)	0.224 (0.1, 0.4)	0.0000
State 4	0	0.000007 (0.0, inf)	1.00 (0.62, 1.5)	-1.00 (-1.5,-0.6)	0.000002
			Right-Hemiparesis		
State 2	0.0788 (0.03, 0.2)	-0.2257 (-0.3,-0.1)	0.1207 (0.05, 0.25)	0	0.026 (0.01, 0.1)
State 3	0.000001	0.4631 (0.3, 0.7)	-0.7643 (-1.1, -0.51)	0.3011 (0.1, 0.6)	0.000
State 4	0	0.000000	0.9948 (0.59, 1.67)	-1.089 (-1.7, -0.6)	0.0944 (0.03,0.3)

Table 6 compares the hazard rates of transition between patients who had left- hemiparesis (arm, leg or face) paralyzed with patients who were paralyzed with right- hemiparesis. The table indicated that, at mild state, patients with left- hemiparesis or right- hemiparesis have similar probability of total recovery (0.08011 or 0.0788

3.1 DISCUSSION OF RESULTS

We incorporated our covariates into a Continuous-time Markov chain model in multi-state modeling to enable us estimate the transitions rates of the covariates. Studies have shown that when data are equally spaced, both the discrete-time Markov chain model and continuous-time Markov model can perform well. Thirty-seven (37) patients were monitored at two months intervals for two years.

The purpose of this study is to enable us to observe the covariate effects of the transition intensities of stroke patients on rehabilitation at some discrete points of time. The model will enable us to determine some risk factors that negatively influence recovery.

Our study revealed that female patients have a better transition rate to a less severe state than their male counterparts. This finding supports [16] on CD4 cell count those transitions from a good state to a bad state is higher on male patients than their female counterparts.

Unfortunately, females are more likely to die at severe state than males. This is consistent with [17]

Table 1 suggested that female patients have a better rate of transiting to less severe state (0.08538, 0.3418, and 0.863) than their male counterparts (0.07732, 0.4942, and 1.133). This findings is supported by [16] on CD4 cell count that transition from good states to bad states is higher on male patients than their female counterparts. Unfortunately, females are more likely to die (0.05483, 0.0029, and 0.1355) than male patients (0.02161, 0.0043, and 0.0523) in all states.

Findings from **Table 2** revealed that the age of a stroke patient could retire recovery about ten (10) times than the baseline probability (0.8067/0.08457) and has the same probability of transiting to death state (0.4062/0.03108). While old and older age groups have a less and similar probability of moving from moderate to severe state (0.0873, 0.6123), the youth is less likely (0.01244) to transit to severe state than these two groups. Older age with severe stroke is more likely to die (0.1491) than old age and the youth (0.000002, 0.000000002). This result is consistent with literature [18].

The outcome of **table 3** gives detail information on the effect of alcohol on stroke survivors. Patients with no history of alcohol may recover more than 5 times (0.4055/0.07475) than patients with history of alcohol at mild state. Findings from our study also indicated a patient admitted with severe stroke and history of alcohol intake have no information of becoming less severe (1.047) unlike their counterparts with 0.4945 probability of moving to a less severe state. This finding is consistent with [5]. Their studies shown that, the relationship between alcohol consumption and functional outcome from stroke is sparse.

The transition intensities in **Table 4** indicated that, the covariate smoking has no effect on stroke severity. The baseline intensity for smoking gives hazard rates to be positive one or more suggesting the covariate have insufficient information in estimating the covariate effect. Several studies shown a strong positive relationship between cigarette smoking and risk of recurrence of stroke [19], [4] and [20]. This finding could mean that a stoke patient who previously smokes and quit smoking during rehabilitation may not have any influence the recovery rate.

We also estimated the transition ratios of the covariate therapeutic type (local/traditional and modern rehabilitation) as in **Table 5**; these estimates predicted that, patients who combined local treatment have similar recovery rate at mild state (0.0799) as compares to patients who never had local treatment (0.08075). Meanwhile, patients in mild state with combination of local treatment adhere to treatment and are less likely to transit to more severe state (0.07897) than patients who never subscribed to local treatment (0.09458). Patients with severe stroke and combines local treatment are more likely to transit to moderate state (0.9721) than patients with no combination of local treatment (1.027= no sign of recovery). Also, in severe state with no combination of local treatment are more likely to die (0.05017, 0.2150) compared with patients who combined treatment with non-hospital medication (0.045, 0.000001). These findings are supported by [21] therapeutic regimen of traditional Chinese Medicine (Acupuncture) combined with modern rehabilitation are effective in improving cognition and has the advantage of being simple, convenient, efficient and inexpensive without severe adverse effect.

Findings from **Table 6** suggested that Right- hemiparesis patients stayed more than 3 times longer (1/0.2257) at mild state before transiting to disease Free State (1/0.1746). Meanwhile recovery at moderate state is faster for right- hemiparesis patients (0.4631) as compared to right- hemiparesis patients (0.4058). Left or right-sided paralyses have similar probabilities of dying at all states except state 4 (0.09447). Thus left- hemiparesis patients are about twice less likely (0.06738) to transit to more severe state than right-hemiparesis (0.1207).

4.0 Conclusion

The purpose of this study is to incorporate some covariates into illness-to-death model (CTMC) that will enable us to observe the effects of the covariates on transition intensities of stroke patients on rehabilitation at some discrete points of time.

The research also revealed that CTMC models best estimated the transition rates of stroke patients who were on rehabilitation at the TTH. The model can estimate the transition intensities for all states (1, 2, 3, 4, and 5). The transition rate from state 2 to state four (4) is zero (0). Also transition from state 2 to state 5 is higher (0.0581) than transition from state 3 to state 5 (0.0003).

The study established that increasing age of a patient suggests a low survival rate (older patients) with severe stroke are less likely to transit to a less severe state compared to the youth.

We therefore recommend that; stroke patients should be advised by medical officers not to combine rehabilitation with local treatment. Combination of local treatment may only be sufficient on patients with severe stroke. Thus, patients should seek local treatment from only known registered stroke rehabilitation centers. Patients who transit to mild state should be advised by medical officers to continue to adhere to treatment to speed up total recovery. Public education on risk factors of stroke should be emphasized. Ministry of Health should undertake public education on the risk factors of stroke both at the National and community base.

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