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Screening of Asymptomatic Intracranial Arterial Stenosis among High Risk Subjects: a Pilot Study from Egypt

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Abstract

Background—Stroke ranks as the second leading cause of death and the leading cause of morbidity worldwide. Large intracranial arterial stenosis (ICAS) is a major cause of stroke.

Methods—This study investigated the prevalence and associated vascular risk factors of ICAS in a high-risk population in Qalyeubia Governorate, Egypt. A cross-sectional pilot survey using transcranial Doppler (TCD) was conducted at Toukh Central Hospital and Aghore El-qubra primary healthcare units in the Qalyeubia Governorate from 1 January 2016 until the end of June 2016.

Results—A total of 153 participants were included in this study. The prevalence of asymptomatic ICAS was 13.1%. Among the modifiable risk factors, cardiac diseases, hypertension, diabetes, obesity, dyslipidemia, physical inactivity, and smoking were the strongest independent predictors of ICAS.

Conclusion—This pilot study concluded that the prevalence of asymptomatic ICAS is relatively high in Egypt, and modifiable risk factors were the strongest predisposing factors of ICAS. TCD is an efficient non-invasive modality for the diagnostic evaluation of ICAS.

Keywords

prevalence; risk factors; stroke; ICAS; TCD

Introduction

Large intracranial arterial stenosis (ICAS) is a major public health problem, as it is a major cause of stroke worldwide. Consequently, stroke is a main cause of long-term disability and mortality [1]. In large controlled studies, the sensitivity, specificity, and positive and negative predictive values of transcranial Doppler (TCD) for diagnosing ICAS are 73%–92%, 89%–99%, 36%–50%, and 85%–86%, respectively [2].

The stroke incidence in Egypt is difficult to estimate because not all stroke patients are admitted to a hospital. Reliable nationwide epidemiological studies are lacking; however, some regional studies indicate that the incidence of stroke is 2.1 per 1000 inhabitants [3]. Another important issue is that intracranial vessels are seldom assessed in stroke patients. The present survey was, therefore, designed to determine the prevalence of asymptomatic ICAS and associated vascular risk factors in high-risk individuals in Qalyeubia Governorate, Egypt.

Methods

A cross-sectional pilot epidemiological study was conducted at Toukh Central Hospital and Aghore El-qubra primary healthcare units in Qalyeubia Governorate, one

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of three governorates within Greater Cairo, the capital city of Egypt, which has an estimated population of 20 million. The study was conducted from 1 January 2016 until the end of June 2016.

Inclusion criteria

a. ≥45 years of age.

b. Presence of one or more of the following risk factors: hypertension, diabetes mellitus, dyslipidemia, hyperuricemia, cardiac diseases, and smoking.

Exclusion criteria

a. History of stroke or transient ischemic attack.

b. The presence of migraine, thyroid disease, anemia, congestive heart failure, or other systemic illnesses that could affect TCD results.

c. The presence of major or severe disability or previous chronic neurological or psychiatric disease.

d. A poor TCD acoustic temporal window.

Informed consent was obtained from all participants prior to completion of the following assessments:

i. Laboratory investigations: The following were parameters were evaluated: fasting and postprandial blood sugar levels, lipid profile (serum cholesterol, triglycerides, low density lipoprotein, and high density lipoprotein), complete blood count, erythrocyte sedimentation rate, C reactive protein level, and serum uric acid.

ii. TCD evaluation: TCD was performed with a portable device (EZ-Dop, DWL, Compumedicus, Germany, GmbH). ICAS was diagnosed according to the internationally published criteria [4].

Statistical Analysis

Statistical analysis of the data was performed using IBM Statistical Package for the Social Sciences version 21. For quantitative variables, the mean and standard deviation were calculated. For categorical variables, the number and percentage were calculated. The statistical analysis was performed using the chi square (χ^2) test. Differences were considered statistically significant at a P value ≤ 0.05.

Results

A total of 153 participants were included in this pilot study. On assessment of the participants by TCD, only 20 participants (13.1%) were diagnosed with ICAS. Of these 20 participants, more than two-thirds (70.0%) were diagnosed with a single stenosis, and the remaining 30.0% were diagnosed with multiple stenoses. All detected stenoses were <50%.

In this study, 44.4% of patients ranged in age from 45 to 55years, 50.3% were male, and approximately two-thirds (64.1%) resided in rural areas. A total of 30.7% of patients had a secondary education, and 39.9% had an active occupation. The vast majority of patients (92.8%) were married, 83.7% had a limited income, and the majority of patients were overweight or obese (45.8%).

The baseline characteristics and the relationship between vascular risk factors and ICAS are shown in Table 1 and Figure 1.

