Original article

Development of a diagnosis score for stroke in the Lebanese population

Maya El-Hajj[a,b,*], Pascale Salameh[a], Samar Rachidi[a], Amal Al-Hajje[a], Hassan Hosseini[b,c]

[a] Lebanese University, Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Hadath, Lebanon
[b] Université Paris-Est, UMR 955, IMRM, Institut Mondor de Recherche Biomédicale, Créteil, France
[c] Service de Neurologie, Hôpital Henri-Mondor, UPEC, Assistance Publique-Hôpitaux de Paris (AP-HP), Créteil, France

ABSTRACT

Stroke is a major cause of death and adult neurologic disability worldwide. Underdiagnosing a stroke at emergency may have devastating consequences on patients. We aim to develop a diagnosis score for stroke at emergency among the Lebanese population by using stroke risk factors and symptoms. A hospital-based case-control study was conducted for the score generation. Data were collected through a designed data collection sheet at two Lebanese tertiary hospitals between January 1st, 2012 and December 31st, 2014. A logistic regression determined the association of stroke risk factors and symptoms, and the rounded coefficients generated the Diagnosis Score for Stroke (DS-Stroke). Another case-control study was conducted for the score validation. Data were collected through a standardized questionnaire at five different Lebanese tertiary hospitals between January 1st, 2015 and December 31st, 2016. DS-Stroke was validated by comparing it to hospitals final diagnosis. DS-Stroke was constructed with good properties, comprising 7 items. The area under the curve was high at 0.980 (0.969–0.990; p < .001). A score < 4 points indicated a high negative predictive value of stroke of 97.3%. A score ≥ 4 points indicated a positive predictive value of stroke of 91.3%. In the validation study, DS-Stroke had an area under the curve of 0.964 (95% CI, 0.951–0.978; p < .001), 93.2% sensitivity, 91.9% specificity, and 84.1% positive predictive value and 96.7% negative predictive value. In conclusion, the DS-Stroke is a useful tool for emergency physicians, non-specialists and front-line clinicians. It is a good diagnosis tool for use to diagnose stroke at emergency, call for further emergency testing if necessary and speed up treatment.

1. Introduction

Stroke, or cerebrovascular accident, is a major cause of death and adult neurologic disability worldwide. Stroke is defined by the World Health Organization as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin".[1] According to the World Health Organization, stroke strikes 15 million people each year, resulting in 5 million deaths and another 5 million permanent disabilities.[2]

Symptoms for cerebrovascular accidents are now well established and rapid and accurate diagnosis of stroke is critical to initiate acute treatment and improve clinical outcome.[3] However, many symptoms accompanying stroke, including headache, dizziness, imbalance, or sudden numbness or weakness on one side of the body may also be symptoms for other diseases such as vestibular dysfunction, multiple sclerosis, hemiplegic migraine, seizures or others. In a cross-sectional study conducted in Lebanon, results found that almost 1 in 8 stroke-free Lebanese residents has had stroke symptoms and that the prevalence of

any stroke symptom is 12.1% in stroke-free people.[4] In the United states, around 4 million people visit the emergency department annually for dizziness and vertigo, and only 4 to 6% of those have cerebrovascular causes.[5,6] Diagnosis of patients with neurological emergencies is actually imperfect in most of the cases where there is significant misdiagnosis of patients, resulting in threatening patients' life, or overtesting, resulting in patient harm and wasting resources.[7]

Underdiagnosing a stroke at emergency department may have devastating consequences on patients. In a prospective study conducted in a large French emergency department, results found that 37.3% of patients had a false positive diagnosis of stroke and 36.6% had a false negative diagnosis produced by emergency physicians.[8] In a tertiary-care teaching hospital in Canada, only 60.4% of cases had a final diagnosis agreeing with the initial diagnosis of the emergency physician.[8] Misdiagnosis of stroke and Transient Ischemic Attack (TIA) is very common when patients present at emergency with weakness, where the rate of misdiagnosis vary widely between 2 to 56%, based on study design.[9,10]

Accurate diagnosis for stroke at emergency department is critical for

fast intervention. Despite having stroke intervention rate in Lebanon higher than other reported rates in developing countries (administration rate of r-tPA [Tissue plasminogen activator] is 10.3% for stroke cases at the largest tertiary care center in Lebanon), this intervention is still very limited due to large time interval between arrival at the hospital and Computerized Tomography (CT) completion (average time 49.4 minutes) and therefore large time interval between arrival and IV r-tPA (average time interval 102.4 minutes).[11]

A recently published retrospective study proposed the use of ABCD2 score [Age, BP (Blood pressure), Clinical features of the TIA, Duration of symptoms, and History of Diabetes] to identify stroke among patients presenting with dizziness at emergency, and a cross-sectional study suggested the use of HINTS [Head, Impulse, Nystagmus, Test-of-Skew] for better screening of stroke among patients with acute vestibular syndrome.[12,13] However, up-to-date, none of these scores has been used in the Lebanese emergency departments as accurate score to diagnose a stroke, and no other score for stroke diagnosis has been developed in Lebanon, or the Middle East. Identifying stroke symptoms and diagnosing a stroke present a significant challenge for emergency physicians because any missed or late diagnosis of stroke would result in missed opportunities for thrombolytic treatment and may confer to increased risk of death and disability. Moreover, distinguishing stroke from other diagnosis is critical and deciding which patient to undergo further testing beyond clinical evaluation at emergency may be difficult for some emergency physicians. We aim to develop a diagnosis score for stroke among the Lebanese population by using a number of significant stroke risk factors and symptoms in order to diagnose stroke patients at emergency department. This score would help emergency physicians, non-specialists and front-line clinicians to have an accurate diagnosis of stroke and call for further emergency testing if necessary.

