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# Etiological Aspects of Lower Extremity Peripheral Arterial Disease: Multicentric Prospective Study of 126 Cases

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**Abstract:** *Introduction:* Atherosclerosis is the main cause of lower extremity peripheral arterial disease (PAD). However, there are other etiologies little reported. The objective of this work was to study the socio-demographic, clinical and etiological aspects of PAD. *Patients and study method:* This was a multicentre, descriptive, cross-sectional study conducted from January 1<sup>st</sup> to October 30<sup>th</sup>, 2021, in Thies and Dakar, Senegal. Any clinically suspected PAD was confirmed by arterial Doppler ultrasound and/or CT angiography. Clinical, biological and ultrasound data were used to establish the etiology and diagnosis criteria of OLIN for the diagnosis of thromboangiitis obliterans (TAO). *Results:* A total of 126 patients were collected, 31 (24.6%) in Thies and 95 (75.4%) in Dakar. There were 72 men (57.1%) and 54 women (42.9%), a male-to-female sex ratio of 1.3. The average age was 62.5 years 10.8 years. The majority of patients had a low socio-economic profile (52%). Etiologies were dominated by atheromatous disease (n= 120; 95.2%) and the cardiovascular risk factors were in order of frequency: physical inactivity (n=98; 77.8%), type 2 diabetes (n=78; 62%), hypertension (n= 69; 54.8%), smoking (n= 46; 36.5%) and dyslipidemia (n=29; 23%). Thromboangiitis obliterans (Buerger's disease) was the second etiology found in 5 patients (3.96% of cases) and concerned only men who regularly used tobacco and cannabis. One case of ANCA-associated vasculitis was also found. In addition, there was a considerable delay in diagnosis with 117 patients (92.8%) at the critical ischemia stage at the time of diagnosis and amputation of varying magnitude in 110 patients (87.3%). This delay in diagnosis was at least due to insufficient screening, limited access to arterial Doppler echo and the lack of specialized services in vascular medicine, outside the capital Dakar. *Conclusion:* The most common etiology of lower extremity PAD was atherosclerosis. Obliterating thromboangiitis was not uncommon. Early detection of PAD and control of risk factors for atherosclerosis must be the rule.

**Keywords:** PAD, Atherosclerosis, TAO, Arterial Ultrasound, Senegal

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## 1. Introduction

Lower extremity peripheral arterial disease (PAD) is a common disease associated with a significant risk of mortality and a significant degradation of quality of life. Although atherosclerosis is the main cause, however, PAD knows other etiologies little reported. The objective of this

work was to study the socio-demographic, clinical and etiological aspects of PAD.

## 2. Patients and Study Methods

This was a multicentre, descriptive, cross-sectional study conducted from January 1<sup>st</sup> to October 30<sup>th</sup>, 2021, in Thies

and Dakar, Senegal. Any clinically suspected PAD was confirmed by arterial Doppler ultrasound and/or CT angiography. Clinical, biological and ultrasound data were used to establish the etiology and diagnosis criteria of OLIN for the diagnosis of thromboangiitis obliterans (TAO).

This was a descriptive, cross-sectional study conducted January 1<sup>st</sup> to October 30<sup>th</sup>, 2021, at Saint Jean de Dieu Hospital, Thies Regional Hospital and the Thoracic and Cardiovascular Surgery Department of Fann University Hospital in Dakar.

Recruitment was consecutive using a standardized form that included the patient's marital status, history and lifestyle, clinical signs, biological, and scan data. The Leriche-Fontaine classification was used to assess severity. All clinically suspected cases of PAD were confirmed by arterial Doppler ultrasound and/or CT angiography. In addition to clinical and biological data, the etiological diagnosis of atherosclerosis was retained by the presence of an atherosclerotic plaque on the ultrasound. And the OLIN criteria were used for the etiological diagnosis of Thrombo-Angiitis Obliterant (TAO).

