The Egyptian Journal of Neurology,
Psychiatry and Neurosurgery

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Ankle-brachial index in ischemic stroke: risk factor correlation and prognostic value

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Abstract

Background: Ankle-brachial index (ABI) is not only a marker of lower limb peripheral arterial disease (PAD), but may also reflect the severity of systemic atherosclerosis.

Objectives: To study the prevalence of abnormal ABI among the studied patients with ischemic stroke compared to general population, to assess the correlation between the ABI abnormality and different risk factors, and to study the relationship between ABI abnormality and severity of stroke.

Materials and methods: A case control observational analytical study for 200 patients, 100 patients with ischemic stroke and 100 patients as control group matched to case group in age and sex excluding patients with cardioembolic stroke, stroke of undetermined etiology, or young patients. We obtained ABI measurement from all participants. Criteria for PAD diagnosis is an ABI of < 0.9. We assessed patients' group using magnetic resonance imaging, transthoracic echocardiography, electrocardiography, carotid duplex, hemoglobin A1C, and lipid profile. Severity of stroke was assessed by the National Institute of Health Stroke Scale (NIHSS).

Results and conclusion: Abnormal ABI relative frequency is higher in stroke group compared to controls. The risk factors most frequently associated with abnormal ABI are diabetes mellitus and dyslipidemia with high statistical significance. In our study, no single stroke patient with abnormal ABI who is not diabetic. In stroke patients, abnormal ABI is relatively more associated with carotid stenosis, recurrent stroke, small vessel disease stroke, and mild to moderate stroke severity by the NIHSS yet with no statistical significance for any of them.

Keywords: Ischemic stroke, Ankle-brachial index, ABI

Introduction

The presence of peripheral arterial disease increases risk of cerebrovascular disease [1]. Ankle-brachial index (ABI) less than 0.9 is broadly acknowledged to indicate peripheral arterial disease (PAD) of the lower limbs. Stroke patients with PAD may have a higher risk of recurrent cardiovascular events and poorer outcomes [2]. ABI is not only a marker of lower limb PAD, but may also reflect the severity of systemic atherosclerosis [3]. PAD was previously described as a strong predictor of stroke and predicts cardiovascular risk and mortality in patients with acute stroke [4]. The prevalence of abnormal ABI in acute ischemic stroke was 26.1% in the stroke subgroup of a Global Atherothrombosis Assessment (AGATHA) study [5]. In another study, among patients with ischemic stroke or transient ischemic attack (TIA), abnormal ABI is reported in 26 to 31% [6]. Also, the association between cerebrovascular disease and other atherosclerotic disorders in different arterial beds namely peripheral vascular and cardiovascular was present in nearly 30% of patients [5]. Low ABI appears to be associated with a higher risk of early recurrent stroke in patients with acute ischemic stroke and no history of symptomatic PAD. So, screening for ABI in acute stroke patients may help to identify patients at high risk of future events [7].

Objectives

The objectives of this paper are to study the relative frequency of abnormal ABI among the studied patients with ischemic stroke compared to general population, to assess the relation between the ABI abnormality and different risk factors of ischemic stroke, and to study the

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relationship between ABI abnormality and severity of stroke by the NIHSS.

Materials and methods

It is a case-control observational analytical study for 200 patients recruited from Ain Shams University Hospitals. We recruited 100 patients admitted with ischemic stroke and 100 patients as control group from outpatient clinics. The active group included patients with transient ischemic attack or ischemic stroke (first ever or recurrent) following the label of large or small vessel according to Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification [8], where the diagnosis established clinically from the history, examination and investigatory tools in patient ≥ 45 years. Control group patients—selected from internal medicine outpatient clinic—were matched to case group in age and sex. We excluded patients with cardioembolic stroke, stroke of undetermined etiology, or patients aged under 45 years.

To determine the ABI with the Doppler method, we followed the American Heart Association recommendation statement. The patient should be at rest for 5 to 10 min in the supine position with the head and heels supported, and the room should be at a comfortable temperature. The blood pressure cuff should contour the limb circumference. Patients must remain still during the measurement. The cuff should be positioned around the ankle with the straight wrapping method, as with brachial measurement, and the lower edge should be 2 cm above the superior aspect of the medial malleolus. Using portable hand held Doppler (model Life Dop L250R with SD8 probe product by Summit Doppler, China), an 8-MHz Doppler probe with gel applied over the sensor, the device was placed in the area of the pulse at a 45° to 60° angle to the skin surface. We move the probe to find the clearest signal. To detect the pressure, the cuff is inflated progressively to 20 mmHg above the level of flow signal disappearance and then slowly deflated to detect signal reappearance. We used also Doppler to detect brachial blood flow during the arm pressure measurement. The same sequence of limb pressure measurement should be used, and the sequence was the same for all patients within our study. If the first arm measurement is 10 mmHg or greater than the other arm, then it should be repeated at the end of the sequence, and the two numbers averaged. For example, when beginning with the right arm and using the counter clockwise sequence (in the following order: right arm, right posterior tibial, right dorsalis pedis, left posterior tibial, left dorsalis pedis, left arm), the right arm measurement would be repeated, and the two measurements should be averaged. However, if the difference between the two numbers is greater than 10 mmHg, only the second measurement should be used

to lessen the white coat effect. The highest systolic blood pressure in the leg was then divided by the average systolic pressure in both arms. Criteria for PAD diagnosis is an ABI of < 0.9 [9].

