AMERICAN UNIVERSITY OF BEIRUT

FACTORS ASSOCIATED WITH DELAYS IN RECEIPT OF EMERGENCY TREATMENT FOR ACUTE STROKE PATIENTS IN LEBANON

by
AHMAD ALI TERMOS

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AHMAD ALI TERMOS

Approved by:

Dr. Samar Noureddine, Professor
Hariri School

First Reader

Dr. Mazen El Sayed, Associate Professor
Department of Emergency Medicine
Faculty of Medicine

Second Reader

Date of project presentation: June 17, 2020

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AN ABSTRACT OF THE PROJECT OF

Ahmad Ali Termos for Master of Science in Nursing

Major: Adult Gerontology Clinical Nurse Specialist

Title: Factors Associated with Delays in Receipt of Emergency Treatment For Acute Stroke Patients In Lebanon

The aim of the study was to explore the characteristics of patients admitted through the Emergency Department (ED) with acute stroke to a private hospital in Lebanon and factors associated with the delay in their seeking emergency treatment.

Stroke is the leading cause of long-term disabilities worldwide. Stroke in Lebanon is considered as the third cause of premature deaths. Ischemic stroke (IS) is the most common type of strokes with an 85% prevalence versus 15% for hemorrhagic strokes. Mortality and morbidity in stroke were found to be associated with delays in receiving effective treatments such as thrombolytic therapy for ischemic stroke. Studies have shown a substantial proportion of patients failing to receive such therapies because they do not reach the emergency department (ED) within the 4.5-hour therapeutic window. In Lebanon, there are no studies to our knowledge that addressed the issue of delay in receipt of treatment in patients with acute stroke.

A retrospective descriptive design was used. Data collection was through a medical record review of all consecutive acute ischemic stroke patients admitted to the ED of the American University of Beirut Medical Center (AUBMC) between January 1st, 2016, and January 1st, 2019. Inclusion criteria included age 18 years and older, diagnosis of stroke, and admission to the hospital. Patients with transient ischemic attacks were excluded. Data included demographic characteristics, medical history, date and time of symptom onset, date and time of arrival to ED, symptoms and ED transport and management.

There was a total of 205 patients who met the study criteria. The median delay time was 4.57 hours, with 49.7% reaching the ED within 4.5 hours of symptom onset. Living outside Beirut, history of prior stroke or having dysphagia predicted longer delays, whereas losing consciousness and coming to the ED by ambulance predicted shorter delays

The study findings highlight the importance of educational campaigns about symptoms of stroke and the importance of prompt seeking emergency care for the treatment to be effective.

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CHAPTER I

BACKGROUND AND SIGNIFICANCE

Stroke or cerebrovascular accident is defined as rapidly developing clinical symptoms and/or signs of focal and at times global loss of brain function, with symptoms lasting more than 24 hours (Pendelbury et al., 2018). Fifteen million people suffer from a stroke each year, out of whom one-third dies and one-third lives with permanent disabilities, reflecting the global burden of stroke (World Health Organization [WHO], 2015). Thus, stroke is considered the leading factor of long-term disabilities worldwide (Hassankhani et al., 2019). Stroke is the fifth leading cause of death in the USA, where 795,000 strokes occur every year (Benjamin et al., 2017). Studies have shown that countries with low to a moderate-income account globally for more than 85% of stroke deaths (Farah et al., 2015). Moreover, the burden of stroke in these countries is expected to increase by 2020 (El-Hajj, Salameh, Rachidi & Hosseini, 2016).

The Middle East (ME) region has a scarcity of reliable studies about the epidemiology of stroke (Farah et al., 2015). Streletz and colleagues (2017) did a systematic review of studies that examined the epidemiology of stroke in the Middle East and North Africa (MENA) region. The authors concluded that healthcare stakeholders and policymakers require more reliable data to develop and implement therapeutic and preventive strategies. Stroke is gradually becoming of major concern in healthcare in these countries, where it is estimated that the present mortality ratios will be doubled by the year 2030 (Farah et al., 2015).

The incidence of stroke has never been studied in Lebanon (Farah et al., 2015). The WHO's statistics showed that 47% of the total annual deaths in Lebanon are related to cardiovascular diseases (CVD), and stroke was reported as the second leading cause of mortality

after ischemic heart disease (WHO, 2015). More recently, the Institute of Health Metrics and Evaluation (2017) estimated stroke to be the third cause of premature deaths in Lebanon. The Ministry of Public Health (2017) reported that diseases of the circulatory system accounted for the largest number of the Ministry's subsidized hospitalizations, out of which stroke ranked fourth in frequency. Moreover, the cost burden of the treatment of stroke was examined in a recent study that estimated the mean hospital cost per stroke patient in Lebanon to be US$ 6,961 ± 15,663, which is significantly high compared to high-income countries such as USA where the estimate is US$ 9,688 (Abdo et al., 2018). Thus, it is important to study stroke and its risk factors.

A. Background

Stroke or cerebrovascular accident includes two types: ischemic and hemorrhagic. Ischemic stroke (IS) is the most common type with an 85% incidence and hemorrhagic strokes account for 15%. Transient ischemic attack (TIA) is a transient stroke manifested by some neurologic signs that resolve spontaneously within less than 24 hours (Pendlebury et al., 2018). To ameliorate the outcomes of acute stroke and TIA, delay in initiating treatments must be minimized by using thrombolytic therapy for ischemic stroke and controlling blood pressure for hemorrhagic stroke (Yanagida et al., 2014).

