

# Clinical and epidemiological study of occlusive peripheral arterial disease of the lower limbs

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**ABSTRACT** *Aim:* study of risk factors for the disease, its clinical manifestations, and laboratory diagnostic elements (vascular functional explorations). *Material and method:* 50 consecutive patients operated in the Department of Surgery no. 1 of the Emergency County Clinical Hospital of Craiova who underwent retroperitoneoscopic lumbar sympathectomy (RLS) are analysed, the study group being a part of a total of 680 patients with occlusive peripheral arterial disease of the lower limbs (PAD), hospitalized and treated in our clinic between 2007 and 2011. *Results:* sex ratio = 1/7.9 in the group which includes all arterial diseases hospitalized (586 males and 74 females), sex ratio = 1/15.6 in patients who underwent sympathectomy (47 males and 3 females). The comorbidity evaluation highlighted the presence of high blood pressure (HBP) in 50% of patients who underwent sympathectomy, which is within the range of data obtained on the entire group (52.5%). Chronic ischemic heart disease (20% in patients who underwent sympathectomy and 48.6% in patients of the entire group), acute myocardial infarction (16% in the RLS group and 11.4% in the PAD group) and ischemic stroke (8% in the RLS group and 4.8% in the PAD group) certify the plurifocality of arterial lesions. Diabetes was present in our study in 26% of patients with PAD and 18% of patients with RLS. Smoking was encountered in 72.6% of patients in the reference group and 70% of RLS patients. Twenty one cases had a history of disease of 1 year or less, while the remaining 29 cases have been suffering even for more than 6 years. The clinical picture was dominated by pain, present in all cases. We found no arterial pulsation in the posterior tibial and pedal arteries in 88% of the cases (44 patients). Changes of the hair and nails were present in 21 cases (42%), and in 28 cases (56%) we found hypotrophy of calf and crural muscles. Trophic lesions were present in a total of 24 patients (48%), assigned as stage IV patients. Oscillometric index values were below the normal range in all cases. Skin temperature values were close to normal values (26°C) in only 13 patients (26%); 27 patients (54%) had a distal systolic index (DSI) < 0.5, corresponding to a severe critical ischemia. *Conclusions:* The development of the disease is caused by the association of several pathogenic factors, the most important ones being age, smoking, diabetes, and HBP. Symptoms at onset were generally mild, insidious, with clinical distress extending over variable periods of time, with oscillating evolution but slowly progressing worsening trend. The clinical picture was dominated by pain. Changes of the skin, hair, nails, and muscles are common objective signs.

**KEY WORDS** *peripheral arterial disease , cardiovascular comorbidities , smoking, diabetes, pain, trophic ulcers, amputation*

## Introduction

Occlusive peripheral arterial disease of the lower limbs (PAD) is a heterogeneous group of disorders with multifactorial etiology and clinical picture dominated by pain, with a wide variety of clinical and anatomical forms (etiopathogenic, morphological, topographical and evolutive), represented by atherosclerotic arteriopathy, vasospastic arteriopathy (Burger disease) and diabetic arteriopathy. They are still an important public health problem because of their debilitating aspect. This is partially due to the severe pain syndrome and evolutive trend of toward trophic lesion development (resulting in reduced functional capacity or even compromised integrity of the affected limb), as well as the frequent association of severe comorbidities (cardiovascular diseases, diabetes, etc.). The presence of PAD indicates the association of coronary cerebral disease [1]. Patients with PAD have a 7-10 times greater risk of cardiovascular ischemic events and a three times higher risk of

short-term mortality [2-4]. The risk of PAD and ischemic events is increased in diabetics due to an increased risk of atherosclerosis [5].

The diagnosis of PAD is usually easy, arterial suffering generating a significant pain syndrome, which quickly directs the patient to the doctor. It is based on subjective and objective clinical signs, complemented by functional vascular explorations and specific imaging investigations, all contained in an algorithm leading to a complete clinical and anatomical diagnosis, allowing a good staging and choice of the best treatment options.

