Original article

UDC: 616.13-008.64-07
doi:10.5633/amm.2016.0307

RELATIONSHIP BETWEEN SUBJECTIVE DISCOMFORTS AND EVALUTION OF DIAGNOSTIC PROCEDURES BASED ON THE STAGES OF CHRONICAL ARTERY INSUFFICIENCY OF LOWER EXTREMITIES

Nebojša Ignjatović[1,2], Miroslav Stojanović[1,2], Goran Stanojević[1,2], Aleksandar Karanikolić[1,2], Milan Radojković[1,2], Saša Živić[2,3], Dragan Stojanov[2,4], Miodrag Đorđević[2], Jelena Ignjatović[4], Daniela Benedeto-Stojanov[2,5], Bobana Milojković[1,2]

Lower-extremity peripheral arterial disease (PAD) represents a group of disorders characterized by narrowing or occlusion of the arteries resulting in gradual reduction of blood supply to the limbs.

The aim of this study was to examine the predominance of subjective discomfort, objective clinical findings and the predominance of localization of steno-occlusive lesions in patients with functional and critical ischemia of chronic arterial insufficiency (CAI) of the lower extremities.

Prospectively, we analyzed a group of 50 patients, admitted at the Vascular Department of Surgical Clinic in Niš during the period from September 2000 to October 2001, with evident symptoms and signs of different stages of CAI of THE lower extremities verified by color Doppler ultrasonography and objective clinical examination.

The critical ischemia was more frequently associated with the change of skin color ($p<0.05$), atrophic changes ($p<0.001$), absent pulsations ($p<0.01$), the occurrence of muscle atrophy ($p<0.01$), gangrene ($p<0.05$). Gangrene was the most dominant clinical occurrence with respect to ulceration ($p<0,05$) in the critical ischemia. The functional ischemia had frequent occurrence of pallor ($p<0.01$), as a significant sign, as well as preserved pulsations of a. poplitelis ($p<0.01$). Asymptomatic steno-occlusive lesions with stenosis of 1-19% were predominant in patients with stage I functional ischemia. Subcritical stenosis with 20-49 % stenosis was characteristic of patients in stage IIa, while critical stenosis with 50-99% stenosis was characteristic of patients in stage IIb and III stage of critical ischemia. Patients in the IV stage of critical ischemia had total occlusion of distal arteries of the lower extremities. In the stage of critical ischemia, the most common steno-occlusive process is localized on femo-ropopliteal segment (a. Femoralis superficialis)

Early detection of PAD is crucial for the timely treatment and prevention of amputation, heart attack, stroke, and death. *Acta Medica Medianae 2016;55(3):44-56.*

Key words: chronical artery insufficiency, functional ischemia, critical ischemia

Surgical General Clinic, Clinical Centre Niš, Niš, Serbia[1]
University of Niš, Faculty of Medicine, Niš, Serbia[2]
Cardiovascular and Transplantation Clinic, Clinical Centre Nis, Nis, Serbia[3]
Department of Radiology, Clinical Centre Niš, Niš, Serbia[4]
Gastroenterology Clinic, Clinical Centre Niš, Niš, Serbia[5]

Contact: Nebojša Ignjatović
Mokranjčeva 29/13, 18000 Niš
e-mail: n.ignjat@gmail.com

Introduction

Lower-extremity atherosclerotic peripheral arterial disease (PAD) is a significant public health problem in the USA, with an estimated 8-10 million affected individuals. Atherosclerotic vascular disease affects large- and medium-sized arteries of most circulatory beds and it is the leading cause of death and disability in developed countries (1).

PAD is a group of disorders characterized by narrowing or occlusion of the arteries, resulting in gradual reduction of blood supply to the limbs. Only a small number of patients is presented with classic intermittent claudication and other symptoms, such as leg pain with exercise and at rest, leg weakness, and balance problems resulting in falls. The prevalence of PAD in people with diabetes has been reported to be as high as 30%, and it is known to have a negative impact on health-related quality of life (QoL) which could further result in chronic pain, intermittent claudication, and loss of mobility and function (2). Although conventional risk factors are known to contribute to the development of PAD, the role of

'novel' biomarkers in pathways of inflammation, thrombosis, lipoprotein metabolism, and oxidative stress in determining susceptibility to PAD is not fully defined. Validation of novel risk markers for PAD may allow earlier detection, an improved understanding of disease etiology and progression and the development of new therapy procedures (1).

The prevalence has been shown to increase with age, particularly in individuals aged 60 years and older. Therefore, as the population ages, PAD will become increasingly prevalent. Despite its high prevalence, PAD remains largely underdiagnosed and undertreated. Evidence suggests the underutilization of inexpensive and widely available diagnostic screening tools, guideline-recommended treatments, and lifestyle modifications. Early detection of PAD is crucial for the timely treatment and prevention of amputation, heart attack, stroke, and death. Individuals with PAD have four to five times greater risk of dying from a cardiovascular event compared to those without PAD, which translates into a mortality risk that is two to three times higher (3).