2. Methods

2.1. Study design

This is a two steps study:

2.1.1. Score generation study

A retrospective hospital-based case-control study was conducted at two Lebanese tertiary hospitals located in the capital Beirut (one private and another governmental) between January 1st, 2012 and December 31st, 2014 to generate the score for stroke diagnosis. The Faculty of Pharmacy at the Lebanese University waived the need for informed consent from the patients whose data was used in this study since it was observational with no traceability for patients. The basic ethical principles were respected including respect for persons, beneficence, and justice.[14]

2.1.2. Score validation study

Another hospital-based case-control study with prospective data collection was conducted at five different tertiary hospitals in Lebanon between January 1st, 2015 and December 31st, 2016 for the score validation. The Faculty of Pharmacy at the Lebanese University waived the approval of this study since it was observational with no traceability of patients. An oral consent was obtained from all included subjects before inclusion in the study.

2.2. Inclusion and exclusion criteria

Hospitalized stroke patients were included if they were Lebanese, 18 years or older, and diagnosed with stroke by CT scan, MRI, or both. Stroke patients were excluded if clinical information was unavailable or CT scan or MRI were not performed.

Control patients were included if they were Lebanese, 18 years or older, and admitted to the same hospitals of stroke patients but with disorders or procedures unrelated to stroke or TIA. Controls were chosen from the departments related to infectious diseases, cancer, endocrinology diseases, respiratory diseases, kidney diseases, and digestive diseases as well as injuries and orthopaedic surgeries.

For the score validation study, giving an oral consent was also a criterion for inclusion for both cases and controls.

2.3. Development of data collection sheet and questionnaire

The data collection sheet and questionnaire were based on different publications' findings, and included four parts. The first part included the socio-demographic characteristics of patients as well as questions about patients' body mass index, the reason of being admitted to the hospital and time of admission, imaging techniques and time, and drug exposure at home. The second part included patients' symptoms on admission and time of symptoms. The third part addressed all potential risk factors of stroke. The last part was related to patients' laboratory data upon admission to the hospital. The data collection sheet was written in English language and information collected were based on patients' medical records at the hospitals. The questionnaire was written in English and administered in Arabic and was based on patients' answers and medical records at the hospitals (The questionnaire is attached as a supplementary material).

2.4. Data collection and definition of certain comorbidities

All variables were collected based on information present in patients' files/physician's diagnosis/patient's answers.

In the score generation study, all data elements of the data collection sheet were collected retrospectively from patients' files at the hospitals.

In the score validation study, all data elements of the questionnaire were collected concurrently after patients' diagnosis at the hospitals. Patients or proxies were interviewed for data collection (A proxy is someone who lives with the patient and knows everything about the patient medical history and medication. A proxy is only interviewed when a stroke patient is in coma or a stroke patient has stroke-induced language disturbances). The socioeconomic and demographic factors and stroke symptoms and risk factors were collected from patients' files at the hospitals and confirmed by patients' responses. The duration and time of symptoms were collected from patients' responses. Patients' diagnosis, laboratory tests, and time of arrival at the hospital and imaging were collected from patients' files at the hospitals.

Evidence of medical history was based on the definition of certain diagnostic categories, the laboratory tests results stated, and the presence of a reported disease history or treatment history.

2.4.1. Stroke

Evidence of stroke and stroke types were collected from the final diagnosis stated in patient's file and from the brain Computed Tomography (CT), Magnetic Resonance Imaging (MRI) results or both.

2.4.2. Hypertension

The definition of hypertension and the classification of the three grades of blood pressure (BP) were adopted from the World Health Organization − International Society of Hypertension (WHO-ISH).[15]

In this study, a history of hypertension is identified based on different approaches, including: reported history of hypertension by the physician, reported antihypertensive treatment, or recorded blood pressure measurements at different time points (admission and mornings for every day after admission) where the mean of blood pressure for three consecutive days' measurements is considered.

2.4.3. Diabetes and dyslipidemia

The definition of diabetes and dyslipidemia was based on the 2006 WHO − International Diabetes Federation (WHO-IDF) and the National Cholesterol Education Program, respectively.[16,17]

Table 1
Study patients Characteristics.

Variables	Total (n = 732) N(%)	Stroke Patients (n = 202) N(%)	Stroke-free Patients (n = 530) N(%)	P value
Age (years; mean ± SD)	64.5 ± 13.4	67.9 ± 13.4	63.2 ± 13.2	< 0.001
Age in years categories				< 0.001
18–44	62 (8.5)	12 (5.9)	50 (9.4)	
45–49	40 (5.5)	12 (5.9)	28 (5.3)	
50–54	49 (6.7)	13 (6.4)	36 (6.8)	
55–59	88 (12.0)	15 (7.4)	73 (13.8)	
60–64	152 (20.8)	15 (7.4)	137 (25.8)	
65–69	66 (9.0)	31 (15.3)	35 (6.6)	
70–74	94 (12.8)	40 (19.8)	54 (10.2)	
75–79	81 (11.1)	28 (13.9)	53 (10)	
80–84	42 (5.7)	12 (5.9)	30 (5.7)	
≥85	58 (7.9)	24 (11.9)	34 (6.4)	
Sex				0.678
Male	401 (54.8)	108 (53.5)	293 (55.3)	
Female	331 (45.2)	94 (46.5)	237 (44.7)	
Insurance				< 0.001
Insured	276 (37.7)	59 (29.2)	217 (40.9)	
Uninsured	456 (62.3)	143 (70.8)	313 (59.1)	
Hypertension	320 (43.7)	146 (72.3)	174 (32.8)	< 0.001
Diabetes Mellitus	226 (30.9)	87 (43.1)	132 (26.2)	< 0.001
Dyslipidemia	197 (26.9)	75 (37.1)	122 (23)	< 0.001
Blood pressure classification				< 0.001
Grade 1	187 (25.5)	60 (29.7)	127 (24)	
Grade 2	85 (11.6)	48 (23.8)	37 (7)	
Grade 3	55 (7.5)	47 (23.3)	8 (1.5)	
Smoking status N (%)				0.003
Smokers	273 (37.5)	92 (46.2)	181 (34.2)	