## Material and methods

The study was conducted on a total of 50 consecutive patients operated on in the Department of Surgery no. 1 of the Emergency County Clinical Hospital of Craiova, who underwent retroperitoneoscopic lumbar sympathectomy (RLS), the study group being a part of a total of 680 patients with PAD,

hospitalized and treated in our clinic between 2007 and 2011., for which all the existing therapeutic options were used, tailored to each individual case, depending on the clinical anatomical form, topography, evolutive stage and biological potential of each patient.

PAD, especially degenerative one, is not isolated, but part of systemic degenerative diseases (atheromatosis and arteriosclerosis), most often with multiple involvement of the cardiovascular system. Therefore, the presence of comorbidities, mostly cardiovascular, provides an overview of the biological terrain in arteriopathic patients. Based on this idea, the study of background as an etiopathogenic factor, focused primarily on the study of cardiovascular comorbidities (Table 1) and their role in the etiopathogenic determinism of PAD. From this point of view, the evaluation of medical history was performed for patients within the RLS group (50 patients), in correlation with the data from the entire group of patients enrolled in the study period, from 2007 to 2011 (680 patients).

**Table 1. Cardiovascular history**

Cardiovascular history	RLS Group		OPADLL 2007-2010	
	No. of cases	%	No. of cases	%
High blood pressure	25	50	357	52,5
Ischemic heart disease	10	20	330	48,6
Acute myocardial infarction	8	16	78	11,4
Stroke	4	8	32	4,8
Arrhythmias	9	18	143	21
Vascular surgery	7	14		
Acute ischemia	1	2		
Cardiac failure	8	16		

The assessment of pain intensity was performed using a visual analog scale (VAS), by which the patient evaluates pain intensity on a scale from 0 (no pain) to 10 (agonizing pain). Physical examination revealed the presence of arterial pulsations in elective foci, the presence of pathological changes of the skin, hair and nails, muscle tone, and trophic lesions, all necessary elements staging and establishing an appropriate therapy. Evaluation of arterial pulse in elective foci allows a proper assessment of the arterial status and is useful in assessment the obstruction.

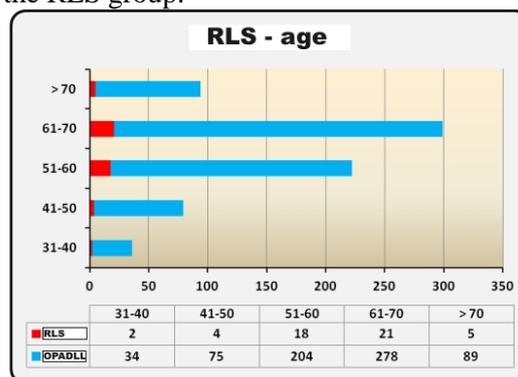
Paraclinical investigations presented in this article are those of the vascular function. Oscillometric evaluation (recording of pulse wave in the studied arterial segment), skin thermography (for our study we used a digital infrared thermometer), and distal systolic index (DSI) or the ankle-arm index were performed.

For the classification of the cases studied we used the Leriche-Fontaine staging system (1920), which recognizes four evolutionary stages:

- Stage I – atypical symptoms: cold feet, pallor, paresthesia, fatigue following effort (after 500 m), discrete sensitivity disorders, intolerance to cold, etc.;
- Stage II – characterized by the presence of intermittent claudication with two substages: II A with claudication after more than 200 m and II B with claudication after less than 200 m;
- Stage III – nocturnal pain, at rest, with early or late onset;
- Stage IV – continuous pain and trophic lesions.

## Results

Our study reflects the distribution of arterial disease according to age, its maximum incidence being between 50 and 70 years of age for atherosclerotic arteriopathy and less than 50 years for patients with thrombangeitis obliterans (Chart 1). Regarding diabetic arteriopathy, its maximum incidence is generally between 40 and 50 years of age. This finding is valid for both the entire group and the RLS group.