Patients' group was assessed using magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) and magnetic resonance angiography (MRA) for intracranial circulation, transthoracic echocardiography, electrocardiography, carotid duplex using the Carotid Endarterectomy Trial North American Symptomatic Method [10] with coordination of radiology department, HA1C, and lipid profile typically including low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, and total cholesterol. Severity of stroke was assessed by the NIHSS and classified as follows: 1–4 minor stroke, 5–15 moderate stroke, 16–20 moderate to severe stroke, and 21–42 severe stroke [11].

Control group underwent the following: clinical history and examination, and ankle-brachial index measurement.

Statistical analysis of data

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013. Descriptive statistics were done for quantitative data as minimum and maximum of the range as well as mean ± SD (standard deviation) for quantitative parametric data, while it was done for qualitative data as the number and percentage. Odd ratio (OR) and its 95% confidence interval (CI) were calculated. Inferential analyses were done for quantitative variables using independent t test in cases of two independent groups with parametric data. In qualitative data, inferential analyses for independent variables were done using chi-square test for differences between proportions. Correlations were done using Pearson correlation for numerical parametric data. The level of significance was taken at P value < 0.050 as significant; otherwise, non-significant. The p value is a statistical measure for the probability that the results observed in a study could have occurred by chance.

Results

A total number of 200 patients were included, divided into 2 groups: (1) patients' group that included 100 patients with ischemic stroke and (2) control group that included 100 patients without stroke. Analysis of the demographic data showed that case group included 59 males (59%) and 41 females (41%), and their age ranged from 45 to 83 with mean age 63.0 ± 9.8. Control group included 58 males (58%) and 42 females (42%), and their age ranged from 48 to 81 with the mean age 61.8 ± 8.3 meaning that the two groups were age and sex matched. On comparison between case and control groups regarding percentage of

subjects with abnormal ABI, case group patients with low ABI (< 0.9) were 20 (20%), while in control group, they were 11 (11%). This shows that abnormal ABI was more pronounced in case group than control group but did not reach statistical significance (P = 0.79) (Table 1).

We also correlated different risk factors to percentage of abnormal ABI and tried to compare this between case and control groups. On comparison between percent frequency for abnormal ABI in subjects with or without HTN in case and control groups, results showed that in patients' group, those with hypertension have lower ankle-brachial index yet with no statistical significance while in control group, the same was found with statistical significance (Table 2).

The same correlation was assessed for DM and abnormal ABI in case and control groups. In case and control group, DM is associated with low ABI in highly significant association. All stroke patients in case group with low ABI suffer from DM (Table 3).

We assessed correlation between each of other risk factors and abnormal ABI in stroke patients. We found that among these risk factors, the one strongly associated with abnormal ABI is dyslipidemia (Table 4). There was no significant relation between smoking and percent of abnormal ABI in stroke patients in case group.

In another perspective for results' analysis, we studied relation of abnormal ABI to the clinical characteristics of stroke namely whether it is first ever or recurrent, in association with carotid stenosis and its classification as small or large vessel disease by the TOAST classification in case group table [4]. Abnormal ABI was more evident in patients with recurrent stroke yet with no marked statistical significance. The same finding was also associated with small vessel stroke showing higher association between abnormal ABI and small vessel disease yet not reaching statistical significance. The percentage of abnormal ABI in stroke patients with carotid stenosis was much higher than patients without carotid stenosis yet with no statistically significant relation mostly due to a few number of cases with carotid stenosis in our sample. We also tried to study the relation between abnormal ABI and severity of stroke through assessment of the NIHSS table [4]. Abnormal ABI is more commonly associated with mild to moderate stroke severity as regards percentage of cases with P value not enough to reach statistical significance.

Table 2 Comparison of percent frequency for abnormal ABI in subjects with or without HTN in case and control groups

Group	HTN		No HTN		P
	N	Low ABI	N	Low ABI	
Case	73	18 (24.7%)	27	2 (7.4%)	0.056
Control	35	8 (22.9%)	65	3 (4.6%)	0.005

ABI ankle brachial index, *HTN* hypertension

Discussion

In the present study, we randomized two groups of subjects matched in age and sex aiming at creating control group to compare results in case group to it. The results of the present study showed that the prevalence of low ABI in group of patients with acute ischemic stroke is higher (20%) compared to 11% in group of normal controls, but this did not show statistical significance on testing. This percentage is lower but not far away compared to most of similar study point for example Fowlkes and colleagues, 2006 stated that "Prevalence of abnormal ankle brachial index (ABI) in acute ischemic stroke was 26.1% in the stroke subgroup of the AGATHA study" [5]. Sanjay and Krishna found that the prevalence of abnormal ABI was 22% in patients with stroke [12]. Non-reaching statistical significance may be related to the presence of silent PAD in control group reaching 11%.

