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# The use of ankle brachial pressure indices in a cohort of black African diabetic patients



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ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> Ankle brachial index (ABI) Diabetes Peripheral arterial disease (PAD) Claudication Screening	<i>Background:</i> Peripheral arterial disease is very common in patients with diabetes, but it remains grossly under- recognized in this type of patients. Ankle brachial index (ABI) is a simple, non-invasive and reproducible method for detection and improving risk stratification. However, the sensitivity appears to be lower in diabetic patients and, false 'high' readings occur because of the arterial calcification of the vessel media which render the vessels incompressible. <i>Materials and methods:</i> The study evaluated the prevalence of a low ABI < 0.9 in diabetic patients in a hospital- based cross sectional observational study. The study has been registered. <i>Results:</i> The prevalence of peripheral arterial disease in diabetics with ABI < 0.9 was 18%. The majority (77%) of responders were asymptomatic with mild PAD (ABI 0.7–0.9). Age > 60 years, hypertension (systolic BP > 140 mmHg) and presence of foot ulcer were identified as independent risk factors. 22 participants (4.4%) of the 500 had ABI greater than 1.3 but were excluded in the analysis. <i>Conclusion:</i> The prevalence of PAD in diabetics measured by the ABI index was low and the majority in our setting had mild PAD and were asymptomatic. ABI could be used in patients with diabetes, but values should be interpreted with precision, according to the clinical situation as higher values are common.

#### 1. Introduction

It is estimated that 170 million individuals have diabetes in the world and it is projected to rise to 360 million by 2030 [1]. Atherosclerotic vascular disease is probably present in all patients with long duration diabetes, and, is responsible for up to 70% of deaths in noninsulin dependent diabetes mellitus (NIDDM) [1,2]. In addition to diabetes accelerating atherosclerosis, the premenopausal protection from vascular disease is lost in female diabetic patients and peripheral vascular disease may be 20 times more common in diabetes [2] Although PAD is very common in patients with diabetes, it remains grossly under-recognized in this population because neuropathy masks the pain of intermittent claudication [3]. PAD is associated with a high risk of lower extremities amputation and an important marker of generalize atherosclerosis. It has a linear relationship with coronary artery disease [4]. The same risk factors also operate and include smoking, hypertension, dyslipidaemia, abnormal fibrinolysis and altered platelet function [5,6]. Doppler-derived arterial pressure measurements should confirm the presence of arterial disease. The Ankle brachial index (ABI) is the ratio of the ankle systolic pressure to the brachial systolic pressure

which is 1.0 or more in normal subjects [7,8]. A low ABPI also indicate a significantly raised relative risk of death from cardiovascular disease [9]. However, the degenerative dystrophic calcification of the media especially common in the major lower limb arteries of the elderly and in patients with diabetes cause false 'high' readings. In these patients toe pressure measurements may be of value [10].

Africa has the lowest rate of diabetes but has the highest rate of undiagnosed patients and thus complications. The prevalence of diabetes is 5.7% in urban Cameroon, W/Africa, but 70% of the population remain undiagnosed [11,12]. In addition, the progression of asymptomatic peripheral arterial disease to claudication has been less widely studied. In the Edinburgh Artery study 15% of those with major, and 7% of those with minor asymptomatic disease developed intermittent claudication in a five-year period [13]. Despite the 'false' high readings with diabetics, the objective of our study was to evaluate the relationship between ABI and cardiovascular (CVS) risk factors in a hospital cohort of adult patients with diabetes. The aim was to evaluate the prevalence and implications of a low ABI < 0.9 in an African diabetic population, and the associated risk factors.