**Chart 1. Distribution according to age group**

Marked male predominance was obvious in both in the group which includes all arteriopathies hospitalized and treated in the period analysed (586 men and 74 women, with a sex ratio of 1/7.9), and the RLS group (47 men and 3 women, with a sex ratio of 1/15.6).

Concerning the patient's place of origin, we found no significant etiopathogenic differences, the urban/rural ratio being almost 1.

Comorbidity assessment highlighted the presence of elevated blood pressure in 50% of the RLS patients, which is within the range of data obtained for the whole group (52.5%). The risk of developing PAD is 2.5 to 4 times higher in hypertensive than in normal individuals, with hypertension being found in 43% of patients with stage II arteriopathy. Chronic ischemic heart disease (20% in RLS patients and 48.6% in the

whole group), myocardial infarction (16% in the RLS group and 11.4% in the PAD group), and ischemic stroke (8% in the RLS group and 4.8 % in the entire PAD group), certify the plurifocality of arterial lesions, our study confirming the data from the literature, according to which between 40% and 60% of patients with PAD also have concurrent coronary lesions, and 5% ischemic strokes. Arrhythmias were present in 18% of the patients in the RLS group and 21% in the general group. Diabetes, another major etiopathogenic risk factor was present in 26% of patients with PAD and 18% of patients with RLS, confirming the data from the literature according to which diabetes is present in 20-30% of patients with PAD, and about 30% of patients with PAD also show carbohydrate metabolism disorders.

Smoking is one of the most frequent and important toxic factors involved (nicotine and carbon monoxide) in the etiopathogenesis of PAD; in our study 72.6% of patients in the reference group and 70% of RLS ones were smokers. The pathogenic role of alcoholism is uncertain; however, alcohol consumption was present in 68% (34 patients) of the RLS group.

The onset of symptoms was generally slow, insidious, with extensive clinical suffering for periods ranging from several months to several years (Chart 2), with oscillating evolution but a slowly progressive worsening trend; 21 of our cases had a history of disease of 1 year or less, while the remaining 29 cases have been suffering even for more than 6 years.

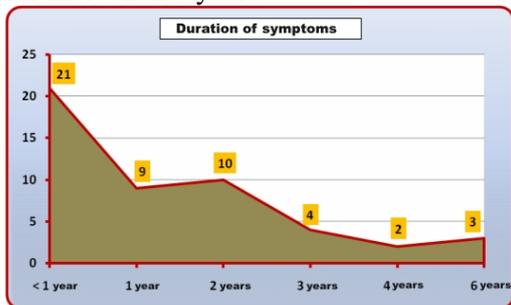


Chart 2. Duration of symptoms

The clinical picture was dominated by pain, one of the criteria constantly used for staging; it was present in all our cases with different clinical forms: intermittent claudication with a claudication index under 200 m (13 cases, 26%), or pain at rest and/or nocturnal (37 cases, 74%), with (24 cases, 48%) or without trophic lesions. We found that on admission, before any therapeutic measures were taken, pain was significant, disabling, evaluated by patients between 7 and 10 on the VAS scale. Paresthesia (66%), foreign body sensation in the affected

extremity, initially felt in vicious positions, then following great efforts, low temperature, and finally in a resting position (54%), and functional impotence (12%), completed the subjective clinical picture of chronic limb ischemia. In the studied cases we found no arterial pulsation in the posterior tibial and pedal arteries in 88% of cases (44 cases); in 16 (32%) cases we found no pulse in the popliteal artery, which, correlated with the presence of femoral pulse, was interpreted as a superficial femoral artery obstruction. Absence of femoral pulse was present in 8 cases, meaning high iliac obstruction.

Changes of the skin, hair, nails and muscles are common objective signs for peripheral obstructive arteriopathies expressing the degree of ischemia. Pallor, found in 46% of cases (23 cases) expresses chronic ischemia, cyanosis (13 cases, 26%) and tissue hypoxia translate into venous stasis, and erythema (10 cases, 20%) is usually the expression of inflammatory processes.

