Association Between the Subtypes of Stroke and the Various Risk Factors of Cerebrovascular Accidents: A Cross-Sectional Study

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Cite this article as: *Shams Vahdati S, Ala A, Mousavi Aghdas SA, Adib A, Mirza-Aghazadeh-Attari M, Aliar F. Association between the subtypes of stroke and the various risk factors of cerebrovascular accidents: A cross-sectional study. Eurasian J Med 2018; 50: 86-90.*

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Received: October 27, 2017
Accepted: December 6, 2017

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DOI 10.5152/eurasianjmed.2018.17322

ABSTRACT

Objective: Stroke is a common heterogeneous disease classified into two subtypes: ischemic and hemorrhagic. Many risk factors have been associated with stroke, and the most well-known is hypertension. Although the relation between stroke and these risk factors has been emphasized before, there is inconclusive evidence about the relation between the different risk factors and the subtypes of stroke. The present study aims to fill this gap.

Materials and Methods: In the present retrospective, cross-sectional study, 827 patients with diagnosed stroke were included. Demographic data and the acquired risk factors were determined using pre-designed questionnaires. Statistical analysis was conducted using chi-square test, Student t-test, and Pearson correlation coefficient.

Results: Among the included 827 patients, 432 (52.2%) were men and 395 (47.8%) were women. The mean±standard deviation of age was 68.41±12.46 y in men and 67.89±11.85 y in women, respectively, and the difference was not significant. Of all the patients, 672 had ischemic strokes and 155 had hemorrhagic strokes. The most common risk factor in the patients was hypertension with a prevalence of 66.7%. Of all the risk factors, only hypertension, atrial fibrillation (AF), age, and a positive family history were significantly related to a subtype of stroke.

Conclusion: Knowing that the prevalence of hypertension, AF, age, and positive family history are significantly different between the two subtypes, the patients having these risk factors can be entered into more specified public health measures, which puts more emphasis on the subtype that they are more prone to.

Keywords: Emergency medicine, neurology, stroke

Introduction

Stroke is an amalgamate disease with two subtypes: ischemic and hemorrhagic [1]. It is estimated that 6.8 million American adults have suffered from stroke, and that 610,000 people experienced it for the first time during 2013. Stroke is the second most common debilitating disease in the United States and financially is a massive burden on the health system [2]. A recent large-scale study has revealed that>90% of the burden of stroke is attributed to the modifiable risk factors, including behavioral (e.g., smoke), metabolic (hypertension, diabetes, hypercholesterolemia, low glomerular filtration rate, and high body mass index), and environmental (air pollution and lead exposure) factors [3].

Arterial hypertension (AH) causes hyaline degeneration and fibrinoid necrosis in the weak and short arteries supplying the base of the brain, including the thalamus, basal ganglia, brain stem, cerebellum, and internal capsule. Other different mechanisms of hypertension contributing to stroke are likewise well-discussed [4, 5]. The patients with diabetes mellitus (DM) are also at an increased risk of recurrent and disabling/fatal lacunar infarcts, which makes them susceptible to ischemic and hemorrhagic strokes [6, 7]. Also, according to two recent meta-analyses, DM and smoking habits differently affect gender in terms of an increase in the risk of stroke. Female diabetic or smoker patients are predisposed to a higher risk of stroke in contrast to males [8, 9]. As another metabolic factor, the elevated levels of low-density lipoprotein particles are related to an increased risk of ischemic strokes [10]. Smoking is implicated in higher stroke mortality, functional disability, and experiencing stroke at younger ages [11]. A meta-analysis reporting on

11,658 stroke patients has shown newly diagnosed atrial fibrillation (AF) [12] in nearly 25% of all the patients, detected by the combination of sequential cardiac monitoring [13]. The patients with AF have a 5-fold increased risk for embolic strokes [14].