A statistically significant increase in the occurrence of ICAS was found among patients who were hypertensive, diabetic, dyslipidemic, overweight, smokers, or physically inactive or had cardiac disease. However, no statistically significant difference was found regarding hyperuricemic patients.

In addition, no statistically significant difference was found between ICAS negative and positive groups regarding age and sex distribution.

Logistic regression was performed for each risk factor to further analyze significant variables and detect independency. As shown in Table 2, adjustment of the odds ratio revealed that the risk of ICAS was higher among diabetic, physically inactive and dyslipidemic patients than in smoking, hypertensive, and cardiac disease patients.

Discussion

In this pilot study asymptomatic ICAS was reported in 20 cases (13.1%), of which a single stenosis was present in 14 cases (9.1%), and multiple stenoses were present in 6 cases (4.0%). These results are consistent with a cross-sectional study using TCD in Hong Kong, which found asymptomatic ICAS in 12.6% of the included cases [5]. In addition, the results of the present study are comparable to those reported by Abd-Allah *et al*. [6], who examined 118 subjects with coronary artery disease and detected ICAS in 14 patients (11.9%). Conversely, Oh *et al*. [7] reported that 3.1% (n = 323) of 10,550 total patients exhibited ICAS, as determined by TCD ultrasonography. This result is lower than that of the present study, which may be due to the large sample size included in their study compared to the small sample size in

Table 1. Characteristics of the study sample and relationships between risk factors and ICAS

Variables	ICAS –ve		ICAS +ve		Total		X^2	*P* value
	No.	%	No.	%	No.	%		
Hypertension								
No	65	84.9	4	20.0	69	45.1	5.85	**0.01***
Yes	68	51.1	16	80.0	84	54.9		
Diabetes mellitus								
No	99	74.4	0	0.0	99	64.7	42.18	**0.00***
Yes	34	25.6	20	100.0	54	35.3		
Cardiac diseases								
No	109	17.4	11	45.0	120	78.4	7.94	**0.00***
Yes	23	82.6	10	55.0	33	21.6		
Dyslipidemia								
No	95	71.4	2	10.0	97	63.4	28.27	**0.00***
Yes	38	28.6	18	90.0	56	36.6		
Hyperuricemia								
No	104	21.8	16	20.0	120	78.4	0.03	**0.85**
Yes	**29**	**78.2**	**4**	**80.0**	33	21.6		
BMI								
Normal weight	38	28.6	1	5.0	39	25.5		
Overweight	55	41.4	15	75.0	70	45.7	8.70	**0.01***
Obese	40	30.1	4	20.0	44	28.8		
Physical activity								
Physically active	129	97.0	8	40.0	**137**	**89.5**	**60.30**	**0.00***
Physically inactive	4	3.0	12	60.0	16	10.5		
Smoking								
Never	116	87.2	2	10.0	118	77.1		
Current smokers	12	9.0	18	90.0	30	**19.6**	72.3	**0.00***
Former smokers	5	3.8	0	0.0	5	3.3		
Total	133	100.0	20	100.0	153	100.0		

* ***P* < 0.05: statistically significant.**

** ***P* < 0.01: highly statistically significant.**

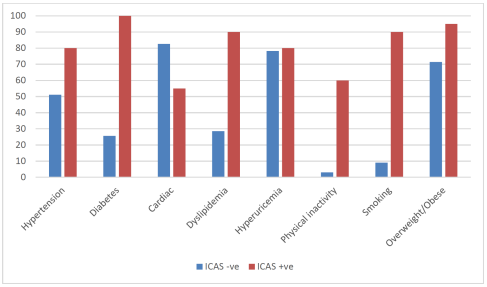

Figure 1. Comparison between Icas +ve and Icas –ve participants regarding vascular risk factors.

Table 2. Logistic regression analysis of ICAS risk factors

Risk factors	ICAS			
	B	*P* value	EXP (B)	95%CI
Hypertension	1.629	0.277	**0.196**	0.01–3.707
Diabetes mellitus	15.468	0.982	**52.798**	0.00–0.000
Cardiac diseases	1.364	0.306	**0.256**	0.01–3.483
Dyslipidemia	2.088	0.093	**8.071**	0.70–92.24
BMI	0.153	0.926	**1.166**	0.04–29.43
Physical inactivity	3.539	0.041	**34.428**	1.15–10.30
Smoking	1.149	0.318	**3.154**	0.33–30.054

the present study. In addition, Luchowski *et al*. [8] reported ICAS in 7.3% of asymptomatic patients scheduled for coronary artery bypass graft surgery.