Table 2. Types of trophic lesions

Type of trophic lesions	cases	%
Calf ulcer	2	4
Gangrene of the forefoot	4	8
Gangrene of toes	18	36
Big toe	9	18
Toes II-IV	4	8
Toe V	5	10

Changes of hair and nails (lack of hair, brittle nails, hyperkeratosis) were present in almost half of the cases studied (21 cases, 42%), and in over half the cases (28 cases, 56%) we found calf and crural muscle hypotrophy, the more important as the arterial suffering is in a more advanced stage.

Trophic lesions were present in a total of 24 (48%) patients, assigned as stage IV; single or multiple, unilateral or bilateral, trophic lesions were located in the fingers, forefoot or leg (Table 2).

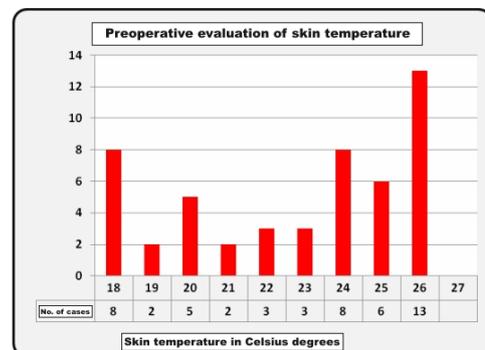


Chart 3. Preoperative evaluation of local skin temperature

Oscillometric index values were below the normal range in all cases studied, consistent with the advanced stages of ischemia.

The values for skin temperature (Chart 3) were close to normal (26°C) only in 13 patients (26%); in 14 cases we recorded a moderate decrease in local temperature (2-3°C), and in the remaining 23 cases (46%) we recorded significant reductions in local skin temperature ( $\geq 4^\circ\text{C}$ ), in 8 of them, the difference being of 9°C.

In our study, 27 patients (54%) had a distal systolic index (DSI)  $< 0.5$ , corresponding to a severe critical ischemia, while the remaining 23 patients (46%) had DSI values of 0.5 (21 patients), and 0.6 (2 patients), falling within the category of stage II and III ischemia (Chart 4).

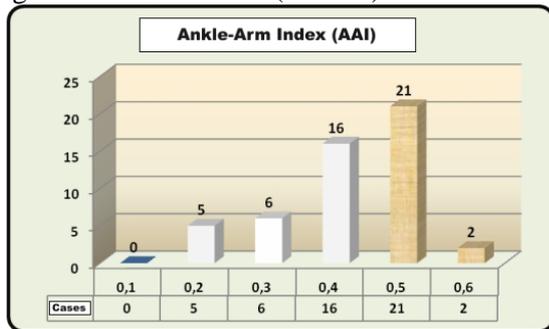


Chart 4. Ankle-Arm index (AAI)

The 50 cases studied included nearly all clinical etiopathogenic and topographical forms of obstructive arteriopathy of the lower limb. Thus, atherosclerotic arteritis held the largest share (26 cases, 52%), followed by diabetic arteriopathy (16 cases, 32%) and thrombangeitis obliterans (6 cases, 12%).

Most cases studied belonged to stage IV (24 cases, 48%), with continuous pain at rest and nocturnal, trophic lesions of varying extent and depth (calf ulcers, gangrene localized to one or more fingers or the forefoot – Table 2), 13 cases (26%) belonged to stage III, with early or late onset nocturnal or rest pain, and 13 cases (26%) belonged to stage II B, with discontinuous claudication and a claudication perimeter under 200 m.

## Discussions

PAD is a public health problem with a very high prevalence that effects the quality of life and functional status and is the leading cause of major limb amputation [6]. PAD is associated with a major deterioration of life quality due to loss of mobility and inability to perform daily activities [7, 8].

