The Correlation of Ankle Brachial Index and the severity of Acute Ischemic Stroke in a Tertiary Hospital in Davao City, Philippines: A Cross-Sectional Study

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ABSTRACT

Introduction: Peripheral arterial disease (PAD) had been shown to have a higher likelihood of developing cardiovascular events as well as cerebrovascular accidents particularly acute ischemic stroke. However, there are limited data on the association between ankle brachial index (ABI) values and the severity of ischemic stroke. This study aimed to determine the correlation of ABI values and the severity of acute ischemic stroke in Southern Philippines Medical Center.

Methods: A prospective cross-sectional study with 112 patients diagnosed with acute ischemic stroke from June to October 2017. The ABI ratio of the subjects were obtained and correlated with the severity of stroke using National Institutes of Health Stroke Scale (NIHSS). Data analyses utilized chi-square test for categorical variables while ANOVA test for continuous variables. Spearman rho was used to determine the association between ABI and NIHSS.

Results: Majority of patients with acute ischemic stroke had PAD with ABI ratio of ≤ 0.9 (51.8%). Using t-test, the NIHSS was significantly higher among patients with PAD having a mean score of 12.43 ± 5.29 compared to patients with normal ABI ratio having a mean score of 5.13 ± 4.09 (p= < 0.001). Furthermore, using Spearman's rho statistics, ABI ratio was negatively correlated with NIHSS score ($p < 0.001$).

Conclusion: Our results confirmed that there is a correlation between low ABI value and the severity of acute ischemic stroke. Routine ABI screening may help physicians intensify treatment strategies for those high-risk patients to prevent future events.

Keywords: Peripheral arterial disease, ankle brachial index, stroke

INTRODUCTION

Stroke is defined as presence of rapidly developing clinical signs of focal or global disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin.[1] This also included patients presenting with clinical signs and symptoms suggestive of subarachnoid hemorrhage, intracerebral hemorrhage, or cerebral infarction.[1]

In 1990, a study on the Global Burden of Disease showed that cerebrovascular diseases ranked as the second leading cause of death after ischemic heart disease in developed regions and was ranked as the third leading cause of death in developing regions.[2] According to Southeast Asian Medical Information Centre (SEAMIC) data in 1995, stroke was among the top 4 leading cause of death in ASEAN countries since 1992.[3] Stroke ranked 1st in Indonesia, 3rd in Japan, Singapore and Philippines and 4th in Brunei, Thailand, and Peninsular Malaysia.[3] In 2014, a study on the real stroke burden in the Philippines revealed that stroke was 2nd to cardiovascular disease as a leading cause of mortality with a prevalence of 0.9%.[4] Ischemic stroke comprises 70% while hemorrhagic stroke comprises 30%.[4]

In the INTERSTROKE study, hypertension, current smoking, abdominal obesity, diet, and physical activity are the five risk factors, which accounted for more than 80% of the global risk in both ischemic and hemorrhagic stroke.[5]

Ankle brachial index (ABI) is the ratio of systolic blood pressure measured at the ankle to systolic blood pressure at the brachial artery.[6] It is a non-invasive diagnostic test that is easy to perform, reproducible and efficient in detecting subclinical peripheral arterial disease (PAD).[7] An ABI of ≤ 0.9 is 95% sensitive and 100% specific for angiographically documented PAD for arterial stenosis ≥ 50% in the lower extremities.[7] In the

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Reduction of Atherothrombosis for Continued Health (REACH) registry, subjects with PAD had a higher likelihood of stroke and other vascular events than coronary heart disease patients.[8] The objective of this study was to determine the correlation of ABI ratio with the severity of acute ischemic stroke. Demographic, clinical, and biochemical profiles were also compared in patients with PAD and normal ABI.

METHODS

Trial design

This was a single-center, prospective, cross sectional study conducted from June to October 2017.

