A retrospective analysis of 254 acute stroke cases admitted to two university hospitals in Beirut: classification and associated factors

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Summary

Lebanon is a developing country where the prevalence of stroke subtypes and their correlation with risk factors have not been studied, even though stroke management is an ongoing major national healthcare challenge. In a retrospective study conducted in two university hospitals, data were collected on all stroke cases admitted in 2012 and 2013. Ischemic strokes were then classified according to a modified TOAST classification. A total of 254 inpatients (mean age 68.41 years ±13.34, 55.1% males) was included in the study; of these, 15% had had a hemorrhagic stroke and was therefore excluded. Conversely to findings from studies in other Arab and Asian countries, where small vessel disease is the most frequent subtype, our study showed a predominance of large artery atherosclerosis (53.5%) which, in comparison with other subtypes, was found to be associated with dyslipidemia (OR= 3.82, 95% CI= [1.76-8.28]; p=0.001). Cardioembolic stroke and small vessel disease were found to be positively associated with aging and living in Beirut, respectively. Larger studies are needed to explain these findings.

KEY WORDS: Beirut, Lebanon, Risk factors, Stroke subtypes, TOAST classification.

Introduction

Stroke is a heterogeneous cerebrovascular disease with a wide variety of phenotypes and underlying etiologies (Amarenco et al., 2009). For this reason, its classification into subtypes is necessary prior to any intervention (Adams et al., 1993). Ischemic stroke is the most common type, accounting for more than 80% of all strokes (Pendlebury et al., 2009). However, its subtyping requires extensive assessment, from the patient's first evaluation to late prognosis (Kim and Kim, 2014). Moreover, studying the association between cerebrovascular risk factors and ischemic subtypes is crucial for implementing an efficacious preventive strategy (Rahim et al., 2014).
Epidemiological studies have shown a large variation between countries in the prevalence of stroke types and ischemic subtypes (Schulz and Rothwell, 2003; Turin et al., 2010; Kim and Kim, 2014). This variation may be related to differences in lifestyles, associated risk factors and preventive measures; differences in study designs and stroke classification tools may also have contributed to discrepancies (Schulz and Rothwell, 2003; Kim and Kim, 2014). Moreover, studies have shown different associations between ischemic subtypes and stroke risk factors (Ihle-Hansen et al., 2012). However, hypertension and diabetes were more linked to small vessel disease, whereas large artery atherosclerosis was more associated with hyperlipidemia and smoking (Khan et al., 2007; Ueshima et al., 2008).
Lebanon, an upper-middle-income country in the Eastern Mediterranean Region (EMR) (World Health Organization WHO, 2015), suffers from a paucity of data on the prevalence of stroke subtypes and their associations with risk factors, even though stroke was classified as the second leading cause of mortality in 2012 (9.4% of all deaths), after ischemic heart disease (31.1%) (WHO, 2015). In fact, over the past two to three decades, as a result of lifestyle modifications, economic growth and urbanization, this country and the region as a whole have seen an epidemiological transition (Rahim et al., 2014). Life expectancy has risen, from 67 years in 1990 to 80 years in 2013, and diseases related to aging are expected to further increase, notably stroke (WHO, 2015). Behavioral risk factors such as smoking (cigarettes 38.5% and waterpipe 22.4%) (Sibai and Hwalla, 2008), insufficient physical activity (38%) (WHO, 2015) and obesity (28%) (Nasreddine et al., 2012) are alarmingly high among Lebanese adults and available data show a high prevalence among adolescents as well (El-Roueiheb et al., 2008; Chacar and Salameh, 2011). Related metabolic diseases, especially diabetes and hyperten-

sion, have their highest prevalence rates in the EMR (13 and 27% respectively) (WHO, 2015).
The current situation in Lebanon warrants urgent epidemiological studies designed to assess stroke prevalence by types and subtypes and the related risk factor associations, thereby making it possible to implement subsequent preventive strategies in an unhealthy aging population. The present study thus analyzed the prevalence of all hemorrhagic stroke and ischemic stroke subtypes in a Lebanese hospital-based inpatient population. Ischemic stroke subtypes were further categorized according to a modified (risk factor-free) TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification (Adams et al., 1993) with the aim of evaluating their correlations with validated stroke risk factors and with sociodemographic characteristics of the sample.