Considering the high prevalence of emergency referrals and hospitalizations due to stroke, it seems that a vast evaluation of the relevant risk factors and their demography is valuable [15]. To the best of our knowledge, there is limited evidence in this field, and it is not well understood if all risk factors contribute as much to the different subtypes of stroke. Understanding the different patterns of the risk factors could benefit policy makers in constructing measures to accurately address the needs of the patients at high risk of stroke. Herein, we have investigated the relation among the above-mentioned risk factors, central and peripheral vascular syndromes, and the subtypes of stroke.

Materials and Methods

Patients

In this retrospective cross-sectional study, we assessed all patients with diagnosed stroke admitted to a referral medical educational hospital. The inclusion period was from January 2015 to January 2017. A total of 846 patients were detected; of which, we excluded those who left the hospital untreated (discharged with personal consent) or who had incomplete documents, i.e., the items of our study. After the exclusion, a total of 827 patients were assessed. The collected data were extracted from the patients' documents according to the variables predetermined in our questionnaire. The variables comprised the demographic data of the patients such as sex, age, stroke subtype (ischemic or hemorrhagic), risk factors (hypertension, diabetes, hyperlipidemia, smoking habits, alcohol consumption, Atrial fibrillation (AF), oral contraceptive use, a history of previous transient ischemic attacks, cerebrovascular accidents (CVAs), acute coronary syndromes, familial predisposition), and the presence of central or peripheral vascular syndromes (strokes, limb arterial thrombosis, and mesenteric artery thrombosis). The risk factors and vascular syndromes were determined by the results of a physical examination during the period in which the patient was hospitalized and by referring to the patient's medical records

Statistical Analysis

The data were analyzed using SPSS® (version 23.0.0, IBM Corp.; Armonk, New York, USA). To describe the sample population, we used mean±standard deviation, frequency, cumulative frequency, frequency distribution table, and cluster bar graphs. For the evaluation of our assumptions regarding the differences among the independent groups, chi-square test, Student t-test, and Pearson correlation coefficient were used. In all items, $p<0.05$ was considered statistically significant. Power of the study was set at 80%.

Ethical Considerations

The present study was approved by the Ethical Board of the University of Medical Sciences wherein the study was conducted. The collected data were anonymously entered in this study. No personal information was extracted from the files; we have provided only general data (not individualized) about our study population. The collected data were recorded in real and non-perverted forms, without selecting particular individuals, to achieve the desired results. To avoid any bias, the assumptions were written in a double-sided layout.

Results

In the present study, of the 846 patients, 827 patients with diagnosed stroke from January 2015 to January 2017 were included.

Of the 827 patients, 432 (52.2%) were males and the remaining 395 (47.8%) were females (sex ratio of 1.09:1), and the difference was not statistically significant (p=0.21).

The mean±standard deviation of age was 68.16±12.38 y with a median of 68 and a mode of 65 y (min=26 and max=95). The age distribution examined with the Kolmogorov–Smirnov test showed that the data distribution was not normal ($p<0.01$) and had a negative skew (skewness=−0.041), showing a higher incidence rate in older patients (Figure 1).

The mean±standard deviation of age in male patients was 68.41±12.46 y and 67.89±11.85 y for female patients, respectively, showing no statistically significant difference (p=0.29).

A total of 672 patients had ischemic stroke (81.3%), leaving the prevalence of hemorrhagic strokes at 18.7% (155 of 872 patients). There was no statistically significant correlation in terms of sex and the subtype of stroke (p=0.47). More information is presented in Figure 2.

The mean age of the patients having ischemic stroke was 68.64±12.41 y, and it was 66.11±12.06 y in patients with hemorrhagic stroke. The difference was statistically significant (p=0.02).

The most common risk factor for stroke was hypertension (66.7%). The other risk factors are presented in Figure 3.

