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Frequency of Asymptomatic Intracranial and Extracranial Arterial Stenosis in a Group of Healthy General Papulation in Kerman (South of Iran)

Farhad Iranmanesh[1], **Kaveh Shafiei**[2], **Fatemeh Bagheri**[3]

Original Article

Abstract

INTRODUCTION: This study aimed to investigate the frequency of asymptomatic intracranial and extracranial artery stenosis in healthy volunteers in Kerman, Iran, in 2019 using Doppler ultrasound imaging.

METHOD: This cross-sectional study was conducted on healthy volunteers in Kerman in 2019 following a public elicitation. After the general examination, 138 healthy volunteers who had no history of any disease and were not treated with any medication underwent cerebrovascular evaluation with Doppler ultrasound. Demographic information, history of addiction, and sonographic findings were recorded in a checklist and then analyzed using SPSS 22.

RESULTS: Stenosis was found in 14.4% of volunteers. The mean age of participants was 45.8±10.12 years, and 74 (54%) of them were male. In volunteers with stenosis, a significant correlation was found between age (P = 0.03) and addiction (P = 0.04) with the involved artery. There was also a significant correlation between addiction and intracranial and extracranial artery stenosis (P = 0.04). Logistic regression analysis showed a significant relationship between being female, addiction, and age with stenosis, as well as between addiction and intracranial artery stenosis (P <0.05).

CONCLUSION: The majority of healthy residents of Kerman have asymptomatic cerebrovascular stenosis, and this is more prevalent in the elderly, addicts, and women.

Keywords: Asymptomatic arterial stenosis, Intracranial, Extra cranial, Doppler ultrasound

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Introduction

Stroke is the third leading cause of death following coronary artery diseases and cancer. Stroke is also a leading cause of long-term disability in developed countries such as the United States, Canada, and Australia [1-3]. Studies show that about 50 to 100 individuals in 100,000 experience a stroke [4]. Some studies have shown a different topography of cerebral arteries stenosis in Eastern and Western countries. For example, CT angiography results in a 2016 study by Ebrahimi et al. showed that intracranial vascular involvement is the most common in patients with thrombotic stroke in Kerman [5]. Numerous risk factors have been reported with cerebral arteries stenosis, including hypertension, cardiac disease, smoking, diabetes, and inactivity [6, 7]. Thus, an early diagnosis of asymptomatic intracranial and extracranial artery stenosis before a stroke is critical. Doppler ultrasound (DU) is a non-invasive and accessible technique without any major complications. So, it can evaluate the hemodynamic status of extra and intracranial arteries with high accuracy [8]. The high value of DU and its association with atherosclerosis risk factors (e.g., hypertension, hyperlipidemia,

1- Professor of Neurology Stroke Fellowship, Neurology Research Center, Kerman Medical University, Kerman, Iran
2- Assistant of Neurology, Neurology Research Center, Kerman Medical University, Kerman, Iran
3- Neurologist, Neurology Research Center, Kerman Medical University, Kerman, Iran

Address for correspondence: Farhad Iranmanesh, Professor of Neurology Stroke Fellowship, Neurology Research Center, Kerman Medical University, Kerman, Iran. E-mail address: fpp_farhad@yahoo.com

diabetes, and smoking) have always been reflected [9]. Some studies have been conducted about asymptomatic cerebrovascular stenosis. The majority of these studies have worked with Doppler ultrasound due to the above-mentioned advantages. For example, López-Cancio et al. investigated the prevalence of asymptomatic cerebrovascular atherosclerosis in their study. The prevalence of asymptomatic intracranial arteries stenosis (ICAS) was 8.6% and diabetes and hypertension were the main risk factors leading to this condition [10, 11]. Bang and colleagues evaluated the prevalence and risk factors of asymptomatic intracranial and extracranial artery stenosis (ECAS) in South Korea. In this study, 27.9% of patients had ICAS and 15% had ECAS [12]. Given the importance of stroke and the lack of any report about asymptomatic cerebral arteries stenosis in Iran, the authors attempt to evaluate the frequency of asymptomatic intracranial and extracranial artery stenosis in the healthy general population in Kerman.

