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Original Article

Prevalence of Cardiac Risk Factors in Ischemic Stroke in a University Medical Center in Tehran

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ABSTRACT

Background: The relative importance of different risk factors of stroke may vary between various etiologies and countries. We sought to describe the cardiac risk factors of ischemic cerebral infarction in a university hospital in Tehran, Iran.

Methods: This prospective, observational study was carried out on 58 consecutive patients admitted to the neurology ward of Baharloo Hospital in Tehran, Iran, with a diagnosis of established ischemic stroke or transient ischemic attack. Data regarding each patient's demographic profile, clinical presentation, medical history (emphasis on risk factors), results of brain imaging, biochemical profile, and other diagnostic tests were recorded in a structured form. Diagnostic neurological studies comprised computed tomography scan of the head and brain, brain magnetic resonance imaging in selected patients, and Doppler ultrasonography of carotid arteries. Cardiologic studies consisted of standard 12-lead ECG, 24-hour Holter monitoring, and 2D transesophageal echocardiography (TEE) obtained over a 7-day period after the onset of symptoms. The recorded data were statistically analyzed for the percentage, mean, and standard deviation of all the variables. SPSS, version 22.0, for Windows was used for all the statistical analyses.

Results: Atrial fibrillation was evident in respectively 6.9% and 15.5% of the ECGs and Holter monitoring cardiograms. The echocardiographic findings of our studied subjects are depicted in detail in Table 2. The most prevalent finding was aortic valve stenosis or calcification in 70.7% of the subjects, followed by aortic arch wall calcification in 55.2%. Patent foramen ovale was observed on the TEE of 14 (24.1%) patients, and 3 patients had mitral annulus calcification. Three patients had rheumatic heart disease. Echocardiography demonstrated simple and severe aortic arch atheroma in 30 (51.7%) and 11 (19.0%) subjects, respectively. Mean left ventricular ejection fraction was 52.67 (SD=5.63) among our participants; 9 (15.5%) of them had impaired left ventricular function (ejection fraction <50%). Mean left atrial appendage flow velocity was 65.77 (SD=25.12), and 17 (29.3%) subjects had left atrial appendage flow velocity <55 cm/sec.

Conclusions: Different cardiac abnormalities were seen among stroke cases of unidentified causes. Because relatively high abnormalities were detected in these patients, the role of immediate cardiologic studies—especially echocardiography and Holter monitoring—in first-time stroke patients should be emphasized. ***(Iranian Heart Journal 2016; 17(1): 57-63)***

Keywords: ■Stroke epidemiology ■ Cardiac abnormalities in stroke ■ Iran ■ Echocardiography

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The rapid loss of brain function due to a disruption in blood supply is called stroke or cerebrovascular accident (CVA). This process may be triggered by ischemia (lack of blood flow) or a hemorrhage.[1] Stroke has become one of the leading causes of mortality and account for 9.7% of all global deaths, significant functional disability, and also long-term neurological impairment. It has been estimated that over 87% disability-adjusted life years (DALYs) from stroke occur in low- and middle-income countries, which is about 7 times the DALYs lost in high-income countries. Thus, in many low- and middle-income countries (including Iran), stroke alongside other noncommunicable diseases is now targeted as a public health priority.[2–5]

Ischemic stroke has several etiologies. The most important causes are large-artery atherosclerosis (macroangiopathy), cardio-embolism (the most common), and cerebral small-vessel disease (microangiopathy). Less common causes include cervical artery dissection, cerebral vasculitis, coagulopathies, and hematological disorders. Even after complete diagnostic workup, a considerable minority of ischemic stroke cases remain with undefined causes. However, there is still scant information on the role of risk factors and the clinical course in etiologic stroke subtypes.[6,7]

In the literature, there is a consensus on the impact of several risk factors of stroke, while others may exert influence on stroke incidence in some studies. Systemic hypertension, myocardial infarction, coronary heart disease, and diabetes mellitus are among well-established risk factors.[8]