In China, population-based studies using TCD have shown asymptomatic ICAS to be present in approximately 6%–7% of presumably healthy adults [9]. In Western countries, studies have shown asymptomatic ICAS in approximately 9% of a Spanish population with moderately high vascular risk (asymptomatic intracranial atherosclerosis study) [10] and approximately 13% of American patients referred for evaluation of asymptomatic carotid artery stenosis [11].

In the present study, no statistically significant difference was observed between ICAS negative and positive groups regarding age and sex distribution. However, the majority of patients with asymptomatic ICAS were in the 56–65 year age group (55.0%), followed by the 45–55 year age group (35.0%), and finally patients over 65 years (10.0%). These results are consistent with those of Park *et al*. [12], who reported no significant association of ICAS with age.

Other studies have shown conflicting data regarding the association between ICAS and age in stroke populations [13,14]. Younger age has been significantly associated with ICAS in some stroke population studies (Sacco *et al*., 1995). In studies with populations that included fewer stroke patients, an older age was a significant predictor of ICAS [15].

Kremer *et al*. [16] reported that gender was equally distributed between groups with and without ICAS (50% vs. 50%). Previous studies addressing possible gender differences provide conflicting results in asymptomatic patients; however, women with symptomatic ICAS enrolled into the Warfarin–Aspirin Symptomatic Intracranial Disease trial [17] were found to have greater risk of stroke and death than men [18].

In the present study, the rate of ICAS was significantly higher among smokers (90%) than among nonsmokers (12.8%). These results are contradictory with those of Kamal *et al*. [19] and Bi *et al*. [20] butare not consistent with those of Alkan *et al*. [21], who found no significant differences in the incidence of ICAS between smokers and non-smokers. This finding can be attributed to the retrospective nature of their study.

In the present work, the rate of hypertension was significantly greater in the ICAS group than in the group without ICAS (80.0% vs. 51.1%). In addition, there were significantly more cases of diabetes mellitus in the ICAS

group (100.0%) than in the group without ICAS (25.6%). These results are consistent with previous studies, suggested that certain risk factors, such as hypertension and diabetes, are significant predictors of cerebral artery atherosclerotic stenosis [22,23].

In addition, Lei *et al*. [24] reported that among their patients with diabetes mellitus, intracranial atherosclerotic lesions were more frequent, especially in patients with multiple stenoses. Furthermore, Logallo *et al*. (2014) reported that diabetes mellitus was the only risk factor that was independently associated with symptomatic ICAS, which is consistent with earlier studies [10,25].

Park *et al*. [12] speculated that the discrepancy in association of hypertension with ICAS could be explained by differences in the proportions of symptomatic stroke patients between studies. Even in studies with populations that included some symptomatic stroke patients (24%–53%), hypertension was also an independent risk factor for ICAS [15]. However, this significant association between hypertension and ICAS was not observed in studies performed solely in stroke patients [9,26]. In studies performed in symptomatic stroke patients, the presence of patients with lacunar infarction in the control group could have caused hypertension to be underestimated due to selection bias.

We also found dyslipidemia to be significantly higher in patients with asymptomatic ICAS than in patients without ICAS (90.0% vs. 28.6%). This supports and extends previous findings that high lipid levels are an independent risk factor for atherosclerosis in patients with ischemic stroke in various ethnic groups [23,27,28].

In the current study, a single stenosis was reported in 70.0% of cases, and multiple stenoses were reported in 30% of cases. These results contradict other studies that reported that multiple intracranial stenoses were found frequently [29], but this finding is consistent with some other studies [13,30].

In the present study, smoking and physical inactivity were found to be risk factors for ICAS. These results contradict those reported by Park *et al*. [12], who found that the significant risk factors for ICAS were an older age (OR = 1.05, 95% CI = 1.00–1.10) and hypertension (OR = 2.40, 95% CI = 1.01–5.69), which did not show a significant association with ICAS in the stroke population. The possible explanation for this contradiction may be due to racial differences or the small sample included in the present study. In addition, Wong *et al*. [5] found that age, hypertension, glycosuria, and family history of stroke were independent factors associated with intracranial atherosclerosis. Other previous noncommunity-based studies in Thailand and Japan reported that age, hypertension, diabetes mellitus, ischemic heart disease, and hyperlipidemia were risk factors [31–33]. All the reported risk factors have been associated with atherosclerosis.

Conclusion

Data from this pilot study showed that the prevalence of asymptomatic ICAS is relatively high in Egypt and that modifiable risk factors are the strongest predisposing factors for ICAS. The Egyptian population is in need of a large-scale study to precisely detect the risk of asymptomatic ICAS. Early detection of individuals with asymptomatic ICAS may lead to the detection of patients with a very high risk for stroke, who could then be targeted for more aggressive preventive interventions.

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