2.5. Statistical methods

Data were analyzed using SPSS version 24. P-value < .05 determined statistical significance. Continuous variables were presented as means with standard deviation and categorical variables as percentages. The differences in baseline characteristics between stroke patients and stroke-free patients were analyzed using chi-square test for qualitative variables and sample t test for quantitative variables. Fisher's Exact test was used when the expected cell size was less than 5.

A stepwise ascending logistic regression was conducted by considering the potential of confounding. Factors included in the analysis were age, gender, insurance, history of hypertension, history of diabetes mellitus, history of dyslipidemia, current cigarette smoking, sudden and strange numbness or dead feeling in face, arm, or leg, sudden and strange weakness in face, arm, or leg such as having difficulties keeping left or right arm raised high or having a drooping appearance on one side of face, sudden loss of coordination on one side of body, sudden trouble in walking, sudden loss in vision in one or both eyes, sudden confusion in understanding what people were saying, trouble expressing oneself verbally or in writing, sudden and severe headache with no known cause just before admission, sudden vomiting away from a GI infection, seizures before admission, and loss of consciousness on admission. Gender and type of insurance were considered as covariates and controlled in this logistic regression. The strength of association between the dependent variable (presence of stroke or not) and independent variables was expressed in odds ratio (OR) through 95% confidence interval. The adjusted ORs obtained were rounded to the nearest units and used as coefficients to determine the score for stroke diagnosis.

An index was constructed using the potential variables found to be associated with stroke in the logistic regression. Those that significantly diagnosed stroke were selected and the index for stroke diagnosis was generated. Factor analysis evaluated the construct validity of this index and was conducted with a varimax rotation to determine the different dimensions of the distribution of the stroke symptoms and risk factors with the different factors loading after ensuring adequate Kaiser-Meyer-Olkin (KMO) and sample adequacy by Bartlett Test. The reliability of the construct was assessed and Cronbach's alpha was calculated.

The score was calculated for each patient, case and control. The Receiver-Operating Characteristics (ROC) curve was sketched in order to determine the cut point of whether a stroke would be diagnosed or not with a great percentage. The sensitivity and specificity as well as the negative and positive predictive values for the new developed score were calculated to assess criterion validity.

For the validation of the generated score, the score was calculated for all patients included in the score validation study and results were compared with the hospital accurate diagnosis of stroke by CT scan, MRI, or both imaging techniques. Sensitivity, specificity, and negative and positive predictive values were also calculated.

Moreover, the developed score was compared to the ABCD2 score to diagnose stroke among patients presenting with dizziness, nausea, and unbalance symptoms at emergency

3. Results

3.1. Summary of primary results

Two hundred and fifty stroke cases were admitted to the interesting hospitals between January 1st, 2012 and December 31st, 2014. Among those, 48 stroke cases were not diagnosed with stroke by CT scan or MRI and therefore were excluded. Overall, 732 patients were included in the score generation study with 202 cases diagnosed with stroke and 530 stroke-free controls. The mean age of stroke was 68 ± 13 years. Males constituted 53.5% of stroke patients. Among stroke patients, 25.7% had TIA, 59.4% had ischemic stroke, and 14.9% had hemorrhagic stroke. The in-hospital stroke mortality rate was 7.4%, with hemorrhagic rate higher than ischemic rate, 20% vs 7.5% respectively.

Due to missing data in regards to patients' address (43.7% of the sample), this sample mainly represented Lebanese patients living in Beirut (46.6% of patients with available address in their hospital file)

Table 2
Stroke Symptoms among Stroke and Stroke-free Patients.

Variables	Total (n = 732) N (%)	Stroke Patients (n = 202) N(%)	Stroke-free Patients (n = 530) N(%)	P value
Sudden and strange numbness or dead feeling in face, arm, or leg	106 (14.5)	99 (49.0)	7 (1.3)	< 0.001
Sudden and strange weakness in face, arm, or leg such as having difficulties keeping left or right arm raised high or having a drooping appearance on one side of face	167 (22.8)	167 (82.7)	0 (0.0)	< 0.001
Sudden loss of coordination on one side of body	82 (11.2)	73 (36.1)	9 (1.7)	< 0.001
Sudden trouble in walking	123 (16.8)	120 (59.4)	3 (0.6)	< 0.001
Sudden loss in vision in one or both eyes	50 (6.8)	46 (22.8)	4 (0.8)	< 0.001
Sudden confusion in understanding what people were saying	41 (5.6)	36 (17.9)	5 (0.9)	< 0.001
Trouble expressing oneself verbally or in writing	120 (16.4)	114 (56.4)	6 (1.1)	< 0.001
Sudden and severe headache with no known cause just before admission	53 (7.2)	47 (23.3)	6 (1.1)	< 0.001
Sudden vomiting away from a GI infection	26 (3.6)	18 (8.9)	8 (1.5)	< 0.001
Seizures before admission	12 (1.6)	2 (1.0)	10 (1.9)	0.527
Loss of consciousness on admission	83 (11.3)	82 (40.6)	1 (0.2)	< 0.001

and Mount Lebanon (44.2%). Only 4.6% of patients with available address lived in Beqaa, 3.6% live in North Lebanon, and 1% live in South Lebanon.

