ORIGINAL ARTICLE

# Prevalence of Peripheral Arterial Diseases in Patients with Large Artery Ischemic Stroke and its Prognostic Value

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Abstract

*Background:* ***Patients who have had a stroke or TIA in the past are at a higher risk of having another vascular event because vascular illness in one artery territory is a powerful predictor of disease in other territories.***

*Aim and objectives:* ***In order to learn how common peripheral arterial disease (PAD) is and how it affects the prognosis of individuals with big artery ischaemic stroke.***

*Subjects and methods:* ***From October 2023 until the end of May 2024, 78 stroke patients with major artery atherosclerotic disease were enrolled in this prospective cohort study. The participants were recruited from Al-Azhar University Hospitals, specifically Al-Hussein and Bab-Elshearya University Hospitals.***

*Results:* ***Diabetes mellitus(DM) and hypertension(HTN) were prevalent in both groups(overall, 74.4% and 76.9%, respectively), with no significant differences observed(p=1.00 and p=0.216, respectively). These findings are consistent with the understanding that both conditions are common comorbidities in populations at risk for vascular diseases, including PAD. The high prevalence rates in both groups suggest that these conditions are critical in the overall risk profile of the study population who presented with acute stroke, but may not differentiate PAD patients from non-PAD individuals in this context.***

*Conclusion:* ***This study highlights the complex interplay of factors influencing PAD and its association with stroke outcomes. Smoking, ABI, and lower limb duplex findings emerged as significant differentiators for PAD, while NIHSS, lower limb duplex, and ABI were the strongest predictors of mortality. The results underscore the importance of comprehensive risk assessment and integrated management in improving outcomes for PAD patients.***

*Keywords:* Peripheral arterial diseases; Artery ischemic stroke

## 1. Introduction

Patients having a history of stroke or transient ischaemic attack are at an increased risk of vascular events due to the significant predictive power of vascular disease in one arterial area.[1]

Reduced arterial perfusion to the lower extremities, or "poor circulation," is a hallmark of peripheral artery disease (PAD). Atherosclerotic plaques typically limit blood flow to the distal extremities by narrowing the arterial flow lumen, a symptom shared by many cases of PAD.

One simple method to compare the systolic pressure of the affected lower extremity with the other is the ankle brachial index (ABI). The ABI test is highly accurate in diagnosing peripheral artery disease, with a sensitivity level above 90% and a specificity level of 95%.[2]

Between 12% and 14% of the population is impacted by PAD.3 In patients older than 60 years, the prevalence of PAD reaches 10%. Regrettably, most people do not exhibit any symptoms and go undetected. The number of patients who do not inform their doctor about their symptoms is even higher, at one-third. Consequently, a population of individuals at high risk goes undiagnosed and gets inadequate care.[3]

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Asymptomatic carotid stenosis becomes more common as ABI decreases. Although carotid angioplasty with stenting and endarterectomy has a low benefit in patients with PAD, screening for asymptomatic carotid stenosis may still play a role.[4]

The researchers set out to determine how common PAD is among people who have suffered a large-artery ischaemic stroke and how it affects their chances of survival.

## 2. Patients and methods

Patients with big artery atherosclerotic disease who had a stroke between October 2023 and May 2024 were enrolled in this prospective cohort study by Al-Azhar University Hospitals (Al-Hussein and Bab-Elshearya University Hospitals).

Ethical Considerations:

The Declaration of Helsinki was followed when conducting this study. Ethical committees of Al-Azhar University's Faculty of Medicine granted IRB permission. At the time of enrolment, all patients were asked to sign an informed consent form.

Inclusion Criteria:

Neuroimaging, magnetic resonance angiography (MRI) of the brain and neck, computed tomography (CT) of the brain and its arteries, or traditional angiography were all used to identify stroke patients with atherosclerotic disease of the large arteries, whether it was inside or outside the brain, and with either anterior or posterior circulation.