Setting and Participants

This study was conducted at the in-patient section of the Department of Internal Medicine of Southern Philippines Medical Center (SPMC), Davao City, Philippines. Male or female patients aged 19 years old and above, admitted and diagnosed with acute ischemic stroke, with cranial CT scan or MRI done were included in the study.

The following exclusion criteria were applied:

1. Diagnosed or had a history of hemorrhagic stroke, cardioembolic stroke and hypercoagulable state
2. Presence of previous vascular surgery in the lower limbs (any kind of arterial surgery)

Study process

The study was approved by the Department of Health XI Cluster Ethics Review Committee (DOH XI CERC) Davao City, Philippines (CERC protocol no. P17032301). Prior to enrollment in the study, the investigator discussed the following to the patient: acute ischemic stroke, what are the known risk factors, the value of ankle brachial index as well as the intent of the study. Written informed consent was obtained from the patients prior to their inclusion in the study.

After fulfilling the inclusion criteria, participants were included in the study population. The primary investigator utilized standard questionnaire and structured interview and physical examination, and solely gathered the information using the data collection form to minimize inter-observer variability. The severity of stroke was determined using the National Institutes of Health Stroke Scale (NIHSS) on patients admitted within 7 days of stroke onset.

The ABI was measured by getting the highest systolic blood pressure in the lower extremity divided by the higher systolic blood pressure in the upper extremity using a handheld Doppler device (Elite Model no. 100).

Variables

The independent variable were the patients' ABI score (ABI score of ≤ 0.9 (PAD), 0.91 - 1.40 (normal) and > 1.40 (non-compressible peripheral arteries) and demographic, clinical and biochemical parameters. Dependent variable was the patients' NIHSS scores.

Outcome measure

The primary outcome of the study was the NIHSS scores of patients with acute ischemic stroke.

Sample Size Computation

Sample size computation was done using the software StatCalc from EpiInfo 7.1.4.0. Estimation was based on the study of Tziomalos et al. and Polisetty et al., wherein the ratio of patients with normal ABI and abnormal ABI is 2.125 and that 64% of patients with normal ABI had stroke, respectively.[9,10] In a computation of odds ratio detecting a 30% difference and carried out at 95% confidence level, a sample size of 112 patients had 80% power of rejecting the null hypothesis if the alternative hypothesis holds.

Data Handling and Analysis

Descriptive statistics was used such as mean, standard deviation, frequency and percentages to summarize the demographic and clinical profile of the respondents. Chi-square test was used to determine the differences on categorical variables while ANOVA test was used for continuous variables. Spearman rho was utilized to determine the significant association between ABI and NIHSS scores. To calculate the odds ratio of having a severe stroke, a cross-sectional odds ratio was done. For factors that significantly increase or decrease the odds ratio of having the outcome, a multivariable logistic regression was done.

RESULTS

A total of 112 patients were included in the study. The patients were grouped based on ABI findings: PAD (ABI score of ≤ 0.9), normal (ABI 0.91 - 1.40) and non-compressible peripheral artery group (ABI > 1.40).

Demographic, clinical profile and biochemical findings

Table I shows the comparison of demographic, clinical profile and biochemical findings of patients included in the study. Based on ABI measurements, the prevalence of PAD was 51.8% (n=58), whereas 47.3% (n=53) had normal ABI. Non-compressible peripheral artery value was only 0.9% (n=1) hence it was not presented in the table.

Half of the patients with PAD (50%) were smokers, compared to 43% with normal ABI. Patients with normal ABI showed longer duration of smoking in terms of mean pack years compared to PAD patients, which was statistically significant 35.20 years (SD ± 24.40); 24.20 years (SD ± 14.00), p=0.046).

The NIHSS was higher in patients with PAD, with mean score of 12.43 (SD ± 5.29) compared to patients with normal ABI of 5.13 (SD ± 4.09), which was statistically significant (p= < 0.001).

