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Original Article

Sex Differences and Risk Factors Analysis of Ankle-Brachial Index in Patients with Cerebral Infarction

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SUMMARY

Purpose: To evaluate the prevalence of peripheral artery disease in patients with cerebral infarction and assess age- and sex-related differences, as well as associated risk factors.
Methods: We enrolled 2,228 stroke patients aged over 40 years with a history of cerebral infarction from our outpatient clinic. Baseline medical conditions and Ankle-Brachial Index (ABI) measurements were recorded.
Results: The prevalence of abnormal ABI was 13.5%. ABI values decreased with advancing age. In the risk factor analysis, diabetes, hypertension, and atrial fibrillation were significantly associated with abnormal ABI values, with odds ratios of 1.47, 1.74, and 2.28, respectively.
Conclusion: Older age was strongly correlated with abnormal ABI values. Additionally, diabetes, hypertension, and atrial fibrillation were identified as significant risk factors for abnormal ABI in stroke patients.

1. Introduction

Atherosclerotic cardiovascular diseases (ASCVD), including peripheral artery disease (PAD) and cerebral infarction, pose a significant global burden.[1] These conditions share common risk factors such as age, sex, hypertension, diabetes, dyslipidemia, and smoking. PAD and cerebral infarction can lead to symptoms such as unsteady gait, limb weakness, and pain, potentially resulting in severe disability and mortality.[2] In 2010, the global prevalence of PAD was estimated to exceed 200 million people, with its incidence increasing alongside aging populations.[3] The Ankle-Brachial Index (ABI), a non-invasive and cost-effective diagnostic tool, measures the ratio of ankle to brachial systolic blood pressure to detect PAD, with ABI values $\leq$ 0.9 indicating its presence.[4] However, the actual prevalence of PAD among patients with cerebral infarction has rarely been studied. Additionally, research on the influence of age, sex, and ABI value asymmetry in infarction patients remains limited.

2. Method

2.1. Study population

Between January and December 2015, patients over 40 years old with a history of cerebral infarction who visited our neurology outpatient clinic were enrolled in the study. All participants voluntarily provided informed consent. Baseline physiological data, including age, sex, height, weight, smoking status, and blood pressure, were collected through questionnaires. Additionally, we assessed participants' histories of hypertension (HTN), diabetes mellitus (DM), atrial fibrillation (AFib), and other relevant conditions.

2.2. Measurement of the Ankle-Brachial Index

In this study, cigarette smoking was defined as currently smoking at least four days per week for more than three months or having a history of smoking (either quitting more than five years ago or within the past five years). Body weight and height were measured using a digital system, and body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

The ABI was determined by calculating the ratio of systolic blood pressure (SBP) measured at the ankle to that measured at the brachial artery. The normal ABI range is 0.91 to 1.4. The commonly used diagnostic threshold for PAD is an ABI of $\leq$ 0.9, as studies have shown this cutoff provides over 90% sensitivity and specificity when compared with angiography. Patients with an ABI > 1.4, indicative of non-compressible arteries due to vessel calcification — commonly seen in individuals with diabetes or chronic kidney disease — were excluded from the study.

2.3. Statistical methods

The statistical analysis was performed using SPSS software, version 24.0 (IBM, Armonk, NY). Continuous variables were presented as mean $\pm$ standard deviation, while categorical variables were reported as counts and percentages. We used the student's t-test and one-way analysis of variance to examine the significance of differences in the

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means of continuous random variables among groups. All tests were two-sided with an alpha level of 0.05. Fisher's exact test was used to analyze associations between categorical variables. Differences in ABI across age groups were assessed using one-way analysis of variance (ANOVA), stratified by sex, with tests for trend across age categories.

Additionally, multivariable logistic regression analysis was performed to identify independent predictive factors while adjusting for potential confounding variables.

This study adhered to the ethical principles of the 1975 Helsinki Declaration on medical research and was reviewed and approved by the Institutional Review Board of MacKay Memorial Hospital (No. 14MMHIS239).

3. Results

A total of 2,228 patients were enrolled and evaluated; data from 20 patients were missing, leaving 2,208 patients for analysis (Table 1). Approximately 62% of the participants were male, with a mean age of 69 years at enrollment. The prevalence of major cardiovascular risk factors —DM, HTN, and dyslipidemia — was 42%, 83%, and 79%, respectively.