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#### 2. Methods

A hospital-based cross-sectional observational study of diabetic patients aged 20 years and above, was carried out in the National Centre for diabetes and hypertension of the Yaounde Central hospital in Cameroon, W/Africa between January and March 2016. The minimum sample size was obtained from the Cochrane formula [14]:  $(N = z^2 p(1 - z^2))$  $p)/d^2$ ) where n is estimated sample size; z is the standard normal variate and for 95% confidence interval it is 1.96; p is the prevalence of PAD in patients with CVS risk factors at the Yaounde General Hospital 2014 reported by Menangal et al. [15] as 16.7%; d the tolerated sampling error (5%). Using the above formula, n (1.96)2 (0.167)(0.833)/ (0.05)2 the minimum sample size was 214 diabetic patients. A convenient consecutive non-probability sampling method was used to enroll those who met the inclusion criteria for the study. The inclusion criteria were 1) patients above 20 years with diabetes and being followed up for at least 12 months, 2) those who consented to the study. The exclusion criteria were 1) those who had deep vein thrombosis (DVT) diagnosed by a positive Homan's sign or a history of DVT, 2) patient who had undergone vascular surgery to lower limbs, 3) those with diagnosed vascular disease, 4) severe terminally ill patients who could not tolerate the ABI measurement procedures, 5) those who did not consent to the study. Of the 510 diabetic patients approached, 7 patients who denied consent and 3 deep vein thrombosis (DVT) patients were excluded from the study. Ankle Brachial pressure Index (ABI) measurements were done for all patients. To measure the Doppler ankle pressure, a sphygmomanometer cuff placed around the ankle was inflated to a suprasystolic level and then slowly deflated. The onset of blood flow detected by the Doppler probe equals the systolic blood pressure. Both the posterior tibial and dorsalis pedis arteries were interrogated and the highest pressure noted. If neither was heard a search was made for the peroneal artery behind the fibula or around the lateral malleolus. ABI values were categorized into three groups; (a) those with ABI < 0.9 were considered as having PAD, (b) those with ABI > 0.9but < 1.3 were considered as having normal ABI and thus no PAD, (c) those with ABI > 1.3 were considered as having incompressible vessels and excluded from the analysis as required further investigations such as the toe-brachial index. 22 (4.4%) patients with ABI > 1.3 were excluded from further analysis. 478 patients with diabetes were administered a pretested questionnaire containing socio-demographic, clinical and paraclinical characteristics. The mean age of participants was 59 years and majority were of the female gender (65%). 99% of participants had type 2 diabetes and the mean duration of diabetes was 8 years. Cardiovascular risk factors were evaluated in all participants. Fasting blood sugar and urinalysis for proteinuria were performed. HbA1c, creatinine, HDL-cholesterol, LDL-cholesterol, total cholesterol and triglyceride levels were noted from the patients' files. The Edinburgh's Claudication Questionnaire (ECQ) [16] was administered to those with ABI < 0.9 and 106 patients responded (Table 3). A data entry form was created in EPI-INFO version 7.0. The data was analyzed using 95% confidence interval with a P-value of 0.05 considered statistically significant. The study has been registered.

# 3. Results

Using a cut of value of ABI < 0.9, out of 478 participants in the analysis, 86 had ABI < 0.9 giving a prevalence of 18%. Of the 106 who responded to the Edinburgh claudication questionnaire 77% were asymptomatic with mild PAD (ABI 0.7–0.9). 23% reported claudication (Table 3) (14% below the knee, 6% above the knee (thigh) and 3% both above and below the knee). 37 (22%) males and 49 (16%) females had PAD as determined by the ankle-brachial index (ABI). In the bivariate analysis using a simple Chi square, PAD was associated with aging (p = 0.033), ethnicity (P 0.04), duration of diabetes (p = 0.006), past history of hypertension (p 0.009), history of MI (p = 0.022), presence of foot ulcers (p = 0.004), high systolic blood pressure (p = 0.011), visceral

 Table 1

 Bivariate analysis of socio-demographic risk factors for PAD.

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	PAD n (%)	NON-PAD n (%)	TOTAL	P-Value
Age				
> 60	59 (68.60)	203(51.79)	262(54.81)	0.033
< 60	27(31.40)	189(48.21)	216(45.19)	
Gender				
Male	37 (43.02)	128(32.65)	165(34.52)	0.619
Female	49 (56.98)	264(67.35)	313(65.48)	
Occupation				
Unemployed	67 (77.91)	295(75.26)	362(75.10)	0.809
employed	19(22.09)	97(24.74)	116(24.90)	
Educational level				
High	52(60.47)	200(51.02)	252(52.72)	0.820
Low	34(39.53)	192(48.98)	226(47.28)	
Ethnicity				
Coastal tropical forest people	8(9.30)	25(6.38)	33(6.9)	0.040
Others	78(90.70)	367(93.62)	445(93.10)	

Bold indicates statistically significant p-value.

#### Table 2

Logistic regression of risk factors of PAD.

