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Original Article

Relation of Stroke Risk Factors with Specific Stroke Subtypes and Territories

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Abstract

Background: Although the risk factors of ischemic strokes are well defined, there is slight information about their relations with the etiologies of ischemic strokes. This study investigated the distribution of ischemic stroke risk factors and their connections to diverse etiologies of cerebrovascular attack (CVA) and specific ischemic regions of brain.

Methods: In this cross sectional study**,** we analyzed the data of patients with definite diagnosis of CVA, excluding hemorrhagic strokes, registered in Imam Hossein Medical Center in Tehran, Iran. The data were collected from entire archived medical records from March 2010 until September 2012, retrospectively.

Results: Out of 1696 cases a total of 1011 subjects, 487 (48.2%) males and 524 (51.8%) females with mean age of 68.91±13.54 yr were included in the study. Patients suffering from atrial fibrillation (AF), valvular heart disease (VHD), and dilated cardiomyopathy were more prone to develop cardioembolic stroke. Those with diabetes mellitus (DM), carotid artery stenosis and dyslipidemia (DLP) had a higher prevalence of macroangiopathic stroke. Ischemic heart disease (IHD), AF, and VHD were associated with stroke in the brain territory supplied by middle cerebral artery (MCA) while DM and carotid artery stenosis were correspondent with posterior cerebral artery (PCA) stroke.

Conclusion: The diagnosis of the weight of each risk factor of ischemic strokes on different etiologies and territories of ischemia can assist care providers for a more efficient prevention of strokes. The results of this study can also be a basis for further investigations to corroborate the pathophysiology of such relations.

Keywords: Stroke, Cerebral arteries, Risk factors, Iran

Introduction

Stroke is defined by the sudden loss of blood circulation to an area of the brain, resulting in partial loss of neurologic function. Strokes are classified as either hemorrhagic or ischemic. Acute ischemic stroke refers to stroke caused by thrombosis or embolism and is more common than hemorrhagic stroke (1). The most common etiologies of ischemic stroke include large-artery atherosclerosis (macroangiopathy) (caused by atherosclerotic lesions in the carotid, vertebrobasilar and cerebral arteries), cardioembolism and cerebral small-vessel disease (microangiopathy). Cervical artery dissection, cerebral vasculitis, coagulopathies and hematologic disorders are less common (2). Although the risk factors of ischemic strokes are well defined, there is slight information about the relation

between these factors and the etiologies of ischemic strokes (3). Some recent articles e.g. Armin J. Grau et al. emphasized the role of risk factors in differentiating etiologies of stroke (4). The data about the relationships between risk factor of strokes and the areas of brain suffer from ischemia is also trivial.

Considering that the prevalence of stroke risk factors rises with aging, the incidence of stroke will increase in further decades as the populations get older. The mortality and morbidity of each stroke pattern is different (5). So realizing the relation between stroke risk factors and its patterns can show the burden of preventing and treating every risk factor on the outcome of stroke.

In this research, we aimed to analyze the relationship between ischemic stroke risk factors and its etiologies. The association of these risk factors and the brain infarcted territories, which are supplied by specific vessels, is also investigated. The results of this study can also be considered as a basis for further investigations to elucidate the pathophysiology of these relations.

Methods

Study design and population

In this cross sectional study, we analyzed the entire archived data of patients with definite diagnosis of cerebrovascular attack (CVA) registered in Imam Hossein Medical Center in Tehran, Iran, from March 2010 until September 2012, retrospectively. Patients having distinct area of infarction, with a clinical deficit lasting more than 24 hours, were included and those recognized with hemorrhagic strokes or stroke with concurrent or undetermined etiologies were excluded. Medical records with missing data about stroke risk factors were also excluded. Therefore, 1011 patients were qualified for this study.

The study was approved by Ethics Committee of the university.

Stroke risk factors

As major stroke risk factors, we collected the data about gender, age, family history of stroke, previous CVA or transient ischemic attack (TIA), history of myocardial infarction (MI), ischemic heart disease (IHD), atrial fibrillation (AF), valvular heart diseases (VHD), left ventricular hypertrophy (LVH), dilated cardiomyopathy, peripheral artery diseases (PAD), hypertension (HTN), diabetes mellitus (DM), carotid artery stenosis, dyslipidemia (DLP), smoking, alcohol consumption, opium addiction, obesity and vasculitis (4, 6).

Etiologies of stroke

Macroangiopathy (Large-Artery Atherosclerosis) is defined as in situ plaque formation or stenosis ≥50% in diameter of cerebral arteries or embolization of atherosclerotic debris from carotid arteries. The occlusion should correspond to clinical symptoms while cardiogenic embolism is excluded.