Direct atherosclerotic plaque visualization has improved our understanding of the development and progression of atherosclerosis. However, little is known about clinical correlates of lower-extremity atherosclerotic plaque characteristics in patients with lowerextremity peripheral arterial disease (PAD) (4). Therefore, adequate visualization of the lower limb arteries is essential prior to arterial reconstruction. Within the last decade several reports have recognized the diagnostic value of ultrasound in peripheral arterial disease (PAD) comparable with that of DSA (5, 6).

The aim of this study was to examine the predominance of subjective discomfort, objective clinical findings and the predominance of localization of steno-occlusive lesions in patients with functional and critical ischemia of chronic arterial insufficiency of the lower extremities.

Method

The prospective clinical study involved a group of 50 patients, admitted at the Vascular Department of Surgical Clinic and Center of Radiology in Niš from September 2000 to October 2001, who manifested the signs and symptoms of the different stages of CAI of the lower extremities, verified by color Doppler ultrasonography. Depending on the progression stage of PAD, the patients were classified into two subgroups: the subgroup of 25 patients in the stage of functional ischemia (Fontaine stage I, IIa and IIb) and the subgroup of 25 patients in the stage of critical ischemia (Fontaine stage III and IV).

Patients were examined in order to obtain significant medical history of the existence, type and the character of subjective complaints in functional stages (stages I and II according to Fontaine, the coldness, numbness, fatigue in the legs and intermittent claudication) and critical ischemia (III and stage IV according to Fontaine, with pain at rest, trophic skin damage and tissue necrosis with the appearance of dry and wet gangrene).

CAI of the lower extremity was determined on the basis of clinical findings and color Doppler duplex scan echosonography results. The control group consisted of 50 patients treated at the Surgical Clinic for other surgical diseases, without clinically manifested signs and symptoms of CAI of the lower extremities. Eligibility criteria for the control group were healthy subjects excluding diabetes mellitus, Raynaud's disease, evident plantar malperfusion, soft tissue inflammation or osteomyelitis, vasculitis, PAO.

Objective clinical examinations

Objective clinical examination was performed by standard principles of the clinical examination, inspection and palpation of the arteries. Inspections are focused on objective signs of the lower limb ischemia in terms of the existence of forced positions, pallor feet in elevation, redness of the skin of the foot in the down position, trophic changes of the soft tissues of the feet, slow capillary and venous filling, ischemic ulceration, and dry and wet gangrene. Change of skin temperature is determined by palpation withthe dorsum of the hand.

Pulse palpation is an essential screening tool wherein a pulse is qualified as abnormal, diminished, or absent. Pulsations of arteries of the lower extremities are easily discovered on the predilection places. The quality of superficial pulsations of arteriesa.femoris, a.poplitea, a.dorsalis-pedis and posterior a.tibialis in patients was determined. Decrease of the pulse amplitude was a sign of the presence of the proximal steno-occlusive lesions, while collateral circulation was rarely sufficient to form the distal pulse, even in cases of the complete occlusion.

Color Doppler ultrasound scanning

All limbs were scanned from the common femoral artery to the pedal arteries using a color Doppler ultrasound scanning (SIEMENS Sienna Sonoline (Diagnostic Ultrasound System, Siemens mead System, Inc., Issaquah, WA 988029-7002, USA) with a probe LINEAR ARREY 7.5 MHz L 40). The femoral and anterior tibial arteries were scanned with the patient in the supine position, whereas the popliteal and the two other crural arteries were examined with the patient in lateral decubitus. Arterial segments were identified by the detection of a color signal or when the artery was occluded, by the identification of a vessel wall accompanied by a vein. The following features were used to diagnose occlusion: segmental loss of signal in the insonated vessel, dampened distal signal compared to the proximal signal and proximal exit collaterals as well as distal re-entry collaterals. All diagnostic segments were classified