Stroke symptoms lasted for less than 10 minutes among 1% of stroke cases and 10–59 minutes and ≥ 60 minutes among 3.9 and 95.1% of cases, respectively. The average time for undergoing CT scan or MRI varied between ≤ 24 hours, 25–48 hours and > 48 hours for 58.7, 15.4 and 25.9% of stroke patients, respectively.

Significant differences were found between stroke and stroke-free patients in regard to age, insurance types, history of hypertension, diabetes and dyslipidemia, stroke symptoms and loss of consciousness on admission (Table 1 and 2).

3.2. Construction of the diagnosis score for stroke (DS-Stroke)

Stepwise ascending logistic regression was performed by considering the potential of confounding. The multiple logistic regression approach provided a good approximation of the association between the different independent variables and the diagnosis of stroke. Gender and type of insurance were considered as covariates and controlled in this logistic regression. Age (≥ 65 years), history of hypertension, presence of sudden and strange numbness or dead feeling in face, arm, or leg, sudden trouble in walking, sudden loss of vision, trouble expressing oneself verbally or in writing and sudden and severe headache with no known cause just before admission were significantly associated with stroke diagnosis in Lebanon (Table 3). Sudden and severe headache with no known cause just before admission had the highest OR (418.81; 95% CI, 27.97–6270.32). Cigarette smoking and a history of dyslipidemia were very close to reach statistically significance in diagnosing a stroke in the Lebanese population.

The Diagnosis Score for Stroke (DS-Stroke) was computed by taking into account the adjusted ORs and rounding to the nearest unit. A

Table 3
Factors validating stroke in the Lebanese population after adjusting for gender, and insurance.

Variable	OR adjusted	95% CI	P value
Age (≥ 65 years)	8.57	1.31-56.01	0.025
History of hypertension	18.10	2.37-138.23	0.005
Sudden and strange numbness or dead feeling in face, arm, or leg	19.62	1.5-257.05	0.023
Sudden trouble in walking	136.95	7.01-2676.99	0.001
Sudden loss in vision in one or both eyes	27.21	1.78-416.87	0.018
Trouble expressing oneself verbally or in writing	376.62	20.51-6915.29	< 0.001
Sudden and severe headache with no known cause just before admission	418.82	27.97-6270.33	< 0.001
History of dyslipidemia	5.31	0.78-36.17	0.088
Cigarette smoking	7.9	0.93-66.9	0.058

Table 4
Diagnosis Score for Stroke (DS-Stroke).

Variables	Clinical features	Diagnosis Score for Stroke
Age ≥ 65 years	No	+0 × 1
	Yes	+1 × 1
History of Hypertension	No	+0 × 2
	Yes	+1 × 2
Sudden and strange numbness or dead feeling in face, arm, or leg	No	+0 × 2
	Yes	+1 × 2
Sudden loss in vision in one or both eyes	No	+0 × 3
	Yes	+1 × 3
Sudden trouble in walking	No	+0 × 15
	Yes	+1 × 15
Trouble expressing oneself verbally or in writing	No	+0 × 42
	Yes	+1 × 42
Sudden and severe headache with no known cause just before admission	No	+0 × 47
	Yes	+1 × 47

simplified version of the DS-Stroke is presented in Table 4.

The DS-Stroke could have a minimum of 0 and a maximum of 112. In the sample, the minimum of the DS-Stroke was 0 and the maximum was 110. In individuals with stroke, the mean of DS-Stroke was 47.3 and the standard deviation 28.2, while in stroke-free patients, the mean was 2.2 and the standard deviation 6.8.

3.3. Construct validity and reliability of stroke risk symptoms index

A factor analysis was conducted and the seven variables identified from the multivariate analysis were entered. Six items were retained and found to be distributed on two factors, explaining 57% of the total variance. Four items loaded on one factor (history of hypertension, sudden and strange numbness or dead feeling in face, arm, or leg, sudden trouble in walking and trouble expressing oneself verbally or in writing) and two items loaded on a second factor (sudden and severe headache with no known cause just before admission and sudden loss in vision in one or both eyes). This index had a good reliability with Cronbach alpha = 0.658 (Table 5).

3.4. DS-Stroke properties and thresholds

The ROC curve for stroke screening is shown in Fig. 1. The area under the curve was high at 0.980 (0.969–0.990; p < .001). We could identify two important cutoff values, one at 2.5 with a sensitivity of 0.990 and a specificity of 0.809, and another at 3.5 with a sensitivity of 0.931 and a specificity of 0.966 (Supplementary material Table I).

3.5. DS-Stroke and diagnosis of stroke

The value of 4 was considered as a cut point for the diagnosis of

Table 5
Principal component and exploratory factor analyses.