Exclusion Criteria:

Atrial fibrillation, transient ischaemic attack, intra-cerebral, subdural, or subarachnoid haemorrhage were all considered clinical evidence of cardio-embolic stroke and would subsequently disqualify a patient from the study.

Every patient underwent a comprehensive clinical evaluation that included a detailed medical history, personal information, and a history of risk factors such as hypertension, diabetes, dyslipidaemia, smoking, and more.

General examination including:

Warning signs that could indicate peripheral artery disease. At 0 days, 7, and 30, a thorough neurological history and examination, as well as the NIHSS, will be conducted to evaluate the severity of the stroke. Healthcare providers use the National Institute of Health Stroke Scale (NIHSS) score, originally developed to evaluate intervention differences in clinical trials, to objectively quantify the impairment caused by a stroke and aid in planning post-acute care disposition. NIHSS is a 15-item impairment scale that was initially developed in 1989 to measure the severity of stroke. Higher scores indicate more seriousness; the scale runs from 0 to 42.

There will be no stroke symptoms or a small stroke if the score is less than 5, a moderate stroke if the score is between 5 and 15, a moderate to severe stroke if the score is between 16 and 20, and a severe stroke if the score is between 21 and 42. Checking for death or recurrence after six months

Laboratory assessment:

Manifested in a variety of laboratory tests, including glucose, insulin, lipids, liver and kidney enzymes, and PT and PTT results.

Imaging Examinations:

Ultrasound with contrast is applied to the veins and arteries of the lower extremities in order to determine the average blood pressure (ABP). The ankle-brachial index (ABI) can be used to evaluate vascular health without the need for invasive procedures. This measurement is derived from the ratio of the systolic blood pressure of the lower extremity (ankle in particular) to that of the upper extremity. This ratio evaluates the blood vessel resistance, wherein the diameter of the vessels is a key component.

A stethoscope or Doppler is used at the brachial, dorsalis pedis, and posterior artery locations for the manual approach. After that, slowly reduce the pressure after inflating the cuff to a pressure 20-30 mm Hg higher than the previous sound heard. The systolic pressure at that location should be recorded at the first heart sound. The ankle systolic pressure divided by the arm systolic pressure is the formula.

MRI scans of the brain (including flair, diffusion-weighted, T1, T2, and T2* images) and magnetic resonance angiography (MRA). The patient may require a carotid duplex, CT angiography of the neck and brain, or traditional angiography in certain cases.

Statistical Analysis:

A thorough analysis and statistical management of all data was performed. Prior to exporting the data to SPSS, all data was entered into the Excel program and cleaned. The statistical package for the social sciences (SPSS Inc., Chicago, IL, USA) version 22 was used for all statistical calculations. When applicable, data were presented statistically using numerical values and percentages. For outcomes with normally distributed data, we used the Student t-test; for outcomes with non-normally distributed data, we used the Mann-Whitney U-test. The Chi-square (x2) test was used to compare categorical data. In cases where the anticipated frequency is below 5, Fischer's Exact test was substituted. The numerical data were correlated using Pearson's correlation test. A significance level of $P<0.05$ was chosen.

## 3. Results

*Table 1. Patient demographic and comorbid data.*

| | FREQUENCY(N=78) | % |
|---|---|---|
| SEX | | |
| MALE | 44 | 56.4 |
| FEMALE | 34 | 43.6 |
| AGE, MEAN±SD | 63.36 | 9.77 |
| COMORBIDITIES | | |
| DM | 58 | 74.4 |
| HTN | 60 | 76.9 |
| SMOKING | 28 | 35.9 |
| PAD SYMPTOMS | 18 | 23.1 |
| RT-CAROTID DUPLEX | | |
| DIFFUSE ATHEROSCLEROSIS | 6 | 7.7 |
| ICA | 30 | 38.5 |
| MILD | 18 | 23.1 |
| NORMAL | 24 | 30.8 |
| LT-CAROTID DUPLEX | | |
| DIFFUSE | 6 | 7.7 |
| HEIGH RI OF VERTEBRAL | 6 | 7.7 |
| ICA | 32 | 41.0 |
| MILD | 16 | 20.5 |
| NORMAL | 18 | 23.1 |
| ECHOCARDIOGRAPHY | | |
| VHD | 4 | 5.1 |
| DD | 30 | 38.5 |
| IHD | 28 | 35.9 |
| LVH | 12 | 15.4 |
| NORMAL | 4 | 5.1 |

