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Lower Extremity Arterial Disease in Patients with Type 2 Diabetes: Prevalence and Associated Factors at the Libreville University Hospital Center

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Abstract

Introduction: Lower extremity arterial disease in diabetic patients has distinct characteristics. **Objectives**: To study the hospital frequency of lower extremity arterial disease and identify associated factors in diabetic patients at the Libreville University Hospital Center (CHUL). **Materials and Methods**: This was a cross-sectional study conducted from July 1, 2023, to January 31, 2024, in the endocrinology department of the CHUL. All patients with type 2 diabetes over the age of 18 admitted to this department, regardless of the reason for hospitalization, who provided informed consent, were included. Socio-demographic data and cardiovascular risk factors were recorded. Personal and family cardiovascular history and functional symptoms were investigated. The physical examination included measuring blood pressure, heart rate, and the ankle-brachial index in all patients. **Results**: A total of 219 patients were included, of whom 75 had lower extremity arterial disease, representing a prevalence of 34.24%. It was compensated in 28 cases (37.33%) and decompensated in 39 patients (52%). In eight cases (10.67%), there was critical chronic ischemia. Cardiovascular risk factors associated with diabetes were physical inactivity (89.5%), hypertension (55.25%), overweight (49.77%), obesity (22.84%), and smoking (10.04%). In multivariate analysis, only hypertension (OR = 2.09; 95% CI: 1.05 - 4.17; p = 0.035) and LDL cholesterol (OR = 2.75; 95% CI: 1.10 - 6.85; p = 0.03) were significantly associated with lower extremity arterial disease in diabetics at the University Hospital of Libreville. **Conclusion**: Lower extremity arterial disease is common in diabetic patients at the University Hospital of Libreville. It is often asymptomatic, thus requiring systematic screening.

Keywords

Lower Extremity Arterial Disease, Diabetes, Hypertension, Ankle-Brachial Index, Gabon

1. Introduction

As a specific manifestation of systemic atherosclerosis, lower extremity arterial disease (LEAD) can increase cardiovascular events like myocardial infarction and stroke by 20% over five years, and overall mortality by 30% [1]. Thus, it is associated with a high cardiovascular risk [2], sharing the same cardiovascular risk factors (CVRF) as cerebrovascular and coronary artery diseases [3] [4] [5] [6]. In diabetic patients, LEAD has unique pathogenetic, clinical, and therapeutic characteristics [7]. It is two to four times more common than in the general population [2] [8], and the mechanism underlying the lesions in diabetic LEAD might differ from that of non-diabetic LEAD. Diabetes itself may play a different role than other CVRFs [9]. Every one percent increase in HbA1c raises the risk of LEAD, microvascular complications, and major amputations by 28% [10] [11]. Furthermore, in diabetic LEAD, the lesions tend to be more distal, often below the knees, while lesions related to smoking are typically more proximal, affecting the aorto-iliac and femoral arteries [11] [12]. Among patients with critical limb ischemia, where 30% are expected to have a leg amputation, a high prevalence of LEAD and diabetes association is observed, exceeding 50% [13] [14]. Early diagnosis is thus the key to a favorable outcome for this pathology, which significantly reduces patients' quality of life [15]. Peripheral neuropathy might also contribute to delayed diagnosis and advanced-stage treatment, emphasizing the need for systematic screening in this patient profile. At the Libreville University Hospital Center (CHUL), which houses the country's primary endocrinology department, the rising incidence of diabetic foot and amputations poses a public health issue. LEAD is associated with diabetic foot in almost 50% of cases[16] [17], suggesting the need for screening among diabetic patients in this department. The aim of this work was to identify the profile of type 2 diabetic patients with LEAD to encourage systematic screening for early treatment of the disease.

2. Methodology

This was a cross-sectional study conducted over a period of seven months, from

July 1, 2023, to January 31, 2024, in the endocrinology department of the University Hospital of Libreville (CHUL). This is the national reference center for diabetes and endocrine pathologies. Patients are admitted here for significant diabetic imbalances complications related to diabetes, including vascular, infectious, neurological complications, and other endocrinopathies.