In patients with PAD, 7% had severe stroke, 23% had moderate to severe stroke, 67% had moderate stroke and 3% had minor stroke. In contrast, among patients with normal ABI, 2% had severe stroke, 2% had moderate

Table I. Comparison of the demographic, clinical profile and biochemical findings of patients with ABI

Characteristics	PAD ABI ≤ 0.90 (n=58)	Normal ABI 0.91 to 1.4 (n=53)	p-value
Mean age ± SD, years	59.56 ± 12.96	55.66 ± 10.02	0.080
Mean BMI ± SD	23.64 ± 2.91	24.80 ± 3.32	0.054
Sex, frequency (%)			
Male	36 (62%)	35 (66%)	0.664
Female	22 (38%)	18 (34%)	
Smoking, frequency (%)	29 (50%)	23 (43%)	0.486
Mean pack years ± SD	24.20 ± 14.00	35.20 ± 24.40	0.046*
Alcohol drinker, frequency (%)	28 (48%)	27 (51%)	0.779
Comorbidities, frequency (%)			
Hypertension	53 (91%)	45 (85%)	0.289
Diabetes	19 (33%)	16 (30%)	0.771
Mean fasting blood sugar ± SD, mmol/L	6.66 ± 2.03	6.95 ± 2.87	0.534
Mean total cholesterol ± SD, mmol/L	4.55 ± 1.24	4.83 ± 1.37	0.261
Mean triglyceride ± SD, mmol/L	1.23 ± 0.64	1.32 ± 0.61	0.452
Mean HDL-C ± SD, mmol/L	0.93 ± 0.33	0.96 ± 0.22	0.532
Mean LDL ± SD, mmol/L	3.02 ± 0.96	3.25 ± 1.13	0.259
Mean VLDL ± SD, mmol/L	0.60 ± 0.41	0.59 ± 0.27	0.812
Mean creatinine ± SD, umol/L	107.00 ± 80.2	97.60 ± 36.20	0.4242
NIHSS Score, mean ± SD	12.43 ± 5.29	5.13 ± 4.09	< 0.001†
NIHSS Score, frequency (%)			
0 (no stroke)	0 (0%)	0 (0%)	< 0.001 †
1 - 4 (minor stroke)	2 (3%)	30 (56%)	
5 - 15 (moderate stroke)	39 (67%)	21 (40%)	
16 -20 (moderate to severe stroke)	13 (23%)	0 (0%)	
21 - 42 (severe stroke)	4 (7%)	2 (2%)	

** Significantly different @ 5% level, † significantly different @ 1% level*

to severe stroke, 40% had moderate stroke and 56% had mild stroke. These findings were statistically significant (p= < 0.001).

In terms of age, BMI, sex, smoking history, alcohol beverage drinking history, co-morbidities and laboratory characteristics, they did not differ among the patient groups.

Table II. Association of the demographic, clinical profile and biochemical findings among patients with severe stroke

Characteristics	Odds ratio (95% CI)	p-value
Age > 50 years	0.89 (0.31 to 2.57)	0.8245
Male	0.72 (0.26 to 1.97)	0.5245
Smoker	0.47 (0.17 to 1.35)	0.1601
Alcohol drinker	0.88 (0.33 to 2.37)	0.8013
Hypertensive	1.14 (0.23 to 5.61)	0.8718
Diabetic	0.97 (0.34 to 2.80)	0.9539
Abnormal ABI ratio ≤ 0.9	10.78 (2.36 to 49.35)	0.0022*
Abnormal ABI ratio >1.4	--	0.9763
Fasting blood sugar > 6.60 mmol/L	0.92 (0.33 to 2.56)	0.8788
Total cholesterol >5.15 mmol/L	0.57 (0.19 to 1.70)	0.3110
Triglyceride >1.95 mmol/L	0.31 (0.04 to 2.54)	0.2771
HDL-C > 1.03 mmol/L	0.59 (0.18 to 1.93)	0.3812
LDL > 1.48 mmol/L	0.38 (0.06 to 2.25)	0.2880
VLDL > 0.43 mmol/L	0.35 (0.13 to 0.96)	0.0408*
Creatinine >113 umol/L	0.57 (0.15 to 2.13)	0.4047

** Significant at p<0.05 level*

Association of ABI ratio and severity of acute ischemic stroke (NIHSS score)

The ABI ratio of the patients and NIHSS score are negatively correlated with a Spearman rho value of -0.482 ($p < 0.01$).