*Table 2. Baseline radiological data distribution among stroke patients with PAD and without PAD.*

| BASELINE RADIOLOGICAL DATA | | WITHOUT PAD (N=40) | | WITH PAD (N=38) | | TEST VALUE | P-VALUE |
|---|---|---|---|---|---|---|---|
| | | Frequency | % | Frequency | % | | |
| RT-CAROTID DUPLEX | Diffuse atherosclerosis | 4 | 10.0 | 2 | 5.3 | 4.71 | 0.201 |
| | ICA | 12 | 30.0 | 18 | 47.4 | | |
| | Mild | 8 | 20.0 | 10 | 26.3 | | |
| | Normal | 16 | 40.0 | 8 | 21.1 | | |
| LT-CAROTID DUPLEX | Diffuse | 4 | 10.0 | 2 | 5.3 | 9.84 | 0.041* |
| | Heigh RI of vertebral | 4 | 10.0 | 2 | 5.3 | | |
| | ICA | 12 | 30.0 | 20 | 52.6 | | |
| | Mild | 6 | 15.0 | 10 | 26.3 | | |
| | Normal | 14 | 35.0 | 4 | 10.5 | | |
| LL-DUPLEX | Marked atherosclerosis | 0 | 0.0 | 10 | 26.3 | 65.99 | <0.001* |
| | Mild atherosclerosis | 4 | 10.0 | 12 | 31.6 | | |
| | Moderate atherosclerosis | 0 | 0.0 | 16 | 42.1 | | |
| | No atherosclerosis | 36 | 90.0 | 0 | 0.0 | | |

The chi-square test with Monte-Carlo method was used for the above comparisons. *:significant p-value≤0.05.

The baseline radiological data distribution among stroke patients, categorized by ABI(ankle-brachial index), reveals significant differences in specific parameters. For patients with ABI≤0.9, left carotid duplex findings show a higher frequency of internal carotid artery(ICA) involvement(52.6%) compared to those with ABI>0.9(30.0%), with a significant p-value of 0.041.

Additionally, marked atherosclerosis in lower limb(LL) duplex is exclusively observed in the ABI≤0.9 group(26.3%), contrasting with no cases in the ABI>0.9 group, yielding a highly significant p-value of<0.001. In terms of mild and moderate atherosclerosis, patients with ABI≤0.9 exhibit a substantially greater prevalence(31.6% and 42.1%, respectively) compared to those with ABI>0.9(10.0% and 0.0%, respectively). Normal findings are predominant in the ABI>0.9 group for both carotid and LL duplexes. These results underscore a notable association between reduced ABI and more severe radiological evidence of vascular disease, emphasizing its potential role as a marker for systemic atherosclerosis in stroke patients,(table 2).

*Table 3. Baseline clinical and laboratory data distribution among stroke patients by ABI≤0.9.*

| BASELINE CLINICAL AND LABORATORY DATA | WITHOUT PAD (N=40) | | WITH PAD (N=38) | | TEST-VALUE | P-VALUE |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| NIHSS(BASELINE) | 17.3 | 2.812 | 17.53 | 2.835 | 0.35 | 0.72 |
| NIHSS(ON DAY-7) | 14.45 | 2.631 | 15.37 | 3.258 | 1.37 | 0.17 |

The independent sample t-test was used for the above comparisons. *:significant p-value≤0.05.