In Lebanon, Lahoud and colleagues (2017) did a retrospective study of 254 medical records of patients admitted to two medical centers with stroke. The authors reported that the majority of cases were ischemic stroke (64.2%), followed by transient ischemic attacks (20.9%) and hemorrhagic stroke (15%). Farah and colleagues (2015) surveyed 1,515 Lebanese stroke and TIA-free residents and reported a prevalence of at least one self-reported stroke symptom at

11.99%. Moreover, risk factors including hypertension, history of heart disease, current water pipe smoking, current, and former cigarette smoking, and psychological distress were identified to be associated with increased risk for stroke symptoms, whereas consumption of the Mediterranean diet and regular physical activity was protective against stroke symptoms (Farah et al., 2015). Other investigators reported similar risk factors for stroke in Lebanon, in addition to diabetes mellitus, atrial fibrillation, socioeconomic status, and history of TIA (Abdo et al., 2019; El-Hajj et al., 2019; Lahoud et al., 2017). Besides, a cross-sectional exploratory study revealed a significant association between self-reported indoor pollution (due to living near pollutant sources) and stroke among the Lebanese population (Salameh et al., 2018). Thus, stroke is a significant health problem in Lebanon, with a serious impact on morbidity and mortality and a significant financial burden. It is important to identify factors associated with stroke to improve patient outcomes. The study aims to explore the characteristics of patients admitted with acute stroke to a tertiary hospital in Lebanon and factors associated with the delay in their treatment.

Delay in seeking emergency care for acute stroke

The treatment of ischemic stroke starts with restoring cerebral blood circulation by dissolving blood clots such as with thrombolytic agents, then rehabilitation measures are put in place to restore neurologic and other deficits (Aroor et al., 2017). The mnemonic BE-FAST (Balance, Eyes, Face, Arm, Speech, and Time) that is used as a screening tool, can capture more than 95% of strokes (Aroor et al., 2017). Moreover, CT brain imaging is done to rule out intracranial hemorrhage and is essential for determining patients who may benefit from thrombolytic therapy or mechanical revascularization (Patel & White, 2017). Multiple randomized clinical trials have shown that patients with large volume occlusion (LVO) have better outcomes with mechanical revascularization compared to those treated with systemic

intravenous thrombolysis (Patel & White, 2017). Recombinant tissue plasminogen activator (r-tPA) is the only approved drug for managing and treating acute ischemic strokes (Hassankhani et al., 2019), but its narrow therapeutic window that is the necessity of giving the treatment within 4.5 hours of symptom onset for it to be effective, is one disadvantage that results in many patients not receiving this treatment (Khandelwal, Yavagal & Sacco, 2016).

Hemorrhagic stroke is a medical emergency where early deterioration is common in the first few hours after intracranial hemorrhage (ICH) onset (Hemphill et al., 2015). Moreover, more than 20% of patients with ICH will run into a significant decrease in the Glasgow Coma Scale (GCS) by two or more points from the time of prehospital emergency medical services (EMS) assessment till the initial assessment in the ED (Hemphill et al., 2015). For hemorrhagic stroke (HS), the acute management centers on blood pressure control then surgical procedures to control the cerebral bleeding. Delay in the treatment may result in neurological deterioration, increased risk for disabilities and death. The American Heart Association (AHA) guidelines for the emergency management of ICH recommend using best emergency diagnosis and assessment methods, maintaining hemostasis and coagulopathy, maintaining systolic blood pressure between 150 and 220 mmHg, management of glucose levels, as well as management of seizures and medical complications such as dysphagia that may result in pneumonia (Hemphill et al., 2015). The ultimate treatment of ICH is by surgery, with measures to prevent recurrence of ICH, and rehabilitation (Hemphill et al., 2015).

B. Significance

In recent years, considerable effort has been made to improve the management of acute ischemic strokes (AIS). However, the effectiveness of therapy was found to be highly time dependent (Hassankhani et al., 2019). In fact, receiving r-tPA within 3 to 4.5 hours decreases the

chances of disabilities resulting from AIS by 7% (Khandelwal et al., 2016). A meta-analysis by Emberson and his colleagues (2014) showed that treating AIS within 3 hours results in desired outcomes as the chance of receiving r-tPA increases as the time between symptom onset and arrival to the emergency department (ED) decreases. Thus in 2018, the AHA in collaboration with the American Stroke Association (ASA) determined the therapeutic time window (onset-to-door time) for determining the eligibility of patients to receive r-tPA, to be within 4.5 hours of stroke symptom onset. Moreover, the door-to-needle time, where the patient will start receiving r-tPA after arriving at the ED, must be 60 minutes or less (Powers et al., 2018).

The data on delay in seeking care for acute stroke is very heterogeneous, with studies exami9ning either prehospital delay, or decision delay or in-hospital delay, and the populations studied including either AIS exclusively, or all patients presenting with acute stroke. Evenson, Foraker, Morris and Rosamon (2009) did a comprehensive review of studies on delay in acute stroke care and a decline in prehospital delay between 1980 and 2007, noting that the decline slowed down in recent years. The authors noted that prehospital delay accounts for the largest proportion of delay time, with the 50^{th} percentile for delay occurring in the range of 3 to 4 hours in the studies done following the year 2000. In-hospital delays, on the other hand, improved less over the years (Evenson et al., 2009). Thus, in recent years, most studies focused on in-hospital delay.

Unfortunately, a comprehensive review of 115 studies published between 1990 and 2016 showed little improvement over the years in the median onset-to-door delay time, i.e. prehospital delay. The majority of studies reported a median onset-to-door time well beyond 3 hours. Factors associated with the delay time that were identified included emergency services pathways, stroke symptomatology, patient and bystander behavior, patient health characteristics, and stroke

treatment awareness (Pulver & Watson, 2017). For instance in Japan living alone, visiting a doctor, and not recognizing stroke symptoms were associated with longer delays whereas knowledge of r-tPA and the use of the emergency medical system was associated with shorter delays (Yanagida et al., 2014). Similar results were reported in China, with shorter delays associated with more severe symptoms and the presence of a witness, whereas longer delays were noted with nighttime symptom onset and not recognizing stroke symptoms (Jiang et al., 2016).