Materials and methods

This study was retrospectively conducted in two university hospitals in Beirut: the Lebanese University Hospital - Geitaoui (LUH) and the Rafic Hariri University Hospital (RHUH). All medical records of inpatients admitted between January 2012 and December 2013, with a discharge diagnosis of stroke, were examined. Sociodemographic characteristics, individual vascular risk factors, medical history, clinical assessment and neuroimaging data of each patient were retrieved for analysis. After consecutive file numbering, patients with hemorrhagic strokes were identified and excluded, whereas ischemic stroke patients were divided into subgroups and analyzed. A stroke was considered ischemic when brain imaging revealed acute infarction or showed no evidence of hemorrhage.

Risk factor recording

Patients were recorded as:
1. hypertensive if they were reported as taking any antihypertensive medication prior to admission or if they had a persistent systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg (James et al., 2014).
2. hyperlipidemic if they were reported as taking a statin or any other lipid lowering agent, or were diagnosed hyperlipidemic according to the 2013 American College of Cardiology/American Heart Association report (Stone et al., 2014).
3. diabetic if they were reported as taking a current medication for diabetes mellitus or had at least two of fasting glucose measurements ≥ 126 mg/dL (7.0 mmol/L) (American Diabetes Association, 2014).
Moreover, any personal history of transient ischemic attack (TIA), stroke, ischemic heart disease (HD), atrial fibrillation (AF), peripheral artery disease (PAD), migraine, and family history of stroke or heart disease was recorded. HD included any history of angina pectoris or myocardial infarction. ECGs and available echocardiograms were checked to confirm medical history. Smoking and alcohol consumption profiles were also recorded, as were levels of physical activity. Current smokers were compared with the group of non-smokers and former smokers, the latter being defined as those who have not smoked for a minimum of 6 months. Daily alcohol consumption was defined as a regular consumption as opposed to occasional, rare or no consumption. Patients doing regular physical activity (daily or weekly, moderate or intense) were considered physically active. Body mass index and metabolic syndrome were not included in the analysis since a large number of medical records lacked waist, weight and height measurements.

Ischemic stroke classification

Ischemic strokes were retrospectively classified according to the modified TOAST classification tool into five etiological categories (Adams et al., 1993):
1. Large artery atherosclerosis (LA): patients with this subtype would have, as clinical findings, a cortical impairment (e.g. aphasia, neglect, focal motor deficit) or brain stem or cerebellar dysfunction (e.g. dysarthria, dizziness, ataxia, diplopia). Paraclinical evidence of a stenosis > 50% of an appropriate intracranial or extracranial artery is also needed, supported by either a brain CT scan or MRI showing the presence of an infarct >1.5 cm in diameter in the subcortical hemispheric area, in the cerebrum or cerebellum, or in the brain stem. This category is usually linked to atherosclerosis or embolism. Potential sources of cardiogenic embolism should be excluded.
2. Cardio-embolism (CE): at least one cardiac source of an embolus must be identified for a possible or probable diagnosis (a valvular heart disease, AF, a history of acute myocardial infarction, or infective endocarditis). Clinical and brain imaging findings are similar to those described for the LA subtype. A decreased level of consciousness and neurological symptoms of abrupt onset with maximal severity at onset help distinguish cardiogenic embolism from other mechanisms of cerebral ischemia.
3. Small vessel disease (SV): this subtype corresponds to small lacunar infarcts; the clinical symptoms are usually those of one of the classical lacunar syndromes (pure motor hemiparesis, pure sensory stroke, sensorimotor stroke, ataxic hemiparesis) without symptoms related to cerebral cortical dysfunction, and they are supported by small infarcts of less than 1.5 cm in diameter on brain MRI or brain CT scan (which occasionally may appear normal). Potential cardiac sources of embolism should be absent, and evaluation of the large extracranial arteries should not demonstrate a stenosis >50% in an ipsilateral artery.
4. Stroke of other determined etiology (Other): this category includes patients with rare causes of stroke, such as non-atherosclerotic vasculopathies, hypercoagulable states, or hematological disorders.
5. Stroke of undetermined etiology (Undetermined): this category includes:
• patients with no evidence of any clear etiology despite an extensive evaluation;
• patients with two or more potential causes of stroke with no clear final diagnosis;
• patients who developed an ischemic stroke but have a negative or incomplete evaluation.
All the study patients were assessed with a brain CT scan and an ECG on admission. Blood samples were systematically drawn to investigate lipid and glycemic profiles. Moreover, 49.6% of the patients had a cerebral MRI.
Stroke risk factors, notably hypertension, hyperlipi-