Association of the demographic, clinical profile and biochemical findings among patients with severe stroke

Table II shows the univariate odds ratio of stroke in terms of demographic, clinical and biochemical findings. Among the variables, abnormal ABI ratio ≤ 0.9 (OR= 10.78; 95% CI 2.36 to 49.35; p=0.0022) had significantly increased odds of having moderate-severe stroke. VLDL > 0.43 mmol/L (OR= 0.35; 95% CI 0.13 to 0.96; p= 0.0408) decreases the odds of having moderate-severe stroke.

DISCUSSION

Key Results

Based on ABI, majority of patients in the study had PAD (51.8%), followed by normal ABI ratio (47.3%) and only 1 patient (0.9%) had non-compressible peripheral artery. The NIHSS was higher in patients with PAD, with a mean score of 12.43 (SD ± 5.29) compared to patients with normal ABI of 5.13 (SD ± 4.09), which was statistically significant ($p = < 0.001$).

The ABI was negatively correlated with NIHSS score ($p < 0.001$). Using a univariate analysis, age, sex, smoking history, history of alcohol intake, hypertension, diabetes, as well as creatinine levels were not associated with severe stroke ($p > 0.05$). However, patients with PAD and elevated VLDL were associated with more severe stroke ($p < 0.05$).

Interpretation

In this cross-sectional study, the severity of stroke using NIHSS was correlated with ABI values. An ABI of ≤ 0.9 was used as a cut off for PAD, which was also used in the guidelines and epidemiologic studies.[11] In our study, patients with low ABI value presented with more severe classification of ischemic stroke.

Majority of the patients in the study had PAD with prevalence of 51.8%. This finding was consistent with several studies wherein there is elevated prevalence of ABI ≤ 0.9 among patients with ischemic stroke.[12,13]

In our population, the mean age of patients with PAD was 59.56 years old (SD ± 12.96), higher than those with normal ABI. This data was lower compared to several studies wherein the mean age range was from 60-70 years old.[9,12-14] Although age has been established to be an important factor in stroke outcome, it was not a predictor of a more severe stroke.[11,15]

The prevalence of smoking history was higher in patients with PAD than those with normal ABI however it was not statistically significant (50% and 43%, respectively; $p=0.046$). In terms of mean smoking pack years, the values were higher in those with normal ABI than those with PAD (35.20 ± 24.4 and 24.2 ± 14, respectively; $p < 0.05$). These results were not consistent in a study done in Greece in which patients with PAD were more frequently current smokers than patients with non-compressible peripheral arteries and patients with normal ABI (25.0, 6.3 and 8.1 %, respectively; $p < 0.05$).[9] The data in our study might not be accurate since we did not classify previous or current smokers. This study also did not account the duration of smoking cessation, which according to previous study was inversely associated with PAD, independent of cardiovascular risk factors.[16]

In our results, the prevalence of the risks factors for ischemic stroke such as hypertension and diabetes mellitus had no significant difference in patients with ABI ≤ 0.9 and in those with normal ABI. This finding was concordant to a previous study, wherein hypertension and diabetes did not differ in PAD and those with normal ABI ($p=0.143$ and $p=0.118$, respectively).[14]