according to diameter reduction: <50% or >50% based on a peak systolic velocity ratio below or above two. Presence or absence of plaque in the iliofemoral arteries was first determined by acquiring images in the short-axis (transversal) view and then reconfirmed in the long-axis (longitudinal) view. In cases where a plaque was found, the ultrasound image was marked up with the help of on-board tools. Plaque was defined as any focal wall thickening >1.5 mm protruding into the lumen of the scanned vessel. The iliofemoral arteries were examined from just below the inguinal ligament with little compression maneuver to compress the adjacent common femoral vein. The transducer was moved downward from the common femoral artery to approximately 2 cm below its bifurcation. To allow segment to segment comparison, the arterial tree was divided into 15 segments; five supragenicular (common femoral, profundafemoris, proximal (superficial) femoral, distal (superficial) femoral and popliteal above the knee) and ten infragenicular segments (popliteal below the knee, tibio-peroneal trunk, anterior tibial, posterior tibial and peroneal arteries each divided into a proximal and distal half, and finally the dorsalis pedis and the plantar artery). Using the conventional method (single-gate) and color Doppler duplex scan, the presence and localization of stenosis, the segmental predominance (with multisegmental forms) and the degree of progression of stenotic-occlusive lesions were verified. Diagnosis of PAD was based on the lower limb arterial duplex carried out in the Center of Radiology. According to arterial duplex results, the participants were found to have either no stenosis (normal), mild stenosis (1–19%), moderate stenosis (20–49%) or severe stenosis (50–99%), orocclusion (100%).

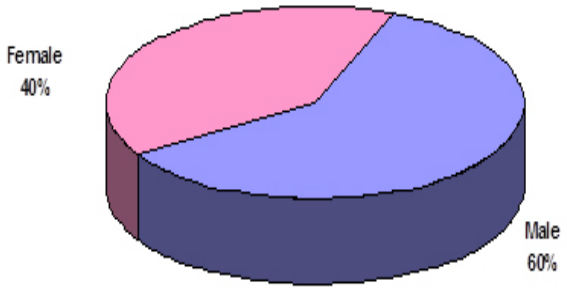
Patients in the studied groups in the clinical stages of functional and critical ischemia according to the morphological characteristics of atherosclerotic plaque were divided into four groups: group I - homogenous plaque material, lipid and fibrolipid plaque (low echogenic), II group - fibrous plaque (moderately echogenic without acoustic shadow), III group - completely calcified plaque (very echogenic), group IV - heterogeneous plaque material, calcified plaque (sonolucent), places necrosis, bleeding, intramural thrombus, lipid depots, with the appearance of complications (a sudden increase in obstruction, rupture of the plaque distal embolization, and/or thrombosis in situ) and the presence of ulceration as a source or a new initiation of site complications.

Results

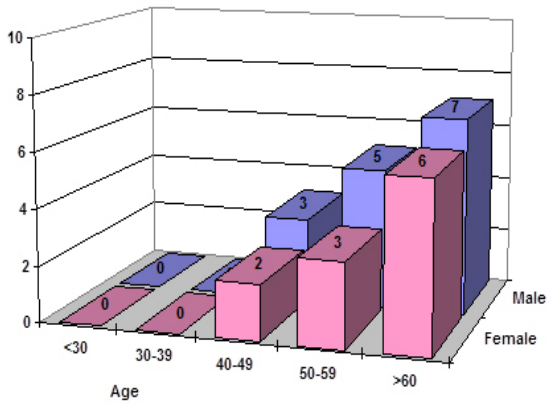
The distribution of patients according to sex and the average age of patients with different stages of CAI of the lower extremities.

In the studied clinical group, there were 50 patients with symptoms and signs of the different stages of CAI of the lower extremities. Depending on the evolutionary stages of the disease patients were divided into two subgroups: a subgroup of 25 patients in the stage of functional ischemia and a subgroup of 25 patients in the stage of critical ischemia. In the study group of the clinical stage functional ischemia there were 25 patients, 15 men (60%), mean age 61.4±7.3 years, and 10 women (40%), mean age 58.6±5.2 years, with male-female ratio of 1.5:1. Elaborated χ^2 test showed no significant difference in the prevalence of functional ischemia according to age groups between the sexes. Student's t-test showed borderline significant difference in years between the sexes ($p<0.1$) (Graph 1, Graph 2, Table 1).

In the study group of the clinical stage critical ischemia there were 25 patients, 17 men (68 %), mean age 64.8±5.2 years, and 8 women (32 %), mean age 59.5±4.8 years, with male-female ratio of 2.12:1, which was statistically significant ($\chi^2=5.97$, $p<0.05$). Elaborated χ^2 test showed no



Graph 1. The distribution of patients according to sex in the stage of functionale ishaemia



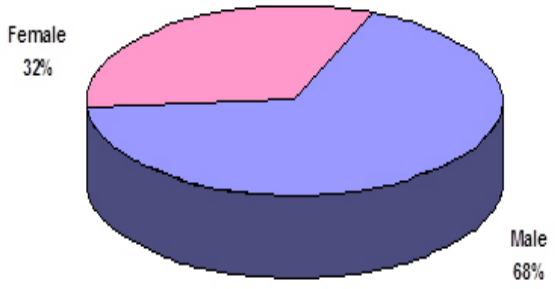
	<30	30-39	40-49	50-59	>60
Male	0	0	3	5	7
Female	0	0	2	3	6

Graph 2. The distribution of patients according to the age in the stage of functionale ishaemia