Microangiopathy (Small-Vessel Disease) is determined as an infarction mostly presented with one of lacunar syndromes like pure motor, sensory or sensorimotor dysfunction. Patients should have a normal brain imaging or infarctions less than 1.5 cm in diameter. Acute cortical dysfunction and cardiogenic strokes should be absent.

Cardioembolism is defined as presenting specific cardiac disorders e.g. valvular heart dysfunction or having prosthetic valve, MI, AF, dilated cardiomyopathy, severe congestive heart failure (CHF) or atrial myxoma. In this category, patients should not have any potential sources of large-artery atherosclerosis (4).

Statistical analysis

Based on Grau et al. research (4), we considered cardiac valve disease, which has the lowest prevalence among other stroke risk factors (4.3%), to calculate the maximum sample size needed for our study. Using confidence level of 95% and the maximum tolerable error in estimation of prevalence of 1.5%, 703 patients were needed as sample size.

In order to present data, we used mean, standard deviation, frequency and percent. To evaluate the relation between different factors and the status of participants, adjusted for the age and gender, odds ratio from multinomial (for multinomial status) and binary (for present of a status) logistic regression were calculated.

All statistical analysis performed by SPSS (version 21.0, IBM Co., Chicago, IL). The most noticeable confounding factors which are available in archived medical records were age and gender, so we adjusted the entire data for them.

Results

A total of 1011 patients, 487 (48.2%) males and 524 (51.8%) females with mean age of 66.84±13.63 and 71.12±13.1 yr respectively (total 68.91±13.54), were included in the study.

The following flowchart shows how we categorize the results in three tables (Fig. 1). Only statistically significant relations are shown in tables.

Stroke etiologies

Table 1 shows the significant relations between CVA risk factors and the etiologies of CVA. Overall, 609 (60.23%) had macroangiopathy strokes, 142 (14.04%) had microangiopathy strokes, and 260 (26.71%) suffered from cardioembolic strokes.