Items	Loading on factor 1	Loading on factor 2
History of hypertension	0.640	
Sudden and strange numbness or dead feeling in face, arm, or leg	0.742	
Sudden trouble in walking	0.730	
Trouble expressing oneself verbally or in writing	0.741	
Sudden and severe headache with no known cause just before admission		0.788
sudden loss in vision in one or both eyes		0.700

KMO = 0.741; Bartlett's test of sphericity p < .001; Cronbach alpha = 0.658.

stroke because it has a good sensitivity, specificity, and importantly high negative and positive prediction values. We more concentrated on having high sensitivity and predictive values because DS-Stroke is a diagnosis test where results of an individual test will be discussed with a patient. We also considered having a cut point with a high negative predictive value because the problems caused by a poor negative predictive value would be worse than for a poor positive predictive value. A score < 4 points indicated a high negative predictive value of stroke of 97.3% (ie, the probability of correctly diagnosing a TIA/stroke free patient at emergency). A score ≥ 4 points indicated a positive predictive value of stroke of 91.3% (ie, the probability of correctly diagnosing a TIA/stroke patient at emergency).

3.6. Validation of DS-Stroke

Around 650 hospitalized patients were included in the score validation study for DS-Stroke validation. Data were collected through a standardized questionnaire for 205 stroke patients and 445 stroke-free patients admitted to five Lebanese tertiary hospitals between January 1st, 2015 and December 31st, 2016. Among included participants, 1.3% of controls had a history of stroke compared to 34.6% of cases. Among stroke cases, ischemic stroke constituted the majority of cases (69.8%) followed by hemorrhagic stroke (15.1%) and transient ischemic attack (15.1%).

Twelve stroke patients were excluded from the study due to lack of imaging or clinical information. Moreover, 75.1% of included stroke cases had a CT scan, 16.1% had an MRI, and 8.8% had both, CI and MRI. None of the controls patients had undergo a CT scan or MRI. The average time for undergoing CT scan or MRI after arrival at the hospital varied between 1–2 hours, 3–6 hours and > 6 hours for 74.6, 9.3 and 16.1% of stroke patients, respectively.

The majority of patients arrived at the hospitals by private transportation. The duration of symptoms varied between less than 10 min for 98% of controls and 8.8% of cases (58.1% of TIA patients), 10–59 minutes for 1.6% of controls and 21.5% of cases (41.9% of TIA patients, 16.8% of ischemic patients, and 22.6% of hemorrhagic patients), and more than 60 minutes for 0.4% of controls and 69.8% of cases (83.2% of ischemic patients and 77.4% of hemorrhagic patients).

DS-Stroke had an area under the curve of 0.964 (95% CI, 0.951–0.978; p < .001) in the score validation study (Fig. 2). Around 423 patients had a DS-Stroke < 4 (among those patients 409 patients
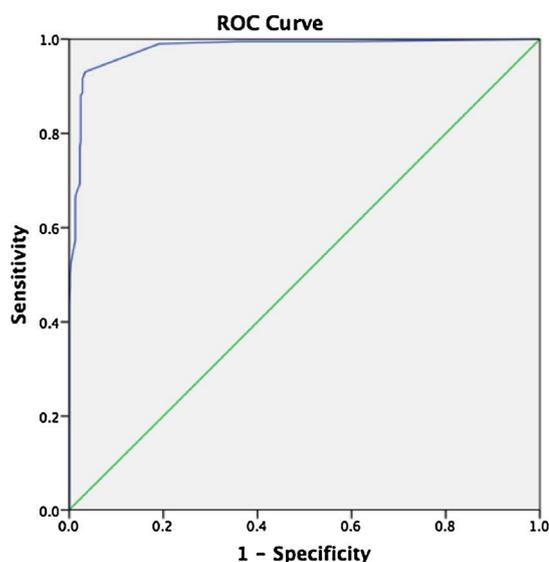
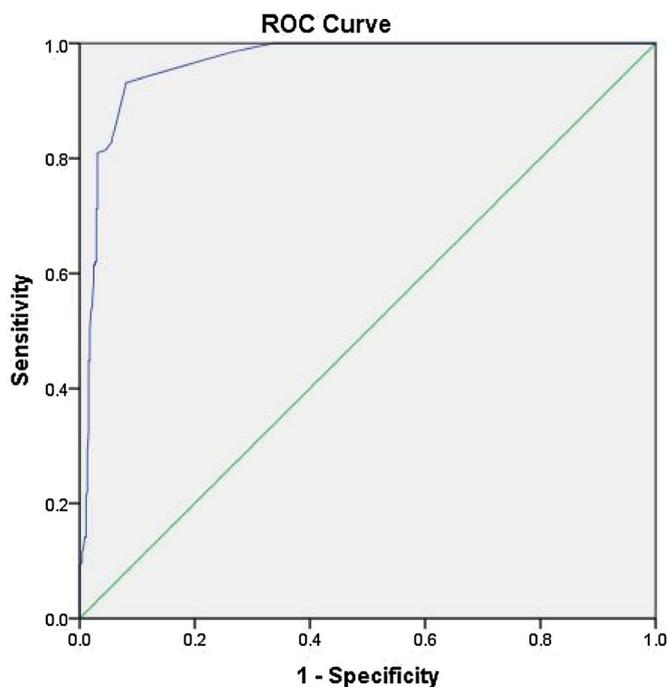**ROC Curve**

Diagonal segments are produced by ties.

Area Under the Curve

Test Result Variable(s): DSStroke

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.980	.005	.000	.969	.990

The test result variable(s): DSStroke has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Fig. 1. Roc curve and area under the curve for DS-Stroke.

ROC Curve

Diagonal segments are produced by ties.