Materials and Methods

This cross-sectional study was conducted on healthy volunteers in Kerman in 2019. Participants were referred following elicitation on the website of the Department of Neurology of Kerman University of Medical Sciences and notifications at medical clinics and health centers. Inclusion criteria were residency in Kerman and signing the consent form to participate in the study. Exclusion criteria included having any underlying disease, using any medication, pregnancy, and age below 18. Participants underwent cerebrovascular evaluation with Doppler ultrasound (DWL, model Multi-Dop X Digital) in Shafa hospital. For each participant, sonography was performed by a trained assistant and under the supervision of a stroke fellowship. The device uses two separate 4 MHZ probes for common carotid arteries (CCA), internal carotid arteries (ICA), and a 2 MHZ probe to check anterior cerebral arteries (ACA), middle cerebral arteries (MCA), posterior cerebral arteries (PCA), vertebral arteries (VA), and basilar arteries (BA). Blood flow of the arteries was checked at the standard depth and for each of the vessels listed, peak systolic velocity, mean flow velocity, and pulsatility index were calculated automatically by the device. Stenosis criteria for MCA and ACA were MFV> 120 cm/sec, and for BA, VA, and PCA was MFV> 100 cm/sec. If the difference was more than 30% in MCA and ACA and 50% in BA, VA, and PCA, both sides of the case were considered as stenosis. Also, for ICA in the siphon of the carotid, MFV was more than 100 cm/sec and in the neck, PSV> 125 cm/sec or ICA/CCA PSV Ratio> 2 was considered as a measure of stenosis [13]. According to the information of a previous study [14] and by using sample size calculation software (PASS version 11), the sample size was calculated as 138 volunteers. The study was approved by the Ethics Committee of Kerman University of Medical Sciences under the code IR.KMU.AH.REC.1398.205. Demographic information, history of addiction, and sonographic findings were recorded in the checklist.

Statistical analysis

The data were analyzed using the Statistical Package for Social Science (SPSS) software version 22. Qualitative variables were reported by frequency and percentage, and quantitative variables were described using mean and standard deviation (SD). The relationship between categorical variables was performed using the chi-square test. If more than 25% of crosstab cells had frequencies less than 5, the Fisher exact test was done instead of the chi-square test. Univariate logistic regression was done. Those variables that have a P-value less than 0.25 entered into multiple logistic regression. The p-value was considered less than 0.05.

Results

In this study, 138 healthy volunteers were evaluated. 74 (53.6%) of volunteers were male and the rest were female. The mean

age of participants was 45.8±10.12 years. 14 of the volunteers were smokers, opium addicts, or both, and 3 of them were female. Stenosis was found in 20 (14.4%) of volunteers. The results of Table 1 show just a difference between the 2 groups in terms of age (P=0.007) and addiction (P<0.001). For evaluation correlation, other statistical methods were used. The most involved arteries were the posterior cerebral artery (PCA) (35%), the middle cerebral artery (MCA) (20%), and stenosis of more than two arteries (15%). A total of 85% of participants had intracranial stenosis and the remaining 15% had extracranial stenosis (Table 2). A significant correlation was found between age (P=0.03) and addiction (P=0.04) with the involved artery (Table 3). There was also a significant correlation between addiction and intracranial or extracranial artery stenosis (P = 0.04) (Table 4). Logistic regression analysis showed a significant relationship for sex [OR=3.47,95% C.I=(3.18,4.01), P<0.001], addiction [OR=2.7,95% C.I=(2.11,3.13), p<0.001] with stenosis, and [OR=4.31, 95% C.I=(4.09,4.76),p<0.001] with intracranial arteries stenosis and age with stenosis [OR=1.61, 95% C.I=(91.11,1.93),P<0.001] (Table 5).

A logistic regression analysis was conducted. For the multiple logistic regression, addiction, age, and sex, which had a p-value of less than 0.25 in the univariate logistic regression, were simultaneously entered into the multiple models. The effect of these variables was adjusted in the presence of other variables.

Table 1. Frequency of variables in subjects

Variable		Stenosis N (%) =20	No stenosis N (%) =118	P-value
Age	45≥	9(45)	88(74.6)	0.007
	45<	11(55)	30(25.4)	
Sex	Male	8(40)	66(55.9)	0.180
	Female	12(60)	52(44.1)	
Addiction	Opium	6(30)	6(5.1)	P<0.001
	Smoking	3(15)	8(8.6)	
	Both	5(25)	5(4.2)	
	Not addicted	9(45)	99(82.1)	

Chi-square test was performed

Table 2. Frequency of involved arteries in subjects.