Table 1. The distribution of patients according to the average age in the stage of functional ishaemia

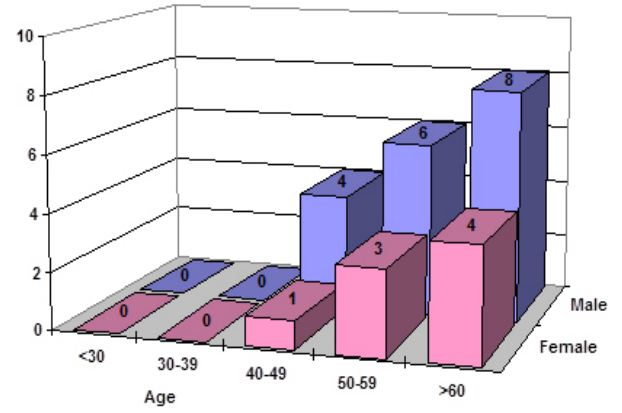
The average age (years)	Male	Female	Total
X	61,4*	58,6	60,2

* p<0,1



* p<0,05

Graph 3. The distribution of patients according to sex in the stage of critical ishaemia



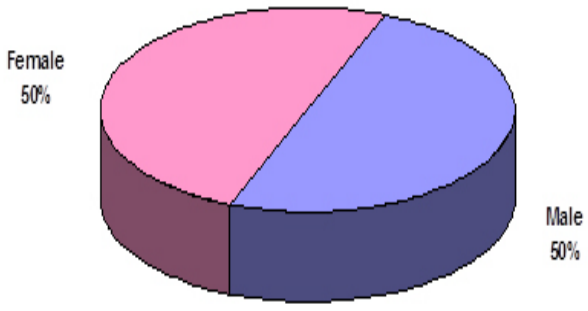
	<30	30-39	40-49	50-59	>60
Male	0	0	4	6	8
Female	0	0	1	3	4

Graph 4. The distribution of patients according to the age in the stage of critical ishaemia

Table 2. The distribution of patients according to the average age in the stage of critical ishaemia

The average age (years)	Male	Female	Total
X	64,8*	59,5	62,7
SD	5,2	4,8	5,1

* p<0,05



Graph 5. The distribution of patients according to sex in control group

significant difference in the prevalence of critical ischemia according to age groups between the sexes. Student's t-test shows the sig-nificance of the difference in years between the sexes ($p < 0.05$). (Graph 3, Graph 4, Table 2).

Frequent occurrence of clinically manifest chronic arterial insufficiency of the lower extremities in the seventh decade were observed, in the older age group and slightly dominant males in both clinical subgroupes, with gradual decline in the incidence in younger patients.

The control group of 50 patients treated for other surgical illnesses without clinically manifested symptoms or signs of the chronic arterial insufficiency of the lower limbs included 25 men (50%) and 25 women (50%), with a male-female ratio of 1:1. The mean age was 55.5±4.8 years. The average age of men was 53.3±4.6 years with a range of 26-78 years of age, the average age of women was 57.6±5.1 years, with a range of age of 32-78 years, with women on average slightly older than men ($p<0.05$) (Graph 5, Graph 6, Table 3).

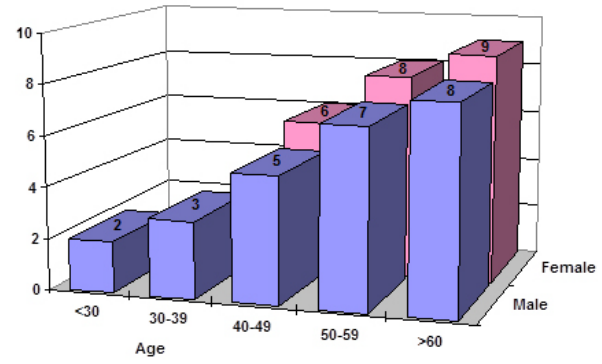
Distribution of patients according to the stage of functional and critical ischemia of CAI of the lower extremities

A total of 25 patients, in the stage of functional ischemia included 9 patients (36%) in stage I and 16 patients (64%) in stage II (IIa stage in 7 patients (28%) and 9 patients in IIb stage (36%). A total of 25 patients, in the stage of critical ischemia, included 13 patients (52%) in stage III, and 12 patients (48%) in the stage four (Graph 7). Elaboration by the Fisher's exact test shows that the difference in the prevalence of stages I and II functional ischemia is statistically significant ($p<0.05$)(Graph 7).