### 3. Operational Values Were Defined as Follows

- 1) Age in years, was calculated from the date of birth that appeared on the national identity card
- 2) The socio-economic level was determined according to the 2013 World Bank criteria that set the poverty index for anyone living on \$1.25 a day in developing countries [1]
- 3) Education was classified into four levels: out-of-school, elementary, secondary and university
- 4) Physical inactivity was defined as the absence of daily physical activity or physical activity of < 120 minutes per week [2]
- 5) Alcohol consumption was assessed by the type of alcohol and the number of drinks per day,
- 6) Tobacco use was measured in packets-years with active or passive, current or former (stopped for 03 years), whether or not cannabis use existed
- 7) Blood pressure was measured in all patients with an OMRON M3 electronic blood pressure meter from OMRON Healthcare. Hypertension was retained for SBP (systolic blood pressure)  $\geq$  140 mm Hg and/or DBP (diastolic blood pressure)  $\geq$  90 mm Hg 02 times at 02 weeks intervals or taking antihypertensive therapy [3]
- 8) Determination of obesity was based on 2003 WHO criteria [4]
- 9) Dyslipidemia was defined according to the NCEP (National Cholesterol Education Program) criteria with normal values of total cholesterol < 2 g/L, LDL-cholesterol < 1.30 g/L, HDL-cholesterol > 0.40 g/L, triglycerides < 2 g/L [5]
- 10) The diagnosis of diabetes was retained when fasting blood glucose  $\geq$  1.26 g/L 02 times or taking diabetes treatment [6]

11) The diagnosis of atherosclerosis was retained by the presence of risk factors of atherosclerosis and atherosclerosis plaque on arterial Doppler ultrasound

12) The diagnosis of TAO was based on the 2000 Olin criteria [7]

13) The search for other etiologies was guided by the clinical presentation and the patient's history, the diagnosis of the suspected disease was retained on the basis of its clinical and/or paraclinical markers, if not already done.

### 4. Ethical Considerations and Declaration of Conflict of Interest

Interviews with the selected patients were conducted in the study setting, in complete confidentiality, with their consent and with respect for their privacy.

The authors do not declare any conflict of interest of the author for this work.

### 5. Data Capture and Analysis

The data entry was done with the EpiData software version 3. 1. The analysis of the data and the preparation of the diagrams and curves were done by the EXCEL and SPSS software. The qualitative variables were expressed by simple enumeration as well as their percentage, the quantitative variables on average with a standard deviation.

### 6. Results

A total of 126 patients were collected, 31 (24.6%) in Thies and 95 (75.4%) in Dakar. It was 72 men (57.1%) and 54 women (42.9%), a male/female sex ratio of 1.3. The average age was 62.5 years  $\pm$  10.8 years and the most represented age group was 60.70 years. In addition, the prevalence of PAD increased with age, peaking around 65 and decreasing after 70 (Figure 1). The majority of patients had a low socio-economic profile (52%) and a low level of education, particularly among women (Figures 2 and 3).

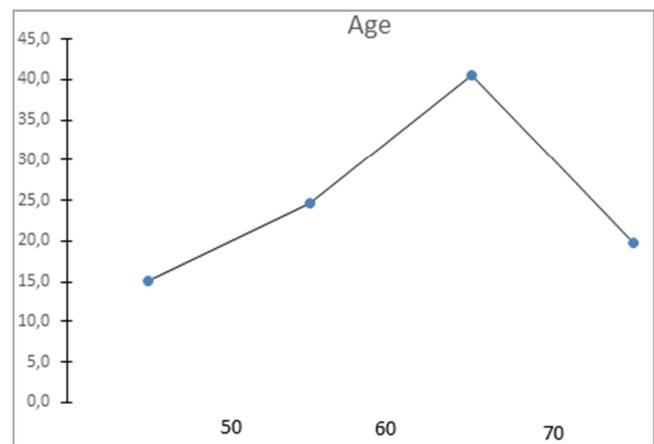


Figure 1. Representative curve of the number of PAD patients by age group.