demia, diabetes and smoking were not included in the classification system used (modified risk factor-free TOAST) so as not to introduce bias into the multivariable analysis of associations of stroke subtypes with risk factors (Jackson and Sudlow, 2005). However, AF and HD were considered in the CE classification and were consequently excluded from the regression models.

Statistical analysis

First, the sample baseline characteristics and prevalence of risk factors among stroke patients were described. We then compared distributions of patient characteristics, medical history and vascular risk factors among the ischemic stroke subtypes. Comparison of means was performed using analysis of variance, with Bonferroni correction on post-hoc tests. Non-parametric tests were used in the case of small subgroups (Kruskal-Wallis). Comparison of proportions was performed using Pearson's Chi-squared test, with further standardized residuals' two-by-two comparison. Fisher's exact test was used for small proportions. In the multivariable analysis, each ischemic stroke subtype was compared with the others for associations with baseline characteristics and risk factors. We estimated the odds of the presence of a risk factor in a particular subtype to the odds of its presence in all the other subtypes. We selected variables that were associated with the outcome with a p-value below 0.2 in bivariate analyses. These were then submitted to a binary logistic regression by forward stepwise selection. After ensuring non-collinearity and sampling adequacy by the Hosmer-Lemeshow test, we reported adjusted odds ratios (aORs). A p-value <0.05 was considered significant. Furthermore, we analyzed the characteristics of patients living in Beirut compared with other patients using a logistic regression. Statistical analysis was performed using SPSS Software for Windows version 18.0.

Results

During the years 2012 and 2013, 254 patients were admitted to LUH and RHUH with a final diagnosis of stroke. They were aged between 31 and 94 years, with a mean age of 68.41 years (±13.34). Male sex was slightly predominant (55.1%) and 51.6% of the patients was living in Beirut. On the basis of clinical and imaging examination, 163 (64.2%) patients were affected by an ischemic stroke, whereas 38 (15.0%) had a hemorrhagic stroke and 53 (20.9%) a TIA. 64 (25.2%) patients had suffered a stroke previously (57 ischemic and 7 hemorrhagic) and were excluded from the subtype classification using the modified TOAST criteria. The most prevalent risk factors among all the patients were hypertension (75.2%), absence of physical activity (89.4%), and diabetes mellitus (40.9%). Further details are presented in Table I.

159 patients (163 ischemic stroke + 53 TIA – 57 recurrent stroke) were thus eligible for subtype classification according to the modified TOAST criteria. They had a mean age of 67.8 years (±13.56) and 84 (52.8%) were males. LA was the most prevalent ischemic stroke subtype (53.5%) followed by CE (16.4%), SV (13.2%), "Undetermined" (15.1%) and "Other" (1.9%). Due to their small number (only 3 patients), strokes of "Other" determined etiology were combined with those of "Undetermined" etiology in the bivariate and multivariable analyses. The prevalence of risk factors in the different TOAST subtypes is presented in Table II. Significant differences between groups were observed for age (patients with CE were older, p=0.004), sex (CE patients were mainly females, unlike other groups, p=0.012), Beirut residency (Beirut residents were highly predominant among SV patients, p=0.005), hypertension (predominant among SV patients, p=0.035), and hyperlipidemia (predominant among LA patients, p=0.005). Relationships between each ischemic stroke subtype and patients' characteristics and risk factors are displayed in Tables III, IV and V. Hyperlipidemia was strongly associated with the LA subtype *versus other* subtypes (OR=3.82, 95%CI= [1.76-8.28]; p=0.001) (Table III). CE was negatively associated with male gender (aOR=0.32, 95%CI= [0.12-0.83]; p=0.020) and hyperlipidemia (aOR=0.26, 95%CI= [0.07-0.96]; p=0.043), and positively associated with age (aOR=1.04, 95%CI= [1.00-1.08]; p=0.047) (Table IV). When comparing the SV subtype with the other groups, living in Beirut was strongly associated with the model (OR=3.25, 95%CI= [1.19-8.88]; p=0.021) (Table V). For the last group (ischemic strokes of Other or Undetermined etiology), age (aOR= 0.97, 95%CI= [0.93-0.99]; p=0.034) and Beirut residency (aOR= 0.346, 95% CI= [0.13-0.95]; p=0.040) were significantly and negatively correlated with the model (data not shown in a Table). As shown in Table VI, stroke patients living in Beirut were found to be significantly older (aOR=1.05, 95%CI= [1.02-1.08]; p=0.001) and more hypertensive (aOR=2.22, 95%CI= [0.97-5.09]; p=0.059) than those living outside the capital when adjusting for other characteristics and risk factors.