Age, gender and constitution are epidemiological factors involved in the etiopathogenesis of PAD. In accordance with the literature, lipid deposition in vascular walls starts at 6 months postpartum and continues slowly for

the rest of the life; ages over 40 favor the development of imbalances in metabolic, endocrine or blood homeostasis that precipitate vascular suffering. The prevalence of PAD in men can be explained on one hand by the fact that before menopause, estrogen contributes to the prevention of vessel damage (after menopause, females also show vascular risk), and on the other hand by the much higher frequency in men of toxic (smoking and alcohol) and/or environmental factors (professions exerted in a cold and wet environment) involved in the etiopathogenesis of peripheral arteriopathies.

PAD affects approximately 29% of individuals over the age of 55 [2, 3, 9, 10] and 60% of those over 85 years [11]. As the population ages and the proportion of older individuals increases, the prevalence of PAD and associated disabilities increases together with the expenses [6]. PAD is very common in advanced age but most patients are asymptomatic [12]. Approximately one third of patients had intermittent claudication described as pain, cramping or numbness in the affected limb that occurs during exercise and disappears at rest [13]. The ratio between symptomatic and asymptomatic PAD is 1:3-1:4. For each patient with symptomatic PAD there are three patients with asymptomatic PAD [14]. One third of patients with asymptomatic PAD have total occlusion of a major artery of the lower limb [15]. In unselected autopsies 15% of men and 5% of women with asymptomatic PAD had a  $> 50\%$  stenosis on an artery of the limb [14]. In the initial stages most patients with PAD are asymptomatic and only 9-11% have intermittent claudication [2, 9, 16, 17]. In advanced PAD critical limb ischemia may develop that causes ischemic foot ulcers with high risk of amputation [18, 19] Critical ischemia represents only 1% of the population over 50 years [2, 9, 16, 17]. It precedes amputation and requires urgent treatment [5].

According to Baker et al. [20] smoking is present in 90-97% of patients with peripheral obstructive arterial disease, especially in people who started smoking at a young age a large numbers of cigarettes (20-40/day); Lagrue et al. [21] believe that smoking multiplies by 4 the role of other risk factors (hyperlipidemia, diabetes, etc.). The pathogenic action mechanism of nicotine is immunological; it acts on the vascular endothelium via a glycoprotein with which it is combined and then secured to the endothelium, becoming antigenic. Nicotine has vasospastic and thrombotic effects. Inhaled carbon monoxide binds to hemoglobin forming carboxyhemoglobin, a complex which secures oxygen and is not

dissociated in tissues, with hypoxia affecting the myocardium, brain and smooth muscle cells of blood vessels, leading to their destruction and development of progressive arteriosclerosis. The relationship between arteriopathy and smoking is best seen Buerger's disease, when giving up smoking results in an improvement of the evolution.

High blood pressure (HBP) would have, according to the latest data from the Framingham study, a similar role to that of smoking and diabetes, contributing to arteriopathies by endothelial damage caused by destructive necrotic lesions of smooth muscle fibers, as well as by an increased permeability of the vascular endothelial to liquids and proteins, which diffuse and impregnate the intimal layer displacing the vessel wall elements [22].

On the other hand, Mayo Clinic studies have shown that the presence of diabetes in arteriopathic patients leads to a worse evolution of arteriopathy, a more frequent development of gangrene and need for amputation, while restorative interventions lead to inferior results compared with those obtained in non-diabetic patients. It is considered that the first change in diabetics is microangiopathy located in the vasa vasorum, with diabetic macroangiopathy developing only after years of evolution. According to Hyvanien [23], arteriopathy develops 10 years earlier in diabetics compared to other patients, and Coremier et al. [24] show that in diabetics arteriopathy is bilateral, develops first in the foot, is multisegmental, and can involve even iliac arteries. Azerad [22] considers that diabetes is the leading cause of arteriopathy in women. PAD affects the quality of life in diabetics [25] and is associated with important functional impotence [26]. Patients with diabetes and PAD have a higher risk for amputation than non-diabetics [27]. Approximately 20-30% of patients with diabetes have PAD [5] and about 20-30% of patients with diabetes have PAD with DSI < 0.9 [28-30]. In diabetic patients PAD is more often associated with ischemic ulcers or gangrene and increased risk of amputation compared to non-diabetic patients [27]. Diabetic patients have a 15 times higher risk of amputation compared to non-diabetics [31]. The distribution of peripheral ASC in diabetics with PAD is frequently more distal than in non-diabetics and involves tibial vessels [32]. Smoking increases by 2.5 times the risk of PAD, and diabetes by 4 times [5].