A recent retrospective chart review in New York state showed that only 96 (20.4%) of 487 patients with ischemic stroke were able to meet the door-to-needle criteria. Out of those, 38 (39.5%) had a delay in brain imaging and 22.9% needed blood pressure control before receiving r-tPA. Moreover, less than 30% of eligible candidates for r-tPA received the treatment in 60 minutes or less from the time of arrival to the ED, which was attributed to ineffective triage protocols and slow interpretations of CT-scan (Mowla et al., 2017).

In Catalonia, an observational multicenter prospective study showed that 37.2% of patients were delayed beyond 6 hours of ischemic stroke symptoms onset. The authors identified educational level, atrial fibrillation, low-income status, living alone, poor knowledge of stroke and its symptoms, and diabetes mellitus as independent predictors of stroke delay, (Abilleira, Lucente, Ribera, Permanyer-Miralda, & Gallofré, 2011). In India, the main reasons for stroke treatment delays included far distances from hospitals, misconceptions about stroke such as not considering stroke symptoms as life-threatening, and patients' beliefs in myths and traditional medicine. On the other hand, living in the city, daytime onset of symptoms, the urgency shown by the witness, availability of transport, and presence of family history were associated with early arrival to the hospital of patients with ischemic stroke (Sankapithilu et al., 2010).

Studies on the time from the onset of stroke symptoms until the patient arrives at the hospital in the MENA region are scarce. In Iran, less than 5% of 283 ischemic stroke patients who presented to the ED received r-tPA, with 80.2% of the sample not meeting intravenous r-tPA eligibility criteria, including 71.82% for reasons related to delayed presentation beyond 4.5 hours (Hassankhani et al., 2019). The investigators found that less than one-third of r-tPA eligible patients received the treatment within 60 minutes or less; this slowdown in the process was due to delayed neurology consultations, unavailability of a stroke team, lack of coordination between emergency medical services and the ED, and ED crowding (Hassankhani et al., 2019).

In summary, delay in seeking care for acute stroke is a problem with multiple causes. In Lebanon, to our knowledge, there are no published studies on delay in treating acute stroke patients and associated factors, although anecdotal evidence suggests that there is delay. Thus, this project aims to study the time from symptom onset to ED arrival and associated factors in acute stroke patients in the ED. The proposed project will be a retrospective medical record review that will rely on the documentation in one hospital in Lebanon.

CHAPTER II

METHODS

A. Design and Setting

A retrospective descriptive design was used in this study. Data collection was performed by reviewing the medical records of all consecutive stroke patients, including ischemic and hemorrhagic admitted to the ED of the American University of Beirut Medical Center (AUBMC) between January 1st, 2016 to January 1st, 2019. Approval was secured from the institutional review board (IRB) of the American University of Beirut, and the administration of the hospital. An official letter was sent to secure the administration's permission to access the medical records. Data extraction was executed with the proper methods to ensure patient confidentiality and privacy via CITRIX.

B. Sample

The sample inclusion criteria were: a) Stroke patients admitted to AUBMC through the Emergency Department, b) Discharge diagnosis of Ischemic or hemorrhagic stroke c) over 18 years of age, d) admission between January 2016 to January 2019. Patients with Transient Ischemic Attacks (TIA) were excluded.

All patients admitted with stroke through the ED during this period (from January 2016 to January 2019) who met the inclusion criteria were targeted.

C. Data Collection

The data was collected using the form shown in the Appendix. The variables were chosen based on the literature and in consultation with the Medical Director of the ED considering what is available in the ED records. An email was sent to the IT team requesting EPIC access, hospital information system (HIS) access, and medical record numbers (MRNs) for stroke patients. A period of five months (from November 2019 till April 2020) was needed to be granted the previous requests, due to the situation in the country. As a result, 494 charts were received and screened via AUB's remote access system (CITRIX). A sample of 206 patients met the criteria of the study and the rest were excluded, including over 100 TIA cases up to January 1, 2019 and others that either were discharged home, went against medical advice from the ED, were transferred to another hospital, or did not have a confirmed diagnosis of stroke upon hospital admission. Out of the 206 patients, one patient who came from Iraq was excluded from the study for exceeding two weeks from the time of onset of stroke symptoms till the time of arrival to the ED. Thus, the final sample included 205 participants.

The dates and times of symptoms onset and arrival to the ED were noted. Patients' age, gender, marital status, nationality, body height and weight, and smoking status were collected from the charts. Place of residence was categorized into five categories by the governorate. Moreover, 23 charts were missing the patients' height and weight. Medical insurance was documented. Time to reach the ED was calculated based on the dates and times of symptom onset and arrival to ED. Moreover, the means of transportation to the ED and witness of the symptoms were documented.

Medical data included the medical diagnosis (hemorrhagic versus ischemic stroke), symptoms at presentation, NIH Scale Score at presentation, as well as risk factors for stroke, CT on admission, receipt of r-tPA, neurologic consultation and destination following the ED visit. In

addition, survival status upon discharge from the hospital was retrieved from the medical records. Datasheets were used with code numbers and no identifiers such as case number or name were included. A sheet linking code numbers with case numbers was stored separately from the datasheet; the purpose is for being identifying any patient who may have presented more than once during the three years 2016-2019 to the ED.

Human subject considerations

This was a minimal risk study as the patient data were treated in an anonymous manner and confidentiality was preserved by reporting results in an aggregate form. As such no consent was asked from the patients. IRB and hospital approval were secured. The data were collected by a CITI certified graduate student. The sheet linking patients' case numbers to the code numbers used on the datasheet was stored separately from the datasheets. Hard copies were kept under lock in the primary investigator's office. Soft copies of data were saved on a password-protected computer in the primary investigator's office.