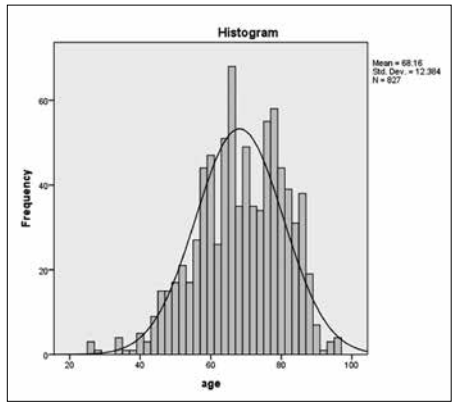

Figure 1. Distribution of age in patients included in the study

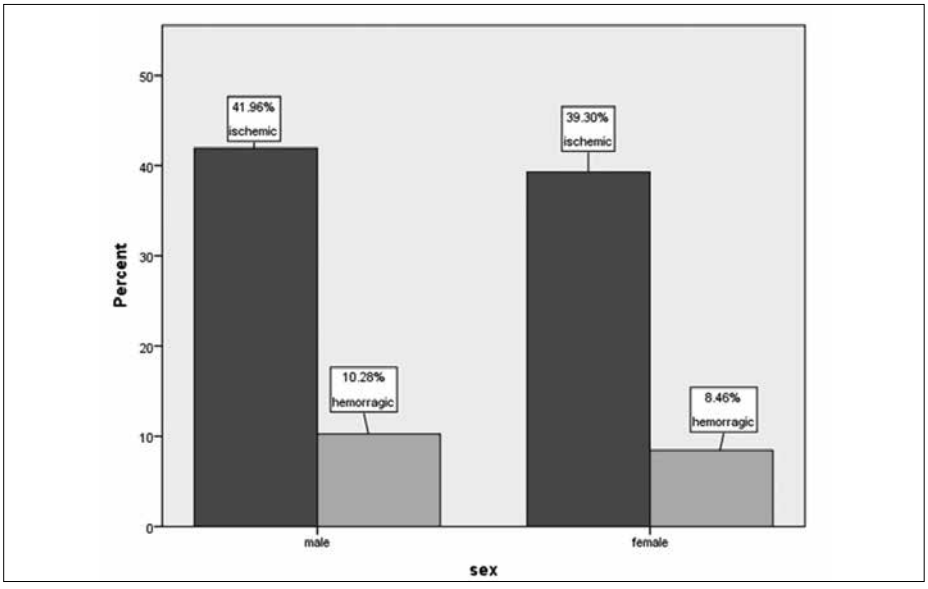

Figure 2. Distribution of patients based on the subtype of stroke separated according to sex

The determination of a relation between the risk factors and the subtypes of stroke showed that there was a significant relation between AH, AF, age, and family history and the subtype of stroke. The other risk factors had no significant relation. More information is presented in Table 1.

Of all the patients, 123 (14.9%) and 26 (3.1%) had peripheral and central vascular syndromes (PVS and CVS), respectively. CVS is defined as the involvement of the vasculature of the central nervous system by any means. Further analysis of the CVSs showed that the most prevalent etiology was the previous episodes of stroke (14.9%). While studying the PVSs, we found that the thromboses of extremity and mesenteric veins with a prevalence of 19 (2.3%) and 7 (0.8%), respectively, were the main causes of PVSs in these patients.

A history of previous stroke(s) was more common in patients with hemorrhagic strokes than that in the patients with ischemic strokes (20.6% vs. 13.4%; p=0.02). The incidence of thrombosis in the extremities was 2.4% in ischemic strokes and 1.9% in hemorrhagic strokes (p=0.73), respectively; further, the incident rate of mesenteric veins thrombosis was 0.7% and 1.3% in the ischemic and hemorrhagic strokes, respectively (p=0.5). There was no statistically significant correlation between the PVSs incidents and the subtype of stroke (p=0.9)