In different subtypes of stroke, the most common cardiac risk factors are respectively angina or myocardial infarction, atrial fibrillation, congestive heart failure, mitral valve disease, aortic arch atheroma, cardiac arrhythmias, patent foramen ovale, and interatrial septal aneurysm.[7,9–12] Some characteristics of a potential cardiac source of brain embolisms include nonprogressive onset, hemianopia without hemiparesis or hemisensory disturbances, Wernicke's aphasia, ideomotor apraxia, involvement of specific territories (posterior division of the middle cerebral artery, anterior cerebral artery, cerebellum, and multiple territories), and a hemorrhagic component.[13]

The relative importance of different risk factors may vary between ethnic groups and countries. Thus, in different regions, studies on stroke risk factors should be carried out, and different types of stroke should be addressed separately. Until now, only a few studies on the risk factors for stroke have been conducted in our country. Our main objective was to describe the cardiac risk factors of cerebral infarction in a university hospital in Tehran, Iran.

METHODS

This prospective, observational study was carried out on 58 consecutive patients admitted to the neurology ward of Baharloo Hospital in Tehran, Iran, with a diagnosis of established ischemic stroke or transient ischemic attack (TIA). The diagnosis was made after patient records (physical examination and brain imaging) were reviewed by an experienced neurologist. Then, data regarding each patient's demographic profile, clinical presentation, medical history (emphasis on risk factors),

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and results of brain imaging and other diagnostic tests were recorded in a structured form. Diabetes mellitus, hypertension, smoking, and dyslipidemia were considered as lifestyle risk factors.

Diagnostic neurological studies consisted of computed tomography (CT) scan of the head and brain, brain magnetic resonance imaging (MRI) in selected patients, and Doppler ultrasonography of carotid arteries. The involved arterial territory (middle, anterior, or posterior cerebral artery or vertebral or basilar artery) was investigated based on the infarcted area on brain CT scan or brain MRI when brain CT was inconclusive. In carotid artery Doppler ultrasonography, internal carotid luminal stenosis >50% was considered significant stenosis. Carotid artery intimal thickness was also investigated by Doppler.

Cardiologic studies consisted of standard 12-lead ECG obtained during a 24-hour period after admission, 24-hour Holter monitoring for all the patients, and 2D transesophageal echocardiography (2D-TEE) obtained during a 7-day period after the onset of symptoms. Standard techniques were used. The measured quantitative parameters in 2D echocardiography were left ventricular ejection fraction (LVEF, %), left atrial appendage flow velocity (LAAV), and aorta intimal thickness. LAAV <55 cm/sec was considered a risk factor for thromboembolism.[14] LVEF <50% was referred to as impaired systolic function,[15] and severe aortic arch atheroma (an index of atherosclerotic disease) was defined as aortic intimal thickness ≥4 mm.[16] The presence of any mass, clot, mitral annulus calcification, patent foramen ovale, interatrial septum aneurysms, aortic valve stenosis or calcification, calcification of aorta, and signs of prior rheumatic heart disease in the mitral or aortic valve was also investigated. Finally, each of the ECG, Holter monitoring, and TEE studies was independently interpreted by at least 2 cardiologists experienced in echocardiography, and any differences were jointly resolved.

The recorded data were statistically analyzed for the percentage, mean, and standard deviation of all the variables. SPSS, version 22.0, for Windows was used for all the statistical analyses. The chi-square test, the Fisher exact test, and the *t*-test were used as appropriate. A P value <0.05 was considered statistically significant.

RESULTS

Our 58 subjects consisted of an equal number of men and women. The mean age of the participants was 66.58 years (SD=12.811), with the youngest and oldest subjects being 31 and 90 years old, respectively. Considering the well-known risk factors among our subjects, 44 (75.9%) patients were hypertensive, 28 (48.3%) diabetic, and 29 (50%) dyslipidemic. Additionally, 7 (12.1%) patients were smokers. The final diagnosis was stroke in 50 (86.2%) and TIA in 8 (13.8%) subjects.