Among patients with a history of stroke, the prevalence of abnormal ABI values was 13.5% (n = 298). Patients in the abnormal ABI group had higher rates of DM, HTN, AFib, and a borderline higher proportion of females.

ABI values were found to be significantly lower in the elderly population (P trend < 0.001). Additionally, ABI measurements from the left side were, on average, 0.015 lower than those from the right side (Table 2).

Compared to the 40–59-year-old group, the odds ratios for having abnormal ABI values were 2.32 in the 60–74-year-old group and 5.76 in the ≥ 75-year-old group (Table 3). In the risk factor analysis, diabetes, hypertension, and AFib were significantly associated with abnormal ABI values, with odds ratios of 1.47, 1.74, and 2.28, respectively (Table 3). However, smoking, BMI, and dyslipidemia were not significantly associated with abnormal ABI values.

4. Discussion

PAD affects 12%–14% of the general population, with its prevalence increasing with age, reaching up to 20% in patients over 75 years old.[5] Abnormal ABI is a well-established marker for PAD. To our knowledge, no studies have previously reported the prevalence of PAD in stroke patients in Taiwan. A prior study indicated that more than 50% of patients with PAD also have concomitant cardiovascular disease (CVD) and face a worse prognosis than those without CVD.[6] In our study, the prevalence of PAD among patients with cerebral in-

Table 2
Age-sex-specific ABI values, divided to left and right side.

	Age			*p* trend
	40–59	60–74	≥ 75	
Male (n)	305	646	413	
Right ABI	1.104 ± 0.115	1.084 ± 0.124	1.035 ± 0.155	< 0.001
Left ABI	1.082 ± 0.117	1.071 ± 0.117	1.029 ± 0.150	< 0.001
Female (n)	120	343	381	
Right ABI	1.088 ± 0.08	1.062 ± 0.101	1.007 ± 0.147	< 0.001
Left ABI	1.067 ± 0.075	1.044 ± 0.095	0.987 ± 0.14	< 0.001

ABI value is average lower 0.015 at Left side (p < 0.001, 95% CI 0.011–0.018, stratified by sex).
ABI, ankle-brachial index.

Table 1
Baseline characteristic of study subjects.

	All patients (n = 2208)	ABI > 0.9 (n = 1910, 86.5%)	ABI ≤ 0.9 (n = 298, 13.5%)	p value
Age	69.35 ± 11.08	68.39 ± 10.86	75.47 ± 10.51	< 0.001
BMI	25.38 ± 3.91	25.48 ± 3.84	24.74 ± 4.25	0.005
Male	61.7%	1,195 (62.5%)	169 (56.7%)	0.053
DM	42.7%	41.4%	51.0%	0.002
HTN	83.5%	82.6%	89.2%	0.004
Dyslipidemia	79%	79.5%	76.1%	0.186
AFib	12.7%	11.2%	22.4%	< 0.001
Ever smoking (quit ≥ 5 years)	9.1%	9.1%	9.4%	0.336
Current smoking or quit < 5 years	25.8%	25.3%	29.2%	0.158
BMI > 27	31%	31.6%	26.8%	0.096

ABI, ankle-brachial index; AFib, atrial fibrillation; BMI, body mass index; DM, diabetes mellitus; HTN, hypertension.

Table 3
Logistics regression for ABI ≤ 0.9.

	Univariate			Multivariate		
	OR	95% CI	p	OR	95% CI	p
Male	0.784	0.612–1.004	0.053			
Age						
40–59	1			1		
60–74	2.329	1.422–3.814	0.001	2.057	1.252–3.382	0.004
≥ 75	5.767	3.571–9.312	< 0.001	5.109	3.148–8.292	< 0.001
DM	1.473	1.153–1.881	0.002	1.580	1.222–2.042	< 0.001
HTN	1.743	1.185–2.562	0.005	1.593	1.069–2.374	0.022
Dyslipidemia	0.823	0.617–1.098	0.186			
AFib	2.287	1.683–3.108	< 0.001	2.015	1.463–2.776	< 0.001
BMI > 27	0.793	0.603–1.043	0.097			
Ever smoked (quit ≥ 5 years)	1.101	0.717–1.689	0.660			
Current smoking (quit < 5 years)	1.23	0.933–1.621	0.142			