Analysis of subjective complaints of the patients in the stages of functional and critical ischemia of CAI of the lower extremities

Intermittent claudication

In the study group in clinical stage II functional ischemia, all of 16 patients (100%) had intermittent claudication as the dominant subjective symptom. Intermittent claudication is manifested in the form of spasm, contraction, fatigue and numbness of muscles, predominantly calf muscle group and gluteal regions. Claudication distance was very different, and ranged from 20-400 m. In stage IIa functional ischemia, claudication was over 200 m in 7 patients (43.75%), while in IIb stage it ranged from 100-200 m in 9 patients (56.25%). In the study group, the clinical stage of critical ischemia with pain at rest, ulceration or gangrene, intermittently claudication was non-dominant ailments that patients are only guidelines.



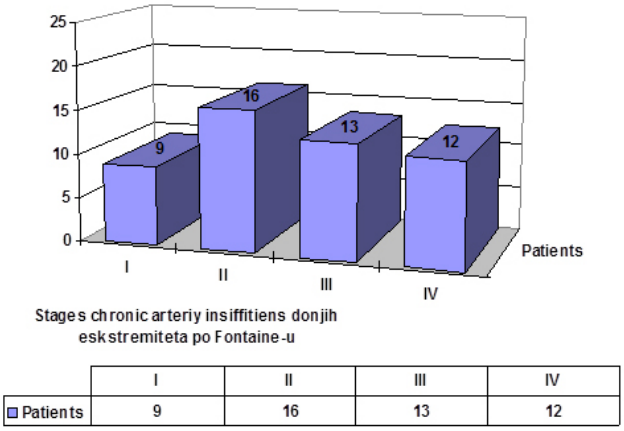
	<30	30-39	40-49	50-59	>60
Male	2	3	5	7	8
Female	0	2	6	8	9

Graph 6. The distribution of patients according to age in control group

Table 3. The distribution of patients according to the the average age in control group

The average age (years)	Male	Female	Total
X	53,3*	57,6	55,5
SD	4,6	5,1	4,8

*p<0.05



	I	II	III	IV
Patients	9	16	13	12

Graph 7. The distribution of patients according to different stages of chronic arterial insufficiency – Fontaine

Rest pain

In the study group, the clinical stage of critical ischemia pain at rest, as a form of ischemic neuritis, was present in 15 patients (60%), and was referred to as the initial symptom in patients who were in stage III, with the subsequent formation of trophic damage to the development of gangrene tissue and entering the fourth stage of critical ischemia.

Cold feet

Cold foot was present in 21 patients (84%) in stage I and II functional ischemia and it was referred to as a non-dominant problem. In 24 patients (96%) in the third and fourth stage of critical ischemia, cold foot was present and listed as an accompanying symptom. This difference was not significant between the groups.

Sensibility disorder

Signs and symptoms of the sensibility disorder in the study group in clinical stage functional ischemia I and II as paresthesia were present in 16 patients (64%). In the studied clinical group III and IV stage of critical ischemia paresthesias were present in 11 patients (44%), hyperesthesia (pain) in 6 patients (24%) and hypoesthesia or anesthesia in 8 patients (32%) (Graph 8).

Mantel-Haenzel's test shows that the disturbances of sensibility in mind hyperesthesia, hypoesthesia and anesthesia were more frequently cited as a symptom in patients with critical ischemia in comparison to patients with functional ischemia (χ^2=4.73, p<0.05 and χ^2=7.29, p<0.01). Critical ischemia was significantly more often associated with disorders of sensibility than functional ischemia (p<0.01).

Analysis of objective clinical findings in patients in stages of functional and critical ischemia

CAI of the lower extremities

Change of skin temperature

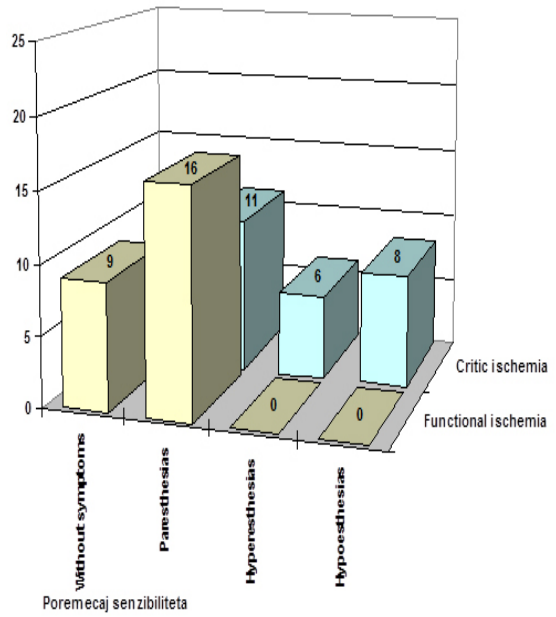
Cold skin was present in the clinical stage I and II functional ischemia in 16 patients (64%), while skin temperature was normal in 9 patients (36%). In the studied clinical group in stages III and IV of critical ischemia, cold skin was present in 21 patients (84%), while normal skin was observed in 4 patients (16%). Changing the temperature of the skin in patients in the stage of functional and critical ischemia showed no statistically significant difference in the distribution between the two groups (Graph 9).