During the study period, all patients over the age of 18 admitted to this department, regardless of the reason for hospitalization, with type 2 diabetes were included after informed consent. Socio-demographic data (age, sex, occupation), cardiovascular risk factors (CVRFs) and their duration were recorded, such as hypertension, smoking, physical inactivity, and obesity. Personal and familial cardiovascular history (cardiovascular heredity) were also studied. Familial heredity included cases of myocardial infarction or sudden death in a father or brother before the age of 55 or a mother or sister before 65, as well as cases of stroke before the age of 45. Functional symptoms sought included pain or muscle cramps in the lower limbs, erectile dysfunction, postprandial abdominal pain, palpitations, dyspnea at any stage, and angina. Erectile dysfunction explained to patients using the more accessible term "male impotence," was evaluated by checking for a recurrent difficulty in achieving or maintaining a full erection sufficient for sexual intercourse. This question was asked twice, in the middle and at the end of the questionnaire, respecting the patient's privacy. Erectile dysfunction was confirmed only if both answers were consistent. Physical inactivity was determined by counting the number of sessions per week of at least moderate-intensity physical activity (PA) lasting at least 30 minutes. It was considered when this number was less than five [18]. The duration of diabetes was determined from the date of the first consultation with abnormal fasting or postprandial blood glucose. Anti-diabetic treatment prior to hospitalization was then recorded. Hypertension was defined as blood pressure ≥140/90 mmHg [19]. Smoking was quantified in package-year. Body mass index (BMI) was calculated after measuring weight and height. The cardiovascular physical examination mainly included blood pressure (BP), heart rate (HR), and ankle-brachial index (ABI) measurements in all patients. ABI was performed using a Doppler for vascular auscultation with an 8 MHz probe, all from SPENGLER, an aneroid sphygmomanometer, and a stethoscope. The 2017 joint recommendations of the European Societies of Cardiology and Vascular Surgery for the diagnosis and treatment of peripheral arterial diseases were followed for the ABI procedure and interpretation [15]. Thus, LEAD was identified based on ABI interpretation. Data were collected by a seventh-year medical student trained in ABI measurement, with a one-month pilot phase where all procedures performed by the student were reviewed for correction. This successful pilot phase with almost 98% validated tests allowed the work to proceed. All doubtful procedures (hard to perform or interpret) were reviewed by a senior physician. The Leriche and Fontaine classification, a clinical examination-based estimate of LEAD severity, was performed only for patients diagnosed with LEAD. An ABI between 0.75 and 0.90 was considered well compensated, between 0.4 and 0.75 poorly compensated or decompensated, and below 0.4 indicated severe impact [20].

The laboratory assessment included glycated hemoglobin (HbA1c), glomerular filtration rate (GFR), microalbuminuria by quantitative measurement, uric acid, and lipid profile: total cholesterol (Total-C), LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), and triglycerides (TG). This evaluation aimed to investigate other CVRFs, especially for assessing micro and macrovascular complications. The investigator focused on the therapeutic protocol used before patients' admission to hospitalization.

The Kobocollect software was used for data collection. Data completeness and consistency were checked daily, then entered and analyzed with the STATA 11 software. First, the distribution of the study population was described. Quantitative variables with a normal distribution were presented with their mean and standard deviation. Asymmetric variables were presented with their median and interquartile range (IQR). Percentages were calculated for qualitative variables. Subsequently, a bivariate analysis with logistic regression was performed to analyze the relationship between LEAD, a binary variable (Presence or Absence), and each of the following independent variables. This analysis aimed to identify associations between LEAD occurrence and CVRFs, their duration, and some cardiovascular personal history (like cerebrovascular accidents, coronary disease, heart failure, and cardiovascular heredity). Associations with some biological parameters like HbA1c, GFR, microalbuminuria, uric acid, lipid profile, and LEAD presence were also investigated.