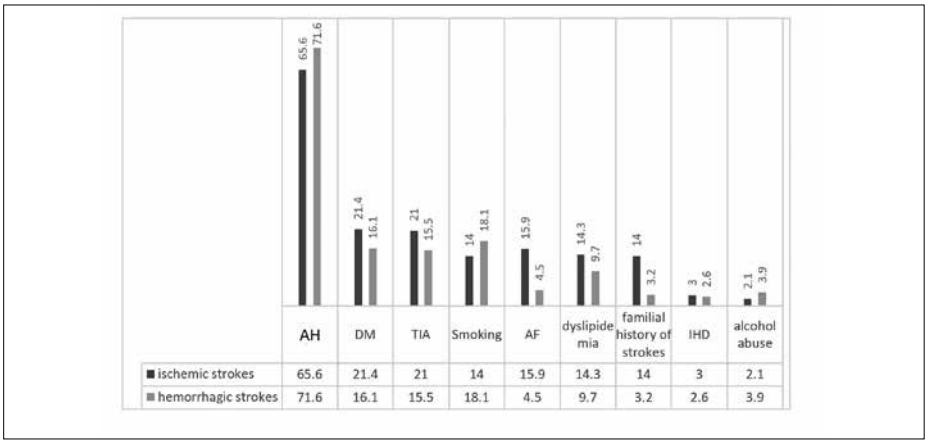

Figure 3. Prevalence of different risk factors in the included patients

Table 1. Relevance of stroke risk factors in accordance with the subtypes of stroke

		B	S.E.	Wald	DF	Sig.	Exp[B]
Variables	DM	−.290	.264	1.203	1	.273	.749
	AH	.680	.220	9.555	1	.002	1.974
	HLP	−.418	.330	1.607	1	.205	.658
	Smoke	.348	.278	1.569	1	.210	1.417
	Alcohol	.910	.598	2.318	1	.128	2.485
	Family History	−2.243	.520	18.627	1	.000	.106
	IHD	−.066	.587	.013	1	.910	.936
	AF	−1.442	.415	12.092	1	.001	.236
	TIA	−.360	.254	2.006	1	.157	.698
	Age	−.035	.008	17.346	1	.000	.966
	Sex	.171	.201	.725	1	.395	1.187
	Constant	.698	.572	1.491	1	.222	2.010

Variable(s) entered on step 1: DM (Diabetes mellitus), AH (Arterial Hypertension), HLP (Hyperlipidemia), Smoke, Alcohol, Familial history, IHD (Ischemic heart disease), Atrial fibrillation (AF), TIA (Transient ischemic attack), age, sex

Discussion

The frequency of ischemic and hemorrhagic strokes was 81.2% and 18.8%, respectively. These findings were in compliance to those of various previous studies, including Andersen et al. [16], Hajat et al. [17], and Zhang et al. [18] who stated that the prevalence of hemorrhagic strokes was between 5% and 25%.

In the study of the stroke risk factors, 64.4% and 20.1% of patients had AH and DM, respectively. The most common risk factors among the patients in Zhang's study were AH and hyperlipidemia. According to these results, the controlling and preventing chronic illnesses such as AH and DM are of high importance while controlling CVAs, particularly now that the prevalence of these conditions is increasing in different societies [19].

According to our study, old age, a history of AF (15.7% vs 3%), and a familial history of CVAs (13.6% vs. 5.2%) were more common among the patients with ischemic strokes. There was no significant difference between the subtype of stroke in terms of sex and the other risk factors. Other studies such as Anderson et al. found that the risk factors such as age, sex, and blood pressure were not predictive of the subtype of stroke [16]. On the other hand, Hajat et al., in a study of 1254 stroke patients that reviewed the risk factors and subtypes of strokes, found that there is a correlation between increased age and the incidence of ischemic strokes [17]. The same results were obtained in the studies performed by Zhang et al. and Grysiewicz et al. [18, 20]. Bilic et al. [21], studying the differences between hemorrhagic and ischemic strokes, found a higher prevalence of AH, an older age, atherosclerotic diseases, and AF in patients suffering from ischemic strokes. The results of the study conducted by Kimura et al. show the predictive value of old age in the occurrence of a second ischemic stroke [22]. All these studies show a positive relation between older age and the incidence of stroke, which is aligned with the findings of the current study, although there were some studies failing to show a correlation among these two factors.