Changes in skin color

In the studied clinical group of patients in the stages of functional ischemia, there was a change in skin color of the lower extremities, which was manifested in paleness of the skin in 16 patients (64%), ischemic rubor in 3 patients (12 %), while skin was without changes in 6 patients (24%).

In the studied clinical group of patients in the stages of critical ischemia there was a change in skin color of the lower extremities in 12 patients (48%), while the atrophic changes were present in 13 patients (52%). Discoloration of the skin with skin pallor were present in 6 patients (24%), cyanosis in 3 patients (12%), ischemic rubor in 1 patient (4%), purple fingers in 2 patients (8%) (Graph 10). The analysis made by Fisher's exact test shows that the critical ischemia was more frequently associated with the change of skin color (p<0.05) and atrophic changes (p<0.001), while

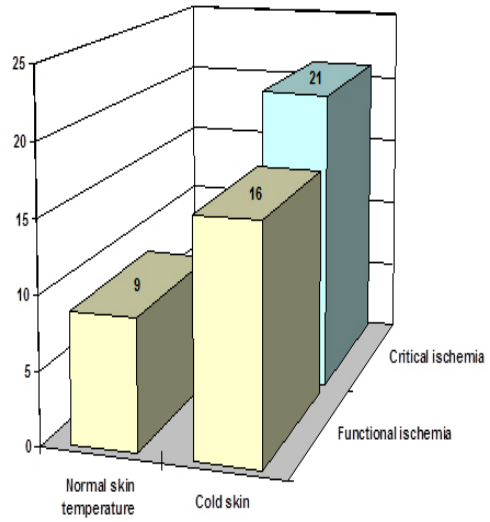
the functional ischemia had frequent occurrence of pallor (p<0.01) as a significant sign. Other indicators did not differ significantly in frequency between the groups.



	Without symptoms	Paresthesias	Hyperesthesias	Hypoesthesias
Functional ischemia	9	16	0	0
Critic ischemia	0	11	6	8

* p<0,05, ** p<0,01

Graph 8. The distribution of patients according to sensibility disorder in the stage of funcional and critical ishemia



	Normal skin temperature	Cold skin
Functional ischemia	9	16
Critical ischemia	4	21

Graph 9. The distribution of patients according to the change of skin temerature in the stage of funcional and critical ishaemia

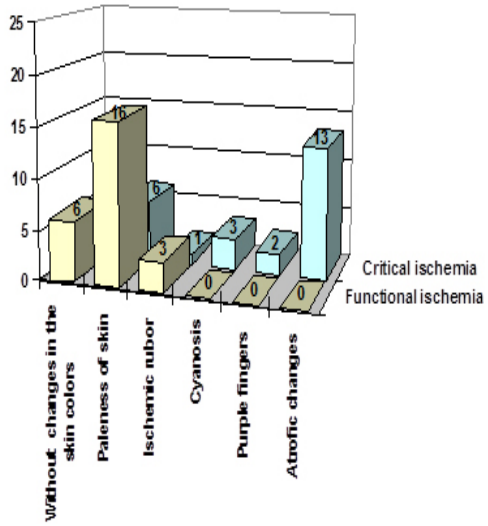
Change of muscle mass

In the patients with chronic arterial insufficiency of the lower extremities, a loss of muscle mass and muscle atrophy depended on the stage of the disease. In the studied clinical group of patients in the stages of functional ischemia, 11 patients (44%) had atrophy of muscles, while muscle mass was normal in 14 patients (56%). In the studied clinical group of patients in the stages of critical ischemia, muscular atrophy was found in 23 patients (92%), while normal muscle mass was present in 2 patients (8%) (Graph 11). This difference in the occurrence of muscle atrophy in the studied group was statistically significant (p<0.01).

Quality pulsations of the arteries in typical places

In the studied clinical group of patients in the stages of functional ischemia, quality pulsations of a.femoris in all of 25 patients (100 %) were normal.

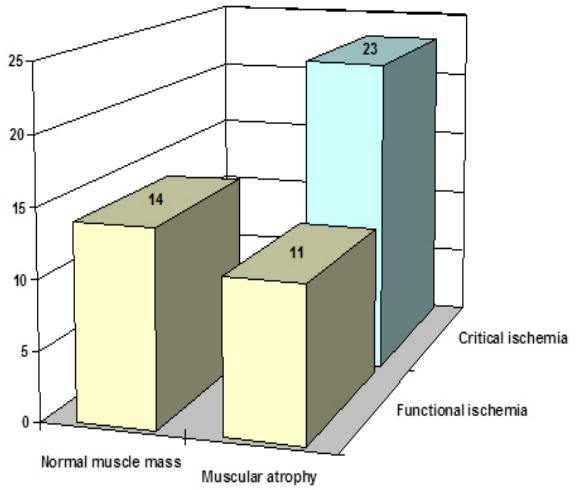
In the studied clinical group of patients in the stages of critical ischemia quality pulsations of a.femoris were normal in 5 patients (20%), was weakened in 12 patients (48%), while in 2 patients (8%) were absent. The predominant finding of a weakened pulse of a.femoris were in patients in stage III of critical ischemia. The difference in quality and pulsations of a. femoris were not statistically significant between these two clinical groups (Graph 12).