ABI, ankle-brachial index; AFib, atrial fibrillation; BMI, body mass index; DM, diabetes mellitus; HTN, hypertension.

farction was 13.5%, significantly lower than that observed in PAD patients with CVD. These findings suggest that, in the progression of atherosclerotic diseases, PAD represents a more advanced stage than infarction and coronary artery disease.[7]

Additionally, our study found that patients with AFib exhibited a higher prevalence of lower ABI values. In recent years, growing evidence has highlighted a strong relationship between AFib and PAD. These conditions frequently coexist, with a bidirectional relationship driven by shared risk factors such as inflammation, endothelial dysfunction, and a prothrombotic state. This association significantly increases the risk of major adverse outcomes, including stroke, myocardial infarction, cardiovascular death, and all-cause mortality.[8] Further research is needed to clarify the underlying mechanisms linking these conditions. The ARAPACIS study reported that 21% of patients with AFib had a low ABI (≤ 0.9), suggesting that a significant proportion of AFib patients may have asymptomatic PAD. Similarly, the prevalence of AFib in PAD patients is considerably higher than in the general population.[9]

Age, diabetes, and hypertension are well-established vascular risk factors. Our study also found a significant association between these factors and lower ABI values. However, smoking, BMI, and dyslipidemia were not significantly associated with abnormal ABI values. Although smoking is a well-known vascular risk factor, nicotine — a key component of tobacco — may exert complex biological effects. While nicotine is associated with increased cardiovascular risk and addiction, it also has potential positive effects, such as promoting neoangiogenesis, cell division, and proliferation. Nicotine influences neural and non-neural cells through specific pathways downstream of nicotinic receptors (nAChRs).[10] Other studies have also supported nicotine's role in promoting angiogenesis.[11] In mouse models, nicotine has been found to enhance cerebral angiogenesis following intracerebral hemorrhage, promoting both neovascularization and neuronal survival.[12]

In obese individuals, a high ABI (> 1.3) is frequently observed, which may be attributed to increased muscle mass and adipose tissue in the lower limbs, reducing arterial compressibility. Additionally, excessive adipose tissue surrounding the arteries can complicate accurate ABI measurement and may be influenced by technical factors, such as the size of the blood pressure cuff used.[13] This may explain why BMI was not found to be a significant factor in our study.

Regarding sex-specific prevalence, the abnormal ABI group was observed at more similar rates in both sexes (56.7% in males vs. 43.3% in females) compared with the normal ABI group (62.5% in males vs. 37.5% in females). The finding was consistent with findings from previous large cohort studies. Estrogen has been reported to have a protective effect against atherosclerosis.[14] However, since PAD patients tend to be older, the protective effect in females diminishes after menopause.

This study has several strengths. First, we included a large number of participants (n = 2,228), all of whom were stroke patients. Additionally, we followed a strict protocol, conducted standardized questionnaire assessments, and performed consistent ABI measurements. These factors enabled us to accurately determine the prevalence and risk factors of PAD in stroke patients. This study has several limitations. First, stroke etiologies were not classified or recorded, limiting the ability to analyze associations between ABI values and specific stroke subtypes. Second, comorbidity data were obtained from patient self-reports or medical chart reviews, introducing the potential for inaccuracies or recall bias. Third, as a cross-sectional study, data were collected at a single point in time, restricting the ability to assess causal relationships or track long-term trends and changes. The study was designed as a cross-sectional study, therefore, the relationship between abnormal ABI and causality has several limitations. To better understand the clinical implications of ABI measurements and their relationship to stroke and other vascular events, longitudinal studies with extended follow-up periods are needed.

5. Conclusion

In patients with cerebral infarction, older age was strongly associated with abnormal ABI values, suggesting that age-related vascular changes play a significant role in the development of PAD. Additionally, diabetes, hypertension, and AFib were identified as major risk factors for abnormal ABI values, highlighting their contribution to systemic atherosclerosis and vascular dysfunction.

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