More importantly, this study showed a significant difference in NIHSS among patients with PAD compared with normal ABI. Based on NIHSS, there was a high prevalence of moderate stroke, moderate to severe stroke, and severe stroke compared to those with normal ABI (67% and 40%, $p<0.001$; 23% and 2%, $p<0.001$; 7% and 2%, $p<0.001$ respectively). The NIHSS score was significantly higher in patients with PAD, with a mean score of 12.43 (SD ± 5.29) ($p = < 0.001$). In addition, using the univariate analysis, patients with ABI values of < 0.9 will have ~10 times odds of having more severe stroke than those with ABI more than ≥ 0.9 ($p <0.05$). This outcome was congruent with previous study in which those with ABI of < 0.9 had a higher mean NIHSS score of 22.5, whereas those with normal ABI had a mean score of 8.3.[10] Initial stroke severity is one of the most important markers for predicting stroke outcome.[17] Moreover, the composite endpoints including recurrent stroke, myocardial infarction, and all-cause mortality occurred more frequently in patients with ABI <0.9 than those with normal ABI (36.6% vs 17.9% respectively, $p=0.018$).[18]

Lipoproteins include high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), intermediate-density lipoprotein cholesterol (IDL-C), very low–density lipoprotein cholesterol (VLDL-C), and chylomicrons.[20] Studies have shown that non-HDL-C (calculated as total cholesterol minus the HDL-C) is a stronger predictor of atherosclerotic cardiovascular disease morbidity and mortality than LDL-C.[20] It has been established that elevated VLDL-C and LDL-C with apolipoprotein C-III correlates with pro-inflammatory and pro-atherogenic effects on endothelial cells in patients with hypertriglyceridemia.[21] A study done among 100 diabetic patients with acute ischemic stroke revealed that elevated VLDL had significant correlation with stroke severity ($p = 0.001$).[22] In our study, an elevated VLDL had decrease odds of having a moderate-severe stroke ($p=0.0408$). This finding can be further investigated in future studies using a larger prospective study.

ABI is not routinely done as a screening tool among patients with ischemic stroke.[14] In our study, ABI showed negative correlation with NIHSS ($p < 0.001$). This means that if the patient has a low ABI ratio, the NIHSS score is higher which pertains to a more severe classification of stroke. It has been determined that ABI is a sensitive, specific, easy to implement, non-invasive and inexpensive form of screening test.[9] Together with the results of our study, we can suggest to include the measurement of ABI in all patients with stroke.

Furthermore, ABI screening can be important in the detection of patients with greater vascular risk, for early treatment and prevention of future events.[13] It has been shown in a meta-analysis that low ABI was associated with increased risk of ischemic stroke (RR 1.83; 95% CI 1.29-2.58) and subsequent stroke (RR 1.43; 95% CI 1.23 – 1.65).[19] In line with this, we could also suggest the inclusion of ABI measurement as a standard practice in physical examination especially in patients with risks factors for cardiovascular and/or cerebrovascular events.

Strengths, Limitations and Recommendations

To the best of our knowledge this is the first study in the Philippines to assess the correlation of ABI and NIHSS among patients with stroke. Majority of the studies on

ABI, both local and international, are focused on cardiovascular disease and rarely on stroke. Our findings can show the importance of including ABI as a routine diagnostic tool in patients with acute ischemic stroke.

However, this study has several limitations. First, the quality and generalizability of our findings will be improved with a bigger sample size. The subscales of NIHSS could have been analyzed independently to appropriately identify patients' stroke severity and to obtain outcome in each category. In smoking history, this study was not able to classify the patient either a previous or current smoker which could lead to a different outcome in association with ABI. Lastly, we could have included the physical activity of the patient in the data gathering to assess if there is a negative correlation with PAD.

Therefore, the following are the recommendations of this study: (1) increase the sample size; (2) categorizing stroke severity as well as differentiation of current and previous smokers could be further analyzed to determine if there is significant association in relation to ABI values; (3) evaluate the possible outcome of the patients during admission which includes the duration of hospitalization, or if there was possible mortality; and (4) long term follow up on the patients preferably 1 year after discharge.

CONCLUSION

This cross-sectional study provides evidence that there is indeed a correlation between low ankle brachial index ratio and the severity of acute ischemic stroke (NIHSS). Routine ABI screening in acute ischemic stroke patients may help identify high-risk patients of future events and may prompt physicians to intensify treatment strategies as well as assure compliance to treatment.

Conflicts of interest: None

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