	Without changes in the skin	Paleness of skin	Ischemic rubor	Cyanosis	Purple fingers	Atrofic changes
Functional ischemia	6	16	3	0	0	0
Critical ischemia	0	6	1	3	2	13

*p<0,.05, ** p<0,01, *** p<0,001

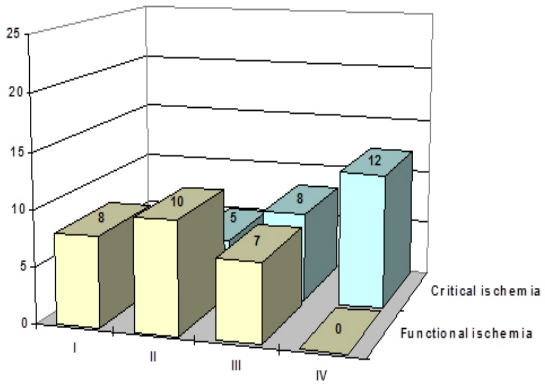
Graph 10. The distribution of patients according to the changes in skin color and atrophic changes in the stage of funcional and critical ishaemia



	Normal muscle mass	Muscular atrophy
Functional ischemia	14	11
Critical ischemia	2	23

*p<0,1, **p<0,05

Graph 15. Localization gangrene and ulceration in the stage of critical ishemia of the lower extremities

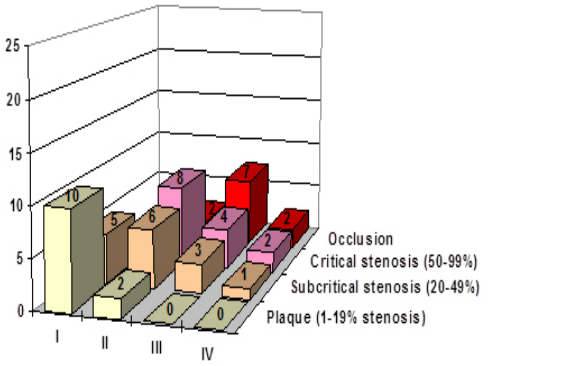


	I	II	III	IV
Functional ischemia	8	10	7	0
Critical ischemia	0	5	8	12

Graph 16. The distribution of patients according to the degree of stenosis of the lumen of the arteries in the stages of functional and critical ischemia

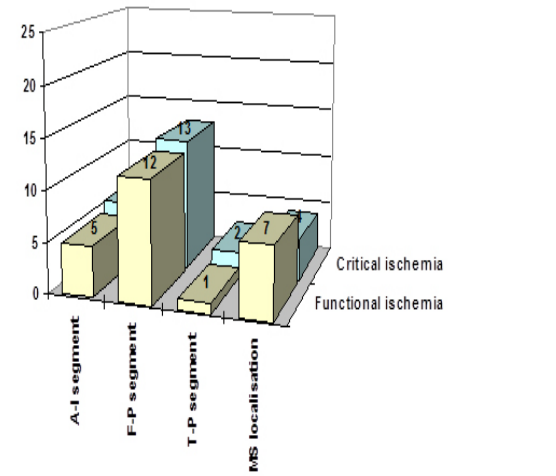
Quality pulsations of a.poplitea in the study group in the clinical stage of functional ischemia: the pulse amplitude was normal in 9 patients (36%), while it was weakened in 16 patients (64 %). Quality pulsations of a.poplitea in the study group in the clinical stage of critical ischemia: the pulse amplitude was normal in 2 patients (8%), in 13 patients (52%) was weakened, while in 10 patients (40%) was absent. In both groups the predominant finding of a weakened pulse was in about half of the patients, while findings of preserved pulsations was significantly more common in functional ischemia and absent pulsations in critical ischemia (p <0.01) (Graph 13).

Quality pulsations of a.dorsalis pedis and a.