Table I - Baseline characteristics of patients (n= 254).

Sociodemographics	N (%)
Male sex	140 (55.1)
Mean age, years (SD)	68.41 (13.34)
Residents of Beirut	131 (51.6)
Covered by an insurance	206 (81.1)
Stroke type	
TIA	53 (20.9)
Ischemic	163 (64.2)
Hemorrhagic	38 (15.0)
Risk factors	
Previous stroke	64 (25.2)
Previous TIA	13 (5.1)
Family stroke history	9 (3.5)
Family heart disease history	13 (5.1)
HD	71 (28.0)
AF	47 (18.5)
PAD	2 (0.8)
Migraine	2 (0.8)
Hypertension	191 (75.2)
Hyperlipidemia	71 (28.0)
Diabetes mellitus	104 (40.9)
Current smoking	90 (35.4)
Daily alcohol consumption	12 (4.7)
No physical activity	227 (89.4)

Abbreviations:SD=standard deviation; TIA=transient ischemic attack; HD=ischemic heart disease, AF=atrial fibrillation; PAD=peripheral artery disease.

Table II - Characteristics of patients classified using the modified TOAST criteria.

	Total n (%)	LA n (%)	CE n (%)	SV n (%)	Other or Undetermined n (%)	p-value*
Patients	159 (100)	85 (53.5)	26 (16.4)	21 (13.2)	27 (17.0)	
Mean Age (y) (SD)	67.80(13.56)	68.35 (13.60)	73.96 (11.27)	66.90 (14.43)	60.81 (12.17)	0.004
≤ 44 y	9 (5.7)	5 (5.9)	0	2 (9.5)	2 (7.4)	0.005
[45-54] y	19 (11.9)	8 (9.4)	2 (7.7)	1 (4.8)	8 (29.6)	
[55-64] y	33 (20.8)	14 (16.5)	2 (7.7)	8 (38.1)	9 (33.3)	
[65-74] y	46 (28.9)	29 (34.1)	9 (34.6)	4 (19)	4 (14.8)	
[75-84] y	32 (20.1)	18 (21.2)	7 (26.9)	3 (14.3)	4 (14.8)	
≥85 y	20 (12.6)	11 (12.9)	6 (23.1)	3 (14.3)	0	
Male sex	84 (52.8)	48 (56.5)	7 (26.9)	10 (47.6)	19 (70.4)	0.012
Beirut residents	75 (47.2)	39 (45.9)	15 (57.7)	15 (71.4)	6 (22.2)	0.005
Previous TIA	8 (5.0)	3 (3.5)	2 (7.7)	1 (4.8)	2 (7.4)	0.786
Family stroke history	3 (1.9)	1 (1.2)	0	1 (4.8)	1 (3.7)	0.513
Family HD history	7 (4.4)	2 (2.4)	2 (7.7)	1 (4.8)	2 (7.4)	0.561
Hypertension	120 (75.5)	66 (77.6)	20 (76.9)	19 (90.5)	15 (55.6)	0.035
Hyper-lipidemia	45 (28.3)	34 (40)	3 (11.5)	4 (19)	4 (14.8)	0.005
Diabetes mellitus	66 (41.5)	36 (42.4)	12 (46.2)	10 (47.6)	8 (29.6)	0.542
Current smoking	62 (39.0)	36 (42.4)	4 (15.4)	7 (33.3)	15 (55.6)	0.050
Daily alcohol consumption	8 (5.0)	6 (7.1)	0	0	2 (7.4)	0.154
No physical activity	136 (85.5)	72 (84.7)	24 (92.3)	17 (81)	23 (85.2)	0.680