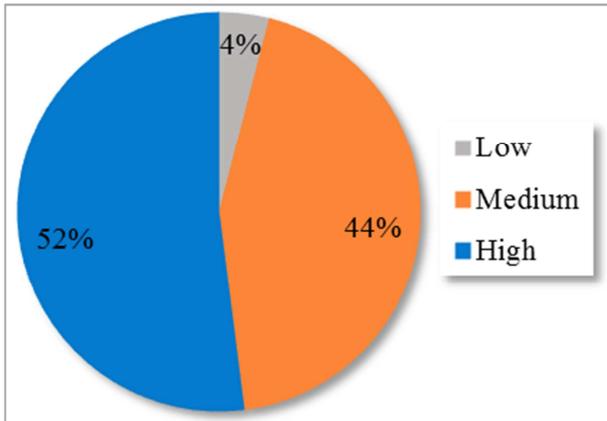


Figure 2. Distribution by socio-economic level.

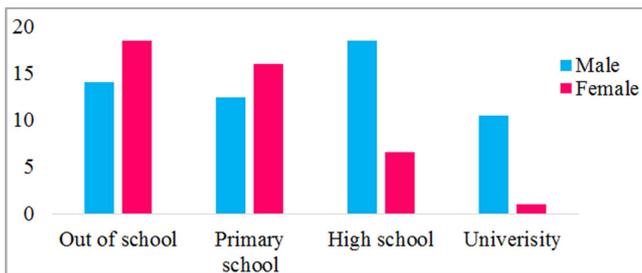


Figure 3. Distribution by educational level and sex.

A considerable delay in diagnosis of PAD was observed. Almost all patients (n= 122; 96.8%) were symptomatic, of which 5 or 4.1% were in stage 2 and 117 or 95.9% in stage 4 of Leriche and Fontaine (Table 1).

Table 1. Distribution of patients by Leriche-Fontaine's classification.

Stages	Number (n)	Percentage (%)
I	04	3,2
II	05	4
III	0	0
IV	117	92,8
Total	126	100



Figure 4. Mixed gangrene of the right foot .



Figure 5. Necrosis in the sock of the right leg.

Gangrene was present in 83 patients (65.8%); it was wet in 49 patients (59.03%), dry in 27 patients (32.53%) and mixed in 7 patients (8.43%). Ulcerative lesions were observed in 34 patients (27%). Their seat was always distal (toes, heel, back of foot, sole of foot) and their depth varied between 0.2 and 3 cm (Figures 4 and 5). One hundred and ten patients (87.3%) had a surgical procedure, of which 40 were major and 70 were minor.

Etiologies were dominated by atheromatous disease (n= 120; 95,2%). The classic risk factors found were in order of frequency, physical inactivity, diabetes, hypertension, tobacco and dyslipidemia (Figure 6).

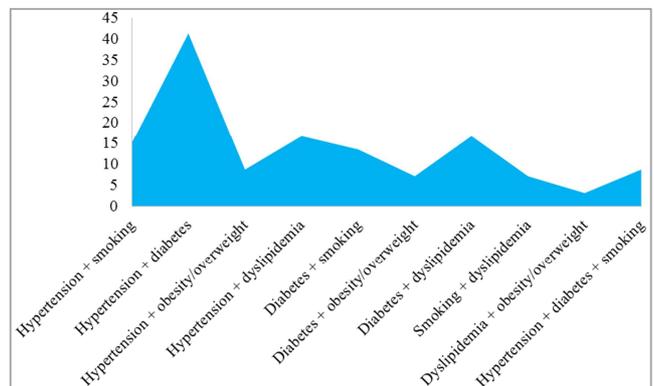


Figure 6. Distribution by risk factors.

Type 2 diabetes was reported in 78 patients (62%). In all cases, type 2 diabetes with a duration of more than 10 years occurred in 51.3% of cases. The age group most affected by diabetes was [60-70] and the prevalence was slightly male (n=40; 51,3%).