Area Under the Curve

Test Result Variable(s): DSSTROKE

			Asymptotic 95% Confidence Interval	
Area	Std. Error[a]	Asymptotic Sig.[b]	Lower Bound	Upper Bound
.964	.007	.000	.951	.978

The test result variable(s): DSSTROKE has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Fig 2. ROC curve and area under the curve for DS-Stroke in the score validation data.

were stroke-free) and 227 patients had a DS-Stroke ≥ 4 (among those patients 191 patients were stroke patients).

Taking into consideration a DS-Stroke score of 4 as a cut point in the score validation study, the DS-Stroke had a sensitivity of 93.2%, specificity of 91.9%, and positive predictive value of 84.1% and negative predictive value of 96.7%.

3.7. Comparison between DS-Stroke and ABCD2

The ABCD2 score is calculated as follows: 1 point for Age ≥ 60 years, 1 point for BP $\geq 140/90$ mmHg, Clinical features of the TIA: 2 points for unilateral weakness/1 point for speech disturbance without weakness/0 point for other symptoms, Duration of symptoms: 2 points for ≥ 60 minutes/1point for 10–59 minutes/0 point for < 10 minutes, and 1 point for a history of diabetes. The ABCD2 factors were collected for patients from the questionnaire and data available for the score validation study.

In the score validation study, 87 patients arrived at the hospital with dizziness, nausea, and unbalance/spinning symptoms and were considered for the comparison between DS-Stroke and ABCD2. An ABCD2 score of ≤ 3 points was considered as low-risk of stroke and an ABCD2 score of ≥ 4 points was considered as intermediate- to high-risk of

stroke. We calculated the area under the curve for the ABCD2 and DS-Stroke and found that DS-Stroke had a better area under the curve, 0.914 (0.848-0.980) and 0.954 (0.916-0.993), respectively (Fig. 3).

DS-Stroke had a sensitivity of 93.5%, specificity of 75.6%, positive predictive value of 81.1%, and negative predictive value of 91.2%. ABCD2 had a sensitivity of 82.6%, specificity of 90.2%, positive predictive value of 90.5%, and negative predictive value of 82.2%.

4. Discussion

The present study shows that age, a history of hypertension, sudden and strange numbness or dead feeling in face, arm, or leg, sudden trouble in walking, trouble expressing oneself verbally or in writing, sudden loss in vision in one or both eyes and sudden and severe headache with no known cause just before admission are significantly associated with stroke diagnosis.

Sudden and severe headache with no known cause just before admission had the highest OR in our study to diagnose a stroke. This finding confirms with the finding of a multicenter, multinational prospective observational study of young stroke across Europe which states that headache at stroke onset is a leading symptom in specific combination of stroke factors.[18] The pathophysiological mechanisms of the

Diagonal segments are produced by ties.
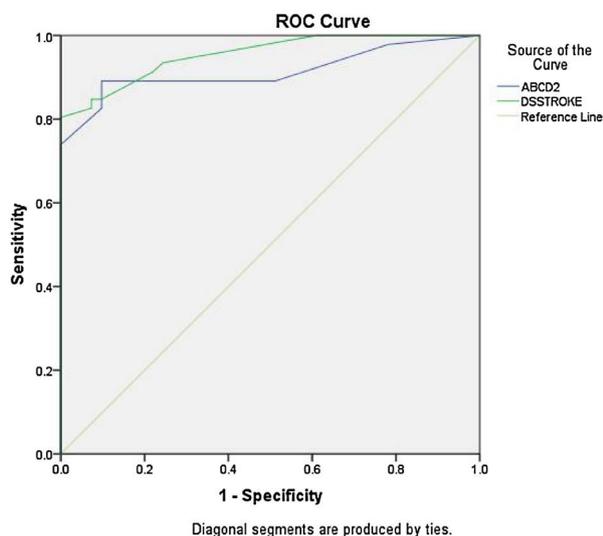
Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
ABCD2	.914	.034	.000	.848	.980
DSSTROKE	.954	.020	.000	.916	.993

The test result variable(s): ABCD2, DSSTROKE has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Fig. 3. ROC curve and area under the curve for DS-Stroke and ABCD2.

sudden and severe headache at stroke onset are not completely understood.[18] Clinical and biomedical markers of inflammation may explain the headache in primary hemorrhagic stroke, while in ischemic stroke, the headache might be explained by the occurrence of severe systolic hypertension during stroke attack, the reactivation of previous primary headache, or a presence of a history of migraine.[18–21]

Many lately conducted prospective randomized trials have shown the clinical benefit of mechanical thrombectomy when acute stroke patients were treated within 6 to 8 hours after stroke symptom onset.[22,23] Despite the extension of the time window between symptom onset and treatment, there is strong evidence that the efficacy of the treatment is highly related to the early time it is introduced. Any misdiagnosis of patients with neurological emergencies may contribute to medical malpractice in the emergency department and patient harm.[7] Moreover, overtesting and increasing radiation exposure have long-term consequences.[24] The use of CT scan by emergency physicians had tripled over the period 1995-2007, not to mention the availability of certain imaging techniques and their high cost, where in Lebanon, their price varies between $275 for CT scans and $355 for MRI based on the medical center where they are performed.[25] Adding to this, although the majority of patients still arrive late at the hospitals due to private transportation, the average time for conducting a CT scan is around 49 minutes after arrival at the hospital and for any intervention (IV r-tPA) is around 102 min.[11] DS-Stroke is a good tool for use to diagnose stroke at emergency department and speed up treatment especially in Lebanon where health insurance depends highly on the private sector and imaging and physician's access depends greatly on insurance approval. The DS-Stroke approach for diagnosing stroke has a crucial

sensitivity in detecting stroke as well as a significant sensibility suggesting that it can be appropriately used to diagnose for stroke at emergency department.