Abbreviations: LA=large artery atherosclerosis; CE=cardio-embolism; SV=small vessel disease; SD=standard deviation; TIA=transient ischemic attack; HD=ischemic heart disease. *Pearson Chi-square for comparison of proportions, Analysis of variance for comparison of means.

Table III - Associations between large artery atherosclerosis (LA) and potential risk factors (reference: CE, SV, Other and Undetermined).

Explanatory variable	Bivariate analysis OR	Multivariable analysis† 95% CI	p-value	OR	95% CI	p-value
Age (y)	1.01	0.98-1.03	0.580			
Male sex	1.37	0.73-2.56	0.325			
Beirut residents	0.90	0.48-1.67	0.727			
Previous TIA	0.51	0.12-2.19	0.361			
Family stroke history	0.43	0.04-4.83	0.493			
Family HD history*	0.33	0.06-1.77	0.196			
Hypertension	1.29	0.62-2.65	0.495			
Hyperlipidemia*	3.82	1.76-8.28	0.001	3.82	1.76-8.28	0.001
Diabetes mellitus	1.08	0.57-2.03	0.817			
Current smoking*	2.42	0.64-9.14	0.191			
Daily alcohol consumption	4.50	0.41-49.6	0.219			
No physical activity	0.87	0.36-2.11	0.750			

Abbreviations: OR=odds ratio; CI=confidence interval; TIA=transient ischemic attack; HD=ischemic heart disease
†Forward Stepwise Selection
*Variables included in the multivariable analysis

Table IV - Associations between cardio-embolism (CE) and potential risk factors (reference: LA, SV, Other and Undetermined).

Explanatory variable	Bivariate analysis			Multivariable analysis†		
	OR	95% CI	p-value	aOR	95% CI	p-value
Age (y)*	1.05	1.01-1.08	0.013	1.04	1.00-1.08	0.047
Male sex*	0.27	0.11-0.68	0.006	0.32	0.12-0.83	0.020
Beirut residents	1.66	0.71-3.88	0.243			
Previous TIA	1.76	0.34-9.27	0.502			
Family HD history	2.13	0.39-11.6	0.381			
Hypertension	1.1	0.41-2.97	0.851			
Hyperlipidemia*	0.28	0.08-0.99	0.049	0.26	0.07-0.96	0.043
Diabetes mellitus	1.25	0.54-2.92	0.600			
Current smoking*	0.18	0.04-0.98	0.047			
No physical activity	2.25	0.49-10.3	0.294			

Abbreviations: OR=odds ratio; CI=confidence interval; aOR=adjusted odds ratio; TIA=transient ischemic attack; HD=ischemic heart disease
†Forward Stepwise Selection
*Variables included in the multivariable analysis

Table V - Associations between small vessel disease (SV) and potential risk factors (reference: LA, CE, Other and Undetermined).

Explanatory variable	Bivariate analysis			Multivariable analysis†		
	OR	95% CI	p-value	OR	95% CI	p-value
Age (y)	0.99	0.96-1.03	0.746			
Male sex	0.79	0.31-1.97	0.608			
Beirut residents*	3.25	1.19-8.88	0.021	3.25	1.19-8.88	0.021
Previous TIA	0.94	0.11-8.01	0.952			
Family stroke history	3.40	0.30-39.2	0.327			
Family HD history	1.10	0.13-9.62	0.931			
Hypertension*	3.48	0.77-15.7	0.104			
Hyperlipidemia	0.56	0.18-1.76	0.318			
Diabetes mellitus	1.33	0.53-3.35	0.543			
Current smoking*	0.34	0.07-1.59	0.170			
No physical activity	0.68	0.21-2.24	0.524			

Abbreviations: OR=odds ratio; CI=confidence interval; TIA=transient ischemic attack; HD=ischemic heart disease
†Forward Stepwise Selection
*Variables included in the multivariable analysis

Table VI - Characteristics of Beirut residents compared to other residents.