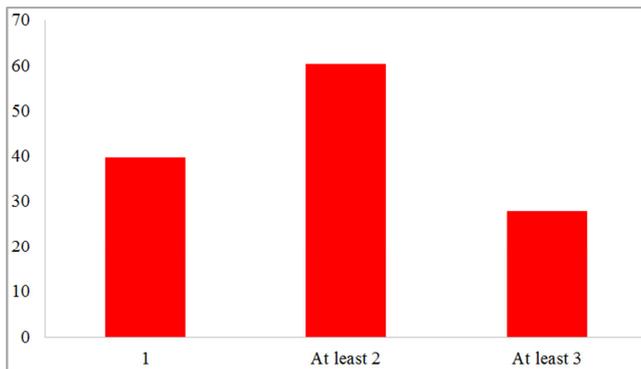
Hypertension was found in 54.8% (n=69) of patients with a clear female predominance (n=39; 56.5%) and a development period of less than 10 years in 58% of cases. The age group most affected (50.8%) by hypertension was [60 -70].

Almost all tobacco was consumed as cigarettes (n=40; 86.96%) of smokers with an average of 25.45 ± 19.75 Packs-Years. The other 6 patients (13.04%) smoked pipe. Twelve patients (26%) were former smokers and 34 (74%) were current users. Three women with PAD were exposed to

passive smoking.

Dyslipidemia was found in 23% of patients (n=29). It was type of total hypercholesterolemia in 13.5%, hyper-LDLc in 14.3%, hypo-HDLc in 12% and hypertriglyceridemia in 0.8% of patients.

Seventy-six patients, or 60.3%, had at least two cardiovascular risk factors and thirty-five (27.8%) had at least three cardiovascular risk factors. Hypertension-diabetes was by far the most common association found in 41.3% of patients (Figure 7).



**Figure 7.** Distribution by number of risk factors.

TAO or Buerger's disease was the second etiology found in 5 patients or 3.96% of cases and concerned only men who regularly used tobacco and cannabis. The average age of diagnosis was  $45.8 \pm 4.08$  years for extremes of 38 and 52 years. The average tobacco consumption was  $21.3 \pm 12.85$  Pack-Years. Cannabis use was found in the 03 youngest patients with a minimum duration of use of 09 years.

A case of ANCA vasculitis was identified in our study population. This was a 45-year-old woman with a very distal involvement with obliteration of the main artery of the right thumb and lateral plantar artery. This clinically resulted in a dry gangrene of the right thumb and a right plantar ulcer about 01 cm deep.

## 7. Comments

In our work, the PAD increased with age to reach a peak reached around 65 and then decrease. Fowkes *et al* [8] also found this increase with age but persisted after 80 years. A similar result was obtained by Maintenant *et al* in 2014, in the EPIDEMCA study conducted in Central Africa [9], and by Rada *et al* [10]. The EPIDEMCA study only targeted people aged 65 and over.

We counted more men than women (57.1% vs 42.9%) with a sex ratio of 1.3. This male predominance observed in our study could be explained by active smoking which was exclusively male and female hormonal protection before menopause. In high-income countries, this male predominance is also described, although the prevalence of PAD tends to equalize between the two sexes over the years due to more frequent female smoking [11]. On the other hand, several studies conducted on the African continent, in both

North and Sub-Saharan Africa, have described a higher prevalence among women. Nevertheless, this work focused on the detection of asymptomatic PAD with older populations than ours (peak age obtained after 70 years), a more consistent female participation and their results seemed to show an asymptomatic association of PAD to the female sex [9, 10, 12].

The economic level was considered low at 52%, average at 44% and high at 4%. This estimate was made directly from patients' monthly incomes and therefore did not take into account the patient's dependents. This means that the level of poverty has likely been underestimated in our work. Nevertheless, our findings are comforted by those in the literature that low socio-economic levels are associated with PAD [13].

In our study, most patients (n=117; 92.8%) were already at stage IV of Leriche and Fontaine at the time of diagnosis and only 05 patients (4%) were diagnosed at the claudication stage.

Norgren *et al* estimated that 10-50% of limping patients did not see a doctor for their symptom [14].

These results reflect the lack of PAD screening in patients with cardiovascular risk factors and the late consultation of patients with claudication resulting in an amputation rate of 87.3% (n=110), 36% minor and 64% major. These amputations were performed in 94% of critical ischemia patients and were well above that of the Hirsch *et al* report which estimated the rate of amputation at 30% at the critical ischemia stage after one year of follow-up [15].