Variables with a p-value less than 10% in bivariate analysis were introduced into a stepwise ascending multivariate regression model. Variables with a p-value greater than or equal to 5% were gradually eliminated until a final model with only variables with a p-value less than 5% was obtained.

3. Results

A total of 219 patients were included, with an average age of 57 ± 11 years, ranging from 28 to 88 years. The sex ratio was one. The proportions of different age groups were: ≤49 years (25.11%), between 50 and 70 years (61.64%), and >70 years (13.25%). The employment status distribution was as follows: public sector workers (20.55%), private sector workers (14.16%), laborers (10.5%), retirees (29.22%), and unemployed (25.57%). CVRFs associated with diabetes were physical inactivity (89.5%), hypertension (55.25%), overweight (49.77%), obesity (22.84%), and smoking (10.04%). The history of smoking was less than ten years in ten patients and over ten years in eleven patients. The history or characteristics of diabetes in the study population are summarized in **Table 1**. Six patients (2.78%) had a history of heart failure. The frequency of symptoms indicative of LEAD was as follows: muscle cramps in the lower limbs (32.78%), lower limb pain (16.44%), and impotence (11.26%). Angina (0.45%), palpitations (1.83%), and effort dyspnea (4.13%) were associated symptoms. The average systolic and diastolic blood pressures were 135.5 ± 18.5 mmHg and 80 ± 12.5 mmHg, respectively, and the average heart rate was 80 ± 13 bpm.

Table 1. History of diabetes in the diabetic population at the University Hospital of Libreville from July 2023 to January 2024.

	Number	Percentage (%)
Diabetes Duration		
<10 years	139	63.47
≥10 years	80	36.53
Associated CVRFs		
Sedentariness	196	89.50
Hypertension (HTA)	121	55.25
Overweight	109	49.77
Obesity	50	22.84
Smoking	22	10.04
High LDL	47	21.46
History of Stroke	12	5.5
History of Acute Coronary Syndrome (ATCD SCA)	3	1.41
Cardiovascular Heredity	71	33.02
Therapeutic		
Untreated	45	20.56
Insulin	46	21
Oral Antidiabetic Drugs (OAD)	106	48.40
Insulin + OAD	22	10.04
Glycemic Control (< 6.5%)		
<6.5	1	1.46
6.5 - 7	10	4.57
7.0 - 9	56	25.57
9.0 - 12	133	60.73
>12	19	8.67
Microvascular Impact GFR (ml/min)		
<30	8	3.65
30 - 60	16	7.30
60 - 120	133	60.73
>120	62	28.32
Microalbuminuria (mg/24h)		
<30	165	75.34
30 - 300	54	24.66
>300	0	0

LDL: Low-density lipoprotein-cholesterol; HbA1c: Glycated hemoglobin; GFR: Glomerular filtration rate; CVRFs: Cardiovascular risk factors.

LEAD was found in 75 patients, representing a prevalence of 34.24%, compensated in 28 cases (37.33%), and decompensated in 39 patients (52%). In eight cases (10.67%), there was critical chronic ischemia and media calcification in 39 patients (17.81%). The average ABI was 1.12 ± 0.94 on the left and 1.07 ± 0.71 on the right. Based on the affected limbs, ABI was abnormal in the left and right lower limbs in eight cases (10.67%) each, and bilateral involvement in 59 patients (78.67%). The Leriche and Fontaine classification of the LEAD population found 77.33% of patients at stage I (asymptomatic), 9.33% at stage II (intermittent claudication), 4.00% at stage III (decubitus pain), and 9.33% at stage IV (partial gangrene, ischemic ulcer with diffuse distal ischemia).