Explanatory variable	Bivariate analysis			Multivariable analysis†		
	OR	95% CI	p-value	aOR	95% CI	p-value
Age*	1.05	1.02-1.08	0.000	1.05	1.02-1.08	0.001
Male sex*	0.56	0.30-1.06	0.075			
AF*	1.95	0.85-4.48	0.118			
HD*	1.70	0.85-3.39	0.133			
Hypertension*	2.91	1.33-6.37	0.008	2.22	0.97-5.09	0.059
Current smoking*	0.34	0.09-1.28	0.110			

Abbreviations: OR=odds ratio; CI=confidence interval; aOR=adjusted odds ratio; AF=atrial fibrillation; HD=ischemic heart disease
†Forward Stepwise Selection
*Variables included in the multivariable analysis

Discussion

Consulting the existing literature, the male predominance observed in our patients is also found in most studies (whether hospital or population based) for ischemic as well as for hemorrhagic stroke (Schulz and Rothwell, 2003; Sallam et al., 2009; Ihle-Hansen et al., 2012). An interesting finding concerned the mean age of our sample, which was older than that reported in studies from Arab countries (EMR) (Bahou et al., 2004; Sallam et al., 2009; Al-Asadi and Habib, 2014), but still younger than the mean age in developed countries (Hajat et al., 2001; Ihle-Hansen et al., 2012; Kolominsky-Rabas et al., 2015). Stroke patients in population-based studies are usually shown to have a higher mean age than those in hospital-based studies (Schulz and Rothwell, 2003).

Hypertension, diabetes mellitus, current smoking and physical inactivity were the most prevalent risk factors for stroke among our population. Hypertension has been found to be the most prevalent risk factor among stroke patients in all countries (Turin et al., 2010; Aljefree and Ahmed, 2015) and its prevalence does not usually differ between hospital- and population-based studies.

However, dyslipidemia, found in 28% of our patients, showed higher rates in many other studies: 55% in Norway (Ihle-Hansen et al., 2012), 57% in Kuwait (Ashkanani et al., 2013) and 78% in low-to-middle-income Arab countries (Abboud et al., 2013).

Diabetes mellitus rates are higher in Lebanon, as in other Arab countries, than in developed countries: 19% in Japan (Turin et al., 2010) and 12% in Norway (Ihle-Hansen et al., 2012) *versus* 56% in Kuwait (Ashkanani et al., 2013) and 46% in the study by Abboud et al. (2013). Population-based studies show lower frequencies of diabetes among stroke patients (Bejot et al., 2008).

The high smoking rate obtained was unsurprising, having been shown in previous studies (Sibai and Hwalla, 2008) and found in many Arab countries (Aljefree and Ahmed, 2015). Lower rates are found in developed countries: 23% in Norway and 26% in Japan (Turin et al., 2010; Ihle-Hansen et al., 2012). Moreover, the frequency of AF (18.5%) among the stroke patients in our sample is high compared with values recorded in other Arab countries (El-Sayed et al., 1999; Hamad et al., 2001; Ashkanani et al., 2013; Al-Asadi and Habib, 2014), but lower than the frequency in Western countries, where the population is older; AF is indeed known to increase with age (Ihle-Hansen et al., 2012).

With regard to the ischemic stroke subtypes defined according to the modified TOAST classification criteria, LA was the most common, accounting for 53.5% of all ischemic strokes, a rate higher than in published data. The high prevalence of smoking may be linked to this finding as might the finding of a higher rate of untreated cases of dyslipidemia, but the association needs further investigation. However, epidemiological findings from French, Korean and some Arab publications also report a higher prevalence of LA, reaching 35.8% (Bejot et al., 2008), 36% (Kim and Kim, 2014) and 38.1% (Deleu et al., 2011) of all ischemic subtypes, respectively. Conversely, the CE subtype is more frequently reported in Western countries (Schulz and Rothwell, 2003; Ueshima et al., 2008; Ihle-Hansen et al., 2012; Kim and Kim, 2014), whereas the SV subtype is reported with high prevalence in Asian and Arab countries (Al-Shammri et al., 2003; Bahou et al., 2004; Khan et al., 2008; Turin et al., 2010).