DS-Stroke was also validated in a score validation study conducted at five different tertiary hospitals in Lebanon with 205 patients diagnosed with stroke with CT scan, MRI, or both and 450 patients hospitalized for conditions other than stroke. DS-Stroke showed a substantial AUC of 0.964 (95% CI, 0.951–0.978; p < .001) in the prospective data with significant sensitivity, specificity, and predictive values. Although this study mainly represented Lebanese people living in Beirut and Mount Lebanon, the score validation study conducted at five different tertiary hospitals in different Lebanese governorates showed that the DS-Stroke is a good assessment tool that may be used in the Lebanese population in order to diagnose stroke at emergency department.

In regard to the comparison between DS-Stroke and the HINTS score, although the HINTS proved to be very sensitive for diagnosing stroke, it requires a skilled examiner to perform the test, while DS-Stroke is much easier to calculate by emergency physicians.

In comparison with the ABCD2 score for stroke diagnosis, the ABCD2 was tested to identify stroke among patients presenting with dizziness at emergency while the DS-Stroke considers all stroke symptoms in order to diagnose stroke at emergency in Lebanon since the prevalence of any stroke symptom is 12.1% in stroke-free people making it better for use in the Lebanese popualtion.[4] However, 87 patients presented at our emergency with dizziness, nausea, and unbalance/spinning and were considered for the comparison between DS-Stroke and ABCD2 to diagnose stroke at emergency department. The AUC showed that DS-stroke is better than ABCD2 at diagnosing stroke

at emergency among this population, AUC 0.954 (95% CI, 0.916-0.993; p < .001). DS-Stroke had also a better sensitivity and negative prediction of stroke than ABCD2 with sensitivity 93.5% vs 82.6%, specificity 75.6% vs 90.2%, positive predictive value 81.1% vs 90.5%, and negative predictive value 91.2% vs 82.2%, respectively. Having a higher sensitivity than ABCD2 indicated that DS-Stroke is better in screening for stroke patients at emergency, and having a better negative prediction value indicated that DS-Stroke is better in assuring the non-presence of stroke in stroke free patients identified by DS-Stroke in order to prevent any complications with misdiagnosis.

The inclusion of certain symptoms such as sudden trouble in walking and sudden and severe headache before admission to the emergency in the DS-Stroke may have increased its accuracy for stroke diagnosis among patients presenting with dizziness at emergency compared to ABCD2 score in the Lebanese population. Moreover, the inclusion of symptom duration in the ABCD2 score may have affected its accuracy in our population since around four stroke-free patients had symptoms that lasted 10–59 or ≥ 60 minutes, and therefore resulted in increasing the chance of classifying those patients as stroke by ABCD2, and by then reduced its accuracy compared to DS-Stroke. Around three patients were misclassified by the DS-Stroke as stroke patients due to the presence of severe headache or trouble in walking before admission. However, DS-Stroke proved to be an accurate diagnosis score for our population and would be a highly recommended to use at emergency department in order to diagnose stroke and speed up treatment if necessary.

This study has several strengths and limitations. The strengths of this study include: this study was the first to develop and validate a diagnosis score for stroke in the Lebanese population; all TIA/stroke diagnosis were based on the hospital CT scan, MRI, or both and on examination by an experienced neurologist; all common types of potential biases in case-control studies were limited including selection bias, recall bias, and observer's bias; adjusted odds ratios were used for the development of DS-Stroke which limited the role of confounders in over or underestimating in ROC diagnosis; the factor analyses used in the retrospective analysis showed the strength of the items constituting DS-Stroke. The limitations of the study include: The large ORs and wide 95% CI indicate the necessity of a larger sample size to better estimate the association between certain symptoms and stroke. DS-Stroke was developed from a retrospective study which might have limited certain data value and affected the results including duration of symptoms for controls presenting certain stroke symptoms. A population cohort might have augmented the predictive accuracy of this score. However, the validation study proved that DS-Stroke has high negative and positive predictive values and AUC which encourage its use in the Lebanese population. Moreover, DS-Stroke proved to be better and more accurate than other international and well-established score (ABCD2).

The Middle East countries share a lot of cultural and behavioral factors. However, there is no available data about the use of different stroke treatments in these countries. Some countries are improving their stroke care including thrombolysis treatment and radiology but some others are still struggling with the number of neurologists available and stroke treatment.[26] It would be interesting to assess the DS-Stroke in the wide Lebanese population and in the Middle East at hospitals emergency departments, before the diagnosis of patients.

5. Conclusion

In summary, we have developed a diagnosis score for stroke at emergency in order to have an accurate diagnosis of stroke, call for further emergency testing if necessary and speed up the treatment for stroke patients. This score might be a useful tool for emergency physicians, non-specialists and front-line clinicians. Moreover, DS-Stroke is beneficial to increase the knowledge of high-risk patients about the most common stroke symptoms in the Lebanese population in order to seek medical treatment urgently. It would be of interest if this score

would be tested at Lebanese hospitals' emergency department and in other Middle East population.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.cegh.2018.01.005.

References

[1]. WHO MONICA Project Investigators. The World Health Organization MONICA project (monitoring trends and determinants in cardiovascular disease). *J Clin Epidemiol.* 1988;41:105–114.

[2]. World Health Organization. *The World Health Report: 2002: Reducing Risks, Promoting Healthy Life.* 2002; 2002.