In bivariate analysis, a relationship was found between LEAD and various factors summarized in **Table 2**. Eight factors or variables were considered, including diabetes duration, anti-diabetic treatment, hypertension, physical activity, HbA1c, uric acid, LDL cholesterol, and total cholesterol. Variables with a p-value less than 10% in bivariate analysis were introduced into a stepwise ascending multivariate regression model. Variables with a p-value greater than or equal to 5% were gradually eliminated until a final model with only variables with a p-value less than 5% was obtained. Thus, in the final model, only hypertension and LDL cholesterol were associated with the occurrence of LEAD.

Table 3 presents the final model of factors associated with LEAD at CHU of Libreville.

Table 2. Bivariate analysis to identify factors associated with LEAD in diabetic patients at CHU of Libreville from July 2023 to January 2024.

	AOMI		OR	95% CI	p-value
	Yes	No			
Tobacco					0.487
Yes	9 (40.91)	13 (59.09)	1.37	0.56 - 3.38	
No	66 (32.50)	131 (66.50)	1	Reference	
Tobacco Duration					1.000
More than 10 years	5 (45.45)	6 (54.55)	1.14	0.42 - 3.08	
Less than 10 years	4 (40.00)	6 (60.00)	1	Reference	
Diabetes Duration					0.0003
More than 10 years	40 (50)	40 (50)	2.97	1.66 - 5.32	
Less than 10 years	35 (25.18)	104 (74.82)	1	Reference	
Anti-diabetes Treatment					0.011
Untreated	11 (24.44)	34 (75.56)	1	Reference	
Insulin	24 (52.17)	22 (47.83)	3.37	1.38 - 8.23	
Oral Anti-diabetic (OAD)	32 (30.19)	74 (69.81)	1.34	0.61 - 3.06	
OAD + Insulin	8 (36.36)	14 (63.64)	1.77	0.59 - 5.32	

Continued

Hypertension					0.0002
Yes	55 (45.45)	66 (54.55)	3.25	1.77 - 5.97	
No	20 (20.41)	78 (79.59)	1	Reference	
Physical Activity					0.034
Yes	3 (13.04)	20 (86.96)	0.36	0.12 - 1.06	
No	72 (36.73)	124 (63.27)	1	Reference	
Body Mass Index (BMI)					0.60
Malnutrition	1 (20.00)	4 (80.00)	0.62	0.10 - 3.67	
Overweight	35 (32.11)	74 (67.89)	0.99	0.50 - 1.99	
Obesity	21 (42.00)	29 (58.00)	1.53	0.69 - 3.38	
Normal	18 (32.14)	38 (67.86)	1	Reference	
Glycated Hemoglobin (HbA1c)					0.004
6.5 - 7	2 (20.00)	8 (80.00)	0.20	0.05 - 0.69	
7 - 9	18 (32.14)	38 (67.86)	0.32	0.22 - 0.47	
9 - 12	48 (36.09)	85 (63.91)	0.36	0.29 - 0.45	
>12	6 (31.58)	13 (68.42)	0.32	0.16 - 0.61	
<6.5	1 (100)	0 (0)	1	Reference	
Glomerular Filtration Rate (GFR)					0.77
<30	2 (25.00)	6 (75.00)	0.65	0.12 - 3.51	
30 - 60	8 (50.00)	8 (50.00)	1.95	0.64 - 5.94	
60 - 120	44 (33.08)	89 (66.92)	0.97	0.51 - 1.83	
>120	21 (33.87)	41 (66.13)	1	Reference	
Microalbuminuria					0.068
<30 mg/24h	51 (30.91)	114 (69.09)	0.56	0.30 - 1.05	
30 - 300 mg/24h	24 (44.44)	30 (55.56)	1	Reference	
>300 mg/24h	00 (00)	00 (00)	-	-	
Uric Acid					0.0097
Low (<310 mmol/L)	33(27.05)	89 (72.95)	0.43	0.23 - 0.81	
Normal (310 - 420 mmol/L)	30 (46.15)	35 (53.85)	1	Reference	
High (>420 mmol/L)	12 (37.50)	20 (62.50)	0.70	0.29 - 1.66	
HDL Cholesterol					0.99
<1 mmol	24 (34.29)	46 (65.71)	1.002	0.55 - 1.82	
≥1.2 mmol	51 (34.23)	98 (65.77)	1	Reference	