The baseline clinical and laboratory data distribution among stroke patients, categorized by ABI(ankle-brachial index), shows no statistically significant differences between the groups. The mean NIHSS score at baseline is similar in patients with ABI>0.9(17.3±2.812) and those with ABI≤0.9(17.53±2.835), with a p-value of 0.72. On day-7, the NIHSS score remains slightly higher in the ABI≤0.9 group(15.37±3.258) compared to the ABI>0.9 group(14.45±2.631); however, this difference is not statistically significant(p=0.17). These findings suggest that ABI status does not significantly influence the initial clinical severity or short-term neurological outcomes as measured by the NIHSS score in stroke patients,(table 3; figures 1&2).

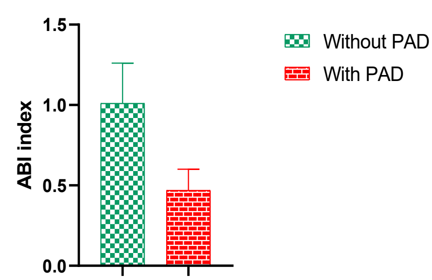


Figure 1. ABI error bar(mean±SD) by PAD

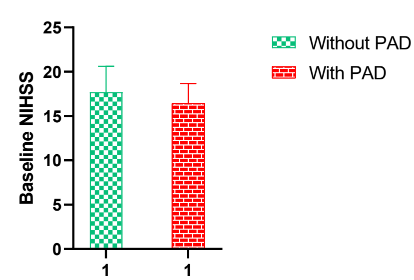


Figure 2. Baseline NIHSS error bar(mean±SD) by PAD Outcomes.

*Table 4. Mortality and recurrence among stroke patients regarding ABI≤0.9.*

| VARIABLES | | WITHOUT PAD (N=40) | | WITH PAD (N=38) | | TEST VALUE | P-VALUE |
|---|---|---|---|---|---|---|---|
| | | Frequency | % | Frequency | % | | |
| MORTALITY | Yes | 0 | 0.0 | 6 | 15.8 | 6.84 | 0.01* |
| | No | 40 | 100.0 | 32 | 84.2 | | |
| RECURRENCE | Yes | 4 | 10.0 | 2 | 5.3 | 0.62 | 0.68 |
| | No | 36 | 90.0 | 36 | 94.7 | | |

The Fisher exact test was used for the above comparisons. *:significant p-value≤0.05.

The outcomes of stroke patients based on ABI(ankle-brachial index) demonstrate significant differences in mortality. In the ABI≤0.9 group, mortality occurs in 15.8% of patients, while no mortality is reported in the ABI>0.9 group, resulting in a statistically significant p-value of 0.01. Regarding stroke recurrence, both groups show similar outcomes, with recurrence rates of 10.0% in the ABI>0.9 group and 5.3% in the ABI≤0.9 group, a difference that is not statistically significant(p=0.68). These results suggest that while ABI≤0.9 is associated with an increased mortality risk, it does not significantly influence stroke recurrence rates,(table 4).

*Table 5. The utility of ABI in predicting mortality and recurrence in stroke patients.*

| OUTCOMES | AREA | SE | P-VALUE | 95% CI | | CUTOFF | SENS. | SPEC. |
|---|---|---|---|---|---|---|---|---|
| MORTALITY | 0.383 | 0.056 | 0.006 | 0.729 | 0.947 | ≤0.65 | 72.2 | 100 |
| RECURRENCE | 0.412 | 0.138 | 0.476 | 0.141 | 0.683 | ≤0.55 | 80.6 | 33.3 |

For ABI index as a predictor of mortality and stroke recurrence, the results are as follows:

The table presents the utility of ABI in predicting mortality and recurrence in stroke patients, with the area under the curve(AUC), standard error(SE), p-value, 95% confidence interval(CI), cutoff value, sensitivity(Sens.), and specificity(Spec.) for each outcome. ABI≤0.65 is a moderately sensitive and perfectly specific predictor for mortality, while ABI≤0.55 is a highly sensitive but less specific predictor for recurrence,(table 5; figures 3&4).