[3]. Edlow JA, Newman-Toker DE, Savitz SI. Diagnosis and initial management of cerebellar infarction. *Lancet Neurol.* 2008;7:951–964.

[4]. Farah R, Zeidan RK, Chahine MN, Asmar R, Chahine P, Salameh P, et al. Prevalence of stroke symptoms among stroke-free residents: first national data from Lebanon. *Int J Stroke.* 2015;10:83–88.

[5]. Saber Tehrani AS, Coughlan D, Hsieh YH, Mantokoudis G, Korley F, Frick K, et al. Rising annual costs of dizziness presentations to US emergency departments. *Acad Emerg Med.* 2013;20:689–696.

[6]. Kerber KA, Brown DL, Lisabeth LD, Smith MA, Morgenstern LB. Stroke among patients with dizziness, vertigo, and imbalance in the emergency department a population-based study. *Stroke.* 2006;37:2484–2487.

[7]. Pope JV, Edlow JA. *Avoiding misdiagnosis in patients with neurological emergencies. Emergency Medicine International [Internet].* 2012; 2012. [cited 2015 Dec 20]. Available from: http://www.hindawi.com/journals/emi/2012/949275/abs/.

[8]. Moeller JJ, Kurniawan J, Gubitz GJ, Ross JA. Diagnostic accuracy of neurological problems in the emergency department. *Can J Neurol Sci.* 2008;35:335–341.

[9]. Ferro JM, Pinto AN, Falcao I, Rodrigues G, Ferreira J, Falcao F, et al. Diagnosis of Stroke by the Nonneurologist a validation study. *Stroke.* 1998;29:1106–1109.

[10]. Hand PJ, Kwan J, Lindley RI, Dennis MS, Wardlaw JM. Distinguishing between stroke and mimic at the bedside the brain attack study. *Stroke.* 2006;37:769–775.

[11]. El Sayed MJ, El Zahran T, Tamim H. *Acute stroke care and thrombolytic therapy use in a tertiary care center in Lebanon. Emergency Medicine International [Internet].* 2014; 2014. [cited 2017 Jan 15. Available from: http://www.hindawi.com/journals/emi/2014/438737/abs/].

[12]. Navi BB, Kamel H, Shah MP, Grossman AW, Wong C, Poisson SN, et al. Application of the ABCD2 score to identify cerebrovascular causes of dizziness in the emergency department. *Stroke.* 2012;43:1484–1489.

[13]. Newman-Toker DE, Kerber KA, Hsieh YH, Pula JH, Omron R, Saber Tehrani AS, et al. HINTS outperforms ABCD2 to screen for stroke in acute continuous vertigo and dizziness. *Acad Emerg Med.* 2013;20:986–996.

[14]. Zoffice for Human Research Protections. *The Belmont Report* 1979; 1979. [cited 2017 Jan 04]. Available from: https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/.

[15]. Moser M. World Health Organization-International Society of Hypertension Guidelines for the management of hypertension-do these differ from the US recommendations? Which guidelines should the practicing physician follow? *J Clin Hypertens.* 1999;1:48–54.

[16]. World Health Organization and International Diabetes Federation. *Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycaemia. WHO/IDF.* 2006; 2006. [cited 2016 Sept 30]. Available from: http://www.who.int/diabetes/publications/Definition%20and%20diagnosis%20of%20diabetes_new.pdf.

[17]. National Cholesterol Education Program. *Detection, valuation, and treatment of high blood cholesterol in adults (adult treatment panel III). National Institutes of Health.* 2001; 2001. [cited 2016 Sept 30]. NIH Publication No. 01–3670. Available from: http://www.nhlbi.nih.gov/files/docs/guidelines/atp3xsum.pdf.

[18]. Kropp P, Holzhausen M, Kolodny E, Becker U, Dichgans M, Diez-Tejedor E, et al. Headache as a symptom at stroke onset in 4,431 young ischaemic stroke patients. Results from the stroke in young fabry patients (SIFAP1) study. *J Neural Transm.* 2013;120:1433–1440.

[19]. Leira R, Castellanos M, Álvarez-Sabín J, Diez-Tejedor E, Davalos A, Castillo J, et al. Headache in cerebral hemorrhage is associated with inflammatory markers and higher residual cavity. *Headache: J Head Face Pain.* 2005;45:1236–1243.

[20]. Hong Y-H, Lee Y-S, Park S-H. Headache as a predictive factor of severe systolic hypertension in acute ischemic stroke. *Can J Neurol Sci.* 2003;30:210–214.

[21]. Verdelho A, Ferro JM, Melo T, Canhao P, Falcao F. Headache in acute stroke: A prospective study in the first 8 days. *Cephalalgia.* 2008;28:346–354.

[22]. Saver JL, Goyal M, Bonafe A, Hans-Christoph D, Levy E, Pereira VM, et al. Stent-retriever thrombectomy after intravenous t-PA vs: t-PA alone in stroke. *N Eng J Med.* 2015;372:2285–2295.

[23]. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al. Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke. *N Eng J Med.* 2015;372:2296–2306.

[24]. Smith-Bindman R. Is computed tomography safe. *N Eng J Med.* 2010;363:1–4.

[25]. Kocher KE, Meurer WJ, Fazel R, Scott PA, Krumholz HM, Nallamothu BK. National trends in use of computed tomography in the emergency department. *Ann Emerg Med.* 2011;58:452–462.

[26]. El-Hajj M, Salameh P, Rachidi S, Hosseini H. The epidemiology of stroke in the middle east. *Eur Stroke J.* 2016;1(3):180–198.