Continued

LDL Cholesterol					0.0001
<3.5 mmol/L	48 (27.91)	124 (72.09)	0.29	0.14 - 0.56	
>3.5 mmol/L	27 (57.45)	20 (42.55)	1	Reference	
Total Cholesterol					0.0001
>5 mmol/L	48 (27.91)	124 (72.09)	0.29	0.22 - 0.76	
≤5 mmol/L	27 (57.45)	20 (42.55)	1	Reference	
Triglycerides					0.06
<0.5 mmol/L	2 (66.67)	1 (33.33)	2.38	1.01 - 5.66	
0.5 - 2 mmol/L	26 (27.96)	67 (72.04)	1	Reference	
>2 mmol/L	47 (38.21)	76 (61.79)	1.59	0.89 - 2.85	

Table 3. Factors associated with peripheral arterial disease in multivariate analysis in diabetic patients at the Libreville University Hospital from July 2023 to January 2024.

Associated Factors	OR	95% CI	p-value
Hypertension (HTA)			
Yes	2.09	1.05 - 4.17	0.035
No	1	Reference	
LDL Cholesterol			
<3.5 mmol/L	2.75	1.10 - 6.85	0.03
>3.5 mmol/L	1	Reference	

4. Discussion

The objectives of this study were to determine the hospital frequency of LEAD and identify associated factors in diabetic patients to implement practical preventive measures within this population. The ABI technique, chosen for this study, is validated by European and ADA recommendations as the first-tier screening method [15] [21].

The prevalence of 34.24% for LEAD in this study aligns with the 35.2% reported by Semporé in 2019 in Bobo-dioulasso [22], but lower than the 41.9% found by Codjo in Parakou in 2013 [23] and the 42.4% from Wanvoegbe in Porto-novo more recently in 2023 [24]; while in Bamako in 2018, Mariko had a hospital frequency of 22.35% [25]. Differences in prevalence between this study and the two mentioned studies from Benin could be due to the significantly lower sex ratio, 0.68 in Parakou and 0.63 in Porto-novo. The prevalence of LEAD in these studies was higher among women than among men, at 45.6% versus 36.4% in Parakou and 51.5% versus 43.8% in Porto-novo. In Bamako, the average age of the diabetic population studied (45.5 ± 11.7) was ten years younger than the Libreville (57 ± 11 years), Parakou (53.7 ± 11.5 years), and

Porto-novo populations (where 57.1% were at least 60 years old). Literature commonly describes LEAD as a condition of older adults, appearing around age 50 with an exponential increase after 65 [17]. In a Taiwanese population with an average age of 63.3 ± 10.8 years, Tseng et al. found a 10% prevalence in 2003, much lower than the values mentioned earlier in sub-Saharan Africa [26].

In Libreville, as in most sub-Saharan hospital studies, the major CVRFs associated with diabetes in this condition were almost identical in varying proportions, including physical inactivity, hypertension, dyslipidemia, obesity, and smoking [25] [27]. Thus, policies focusing on public awareness and education should be prioritized to combat these CVRFs effectively and reduce their morbidity and mortality burden. Asymptomatic cases dominate, 77.33% in this study, 77.5% in Marrakech, and 70.8% in Tunis and Madagascar, justifying the need for systematic screening among this patient population [27] [28] [29].