D. Data Analysis

All data analyses were performed using SPSS (Statistical Package for the Social Sciences (SPSS) version 25. Sample characteristics were described using frequency and percent for categorical variables, mean and standard deviation for continuous variables, and median with interquartile range for the delay time. The delay time variable was skewed to the right, so it was logarithmically transformed for the bivariate and multivariate analyses. Moreover, marital status was recoded into 2 categories: married versus not. Governorate was recoded into two categories: Beirut versus outside Beirut. Living arrangement was recoded into five categories: Alone, with a spouse, with spouse and children, with other family member, and with a maid. Destination from

the emergency department was also recoded into four categories: Regular unit, ICU/CCU/Neurology ICU, Neurology inpatient unit, and Morgue. Moreover, the stroke witness variable was recoded into four categories: Spouse, Other family, Friend or maid, and Stranger or no one.

Independent sample t-test, Pearson r correlation coefficient and ANOVA were used to test the association between delay time and the variables of interest depending on their level of measurement. Multiple linear regression analysis was used for multivariate analyses to identify predictors of delay time using those variables that were significantly correlated with delay time at the bivariate level of analysis. The log-transformed delay time was used in the bivariate and multivariate analyses.

CHAPTER III

RESULTS

A. Sample Characteristics

Table 1 shows the demographic characteristics of the sample. The majority of the sample (69.3%) was married and included more males (51.7%) than females, with a mean age of 73.33 (standard deviation 13.47 years, and range of 25 to 98 years. There was no data about the level of education of the patients. The majority of patients (67.8%) lived in Beirut, with their spouse and children (48.3%) and were of Lebanese nationality (90.2%). There were 11.7% of the sample who were working, and over two third (65.4%) had medical insurance, out of whom 80.6% had private insurance. Finally, the majority of patients (64.4%) were witnessed by their children or other family members when they had the stroke.

Table 1. Demographic Characteristics of the sample (N = 205)

Variable	**N**	**%**
Age (mean ± standard deviation)	73.33 ± 13.47	
Gender (Male)	106	51.7
Marital status:		
• Married	142	69.3
• Divorced or widowed	53	25.8
• Single	10	4.9
Governorate		
• Beirut	139	67.8
• Mount Lebanon	51	24.9
• Bekaa	7	3.4
• South	5	2.4
• North Lebanon	3	1.5

Nationality		
• Lebanese	185	90.2
• Iraqi	7	3.4
• Syrian	4	2.0
• Palestinian	3	1.5
• Other	6	2.9
Living arrangement		
• Alone	14	6.8
• With spouse only	34	16.6
• With spouse and children	99	48.3
• With other family	50	24.5
• With maid	8	3.9
Work status		
• Working	24	11.7
• Retired	92	44.9
• Housewife	79	38.5
• Disability	10	4.9
Has medical insurance	134	65.4
Self-Payer	71	34.6
Type of insurance (out of 134 who reported having insurance)		
• Private insurance	108	80.60
• NSSF	24	17.91
• Cooperative	2	1.41
Witness of the stroke		
• Spouse	49	23.9
• Children or other family members	132	64.4
• Friend or maid	16	7.8
• Stranger or no one	8	3.9

Table 2 shows the clinical characteristics of the sample. The most prevalent medical diagnosis was ischemic stroke in 96.6% of the participants. The mean delay time from onset of symptoms to arrival to the ED was 15.78 hours (standard deviation 29.76), with a range of 28 minutes up to 11 days. The median delay time was 4.57 hours, interquartile range 1.92, 16.21. Almost half the sample (49.8%) reached the ED within 4.5 hours of symptom onset. The most common symptoms were speech disturbance (43.9%), followed by left sided weakness in 41%,

right sided weakness in 34.6%, aphasia in 23.4%, reduced level of consciousness in 19% and left facial drooping in 15.6%. All other symptoms were documented in less than 10% of patients.

Regarding risk factors for stroke, 78% of participants were hypertensive, 44.4% hyperlipidemic, 43.9% diabetic, 27.8% had coronary artery disease, 27.8% current smokers, 25.5% had previous strokes, 23.9% had history of atrial fibrillation, and 3.9% had history of TIAs. The mean body mass index was 28.85 ± 5.71 kg/m^2, including 37.7% who were obese (BMI > 30 kg/m^2) and 31.5% who were overweight (BMI between 25.0 and 30.0 kg/m^2).

Out of the 102 (49.8%) participants who arrived at the emergency room within 4.5 hours of symptoms onset, 27.4% of them received rtPA, which contributes to 13.7% of all participants. Moreover, 147 (71.7%) arrived to the ED by ambulance. In addition, 99.5% of the participants were seen by a neurologist upon arrival to the ED and 99.5% also had a CT-scan. Moreover, the National Institutes of Health Stroke Scale (NIHSS) of all participants had a mean of 10.84 ± 6.45.

The destination of the participants from the ED were mostly to a neurology unit (64.4%) followed by critical care units (20%), regular units (15.1%), and only one patient passing away in the ED. Finally, 91.7% survived till their discharge from the hospital whereas 8.3% did not (see Table 2).