Based on brain CT imaging or brain MRI, the most prevalent arterial territory involved was the middle cerebral artery evident in 35 (60.3%) and 5 (8.6%) of the subjects' imaging, respectively. None of the patients had infarction in the territory of the vertebral artery. In carotid Doppler sonograms, 45 (77.6%) and 43 (74.1%) of the subjects had no stenosis in respectively the right and left carotid arteries. Carotid artery atheroma was only evident in 6 subjects; 1 was severe atheroma (Table 1).

Table 1. Results of the subjects' neurological studies

Type of study	Category	Number	Percentage
Involved vascular territory in brain CT/MRI	MCA	35	60.3
	ACA	2	3.4
	PCA	10	17.2
	Vertebral artery	0	0
	Basilar artery	5	8.6
	Not seen	6	10.3
Right internal carotid artery stenosis	Significant	4	6.9
	Nonsignificant	9	15.5
	None	45	77.6
Left internal carotid artery stenosis	Significant	4	6.9
	Nonsignificant	11	19.0
	None	43	74.1
Carotid artery atheroma	Severe	1	1.7
	Non-severe	5	8.6
	None	52	89.7

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In addition, 53 (91.4%) patients had normal ECGs during the 24-hour period after admission (Table 2).

Table 2. Results of the subjects' cardiologic studies

Type of study	Category	Number	Percentage
ECG	Normal sinus rhythm	53	91.4%
	AF/AFL	4	6.9%
	Other abnormalities	1	1.7%
Holter monitoring	Normal sinus rhythm	18	31%
	AF/AFL	9	15.5%
	SVT	10	17.2%
	Premature beats	21	36.2%
Echocardiography	Clot	3	5.2%
	Mass	3	5.2%
	MAC	3	5.2%
	PFO	14	24.1%
	IAS Aneurysm	7	12.1%
	AV stenosis/calcification	41	70.7%
	RHD	3	5.2%
	Aortic wall calcification	32	55.2%
Aortic arch atheroma	Severe	11	19.0%
	Simple	30	51.7%
	None	17	29.3%
Left ventricular EF	< 50%	9	15.5%
	≥ 50%	49	84.5%
LAAV	< 55 m/s	17	29.3%
	≥ 55 m/s	41	70.7%

AF, Atrial fibrillation/flutter; SVT, Supraventricular tachycardia; MAC, Mitral annulus calcification; PFO, Patent foramen ovale; IAS, Inter-atrial septum; AV, Aortic valve ; RHD, Rheumatic heart disease; LAAV, Left atrial appendage flow velocity

Atrial fibrillation was evident in respectively 6.9% and 15.5% of the ECGs and Holter monitoring cardiograms. The echocardiographic findings of our studied subjects are depicted in detail in Table 2. The most prevalent finding was aortic valve stenosis or calcification in 70.7%, followed by aortic arch wall calcification in 55.2% of the subjects. TEE illustrated patent foramen ovale in 14 (24.1%) patients. Three (5.2%) of our subjects had clot or mass in their cardiac chambers, and 3 had mitral annulus calcification. Three patients had rheumatic heart disease. Simple and severe aortic arch atheroma were seen in 30 (51.7%) and 11 (19.0%) of the subjects' echocardiograms, respectively. Mean LVEF was 52.67 (SD=5.63) among our participants; 9 (15.5%) of them had impaired LV function (EF<50%). Mean LAAV was 65.77 (SD=25.12), and 17 (29.3%) patients had LAAV <55 cm/sec.

DISCUSSION

As is shown in the results section, among the established risk factors for stroke, hypertension was the most prevalent among our subjects (75.9%). Ellekjaer et al.[17] showed that the prevalence of stroke among hypertensive people was 3 times the normal population.

In the present study, among the cardiac risk factors of idiopathic ischemic stroke, the most prevalent factors were aortic valve stenosis or calcification and aortic arch wall calcification. Among cardiac arrhythmias observed, atrial fibrillation and supraventricular tachycardia accounted for 15.5% and 17.2% of the cases in Holter monitoring cardiograms. Fernandez et al.[10] reported that 29.5% of their stroke patients had significant cardiac arrhythmias, including 27.1% cases of tachyarrhythmia. Ravari et al.[18] reported that 19.9% of their stroke patients had atrial fibrillation, while El Sayed et al.[19] reported that 7.3% of their ischemic stroke cases had atrial fibrillation. In our study, about 32.7% of the patients had significant tachyarrhythmias, which included atrial fibrillation and other supraventricular tachycardia. The difference may be due to the difference in stroke etiologies addressed in these studies; our study population comprised idiopathic ischemic stroke patients.