Jørgensen et al. [23] found no correlation between AF and the occurrence of stroke, but there were studies stating that there is a higher risk of having an ischemic stroke, particularly among the patients with a history of AF, and another study showed an overall higher risk of suffering from strokes regardless of the subtype in patients with a history of AF [17, 18, 21, 22, 24]. Focusing on these results and the fact that AF has a prevalence of 19% in patients with a history of stroke and that this rate increases to 40% with an increase in age, we notice the importance of an early diagnosis and the treatment of AF in preventing strokes, particularly the ischemic subtype [25].

Age, sex, race, and a familial history of stroke are all risk factors of ischemic strokes, which cannot be changed, cured, or prevented [20].

In a study performed by Zhang et al., it was shown that having a familial history of stroke was suggestive of experiencing an ischemic stroke rather than a hemorrhagic stroke (9.8% vs. 3.3%) [18]. The results of the current recent study show a correlation between ischemic strokes and a familial history of strokes. These results were proven by Yamada et al. [26]at a cellular and molecular level, suggesting a genetic basis for ischemic strokes.

An evaluation of the PVSs and CVSs showed a history of these conditions in 3.1% and 14.9% of the cases, respectively. Zhang et al. [18] reported only a history of peripheral vascular diseases equivalent to 1.8% in patients with ischemic strokes. A history of past strokes in patients suffering from hemorrhagic strokes was more common as compared with that in patients suffering from ischemic ones (20.6% vs. 13.4%) with a p-value of 0.02. No correlations were found between the incidence of PVSs and the subtypes of stroke. In a study, Skaf et al. [27] showed that the prevalence of venous thromboembolism was higher in the patients with hemorrhagic strokes than that in the patients with ischemic strokes. Another study performed by Turnipseed et al. [16] reported five cases of stroke and two cases of transient ischemic attacks in 160 patients referred with peripheral vascular problems [28].

There is also a study that showed a 22.5% risk of experiencing a second episode of stroke in 5 years after experiencing the first stroke, which risk is particularly higher in the first 6 months following the initial incident. According to this study, the incidence rate of the second stroke is in correlation with the hemorrhagic index [28], and Baily et al. [29] claimed that 75% of the strokes in the patients experiencing a second episode were hemorrhagic rather than ischemic.

The present study aimed to address the differences between the two main subtypes of stroke and their different risk factor patterns. A limitation of this study is that the sample population was not large enough to make definite conclusion on the risk factors and the subtypes; it rather provides preliminary information on the subject. Also, all patients in the present study were from a single tertiary care, referral center. Multicenter studies would be of more merit. Needless to say, cohort studies focusing on the risk factors would help in constructing a definite correlation.

Most of the patients had an ischemic-subtype stroke. The age difference between the ischemic and hemorrhagic stroke group was statistically significant, suggesting a need for intense public health measures in the elderly. The most common risk factor among the patients was AH, emphasizing the importance of tight control of this factor. The only factors associated with the stroke subtype were AH, AF, age, and family history. The other risk factors were not significantly associated with a particular subtype of stroke.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics board of research deputy of Azad University School of Medicine, Tabriz branch.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.S.V., A.A.; Design - S.S.V., A.A.; Supervision – S.S.V., A.A.; Resources - F.A., A.A.; Materials - S.S.V., F.A.; Data Collection and/or Processing - M.M.A.A., A.A.; Analysis and/or Interpretation - S.A.M.A., A.A.; Literature Search - M.M.A.A., F.A.; Writing Manuscript - M.M.A.A., A.A., S.A.M.A.; Critical Review - A.A., S.S.V.; M.M.A.A.

Acknowledgements: The Authors would like to thank the deputy of research of Tabriz University of Medical Sciences for their support.

Conflict of Interest: Authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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