Table 2. Clinical Characteristics of the sample (N = 205)

Variable	**N**	**%**
Delay time from symptom onset till arrival to ED (mean ±SD; median [quartile range])	15.78 ± 29.76; 4.57 [1.92, 16.21]	
Body mass index(mean ± SD)	28.85 ± 5.71	
NIH stroke scale (mean ± SD)	10.84 ± 6.45	
Diagnosis:		
• Ischemic stroke	198	96.6
• Hemorrhagic stroke	7	3.4

Left Facial droop	32	15.6
Right facial droop	18	8.8
Speech disturbance/ Aphasia	90/48	43.9/23.4
Ataxia	19	9.3
Vomiting	8	3.9
Headache	19	9.3
Dysphagia	14	6.8
Visual disturbance	15	7.3
Left sided weakness	84	41.0
Right sided weakness	71	34.6
Decreased level of consciousness/ Loss of consciousness	39/9	19.0/4.4
Smoking status		
• Never/Ex-smoker	120/28	58.5/13.7
• Current smoker	57	27.8
History of hypertension	160	78.0
History of diabetes	90	43.9
History of hyperlipidemia	91	44.4
History of TIA	8	3.9
History of prior stroke	52	25.5
Family history of stroke	0	0.0
History of coronary artery disease	57	27.8
History of atrial fibrillation	49	23.9
Method of transportation to the ED		
• Ambulance	147	71.7
• Private car/ Walking	57/1	27.8/0.5
CT scan of brain done on admission	204	99.5
Neurological consultation done in ED	204	99.5
Arrived to ED within 4.5 hours from symptom onset	102	49.8
Received rtPA (out of the whole sample)	28	13.7
Received rtPA (out of those who arrived within 4.5 hours)	28	27.4
Destination from ED		
• Neurology inpatient unit	132	64.4
• ICU/CCU/Neurology ICU	41	20.0
• Regular unit	31	15.1
• Morgue	1	0.5
Survived by discharge from hospital	188	91.7

Legend: CT: computerized tomography; ED: emergency department; ICU: intensive care unit; NIH: national institutes of health; SD: standard deviation; TIA: transient ischemic attack

B. Demographics Related to Delay

Table 3 illustrates the significant results of bivariate associations between delay time (log transformed) and the various demographic and clinical variables. Gender, age, nationality, BMI, smoking status, living arrangements, working status, and stroke risk factors were not

significantly associated with delay time to the ED. Moreover, although married participants delayed more than the non-married (17.01 ± 26.96 versus 12.97 ± 35.46), the difference did not reach statistical significance results (P=0.08), as shown in Table 3. Similarly, participants living outside Beirut delayed more than the ones living in Beirut (17.21 ± 23.50 versus 15.10 ± 32.36), p= 0.054. There was also a trend for those with medical insurance to come faster to the ED than those with no insurance (13.49 ± 20.92 versus 20.13 ± 41.48, p = 0.113).

The mode of transportation to the ED was significantly associated with delay time (p < 0.001), with those coming by ambulance arriving significantly sooner to the ED than those who came by private car (11.77 ± 27.75 versus 25.52 ± 32.51) as shown in Table 3. Finally, the difference in delay time by destination from ED did not reach statistical significance (p = 0.07), although patients admitted to regular units delayed much longer (29.83±44.02) than those admitted to neuro-in unit (12.45±17.82). .

C. Responses to Stroke Symptoms in Relation to Delay Time

As shown in Table 3, medical diagnosis was significantly associated with delay time, with those diagnosed with ischemic stroke delayed more than those with hemorrhagic stroke (16.23 ± 30.19 versus 3.32 ± 2.38; p = 0.027. Moreover, participants with history of prior strokes (21.47 ± 40.29) delayed significantly more than those with none (13.94 ± 25.14), P=0.008).

As expected, patients who presented with loss of consciousness came much faster to the ED (1.86 ± 1.72) than those who did not (16.43 ± 30.28), p = 0.001. In relation to symptoms, participants with aphasia (8.63 ± 15.96) were significantly more likely to present faster to the ED than those with no aphasia (17.97±32.57), P=0.008). On the contrary, the ones with speech problems (21.38 ± 39.06) delayed significantly more coming to the ED than those without

speech problems (11.41 ± 18.69), P=0.014. Likewise, participants with symptoms of dysphagia (19.32 ± 19.56) delayed more than those without dysphagia (15.53 ± 30.39), with p=0.040. Finally, those who received rtPA delayed less (1.50 ± 0.91) than those who did not receive rtPA (18.05 ± 31.44), with p < .001. (see Table 3). Finally, it is worth noting that the NIH Stroke Scale score was significantly associated with delay time, with Spearman Rho correlation coefficient of -0.154, p = 0.028, thus the more the neurologic impairment, the shorter the delay in coming to the ED in the sample.

Table 3. Significant differences in delay time (2 group differences). N = 205

Variable	N	Mean ± SD	T$^{\perp}$	P value$^{\perp}$
Marital status				
• **Married**	143	17.01 ± 26.97	1.76	0.080
• **Widow/divorced/single**	62	12.97 ± 35.46		
Transport to ED				
• **Ambulance**	147	11.77 ± 27.75	-4.77	0.000
• **Private car**	58	25.52 ± 32.51		
Residence				
• **Beirut**	139	15.10 ± 32.36	-1.94	0.054
• **Outside Beirut**	66	17.21 ± 23.50		
Diagnosis				
• **Ischemic**	198	16.23 ± 30.19	1.21	0.027
• **Hemorrhagic**	7	3.32 ± 2.38		
History of prior stroke				
• **Yes**	52	21.47 ± 40.29	-2.68	0.008
• **No**	152	13.94 ± 25.14		
Loss of consciousness				
• **Yes**	9	1.86 ± 1.72	3.23	0.001
• **No**	196	16.43 ± 30.28		
Aphasia				
• **Yes**	48	8.63 ± 15.96	2.46	0.008
• **No**	157	17.97±32.57		
Speech problems				
• **Yes**	90	21.38 ± 39.06	-2.48	0.014
• **No**	115	11.41 ± 18.69		
Dysphagia				

• **Yes**	14	19.31 ± 19.56	-2.06	0.040
• **No**	191	15.53 ± 30.39		
Received rtPA				
• **Yes**	28	1.50 ± 0.91	6.10	0.000
• **No**	177	18.05 ± 31.44		

Legend: rtPA: recombinant tissue plasminogen activator; SD = Standard deviation; ⊥: Values of the analyses done with the log transformed delay time variable.