Among the most important echocardiographic findings in stroke patients are patient foramen ovale and interatrial septum aneurysms.[20] Patent foramen ovale may cause ischemic stroke by paradoxical embolism. Patent foramen ovale is common in one-third of all stroke patients and 40% of cases >50 years of age.[21] In the present study, the prevalence of patient foramen ovale was 24.1%, which is slightly lower than that in the previous reports. This difference is because TEE, despite its ability to demonstrate the shunt between the 2 atria, is user-dependent. Atrial

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septal aneurysm can cause stroke by paradoxical embolism of a thrombus originating in the aneurysm or by inducing supraventricular arrhythmia. Albers et al.[22] mainly emphasized on the importance of TEE and reported that 21% of their cerebral infarct and 46% of their lacunar infarct (microangiopathic stroke) cases had interatrial septal aneurysms. We also employed TEE and found that in unexplained stroke patients, 12.1% had interatrial septum aneurysms.

Stenotic or nonstenotic aortic valve calcification and mitral annular calcification are considered as the manifestations of generalized atherosclerosis.[23] Calcific deposits lead to cardiac conduction abnormalities or to embolism due to the dislodgement of the calcified material in the blood stream. Aortic valve calcification with or without stenosis was evident in a considerable proportion of our patients (70.7%), although only 5.2% of our patients showed echocardiographic signs of mitral annular calcification. Also, aortic wall calcification is an independent risk factor for stroke, whose incidence increases by about 1.89 times.[24] In our study, accordingly, the majority of the patients suffered from aortic arch calcifications (55.2%), which is a sign of atherosclerotic disease leading to cerebral ischemia.

EF is an echocardiographic measure of LV systolic function.[25] Interestingly, Hays et al.[26] found that in all age, gender, and ethnic groups, even mild degrees of LV dysfunction (EF 41% to 50%) were associated with an increased risk of ischemic stroke. Moreover, the authors found that the every 1 degree decrease in EF was associated with 3.92 times the risk of ischemic stroke. In our study, 15.5% of the patients had impaired systolic function (EF<50%); this difference could be because of the different methods used for evaluating EF—which were mainly affected by echocardiographic image quality.[26]

Slow blood flow in the left atrium is a strong risk factor for thrombus formation. LVEF, left atrial size, (paroxysmal) atrial fibrillation, age, and sex are independent parameters influencing LAAV.[14] It is deserving of note that 29.3% of our study participants had slow left atrial appendage flow, placing them at a greater risk for stroke recurrence of embolic origin.

Atheroma in the ascending aorta and aortic arch, independent of other well-established risk factors—including high-grade carotid stenosis—is a significant risk factor for cerebral ischemia; the chance of simple and severe atheroma in ischemic stroke patients is 2.3 and 7.1 times that of the normal population.[27] In our study, aortic arch atheroma was evident in the echocardiograms of 41 (70.7%) patients: 11 cases were severe (19.0%) and 30 (51.7%) were simple. In the available literature, the rate of aortic atheroma in stroke patients has been reported in between 14% and 57% of stroke cases.[12] These rates belong to cerebral infarction due to several identifiable and unidentifiable causes, and this point explains the wide range.

The current study addressed the distribution of various cardiac abnormalities among stroke cases of identified causes. One of the major limitations of our study was its descriptive design, which cannot yield the strength of the relationship between the different risk factors and the outcome. One of the strengths of our study was the echocardiographic method that we used (i.e., TEE), which is the preferred method in assessing stroke patients.

Finally, we recommend full cardiologic workup of patients admitted with an impression of stroke or TIA—including Holter monitoring and TEE studies.

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