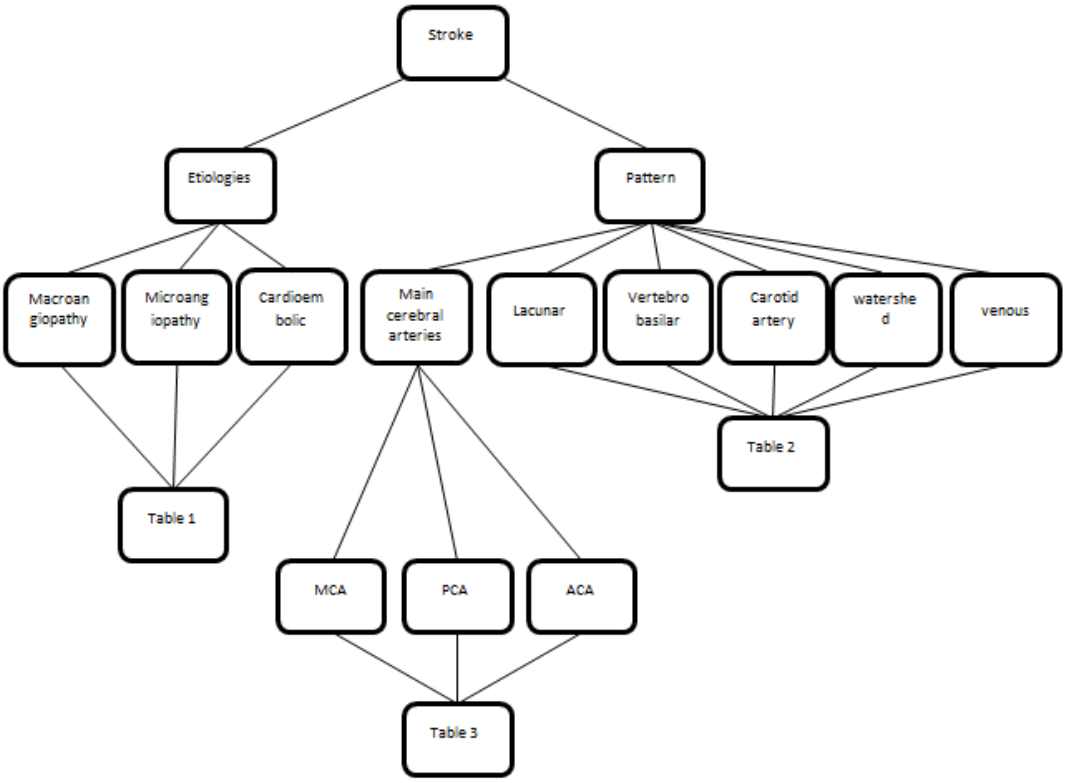

Fig.1: Results categorization in tables

Macroangiopathic

Diabetic subjects were more susceptible to develop macroangiopathic stroke (OR (%95CI): 1.83 (1.37-2.43). Subjects with carotid stenosis were more than 5-fold probable to develop macroangiopathic stroke compared to patients without this risk factor (OR (%95CI): 5.75 (3.89-8.48)). Cases with DLP established macroangiopathic stroke more than other etiologies of CVA (OR (%95CI): 1.35 (1.02-1.79)).

Cardioembolic

AF, VHD and dilated cardiomyopathy were strongly associated with cardioembolic stroke subtype (OR (95%CI): 19.33 (11.98-31.17) 31.91 (21.69-41.96), 22.73 (6.73-76.75) respectively) (Table 1).

Stroke patterns

In Table 2, the significant associations between stroke risk factors and several patterns of ischemia are evaluated.

In Table 3 the relations between risk factors of CVA and the ischemic brain areas supplied by middle, anterior, and posterior cerebral artery (MCA, ACA, and PCA) are analyzed. In some cases, CVA occurred in brain areas which supplied by more than one main cerebral artery. Among the ischemic strokes, the stenosis in main cerebral arteries was seen in 709 (70.1%) patients, consisting of 488 MCA strokes, 208 PCA strokes, and 53 ACA strokes.

In 59 and 182 patients, the vertebrobasilar and carotid arteries were respectively affected. Twenty-three cases had watershed stroke, three suffered from venous stroke, and lacunar stroke occurred in 35 of the cases.

Table 1: Significant relationships between the etiologies of CVA and its risk factors

Etiology n (%)	**Risk factors n (%)**	**ORs (95%CIs)**
Macroangiopathy 609 (60.23%)	DM 218 (35.79%)	1.83 (1.37-2.43)
	Carotid artery stenosis 211 (34.64%)	5.75 (3.89-8.48)
	Dyslipidemia 210 (34.48%)	1.35 (1.02-1.79)
Microangiopathy 142 (14.04%)	–	–
Cardioembolic 260 (25.71%)	AF 101 (49.02%)	19.33 (11.98-31.17)
	Valvular heart disease 185 (71.15%)	31.91 (21.69-41.96)
	Dilated cardiomyopathy 22 (8.46%)	22.73 (6.73-76.75)

Table 2: Significant relationships between the territories of CVA and its risk factors

Brain territory n (%)	**Risk factors n (%)**	**ORs (95%CIs)**
Watershed 23 (2.27%)	Peripheral artery disease 1 (4.34%)	13.27 (1.30-134.61)
	Smoking 7 (30.43%)	4.13 (1.45-11.73)
Carotid arteries 182 (18.00%)	Opium addiction 14 (7.69%)	4.15 (1.75-9.83)
Other territories (except main cerebral arteries) 309 (30.56%)	–	–

AF: atrial fibrillation, DM: diabetes mellitus,

Table 3: Significant relationships between CVA in main cerebral arteries and its risk factors

Main cerebral artery n (%)*	Risk factors n (%)	ORs (95%CIs)
MCA 488 (48.26%)	Ischemic heart disease 216 (44.26%)	1.39 (1.08-1.79)
	AF 79 (16.18%)	1.96 (1.33-2.89)
	Valvular heart disease 130 (26.63%)	1.38 (1.03-1.85)
PCA 208 (20.57%)	DM 79 (37.98%)	1.46 (1.06-2.01)
	Carotid artery stenosis 62 (29.80%)	1.47 (1.04-2.08)
ACA 53 (5.24%)	–	–

ACA: anterior cerebral artery, AF: atrial fibrillation, DM: diabetes mellitus, MCA: middle cerebral artery, PCA: posterior cerebral artery/*In some cases, CVA occurred in brain areas which supplied by more than one main cerebral artery

Watershed

Smoking was only associated with a higher prevalence of watershed infarct (OR (%95 CI): 4.13 (1.45 - 11.73)) compared to nonsmoker patients. Suffering from PAD had a positive relation with watershed CVAs (OR (%95CI): 13.27 (1.30 – 134.61)).

Carotid arteries

Opium addiction increased the risk of stroke in the carotid arteries (OR (%95 CI): 4.15 (1.759 - 9.835)).