D. Predictors of Delay Time

A linear multiple regression analysis was made with variables that were significantly or marginally correlated with delay time in this study (see Table 4). The predictors that were entered were marital status, residence, medical insurance, mode of transport to the ED, medical diagnosis, prior stroke, speech problems, aphasia, loss of consciousness, dysphagia, and the NIH stroke scale. The model explained 27.2% of the variance in delay time (adjusted $R^2 = 0.230$). The significant predictors were place of residence (P=0.026), mode of transport to the hospital ($p < 0.001$), history of prior stroke ($p = 0.006$), loss of consciousness (P=0.007), dysphagia ($p = 0.011$) and speech disturbance showed marginal significance as predictor (p=0.082). Thus, living in Beirut, coming to the ED by ambulance and presenting with loss of consciousness predicted shorter delay time whereas presenting with dysphagia and having a history of prior stroke predicted longer delay times.

Table 4. Multiple regression analysis for delay time (N = 205)

Variable	B	Standard error	Confidence interval of B	Beta	P value
Marital status	-0.100	0.091	-0.279, 0.078	-0.071	0.270
Residence (Beirut versus outside Beirut)	0.197	0.088	0.023, 0.371	0.143	0.026
Medical insurance	-0.111	0.085	-0.279, 0.057	-0.082	0.194
Transport to ED (ambulance or not)	0.417	0.093	0.2344, 0.601	0.293	0.000
Medical diagnosis	-0.248	0.223	-0.689, 0.192	-0.070	0.267
Prior stroke	0.257	0.092	0.075, 0.439	0.174	0.006
Speech problems	0.156	0.089	-0.020, 0.332	0.120	0.082
Aphasia	-0.109	0.110	-0.326, 0.108	-0.072	0.323
Loss of consciousness	-0.553	0.202	-0.952, -0.154	-0.176	0.007
Dysphagia	0.410	0.160	0.093, 0.762	0.161	0.011
NIH stroke scale	-0.006	0.007	-0.019, 0.008	-0.057	0.404

Legend: NIH: National Institutes of Health; rtPA: recombinant tissue plasminogen activator

CHAPTER IV

DISCUSSION

This study examined the characteristics of 205 patients admitted with acute stroke to a major tertiary referral center in Beirut, the time from symptom onset to arrival to the emergency department (delay time) and factors associated with the delay. The results revealed that most of the patients had ischemic stroke (96.6%), and only 49.8% of the patients reached the ED within 4.5 hours, which is the time period needed for lifesaving thrombolytic therapy to be effective for those with ischemic stroke. Delay time in the current study had a mean of 15.78 hours (median 4.57 hours), with a range of 28 minutes to 11 days. Predictors of delay in the multivariate analysis were place of residence, mode of transport to the hospital, history of prior stroke, dysphagia at presentation, and receipt of rtPA in the ED.

A. Profile of Acute Stroke Patients

The characteristics of the sample in the current study were compared to those of the sample in the study of Lahoud and colleagues (2017), which was conducted in two other medical centers in Lebanon but included also patients with TIA. The gender distribution was similar in both studies, with males constituting 51.7% of the sample in the current study and 55% of that in Lahoud et al.'s study (2017). The patients in this study were older (mean age 73.33 years versus 68.41%). More patients in this study lived in Beirut (67.8%) compared to the other study (51.6%), but fewer patients had medical insurance (65.4% versus 81.1%). Both studies showed that ischemic stroke is more prevalent than hemorrhagic stroke in Lebanon. However, ischemic strokes showed higher percentages in this study compared to Lahoud et al. (96.6% versus

64.2%), due to the exclusion of patients with transient ischemic attacks (TIA) in our sample. When excluding the patients with TIA from the sample in Lahoud, et al.'s (2017) study, it is noted that 81.09% of their remaining patients had ischemic stroke. In terms of risk factors, the current sample had similar history of prior stroke (25.5% vs. 25.2%), coronary artery disease (27.8% vs. 28%) and slightly more hypertension (78% vs. 75.2%), but lower history of TIA (3.9% vs. 5.1%), family history of stroke (0% vs. 3.5%) and current smoking (27.8% vs. 35.4%). On the other hand, the sample in this study had higher history of diabetes (43.9% vs. 40.9%), hyperlipidemia (44.4% vs. 28%), and atrial fibrillation (23.9% vs 18.5%) compared to that of Lahoud et al.'s study. These differences may be attributed to the age difference between the two samples.

Hemiparesis (41% left sided and 34.6% right sided) and speech disturbance (43.9%) were the most frequently presenting symptoms in this study, followed by lethargy and obtundation (19% reduced level of consciousness) and left facial droop (15%). These findings are similar to those reported by Mosley and his colleagues (2014) and Hassankhani et al. (2019). Lahoud et al. (2017) did not report about symptoms in their sample.

In this study, all patients (except for one) had CT imaging of the brain. The patient who did not receive an instant CT-brain imaging was misdiagnosed on admission for his young age (25 years-old) and having only headache as a symptom. When he was admitted, a CT-brain imaging was done the next day since he developed left-sided weakness and the CT showed an acute stroke. Likewise, all patients had neurological consultation except for one. The patient who was not seen by a neurologist on admission was an Iraqi patient who was previously diagnosed in his country for acute stroke three days prior admission and was transferred to AUBMC to pursue treatment. Moreover, only 14.1% of those with ischemic stroke received rtPA although 49%

arrived to the ED within 4.5 hours of symptom onset; it maybe that there were contraindications to the administration of rtPA, which was not investigated in this project. Still these results are better than those by Hassankhani et al (2019) in Iran, where less than 5% received rtPA, and those of a Norwegian study where only 7.1% of the patients with acute ischemic stroke received rtPA (Faiz et al., 2014). The differences between these studies may be linked to the delay in coming to the ED, such as in the study by Hassankhani et al. (2019), where less than one third arrived within 4.5 hours. Alternatively, delays in CT imaging or the need to control hypertension were reported by Mowla et al. (2017), which could contribute to not providing thrombolytic therapy. Only one patient passed away in the ED in this study, and 91.7% survived till hospital discharge, which reflects adequate and effective treatment of these patients.