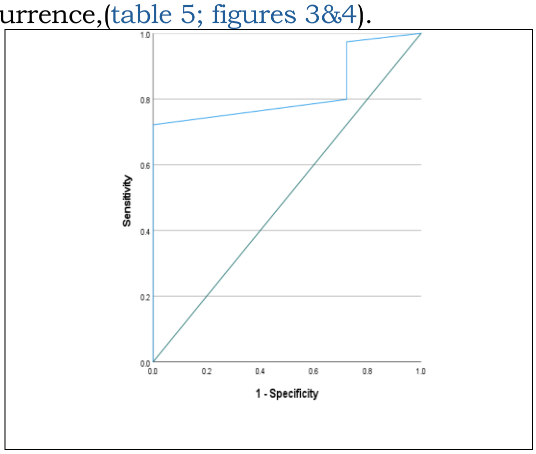


Figure 3. Six-month mortality prediction utilizing the ABI index.

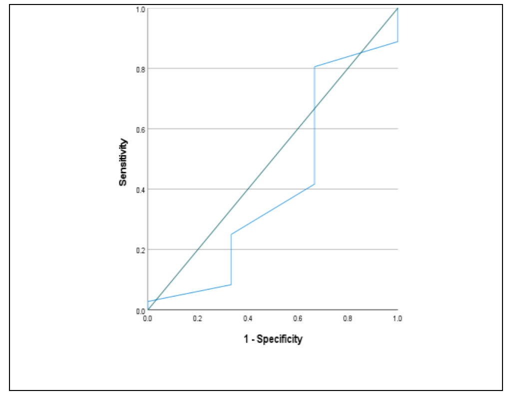


Figure 4. Six-month stroke recurrence prediction utilizing the ABI index.

Cases presentation:

Case (1):

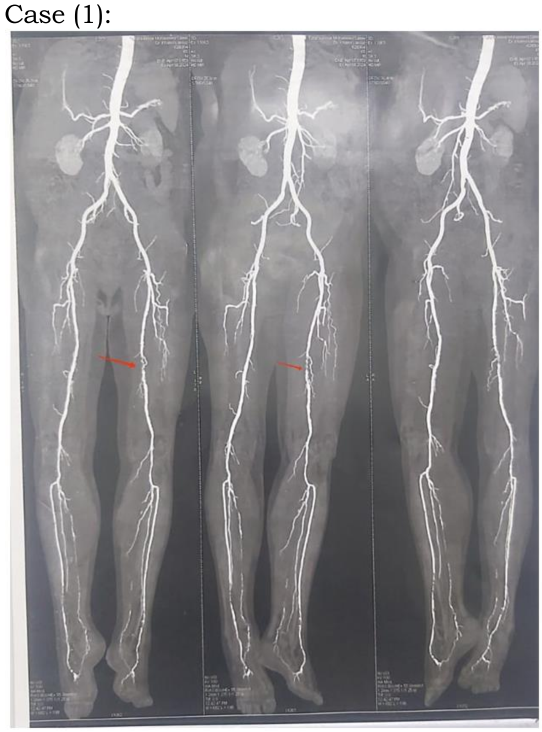

Figure 5. 67-year, male, presented with acute ischemic stroke(left superior MCA infarction), left calf pain, claudication CTA of both lower limbs showed left superficial femoral a. Stenosis.

Case (2):

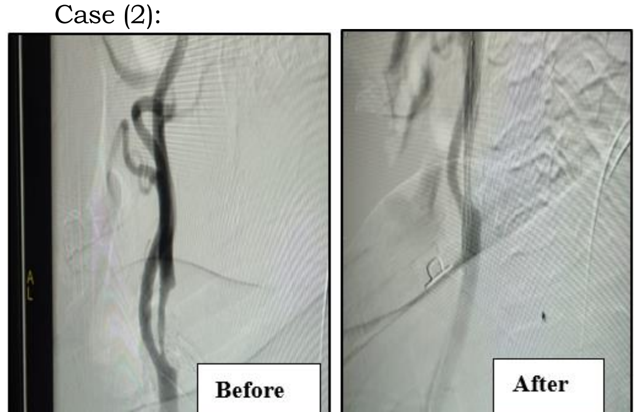


Figure 6. 56-year female, D, HTN, presented with acute ischemic stroke (left incomplete MCA

infarction), DSA showed left ICA stenosis 80 % and Balloon dilatation with stenting was done.