Location	Artery	N(%)
Intracranial	PCA	7(35)
	MCA	4(20)
	MCA+PCA	1(5)
	More than 2 arteries	3(15)
	BA	1(5)
	VR	1(5)
Extracranial	ICA	3(15)

Table 3. Frequency of variables according to involved arteries in stenotic group

Variable		More than 2 arteries 3 N (%)	BA 1 N (%)	ICA 3 N (%)	MCA 4 N(%)	MCA+PCA 1 N (%)	PCA 7 N (%)	VR 1 N (%)	P-value
Sex	Male	1(33.3)	1(100)	2(66.7)	2(50)	0(0)	2(28.6)	0(0)	0.63
	Female	2(66.7)	0(0)	1(33.3)	2(50)	1(100)	5(74.1)	1(100)	
Age	≥45	3(100)	0(0)	0(0)	3(75)	1(100)	2(26.6)	0(0)	0.03
	< 45	0(0)	1(100)	3(100)	1(25)	0(0)	5(74.4)	1(100)	
Addiction	Yes	1(33.3)	1(100)	3(100)	2(50)	1(100)	5(71.4)	1(100)	0.04
	No	2(66.7)	0(0)	0(0)	2(50)	0(0)	2(28.6)	0(0)	

Fisher exact test was done

Table 4. Frequency of variables according to intra or extracranial involvement in stenotic group

Variable		Intracranial N(%)=17	Extracranial N(%)=3	P-value
Sex	Male	6(35.3)	2(66.7)	0.53
	Female	11(64.7)	1(33.3)	
Age	≥ 45	9(52.9)	0(0)	0.21
	45>	8(47.1)	3(100)	
Addiction	Yes	11(64.7)	3(100)	0.04
	No	6(35.3)	0(0)	

Fisher exact test was done

Table 5. Results of univariate and multiple logistic regressions analysis (Adjusted)

Variable		Univariate			Multiple		
		OR	95%CI for OR	p-value	OR	95%CI for OR	P-value
Stenosis	Addiction	3.1	1.21,3.92	0.001	2.7	2.11,3.13	<0.001
	Sex(female)	3.81	2.32,4.12	<0.001	3.47	3.18,4.01	<0.001
	Age(older than 45 years)	1.93	1.02,2.15	<0.001	1.61	1.11,1.93	<0.001
Intracranial arteries stenosis	Addiction	4.52	4.11,4.72	0.003	4.31	4.09,4.76	<0.001
	Female	0.82	0.77,1.32	0.181	0.67	0.54,1.28	0.321
	Age ≥45	0.91	0.65,1.63	0.132	0.87	0.61,1.42	0.67

Discussion

This study was conducted with the aim of investigating the prevalence of asymptomatic intracranial and extracranial artery stenosis in a healthy general population group in Kerman, Iran. The frequency of cerebrovascular stenosis in participants was 14.4%. The frequency of asymptomatic ECAS and ICAS was 2.2% and 12.2%, respectively. In this study, volunteers with underlying diseases (e.g., diabetes and hypertension), which could potentially increase the incidence of stroke, were excluded. Therefore, when including such individuals in the study, it can be claimed that a large portion of Kerman's residents have asymptomatic stenosis. There is no similar study in Iran for comparison, but some studies