On revising results assessing different risk factors correlation with the presence of low ABI in stroke patients, the most evident was correlation with DM. This showed high statistical significance in stroke group and in control group. We can state that in our study, there was no single patient with ischemic stroke and DM who does not have low ABI. This comes in agreement with Purroy and colleagues, who found high prevalence of risk factors for PAD in patients with ischemic stroke, particularly DM [13].

At the present study, patients with ischemic stroke and dyslipidemia had lower ABI in comparison to non-dyslipidemic patients with stroke in statistically significant results. This comes in agreement with Lee and colleagues, who found significant association between dyslipidemia and low ABI in patients with acute ischemia stroke [14].

The present study revealed non-significant correlation between smoking and low ABI. This comes in agreement

Table 1 Comparison between case and control groups about abnormal ABI

ABI measurement	Case (N = 100)	Control (N = 100)	P
< 0.90	20 (20.0%)	11 (11.0%)	0.079
≥ 0.90	80 (80.0%)	89 (89.0%)	

ABI ankle brachial index

Table 3 Comparison of percent frequency for abnormal ABI in subjects with or without HTN in case and control groups

Group	DM		No DM		P
	N	Low ABI	N	Low ABI	
Case	42	20 (47.6%)	58	0 (0.0%)	< 0.001
Control	18	9 (50.0%)	82	2 (2.4%)	< 0.001

ABI ankle brachial index, *DM* diabetes mellitus

Table 4 Relation between abnormal ABI and some risk factors and clinical characteristics of stroke in patients' group

Clinical characteristic		N	Number and percentage of low ABI	P value
Smoking	Smoker	46	7 (15.2%)	0.27
	Non-smoker	54	13 (24.1%)	
Lipid profile	Dyslipidemic	22	9 (40.9%)	0.006
	Non-dyslipidemic	78	11 (14.1%)	
Stroke	First	20	5 (25%)	0.532
	Recurrent	80	15 (18.8%)	
TOAST classification§	Large vessel	49	7 (14.3%)	0.161
	Small vessel	51	13 (25.5%)	
Carotid stenosis	> 50%	5	2 (40.0%)	0.532
	< 50%	95	18 (18.9%)	
NIHSS‖	Mild to moderate(≤ 15)	90	19 (21%)	0.404
	Moderate to severe(≥ 16)	10	1 (10%)	

ABI ankle brachial index, TOAST Trial of ORG 10172 for Acute Stroke Treatment classification, NIHSS National Institute of Health Stroke Scale

with Lee and colleagues, who found no significant association between smoking and low ABI in patients with acute ischemic stroke [14].

Percentage of stroke patients with carotid artery stenosis had lower ABI than patients without stenosis, but this was statistically non-significant, and the main explanation is that we had very few cases of significant carotid stenosis in our sample reaching only 5 out of 100 patients. This finding was also present in AGATHA study [5]. Also, patients with small artery occlusion had lower ABI than patients with large artery occlusion, but this was statistically non-significant. This agrees with the finding that patient with peripheral arterial disease especially diabetic patients tend to suffer from small vessel disease in the cerebrovascular circulation.

Patients with recurrent ischemic stroke had lower ABI than patients with first ever stroke, but this did not reach statistical significance. However, Georgios and colleagues found the relationship of asymptomatic PAD and low ABI with higher rates of stroke recurrence and reported that low ABI is an independent predictor of stroke recurrence in patients hospitalized with symptoms of acute cerebral ischemia [15]. The accruing evidence that highlights the potential role of low ABI as an independent predictor of stroke recurrence may raise certain clinical implications by giving advice to screen for low ABI in the first-ever stroke to maximize treatment to prevent stroke recurrence, and of course, such recommendation requires clinical research validation.

On using the NIHSS in the present study, low ABI in stroke group was not correlated with severity of stroke assessed by the NIHSS. However, Lee and colleagues found that, a low ABI was associated with severe presentation of ischemic stroke [14].

Conclusion

Abnormal ABI relative frequency is higher in stroke group compared to controls. The risk factors most frequently associated with abnormal ABI are diabetes mellitus and dyslipidemia with high statistical significance. In our study, no single stroke patient with abnormal ABI who is not diabetic. In stroke patients, abnormal ABI is associated with carotid stenosis, recurrent stroke, small vessel disease stroke, and mild to moderate stroke severity by the NIHSS yet with no statistical significance for any of them.

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