Intermittent claudication occurs during walking, because of the altered adaptation capacity of the arteries, blood flow becoming

inadequate and leading to ischemia of muscle mass with the formation of strongly algogenic catabolites that produce local pain. The location of claudication may suggest the obstruction site. In our study, the most frequent location of claudication was the calf, suggesting involvement of femoral or popliteal arteries. In all our cases, intermittent claudication had a claudication index below 200 m, suggesting a stage IIB diagnosis.

Rest pain (37 cases, 74%) characterized advanced stages (III and IV), when the flow is so low that it can not provide nutrition, even in a resting state. Located at the distal end of the affected limb, especially the big toe, foot or ankle, it is sometimes atrocious, is sometimes associated with local burning feeling and produces advanced mental depression and extreme anxiety. Nocturnal rest pain forced patients to sleep with the affected leg hanging from the bed, leading in time to the development of local edema with frequent fibrous organization or skin lesions (24 cases, 48%).

In our study, oscillometry, although replaced in modern vascular surgery services with complex functional tests, was used for its simplicity, adaptability and low time consumption. In accordance with the literature, only complete disappearance of oscillations was considered a clear sign of peripheral arterial obstruction, because the reduction of fluctuations below the above mentioned values, although rising suspicion of arterial obstruction, can be found in a number of other pathological circumstances as hypotension, chronic lower limb edema, heart failure, obesity, hypothyroidism, vasomotor hypotonia.

Cutaneous thermography provides data on the status of collateral vessels, skin temperature being proportional to local blood perfusion. We used this functional exploration in order to objectify changes in skin temperature consecutive to local perfusion decrease, as well as to assess the effectiveness of RLS by pre- and post-operative comparative study of this parameter.

Distal systolic index (DSI) or ankle-arm index, credited with a sensitivity of 90-95% and a specificity of 98-100% for angiographically verified stenosis, was one of the criteria we use for the evaluation and staging of chronic arterial obstruction. Limitations of this method are that it is ineffective in patients with calcified vessels (patients with diabetes or renal failure), calcified vessels being uncompressible even at pressures of 250 mmHg. DSI decrease is correlated with the number and location of significant arterial lesions (occlusion/stenosis > 50%) with imagistic confirmation. Patients with single segment lesion

(aortic-iliac, femoral-popliteal and tibial-peroneal segment) often show DSI values over 0.5, while multisegmental lesions are associated with severe ischemia.

## Conclusions

1. The development of the disease is caused by the association of several pathogenic factors, the most important being age, smoking, diabetes, and high blood pressure. According to Băcanu [33], the combination of two major risk factors increases the frequency of atheromatosis by 2.5 times, the combination of 3 factors by 7.7 times, and if 4 risk factors are present by 15.2 times compared to normal individuals.

2. Onset of symptoms was generally slow, insidious, with clinical suffering extending over periods ranging from several months to several years, with oscillating evolution but slow, progressive worsening trend.

3. The clinical picture was dominated by pain, one of the criteria constantly used for staging, present in all our cases as different clinical forms.

4. Changes in the skin, hair, nails and muscles are objective signs of peripheral obstructive arteriopathies which express the degree of ischemia.

5. We recorded trophic lesions in 48% of patients, so most of the cases were diagnosed in in stage IV.

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