Case(3):

Figure 7. 76-year, male, D, HTN, smoker presented with acute ischemic stroke, History of chronic severe sole pain, foot ulcers, ischemic changes in both legs. CTA of both lower limbs showed bilateral stenosis of both femoral arteries.

## 4. Discussion

Our study found that the prevalence of PAD among stroke patients was 23.1%, while moderate to severe atherosclerosis was observed in 33.3%, indicating a significant prevalence of these conditions.

Our results are in line with those of the Systemic Risk Score Evaluation in Ischaemic Stroke Patients (SCALA) study (51% of patients) and the Polyvascular Atherothrombosis Observational Study (PATHOS) (33.5%), which both documented PAD as determined by ABI in patients with stroke or TIA; however, only 10% of these patients actually displayed symptoms of PAD.[5,6]

A prospective cohort study that followed stroke and TIA patients for an average of 2.1 years found that some of them had asymptomatic PAD (with an ABI < 0.9), which is consistent with our findings. A lower percentage of patients with asymptomatic PAD did not experience vascular events, according to the Kaplan-Meier curve (48% vs. 84%; P=0.0001). Pre- and post-confounders analysis showed a statistically significant association between asymptomatic PAD and composite vascular events (HR, 4.2; 95% CI, 1.9-9.3; P=0.0003) and stroke (HR, 6.5; 95% CI, 2.1-19.9; P=0.001), respectively.[7]

The present study reveals that DM and HTN were prevalent in both groups(overall, 74.4% and 76.9%, respectively), with no significant differences observed(p=1.00 and p=0.216, respectively). These findings are consistent with the understanding that both conditions are common comorbidities in populations at risk for vascular diseases, including PAD. The high prevalence rates in both groups suggest that these conditions are critical in the overall risk profile of the study population who presented with acute stroke, but may not differentiate PAD patients from non-PAD individuals in this context.

Research using multivariable Cox models to determine hazard ratios, population-attributable risk (PAR), and 95% confidence intervals (CIs) in a multiethnic urban population was in agreement with our results. The sample size was 3,298 people. Diabetes had a PAR of 19.5% (95% 12.4-26.5), whereas hypertension (HTN) contributing to stroke had a PAR of 29.9% (95% CI: 12.5-47.4).[8] These results align with our observation of high rates of HTN and diabetes among patients with acute stroke in our study population.

In the present study, the mean age was slightly higher in the PAD group(65.6±13.9 years) compared to the non-PAD group(62.7±8.2 years), but the difference was not statistically significant(p=0.42). While age is a recognized risk factor for PAD due to cumulative vascular damage, the lack of significance in this study may reflect the relatively small sample size or the influence of other confounding factors. Additionally, the study population consisted of stroke patients, which may have made age a common risk factor across both groups.

The carotid duplex findings did not reveal statistically significant differences between the PAD and non-PAD groups for either the right(p=0.26) or left carotid artery(p=0.31). ICA changes were more frequently observed in the PAD group(55.56% on the right, 55.56% on the left) compared to the non-PAD group(33.33% on the right, 36.67% on the left). However, these differences were not significant. These findings suggest that while carotid artery changes are common in individuals with vascular disease, their presence alone may not distinguish PAD patients in this cohort. This aligns with studies indicating that carotid atherosclerosis and PAD often coexist but are influenced by overlapping and independent pathophysiological mechanisms.[9]

Our results are in agreement with those of the Second Manifestations of Arterial Disease (SMART) study, which found that the prevalence of internal carotid artery stenosis increased by 50% in patients with PAD or a history of PAD. The study included 162 patients who were initially free of internal carotid artery stenosis, did not have cerebrovascular symptoms, and had not undergone a carotid endarterectomy. This subset of patients was chosen from the initial 600 participants in the SMART study.[10]

No statistically significant differences were seen between the groups in our study's echocardiographic data (p=0.53). There was no significant difference in the presence or absence of VHD, DD, IHD, and LVH between the two groups. The fact that such cardiac problems can manifest in both PAD and non-PAD patients demonstrates how atherosclerosis affects various vascular regions in stroke sufferers. Although not statistically significant, the fact that 11.11 percent of PAD patients had normal echocardiographic findings compared to 3.33 percent of non-PAD individuals suggests that PAD may interact with cardiac function in some way that needs to be explored further.