Atherosclerosis was by far the main etiology of PAD in our work (n= 120, 95.2%) as reported by all authors [8-12]. However, we found in young subjects, aged less than 50 years, a lower proportion of atherosclerosis (n=12; 68.4%) and TAO was more common (n=4; 21,1%). This observation is also made by Sauvanier *et al* [16]. In addition, autoimmune diseases found in 4 of our patients, accelerated the process of atherosclerosis and should be sought in the young subject with PAD [16].

Our study population was largely sedentary. The role of sedentary lifestyles in increasing the risk of type 2 diabetes and cardiovascular disease is now indisputable and its association with PAD tends to aggravate it because of its disabling disease quality [17].

Diabetes had the highest prevalence after physical inactivity. This was exclusively type 2 diabetes. Diabetes is indeed a powerful and independent risk factor for the occurrence of PAD [13] with a prevalence ranging from 22 to 71% and this prevalence increases with age, age of diabetes [14-16]. The results of our study are consistent with data from the literature as diabetes was associated with age > 60 years (69.2%), an evolution duration greater than 10 years (51.3%), critical ischemia and 75.6% to another cardiovascular risk factors. Moreover, the high prevalence of PAD in diabetics and the association of diabetes with critical ischemia easily explains the high prevalence of diabetes in our study population (62%).

Hypertension had the third highest prevalence at 54.8%.

Its distribution by age group follows that of diabetes with which it is strongly associated (75.4%). His seniority does not seem to impact the occurrence of PAD. Hypertension is described in the literature as a factor representing a lower relative risk for diabetes or tobacco [14] and by comparing these three factors in our population in terms of single cases we found a three (03) times lower prevalence of hypertension (diabetes=15.1% vs tobacco=14.3% vs hypertension=4.8%).

Smoking was followed in our study population, which was found in 46 patients (36.5%) at a lower rate than in the western series [13,16]. Tobacco has a double implication in the occurrence of PAD, on the one hand through atherosclerosis and on the other hand through Buerger's disease. The atherogenic role of smoking is well established and its association with peripheral arterial involvement is stronger than that with coronary disease [13, 16, 21]. On the other hand, the lower prevalence of smoking in our work compared to the western series could be explained by a lesser use of tobacco in the population especially female.

Dyslipidemia was the fifth risk factor in our population (23%). Hypercholesterolemia is considered a moderate factor in the occurrence of PAD [13]. Joosten et al estimated the taxpayer share of hypercholesterolemia among American workers at 17% and this was less important than tobacco, diabetes, and hypertension [22] as was the case in our study. On the other hand, a study conducted in Guadeloupe in 2016 found different results on the ranking of cardiovascular risk factors and a much higher prevalence of dyslipidemia than ours of 45% [23]. A significant link between PAD and hypertriglyceridemia was mentioned in the literature [7] but we could not verify this because this entity was present in only one patient.

Obesity was the least common risk factor in our population despite being very sedentary. His association with PAD is a controversial issue in the literature or sometimes a "U" relationship is highlighted between the two [13]. In contrast, the EPIDEMCA study found a significant association between undernutrition and PAD in Central Africa [9]. However, the proportion of undernutrition in our population was lower, at 6.3%.

The association of cardiovascular risk factors was very important in our population, especially that of hypertension to diabetes which concerned 52 patients (41.26%) of our workforce. Many studies report the high prevalence of hypertension in patients with PAD and diabetes, so that some even consider it a predictor of PAD occurrence. This prevalence varies between 51% and 70% depending on the studies and it is around 66.7% in our diabetic population [18, 19, 20].

The diagnosis of TAO is not always simple due to the lack of consensus on diagnostic criteria. Trophic disorders are the primary expression of this disease [16, 24, 25]. Cannabis and especially tobacco are the two factors involved in the occurrence of TAO [26, 27].

## 8. Conclusion

The most common etiology of lower extremity PAD was atherosclerosis. Obliterating thromboangiitis was not uncommon. Early detection of lower limbs PAD by pulse palpation and systolic pressure index in subjects with cardiovascular risk factors should be the rule.

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