Risk Factor	p-value	95% Confidence interval	Odds Ratio
Age( $\geq 60$ vs. < 60 years)	0.004	1.23–3.34	2.03
Ethnicity coastal tropical forest people vs. Others	0.625	0.4–3.14	0.083
Duration of Diabetes ( $\geq 10$ vs. < 10 years)	0.234	1.01-5.21	1.70
Past History of Hypertension (Yes vs No)	0.737	3.24–10.52	4.42
Myocardial Infarction (Yes vs No)	0.999	1.67-8.21	2.3
Presence Of Foot Ulcer(s) (Yes vs No)	0.0002	2.29-63.13	12.03
Taking Antiplatelet drugs (Yes vs No)	0.084	0.32-2.11	0.54
Systolic BP(mmHg) ( $\geq$ 140 vs < 140 mmHg)	0.005	1.21-3.16	1.96
Visceral Obesity (Yes vs No)	0.761	1.04-3.92	2.10
Creatinine (> 1.2 vs $\leq$ 1.2 mg/dL)	0.778	0.21-3.1	0.65
Proteinuria (Yes vs No)	0.061	1.42-4.60	2.55
HDLc ( $< 50 \text{ vs} \ge 150 \text{ mg/dL}$ )	0.899	0.64-1.32	0.92
LDLc ( $> 100 \text{ vs} \le 100 \text{ mg/dL})$	0.498	2.23-9.52	5.10

Bold indicates statistically significant p-value.

#### Table 3

The Rutherford classification of participants with PAD.

Grade	Categories/ stages/ABI	Description	Number of participants	Percentage (%)
0	0 (ABI 0.91–1.3)	asymptomatic	66	76.64
1		Claudication	20	23.26
	1(ABI	Mild(> 200 m)	16	80
	0.70-0.9)			
	2(ABI	Moderate	4	20
	0.40-0.69)	(100–200 m)		
	3(ABI < 0.4)	Severe (< 100 m)	0	0
II	4	Rest pain	0	0
III	5	Minor tissue loss	0	0
IV	6	Major tissue loss	0	0

obesity (p = 0.001), proteinuria (p= 0.001), low levels of HDLc (p < 0.001) and high levels of LDLc (p = 0.022) (Tables 1, 4–7). In multivariate analysis using logistic regression, PAD was independently associated with age > 60 years (p = 0.004), OR 2.03, CI: 1.24–3.34), presence of foot ulcers (p = 0.002, OR 12.03, CI: 2.29–63.13) and systolic BP > 140 mmHg (p = 0.005, OR 1.96, CI: 1.21–3.16) (Table 2). 22 (4.4%) participants of the 500 had ABI greater than 1.3 and were excluded in the analysis.

#### Table 4

Bivariate analysis of clinical characteristics of PAD.

	PAD n(%)	No PAD n(%)	TOTAL	P- Value
Past diagnosis of h	ypertension			
YES	56(65.12)	216(55.10)	272(56.90)	0.009
NO	30(34.88)	176(44.96)	206(43.10)	
Dyslipidemia				
YES	20(23.26)	69(17.60)	89(18.62)	0.714
NO	66(76.74)	"é"(82.40)	389(81.38)	
CKD				
YES	5(5.84)	13(3.32)	18(3.77)	0.158
NO	81(94.19)	379(96.65)	460(96.32)	
HIV				
POSITIVE	1(1.16)	9(2.30)	10(2.09)	0.665
Neg/no idea	85(98.84)	383(97.70)	468(97.91)	

#### Table 5

Bivariate analysis of clinical characteristics of PAD continued.

	PAD n(%)	No PAD n(%)	TOTAL	P- Value
SMOKING				
smoked	16(18.60)	47(11.99)	63(13.18)	0.752
Never smoked	70(81.40)	345(88.01)	415(86.82)	
Chewing tobacco				
Yes	4(4.65)	10(2.55)	14(2.93)	0.944
No	82(95.35)	382(97.45)	464(97.07)	
Alcohol Abuse ( $> 2$	1 units for males	or $> 14$ units for	female)	
Yes	7(8.14)	15(3.83)	22(4.60)	0.364
No	79(91.86)	377(çè.17)	456(93.40)	
Oral contraception				
Yes	10(11.63)	29(7.40)	39(8.16)	0.318
No	76(88.37)	363(92.62)	439(91.84)	
Myocardial infarctio	n			
Yes	4(4.65)	3(0.77)	7(1.46)	0.022
No	82(95.35)	389(99.23)	471(98.54)	

#### Table 6

Bivariate analysis of clinical characteristics of PAD continued.