Furthermore, the present study shows a significant association between ischemic stroke subtypes and specific risk factors. In line with data from the literature, lipid abnormalities were found to be strong predictors of LA and negative predictors of CE (Schulz and Rothwell, 2003; Khan et al., 2007). However, the study by Schulz and Rothwell (2003) showed a lower aOR for the association (aOR=2.10, 95%CI= [1.55-2.83], p<0.0001). Moreover, we found that CE was negatively associated with male gender, a finding also reported by Schulz and Rothwell (aOR=0.7, 95%CI= [0.6-0.9], p=0.01). In line with existing data (Schulz and Rothwell, 2003; Bejot et al., 2008; Turin et al., 2010), we also found that aging was a predictor of CE, as the incidence of AF increases with age. The SV subtype was found to be correlated only with Beirut residency after adjusting for other variables. Hypertension, although higher among SV patients (p=0.035), was not found to be significantly associated with this subtype in the multivariable regression, contrary to the findings of others (Khan et al., 2007). This could be linked to the relatively small sample size in the present study especially given that Beirut residents are found to be more hypertensive than other residents in the multivariable model. Furthermore, a recent study (Gebeily et al., 2014) found hypertension and age to be associated with cerebral white matter hyperintensities found on brain imaging in Lebanese patients, and these hyperintensities are known to be more commonly seen among SV patients (Chen et al., 2009). Thus, the association between Beirut residency SV could be mediated by these two factors: people living in Beirut were older and more hypertensive. From another perspective, some studies have suggested an association between air pollution and SV (Andersen et al., 2010; O'Donnell et al., 2011; Corea et al., 2012). In fact, air pollution may trigger various mechanisms related to the development of SV, such as systemic inflammation, activation of thrombosis pathways, arteriolar narrowing and impaired vasodilation, and accelerated progression of atherosclerosis (Brook, 2008). However, the capital, Beirut, is the most populated city in Lebanon and also highly polluted (Afif et al., 2009; Borgie et al., 2014), and this may further explain the correlation between Beirut residency and the SV subtype in our study. Another hypothesis that should be tested in future studies is the relationship between stroke subtypes and obesity, a potential residual confounding risk factor in the multivariable regressions.

The modified risk factor-free method (modified TOAST criteria) used to classify ischemic stroke cases into subtypes strengthens the validity of our results. However, there are some limitations to be underlined. First, the data collection was conducted retrospectively, which may introduce an information/classification bias. Although the TOAST classification has previously been applied retrospectively with accurate and reproducible results (Goldstein et al., 2001), it would have been preferable to prospectively subtype the ischemic stroke cases. It would also have been more appropriate to have the medical records analyzed separately by two neurologists, then measuring the degree of agreement between the two classifications. Second, an inclusion bias may exist due to the hospital-based nature of the study. In fact, some differences in the prevalence of is-

chemic stroke subtypes, and their associations with risk factors, have been reported between hospital- and population-based studies (Schulz and Rothwell, 2003). Hospital-based studies may include more severe stroke cases, cases occurring in a younger population, or cases with different frequencies of risk factors, as shown previously (Giroud et al., 1997). Moreover, the fact that both recruiting centers were in Beirut may have biased the results and the prevalence of the LA subtype, which may not be representative of the whole Lebanese population. Thus, larger population-based studies should be conducted in the future to confirm our findings.

This is the first epidemiological study to assess stroke subtypes in Lebanon using the modified TOAST classification. The LA ischemic subtype may be predominant among hospitalized patients, and associated with a high percentage of uncontrolled cases of dyslipidemia. Interestingly, the SV subtype may be more frequent among Beirut residents, an association that may be partly explained by the high level of pollution in the capital. Thus, a larger population-based survey is needed to further confirm these findings and lead towards better risk factor identification and control. The implementation of a comprehensive stroke prevention strategy at national level is, furthermore, urgent in an unhealthy aging population.

Finally, this study was conducted for observational purposes with no traceability of participants. Thus, no ethical approval was found to be necessary by the Lebanese University ethics committee and by the hospitals' ethics committees.

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