have been conducted in other countries. López-Cancio et al. reported an 8.6% prevalence of asymptomatic ICAS in participants in Spain [10, 11]. Bang and colleagues evaluated the prevalence of asymptomatic ICAS in South Korea. They found that 27.9% of patients were in the ICAS group and 15% were in the ECAS group [12]. In a cross-sectional study in Japan, Matsui et al. reported a 5.9% prevalence of asymptomatic ICAS in individuals with a normal neurological condition. Moreover, moderate and mild stenosis cases were 1.5% and 4.4%, respectively [15]. Wang et al. reported an overall 7.6% prevalence of asymptomatic ICAS in the middle-aged and elderly population in China [16]. Jin et al. investigated the prevalence and risk factors of ECAS and ICAS in asymptomatic rural residents of 13 villages in China. In their study, 4.7% of residents had ICAS and 2.2% had ECAS [17]. Sun et al. reported an overall 6.6% prevalence of asymptomatic carotid stenosis. In their study, the prevalence of moderate to severe asymptomatic carotid stenosis was 5% [18]. Overall, studies show the asymptomatic ICAS prevalence of 4% to 29% (14), moderate asymptomatic carotid stenosis prevalence of 0% to 7.5%, and severe asymptomatic carotid stenosis prevalence of 0% to 3.1% [19]. Variation in results is mainly due to different population studies, including or excluding vascular risk factors, and the evaluation technique. For example, Kamran Kamal et al. used brain MRA for their study, and Jin et al. used transcranial Doppler sonography in a pure rural population of North China [14, 17]. Similar to other published studies, intracranial vascular involvement was more prevalent than extracranial vascular involvement in the authors' study. Most studies on patients with stroke show similar results [12, 20-23]. In Saber et al.'s study, however, the prevalence of extracranial stenosis (78%) was significantly higher than intracranial vessels (22%) [24]. Likewise, Luchowski et al. found that the prevalence of ECAS cases is higher than ICAS cases in Poland [25]. Also, ECAS was more prevalent in studies by Liu et al. [26] and Park et al. [27], indicating a variable pattern of stenosis prevalence in different communities [5]. In the authors' study, the most involved arteries were the posterior cerebral artery (PCA) (35%) and the middle cerebral artery (MCA) (20%). Wong et al. showed that 12.6% of participants have middle cerebral artery (MCA) stenosis [28]. Samaei et al. also reported MCA stenosis as the most common artery involved [29]. MCA and PCA seem to be the most common arteries involved in the Iranian population, according to the results [5].

Similar to other results, the frequency of asymptomatic stenosis was increased with age in our study. Wang et al. showed that the prevalence of this condition increases significantly with age, from 5.1% in individuals 40-49 years to 12.7% in individuals over 70 years [16]. Matsui [15] and Jin [17] also confirmed the effect of age on the progress of atherosclerosis and, eventually, vascular stenosis. In the study conducted by the authors, a significant correlation was identified between stenosis and addiction. Numerous other studies have likewise affirmed the role of smoking and addiction in atherosclerosis and asymptomatic stenosis [20]. The relationship between asymptomatic stenosis with vascular factors such as hypertension and hyperlipidemia diabetes was found [16, 18, 20]. For example, Jin et al. showed that the three risk factors associated with ICAS are age, hypertension, and diabetes mellitus. Likewise, risk factors associated with ECAS were age, being male, diabetes mellitus, having a high systolic blood pressure, and high total cholesterol [17]. In our study, female was correlated with asymptomatic stenosis and intracranial artery stenosis. Since in most of the studies men have reported to be more prone to this condition [11, 15], further evaluations are required to find out whether our finding is incidental or women in Kerman are more prone to asymptomatic stenosis.

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progression of atherosclerosis and, eventually, vascular stenosis. In the authors' study, a meaningful relationship was also found between stenosis and addiction. Many other studies have similarly confirmed the role of smoking and addiction in atherosclerosis and asymptomatic stenosis [20]. The relationship between asymptomatic stenosis and vascular factors such as hypertension and hyperlipidemia diabetes was found [16, 18, 20]. For example, Jin et al. showed that the three risk factors associated with ICAS are age, hypertension, and diabetes mellitus. Likewise, risk factors associated with ECAS were age, being male, diabetes mellitus, having high systolic blood pressure, and high total cholesterol [17]. In the authors' study, being female was correlated with asymptomatic stenosis and intracranial artery stenosis. Since in most of the studies men have been reported to be more prone to this condition [11, 15], further evaluations are required to find out whether the authors' finding is incidental or women in Kerman are more prone to asymptomatic stenosis.

Limitations

The authors had some limitations in this study that should be considered in future studies: First, they worked with Doppler ultrasound, which, although is used in stenosis diagnosis, fails to detect mild cases of stenosis. Thus, duplex ultrasonography is recommended to be used in subsequent studies. Second, the health situation of participants was assessed based on the patient's history that needs to be considered in other studies. Third, it was a preliminary study, and future research should be done with larger sample sizes to achieve reliable results for decision-making on prevention and screening policies for high-risk individuals. Finally, the absence of a description about the severity of stenosis was another study limitation.

Conclusion

In conclusion, the majority of the healthy general population of Kerman have asymptomatic cerebrovascular stenosis, and this is a relevant finding to consider especially in the elderly, addicts, and women. The authors' findings highlight the importance of conducting similar research in other regions of Iran.

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Conflict of Interests

The authors have no conflict of interest.

Authors' Contribution

First and second author contributed to all the procedures. The third author did Doppler sonography and helped to data collection and manuscript preparation.

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