In bivariate analysis, diabetes duration ($p = 0.0003$), anti-diabetic treatment, especially insulin-based treatment (OR at 3.37; 95% CI: 1.38 - 8.23; $p = 0.011$), hypertension ($p = 0.0002$), physical inactivity ($p = 0.034$), HbA1c ($p = 0.004$), uric acid ($p = 0.0097$), LDL cholesterol ($p = 0.0001$), and total cholesterol ($p = 0.0001$) were associated with the occurrence of LEAD in this study. Similar results have been reported by many African studies, with varying proportions [24] [25] [27] [30]. Diabetes duration is one of the most correlated factors with LEAD in both Western and African literature [31]. Guan et al. showed that in a population of 1397 Chinese diabetic patients aged at least 50 from 15 different hospitals in seven major cities, the LEAD prevalence increased from 15.78% to 23.84% when diabetes duration ranged from five to ten years [32]. However, in several studies, this association was not confirmed in multivariate analysis, as reported by Tseng [33]. Insulin therapy, especially at high doses, was also suspected to be associated with the occurrence of LEAD, particularly in female diabetic patients [33]. In this study, the doses of insulin used were not examined, nor the arterial impact of this treatment by gender. Further studies on this association could confirm or refute it. HbA1c's link with LEAD has been described by many authors [23] [32] [34]. Sartore's work confirms the crucial role of this biological parameter in micro and macrovascular complications in diabetic patients [35]. Uric acid has also been linked to LEAD in diabetic patients, as noted by Chen [34].

However, the absence of smoking among the factors associated with LEAD in several African studies [22] [27] [30], including those from North Africa, in contrast to Western studies where it is a major CVRF after diabetes [36], suggests the possible role of genetic factors in the pathogenesis of this condition [17] [36].

In multivariate analysis, only hypertension (OR = 2.09; 95% CI: 1.05 - 4.17; $p = 0.035$) and LDL cholesterol (OR = 2.75; 95% CI: 1.10 - 6.85; $p = 0.03$) were significantly associated with LEAD occurrence in diabetics at CHU in Libreville. Endothelial dysfunction and increased arterial wall stiffness play a significant role in the pathogenesis of LEAD in diabetic patients [37] [38], which may explain the links between this condition, hypertension, and LDL cholesterol. It is known that the risk of LEAD increases with systolic blood pressure (SBP) levels and is particularly associated with pulse pressure [39]. The UKPDS study showed that every 10 mmHg reduction in SBP was associated with a 16% decrease in LEAD risk [40]. Likewise, several studies have linked LDL cholesterol to peripheral artery disease in diabetic patients [41] [42]. However, these results should be interpreted with caution, as many studies implicate chronic arsenic poisoning in drinking water in the occurrence of systemic atherosclerosis and thus LEAD [43]. Many countries do not yet comply with the World Health Organization's recommended standards for drinking water safety [44], and Gabon, like many other countries in the region, could be affected by this.

This work has limitations, as the methodology did not account for some CVRFs, such as lipoprotein Lp(a), or certain genetic factors that could interact with classical CVRFs like hypertension and smoking. Additionally, CVRFs associated with LEAD may vary by age and gender, suggesting that subgroup analyses by age and gender would have been beneficial. Nevertheless, this study provides initial epidemiological data that can be improved by more in-depth subsequent studies.

5. Conclusion

The hospital frequency of LEAD in diabetic patients at CHUL is high: one in three diabetic patients is affected. These are relatively young patients at high cardiovascular risk, combining multiple other CVRFs with diabetes. This condition is asymptomatic in nearly eight out of ten patients. Thus, in diabetic patients, especially those with hypertension and LDL cholesterol dyslipidemia, systematic LEAD screening should be implemented. Combatting other major CVRFs remains critical.

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Allognon MC and Ayo Bivigou E. designed the study, interpreted the results, and drafted the final manuscript. Nnang Essone JF, Kinga A, and Mpori JM conducted the literature search. Ndoume Obiang F, Akagha Kondé C, Ntoutoume Mvé A, Ndjibah Alakoua C, Yékini CF, and Babongui Boussougou L collected the data. Ecke Nzengue JE and Houenassi DM improved the study design, analyzed the results, and revised the manuscript. Boguikouma JB revised the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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