MCA

Patients with a history of AF or IHD were more susceptible to develop stroke in brain territories supplied by MCA (OR (%95CI):1.96 (1.33-2.89), 1.39 (1.08-1.79) respectively). The relationship between VHD and CVA because of MCA stenosis were statistically noticeable (OR (%CI):1.38 (1.03-1.85)).

PCA

DM and carotid stenosis both increased the risk of stenosis in PCA (OR (95%CI): 1.46 (1.06-2.01), 1.47 (1.04-2.08) respectively)).

Having previous history of TIA or CVA, positive family history, dilated cardiomyopathy, LVH, HTN, DLP, and vasculitis were not associated with ischemia in any specific part of the brain.

Discussion

Ischemic strokes comprise the majority of stroke subtypes in both developing and developed countries (7). This retrospective study investigated the distribution of ischemic stroke risk factors and their relations to diverse etiologies of CVA and specific ischemic regions of brain.

The prevalence of cardioemolic strokes in our study was in consistence with other previous researches as second etiology of CVA (260 out of 1011 cases) (8). The prevalence of macroangiopathic stroke was higher than microangiopathic subtype, which is in line with studies from western countries and Latin America (3, 4, 9).

Ischemic Stroke and Cardiac risk factors

The more common high risk cardioembolic conditions are AF, recent MI (within the past six months), mechanical prosthetic valve, dilated cardiomyopathy, and mitral rheumatic stenosis (8). Therefore, as we expected in our research, AF, dilated cardiomyopathy and VHD were considerably associated with the presence of cardioembolic stroke. Cardioembolism was reported to be the most common cause of stroke especially in elderly (3, 4); however, this may be due to increased prevalence of AF parallel to aging (10-12).

Ischemic Stroke and DM

Diabetes is associated with increased level of coagulation factors and hyperinsulinemia that have an important role in the development of microangiopathic stroke. It also accelerates the atherosclerotic process of large cerebral arteries, which causes macroangiopathic infarction (13). Our results revealed that DM was associated with macroangiopathic strokes and CVA in brain territories supplied by PCA. In a Brazilian study, macroangiopathic and microangipathic strokes were the most common stroke etiologies in diabetic patients (14).

Ischemic Stroke and Smoking

Smoking is a widely accepted risk factor for stroke in any population (15). It causes cerebral infarction mainly through reversible parameters, such as increased platelet aggregation and arterial vasoconstriction, mainly due to higher sympathetic activity rather than through atherogenic parameters (13). Although in several studies smoking is associated with the occurrence of lacunar infarction in men (13, 15), in our study smoker patients were more susceptible to develop watershed strokes.

Ischemic Stroke and DLP

Previous studies showed a significant relationship between high cholesterol level and risk of cerebral infarction (9, 16). In a research done in Japan, a negative association was reported between total cholesterol level and the risk of cardioembolic infarction in female subjects (13). This can be justified by the hypothesis that higher serum cholesterol level is associated with a higher prevalence of minor CVAs (17). DLP was associated with both PCA and ACA CVAs equally (18); however, this risk factor was not associated with stroke in any of the brain specific territories in our study.

Ischemic Stroke and PAD

In our study, PAD was positively accompanied with watershed stroke; nonetheless, this relation needs further investigations to corroborate while a few patients with PAD were included in our study.

Ischemic Stroke and Opium addiction

The chance of neuropsychological impairment is greater in opiate abusers compared to patients with no history of drug abuse (19). 9.59% of our patients were addicted to opiates and had more chance of stroke in carotid arteries than other brain vessels.

Ischemic Stroke and Carotid stenosis

Different aspects of carotid stenosis like atherosclerotic plaque composition and carotid plaque rupture play a role in the pathogenesis of ischemic stroke and make the severity of carotid stenosis more obvious (20). In our study, macroangiopathic strokes (Table 1) were more probable in patients suffering from carotid stenosis and they also had greater risk of PCA stroke compared to other brain vessels.

Study Limitations

Being a hospital-based study is one of the limitations of our study. Rarely occurred risk factors of stroke such as PAD and vasculitis in our patients were our other limitations, so further multicentral investigations with specific consideration on low happened stroke risk factors is recommended.

Conclusion

Although the risk factors of stroke are well known conventionally, their relations with etiologies of stroke and specific ischemic brain areas are not scrutinized in details. In this study, we observed many statistically significant connections, which can be an initiation not only for further researches to find out the pathophysiology of these relationships but also for a more efficient prevention of strokes.

Ethical Considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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