	PAD n(%)	No PAD n(%)	TOTAL	P- Value
Stroke				
Yes	5(5.81)	3(0.77)	8(1.67)	0.885
No	81(94.19)	390(99.23)	470(98.33)	
Presence of	of foot ulcers			
Yes	5(5.81)	2(0.51)	7(1.46)	0.041
No	81(94.19)	390(99.49)	471(98.54)	
On Antiple	atelet drug			
Yes	16(18.60)	27(6.89)	43(9.0)	0.001
No	70(81.40)	365(93.11)	435(91.0)	
Family his	tory of PAD			
Yes	3(3.49)	12(3.1)	15(3.14)	0.764
No	83(96.51)	308(96.9)	463(96.86)	

## 4. Discussion

The study demonstrated a prevalence of PAD in 18% of a large cohort of black African diabetic patients using Doppler Ankle brachial index (ABI) measurements. 99% of participants had type 2 diabetes and the mean duration of diabetes was 8 years. This was closely similar to a prevalence of 16.7% in patients with cardiovascular risk factors reported by Menanga et al. in the same setting although just 5 out of the 42 participants were diabetics [15]. Studies in Uganda and Nigeria on diabetic patients with advanced age showed a prevalence of 39% and 52.5% respectively [17,18]. In this study the majority (77%) were asymptomatic with mild PAD. Age > 60 years, hypertension (systolic BP > 140 mmHg) and presence of foot ulcer were identified as independent risk factors. Several studies have shown that ABI has a sensitivity of 95% and specificity of 100% [19]. A positive predictive value of 90%, a negative predictive value of 99% and an overall

Table 7
Bivariate analysis of clinical characteristics of PAD Continued.

	PAD n(%)	No PAD n(%)	TOTAL	P- Value
Urinalysis (Pre	sence of proteinur	ia)		
Yes	31(36.05)	77(19.64)	108(22.59)	0.001
No	55(63.95)	315(80.36)	370(77.41)	
Total Cholester	ol (mg/dL)			
> 200	12(13.95)	49(21.40)	61(19.37)	0.183
$\leq 200$	74(86.05)	180(78.60)	254(80.63)	
HDLc(mg/dL)				
> 50	13(15.12)	114(49.78)	127(40.32)	< 0.001
≤50	73(84.88)	115(50.22)	188(59.68)	
LDLc(mg/dL)				
> 100	29(33.72)	110(48.06)	139(44.13)	0.022
≤100	57(66.28)	119(51.94)	176(55.87)	
TG(mg/dL)				
> 150	13(15.12)	40(12.47)	53(16.83)	0.619
≤150	73(84.88)	189(12.47)	262(83.17)	

accuracy of 98% favour the use of ABI as a screening test or a diagnostic tool in non-diabetics [20-23]. If Doppler ankle pressures are normal in a patient with a good history of claudication, the sensitivity of the test is increased after exercise on a treadmill for 1 min [24]. Unfortunately, it remains a problem in the diabetic patient with evidence of both arterial occlusive disease and neurological symptoms. In addition, apart from being diagnostic, ABI values reflect the severity of PAD (Tables 3 and 8) [7,8,20,25], making it a widely used marker for the presence and progression of PAD in major cardiovascular trials [26-32]. Normal subjects should have an ABI of 1.0 or more, whereas in claudicants it is usually less than 0.9. Critical ischaemia has been defined by the European working group as persistent rest pain for more than 2 weeks and/ or ulceration or gangrene, plus an ankle systolic pressure of less than 50 mmHg (ABI < 0.5) [33] (Tables 3 and 8). Calcification of the arterial media which is common in diabetes, may lead to falsely elevated pressures greater than 1.3 due to incompressible arteries. However, an experienced operator will be alerted by the damped flow signals if proximal disease is present (waveform analysis) [34]. Toe (digital) arteries are less likely to be affected by calcification but require small cuffs and are more difficult to measure routinely. However, a toe-brachial index (TBI) measurement may be of value, and toe and/or oxygen pressures have been shown to enhance the detection of critical ischaemia [8]. The prevalence of a low or falsely elevated (pathological ABI) is high in diabetic subjects with symptomatic peripheral vascular disease and frequently associated with diabetic neuropathy (possibly ischaemic in cause) and chronic renal failure (CRF) [35-38] It relates with age, duration of diabetes and the presence of vascular disease in another vascular bed [22,37-39]. In addition, an ABI > 1.3 in CRF is frequently associated with hyperparathyroidism, suggesting a possible role of the disturbances in calcium and phosphorus metabolism in the occurrence of media calcification [38]. PAD is strongly associated with similar risk factors for other cardiovascular diseases. 70% of PAD are associated with old age (> 60 years), hypertension, smoking, diabetes, dyslipidemia, chronic renal disease, oral contraception, alcohol, HIV as demonstrated in this study (Tables 2, 4-7) [39,40]. The statistical significance of ethnicity may indicate a contribution from demography and genetics to PAD. Because of the effect of the duration of diabetes, it would have been interesting to group these patients according to the years of evolution of the disease and, also contrast with type 1 diabetes.