B. Delay time and associated factors

In this study, the median delay time was 4.57 hours, which is slightly above the 3 to 4 hours median delay reported in a comprehensive review of pre-hospital delay in acute stroke patients (Evenson et al., 2009), and more than the median of 3.8 hours reported by Faiz et al. in a sample of 350 patients who included those with TIA. The median delay time in this study falls within that of the majority of the studies reviewed by Pulver and Watson (2017), which they reported to be over 3 hours. Almost half (49%) of patients arrived within 4.5 hours to the ED, which is better than that reported by Hassankhani et al. (2018), where only 28.18% of patients with ischemic stroke reached the ED within 4.5 hours from symptom onset. Abilleira et al. (2011) reported that 37.2% of their acute stroke patients had a delay time longer than six hours, compared to 43.4% in this study.

Since the majority of the sample in this study (96.59%) had ischemic stroke, then up to half the patients may have been deprived of the benefit of thrombolytic therapy, given that their delay was longer than 4.5 hours. The prolonged delay in this study may be related to the lack of sufficient knowledge among the Lebanese population of symptoms of acute stroke, as was found in a community survey of 390 adults older than 50 years (mean age 62.03 years) who were recruited from pharmacies all over Lebanon and included 16 (4.1%) who had prior stroke (Khalil & Lahoud, 2020). In that study, only 68% were able to spontaneously recall at least one symptom of stroke, with the most frequently recalled ones being headache, hemiparesis and dizziness. Although that was not a clinical sample of stroke patients, the finding has implications for family members or witnesses of stroke patients. This suboptimal knowledge could be an alarming indication for the need to educate the public about stroke.

In this study, 71.7% of patients came to the hospital by ambulance compared to 64.9% of patients in the study of Faiz et al. (2014). In this study, those who used the ambulance reached the hospital significantly faster than those who came by private car. Similarly, a study done by Arrate and his colleagues (2019) showed that using emergency medical services (EMS) such as ambulances was strongly associated with early hospital arrival from the time of stroke onset. Thus, there is room for improvement in educating the public about the importance of using an ambulance to escort patients with stroke to the ED in order to reduce delays in treatment.

Patients with hemorrhagic strokes delayed coming to the ED significantly less than those with ischemic stroke. Similarly, Andersson Hagiwara et al. (2018) reported that patients with hemorrhagic strokes had more frequent and rapid activation of emergency medical services (EMS) than those with ischemic stroke, with only 22% of ischemic stroke patients arriving to the ED within three hours of symptom onset, compared to 37.4% of the 198 patients with ischemic

stroke in the current study. This difference might be linked to the higher severity of symptoms and the more rapid deterioration of health status seen in patients with hemorrhagic strokes compared to ischemic stroke.

None of the demographic characteristics were significantly associated with delay time, as was found in a study in the US (Ader et al., 2019). However, Ader and colleagues (2019) reported that driving longer distances resulted in delay in rtPA administration and longer symptom onset to arrival time to the ED. Similarly, this study showed that people living in Beirut area delayed significantly less than those living outside Beirut. AUBMC lies in the center of Beirut so the patients living outside Beirut are delayed for multiple factors such as traffic congestion and the unavailability of modes of transportation that can hamper the arrival to AUBMC within 4.5 even from nearby cities.

In terms of symptoms, having aphasia and loss of consciousness were associated with shorter delays, whereas speech problems and dysphagia were associated with longer delays. This finding suggests that people wait until symptoms become very severe before coming to the ED. This finding concurs with the significant negative association between the NIHSS score and the delay time in this study, where the more severe the neurologic impairment, the shorter the delay time. Alternatively, patients may not recognize all possible symptoms of stroke. An Irish study showed that stroke's warning signs such as by dizziness, numbness, weakness and headache were identified by only 5% of a community sample of older adults, whereas slurred speech was recognized as a stroke symptom by half of the sample (Hickey et al., 2009). In this study, although aphasia and loss of consciousness were associated with reduced delay, other important signs such as ataxia, hemiparesis, visual problems, and facial drooping did not show any significant association with delay. These results show that our Lebanese population may be only

recalling one of the BE-FAST (Balance, Eye, Face, Arm, Speech, Time) and dismissing the rest of symptoms. BE-FAST is an effective tool that captures > 95% of acute ischemic stroke patients (Aroor et al., 2017). Thus, educational campaigns for the public regarding "BE-FAST" are needed to be initiated on media and social networks in order to promote identification of stroke symptoms, early EMS activation, and timely administration of rtPA. This education needs to be provided also to prehospital emergency personnel to promote early recognition and appropriate treatment of stroke.

Although risk factors did not relate to delay time, including hypertension, history of heart disease, current and former cigarette smoking, diabetes mellitus, atrial fibrillation, and history of TIA, they are frequently seen in stroke patients. The lack of association may be accounted for by lack of knowledge of risk factors for stroke, as was found in an Irish study where less than half of a community sample of older adults that included 6% with history of stroke or TIA knew established risk factors like smoking and hyperlipidemia, but 74% knew that hypertension was a risk factor for stroke (Hickey et al., 2009). In Lebanon, a recent study showed that half of the sample of older adults that included 4.1% with history of stroke could not recognize hypertension as a risk factor (Khalil & Lahoud, 2020).