Although this study did not find any evidence of left ventricular dysfunction in outpatients with symptomatic PAD, previous research has shown that PAD is a strong predictor of clinically significant abnormalities on transthoracic echocardiograms (TTEs), such as this condition. Compared to patients without PAD (n=84), this was seen in patients with confirmed PAD (ABI≤0.9, n=120). Since our study only included stroke patients (with or without PAD), and since most of them had normal echocardiography results, we cannot draw any firm conclusions about the differences between the groups. Outpatients who were generally in better health were the subjects of the aforementioned investigation.[11]

Compared to non-PAD persons, 44.44% of PAD patients exhibited substantial atherosclerosis in the lower limb duplex, according to the present study. The association between the two was statistically significant (p<0.001). Similarly, the prevalence of moderate atherosclerosis was 55.56 percent in the PAD group compared to 1.00 percent in the non-PAD group. To the contrary, the PAD group did not exhibit any instances of moderate or nonexistent atherosclerosis. The results show that lower limb duplex imaging is useful for PAD diagnosis and that a significant feature of PAD patients is the degree of atherosclerosis.

This observation aligns with established evidence linking lower extremity atherosclerosis with PAD diagnosis and severity.[12]

Moreover, marked atherosclerosis in the lower limbs was significantly associated with mortality(p=0.006), with a higher proportion of deaths occurring among patients with severe atherosclerosis. This finding underscores the prognostic value of atherosclerosis severity in predicting stroke outcomes. Conversely, atherosclerosis severity was not significantly associated with recurrence(p=0.45), suggesting that other factors may play a more prominent role in stroke recurrence.

Our results are supported by multivariate models that account for cardiovascular disease risk factors. These models show that among 508 subjects (59 women and 449 men) from two San Diego, California, hospital vascular laboratories, there is a significant association between very low (<0.70) and low (0.70≤ABI<0.90) ABIs measured at visit 2 and an increased risk of death from all causes and CVD.[6]

ABI demonstrated significant predictive value for mortality, with an AUC of 0.383 and a cutoff value of≤0.65 yielding a sensitivity of 72.2% and specificity of 100%(p=0.006). This highlights ABI’s utility as a prognostic marker in identifying high-risk patients. However, ABI was not a significant predictor of recurrence(p=0.476), suggesting its limited role in this context.

A retrospective analysis of 2,159 patients with suspected PAD who had ABI measured by photoplethysmography found statistically significant differences in mortality after an average of 39 months of follow-up, which is in line with the current results. The abnormal ABI group had the greatest mortality rate of 65.8% out of 576 deaths (26.7%), compared to 16.0% in the normal ABI group (p<0.001). With a cut-off of 0.9, patients with aberrant ABI were found to have an independent association between PAD and total mortality (OR:2.21; 95% CI:1.01-4.85) and cardiovascular mortality (OR:4.90; 95% CI:1.50-16.04).[13]

### *4. Conclusion*

This study highlights the complex interplay of factors influencing PAD and its association with stroke outcomes. Smoking, ABI, and lower limb duplex findings emerged as significant differentiators for PAD, while NIHSS, lower limb duplex, and ABI were the strongest predictors of mortality. The results underscore the importance of comprehensive risk assessment and integrated management in improving outcomes for PAD patients..

## Disclosure

The authors have no financial interest to declare in relation to the content of this article.

## Authorship

All authors have a substantial contribution to the article

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## Conflicts of interest

There are no conflicts of interest.

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