Table 8	

The Fontaine classification of peripheral arterial disease.

Fontaine 1	Asymptomatic lower limb arterial disease
Fontaine IIa	Claudication > 200 m
Fontaine IIb	Claudication < 200 m
Fontaine III	Rest pain
Fontaine IV	Ulceration and/or gangrene

Although diabetes accelerates atherosclerosis, the distribution of vascular disease in the lower limb is thought to be different from the non-diabetic. There is more frequent involvement of vessels below the knee affecting the popliteal trifurcation and tibial arteries demonstrated as 62% in this study [41]. The distal profunda artery is also often affected which reduces the ability for collaterals to develop around the more common superficial femoral artery occlusion [42]. Despite these problems revascularization procedures are frequently successful, although a more distal anastomosis may be required [43,44]. Despite advances in non-invasive investigations, arteriography (which must include pedal arteries) remains the gold standard both for diagnosis and planning of treatment. Care is, however, needed with contrast media in patients with renal impairment.

### 4.1. Study limitations

The exclusion in the analysis of 22 (4.4%) participants of the 500 who had ABI greater than 1.3 would have eliminated further patients with PVD. Toe-brachial indices may have included these. The 'questionnaire' method of assessing claudication could be subjective and a detailed history and examination paying particular attention to the cardiovascular system is essential. The distribution of vascular disease cannot be determined by symptoms alone and require vascular imaging. Most patients with claudication are middle-aged or elderly and often have coexisting degenerative musculoskeletal disease such as hip or knee osteoarthritis which can mimic claudication. Some medications such as beta blockers for hypertension may exacerbate claudication. Symptoms of painful diabetic neuropathy are sometimes mistaken for intermittent claudication [45]. In addition, probably because neuropathy may mask the pain, claudication which is the hallmark of PAD is not commonly manifested in diabetics. Only a third of diabetic patients with PAD would report intermittent claudication as corroborated in this study [1-6].

### 5. Conclusions

Ankle brachial index (ABI) is a non-invasive vascular screening test of large vessel, peripheral arterial disease. The prevalence of peripheral arterial disease (PAD) in diabetics with ABI < 0.9 was 18% and the majority (77%) were asymptomatic with mild PAD. This is consistent with the known limitations of the use of ankle brachial indices in assessing peripheral vascular disease in diabetic patients. However, ABI can still provide useful information in patients with diabetes if values are interpreted according to the clinical situation as higher values are common. Age > 60 years, hypertension (systolic BP > 140 mmHg) and presence of foot ulcer were identified as independent risk factors.

### **Ethical approval**

The research study was registered prospectively by the University of Douala, Cameroon. The work was approved by the ethical committee of the University of Douala, Cameroon and subjects gave informed consent to the work.

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None.

# Author contribution

Elroy Patrick Weledji carried out the study design, data analysis, interpretation, writing of paper and literature search; Neville Telelen Alemnju carried out the study design, data collection, data analysis and literature search; Christophe Nouediou developed the study concept, design and data collection. All authors have read and approved the final manuscript.

# **Conflicts of interest**

The author has no conflict of Interest.

#### Research registration number

Research Registry UIN 3859.

# Guarantor

Professor Christophe Nouediou, National Centre for Diabetes and hypertension, Yaounde, Cameroon; Professor Marcelin Ngowe Ngowe, Dean of the faculty of Health Sciences, University of Buea.

### Consent

The work was approved by the ethical committee of the University of Douala, Cameroon and subjects gave informed consent to the work.

# Contributors

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#### Provenance and peer review

Not commissioned, peer reviewed.

# List of abbreviations

ABI	Ankle Brachial Index
PAD	Peripheral Arterial Disease
HDLc	High Density Lipoprotein cholesterol
LDLc	Low Density Lipoprotein cholesterol
ECQ	Edinburgh's Claudication Questionnaire
MI	Myocardial Infarction

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2018.09.009.

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