The only risk factor associated with delay in this study was history of stroke, whereby patients with previous stroke delayed significantly more coming to the ED. This finding raises concern as prior stroke makes people vulnerable to a recurrent attack of stroke, and suggests the need for effective health education upon discharge from previous stroke hospitalization by providing patients with instructions on how to react appropriately in the event of symptoms recurrence. This education needs to be emphasized again in the outpatient settings like clinics and primary health care centers. Recognition of risk factors associated with stroke is also

essential for stroke prediction. However, the Lebanese population has limited knowledge of stroke risk factors (Khalil & Lahoud, 2020). Knowledge of stroke and its risk factors was not assessed in this study, but it could shed light on the causes of delay in this sample.

As expected, patients who came faster to the ED were significantly more likely to receive rtPA than those who came later rand as mentioned earlier, only 29% of those with ischemic stroke who reached the ED within 4.5 hours were given rtPA. It is not clear from the data why not all early comers to the ED received rtPA; one factor may be patients having contraindication to rtPA, data that were not collected for this project. Mowla et. al (2017) reported that ineffective triage protocols and slow interpretations of CT-scan may account for delay in provision of r-tPA in eligible patients. This concern points out the importance of following up-to-date clinical guidelines for acute stroke at the emergency departments and generating evidence-based protocols in addition to stroke team activation. Time to CT and time to rtPA were not assessed in this study and must be part of the performance indicators that must be regularly measured to evaluate the quality of care provided.

Results of the multiple regression showed that living outside Beirut, history of prior stroke or having dysphagia predicted longer delays whereas losing consciousness and coming to the ED by ambulance predicted shorter delays. This finding highlights the importance of educational campaigns about symptoms of stroke and the importance of prompt seeking of emergency care for them in order for the treatment to be effective. Moreover, use of ambulance to bring patients to the ED needs to be emphasized. The education must target both the general community as well as patients with stroke.

C. Limitations

Several limitations should be considered in interpreting the results of this study. The extraction of data collected for this study was completely dependent on medical records. Thus, accurate out-of-hospital events, especially when it comes to the time of onset of stroke symptoms and patients' last seen healthy, were not precisely documented in some of the ED charts. For example, some delay times were recorded by nurses, emergency residents, and neurologists in a dichotomous manner (such as within 4.5-hour window, last night, 2 days ago, etc…). Thus, the time of symptoms onset required estimation of time in those cases. The other limitation was related to missing data such as level of education and type of occupation that are not usually documented in medical records, in addition to 23 charts missing height and weight data. Finally, this study was done on one major tertiary medical center in Beirut where more than two thirds of the study sample were living in Beirut and its suburbs, so may not represent the Lebanese population of stroke patients. Thus, a multi-center study is needed to determine factors associated with stroke delay in receiving medical treatment in Lebanon.

One implication for practice that transpires from the findings of the study involves improving documentation, such as more accurate documentation of the time from symptom onset and the reason for not administering rtPA, in addition to time till CT. Future prospective studies are needed to capture the exact time of symptom onset and relevant factors that could not be addressed in this study, such as the level of education of patients, their knowledge about stroke and its symptoms, and the bystander response among the Lebanese population.

In conclusion, this study revealed that stroke patients delay significantly coming to the ED when they experience a stroke. Those living far distances from medical centers take a lot of time reaching the ED, which has major effects on their treatment. Moreover, calling an ambulance when stroke symptoms occur can save lives. Acquainting the public with the

mnemonic “BE-FAST” can be an effective method in reducing stroke incidence. Thus, medical centers and the Ministry of Public Health should raise awareness about stroke symptoms by using advertisements and social media to educate the public about stroke and its unfavorable effects. Moreover, health care professionals in primary health care settings can help guide the Lebanese society to recognize a stroke and how to react when symptoms occur. Finally, prehospital emergency personnel need to be trained in the assessment and recognition of acute stroke.

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APPENDIX

Medical Record Chart Review for Stroke

Code number:_____

Gender: □Male □Female Age: _____ years.

Nationality: □ Lebanese □ Syrian □Iraqi □Palestinian □other_____

Place of residence:

Time and date of arrival to ED:

Marital status: □Married □Widowed □Divorced □Single

Height: Weight: BMI:

Smoking history:

□ never smoked

□ current smoker (cigarettes/day): _____

□ previous smoker, time of quitting: _____

Education: □Elementary □Intermediate □Secondary □Technical □University □Graduate

Work status: □Working □Retired □Housewife □On disability

If working, Occupation: _____

Medical insurance: □ No □ Yes. If yes, what type: □National Social Security Fund (NSSF/public) □Private insurance

Living arrangement: □Alone □With spouse □With spouse and children □With children

Medical diagnosis: □Ischemic stroke □Hemorrhagic stroke

Time and date of onset of stroke: _____

Clinical Presentation:

□Left facial drooping □Right facial drooping □ Aphasia □ Ataxia

□Vomiting □Headache □Speech disturbances □Visual disturbances

□Other: _____

Patient was transported to the ED by: □ Ambulance □ Private car

Witness of symptoms: □Relative □Stranger □Friend □None

Risk factors:

□Hypertension □Diabetes mellitus □Hyperlipidemia □ Old TIA □Prior stroke

□Family history of stroke □Coronary artery disease □Atrial Fibrillation

NIH Scale Score on admission:

CT-Scan on admission: □Yes □No

Recombinant tissue plasminogen Activator (r-tPA) received: □Yes □No

Neurology consultation upon arrival: □Yes □No

Patient's destination: □Home □Regular floor □ICU □Morgue

Survival up to discharge from hospital: □Yes □No