	I	II	III	IV
Plaque (1-19% stenosis)	10	2	0	0
Subcritical stenosis (20-49%)	5	6	3	1
Critical stenosis (50-99%)	1	8	4	2
Occlusion	0	2	7	2

Graph 17. Morphological changes of atherosclerotic plaque within patients in the stage of chronic arterial insufficiency of the lower extremities



	A-I segment	F-P segment	T-P segment	MS localisation
Functional ischemia	5	12	1	7
Critical ischemia	6	13	2	4

Graph 18. The localization of stenotic-occlusive lesion within patients in the stages of functional and critical ischemia

tibialis posterior in the study group in the clinical stage of functional ischemia: the pulse amplitudes were weakened in 7 patients (28%), while were absent in 18 patients (72%). Quality pulsations of a.dorsalis pedis and posterior a.tibialis in the study group in the clinical stage of critical ischemia were weakened in 4 patients (16%), while in 21 patients (84%) were absent. Performed statistical analysis showed no significant difference in the quality of the pulse between the groups (Graph 14).

Trophic changes

Trophic changes of the skin and tissue necro-

sis caused by anoxia, which occur on toes, ball of foot and lower leg in the form of ulceration and gangrene were seen in 12 patients (48%) in the study group in the clinical stage IV critical ischemia. The ulcers were present in 2 patients (8 %), and gangrene in 10 patients (40%). Localized trophic changes of the fingers were observed in 6 patients (24%), of foot in 4 patients (16%), and of the lower leg in 1 patient (4%). Trophic changes of the toes observed in 8 patients (32%) were more frequent compared to the other sites found in 5 patients (20%)($p<0.1$), gangrene was a clinically dominant presentation with respect to ulceration ($p<0.05$) (Graph 15).

Analysis of color Doppler duplex scan ultrasonography in patients in stages of functional and critical ischemia of CAI of the lower extremities.

Analysis of the hemodynamic changes

In order to assess the degree of stenosis of arterial lumen, using sonogram, in patients with the stages of functional and critical ischemia, four groups were made: Group I – 1%-19% stenosis, plaque without significant hemodynamic changes, in 8 patients (32%) instage functional ischemia; Group II – 20 %-49% stenosis, subcritical stenosis in 1 patient (4%) in I stage, 7 patients (28%) in stage IIa, 2 patients (8%) in stage IIb functional ischemia and 5 patients (20%) in III stage in critical ischemia. Group III– 50%-99% stenosis, critical stenosis in 7 patients (28%) in stage IIb

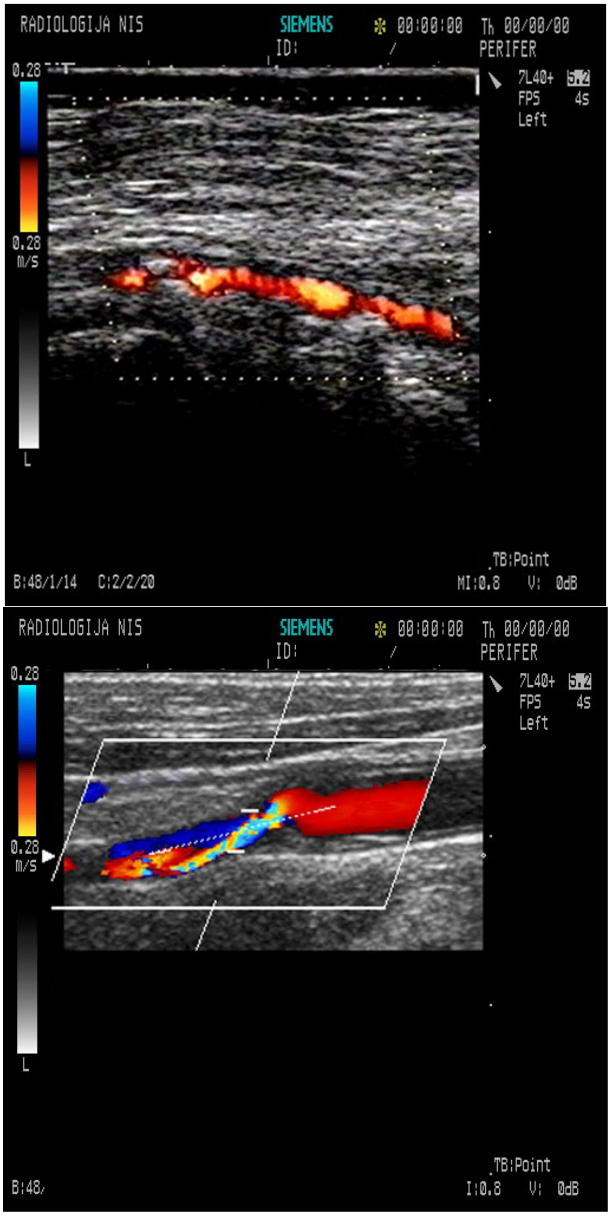


Figure 1. Color Doppler of multisegmental subcritic stenosis AFS, with the reduction of flow and significant hemodynamic disorders (left) and critical stenosis (high percent) PoplA (right)

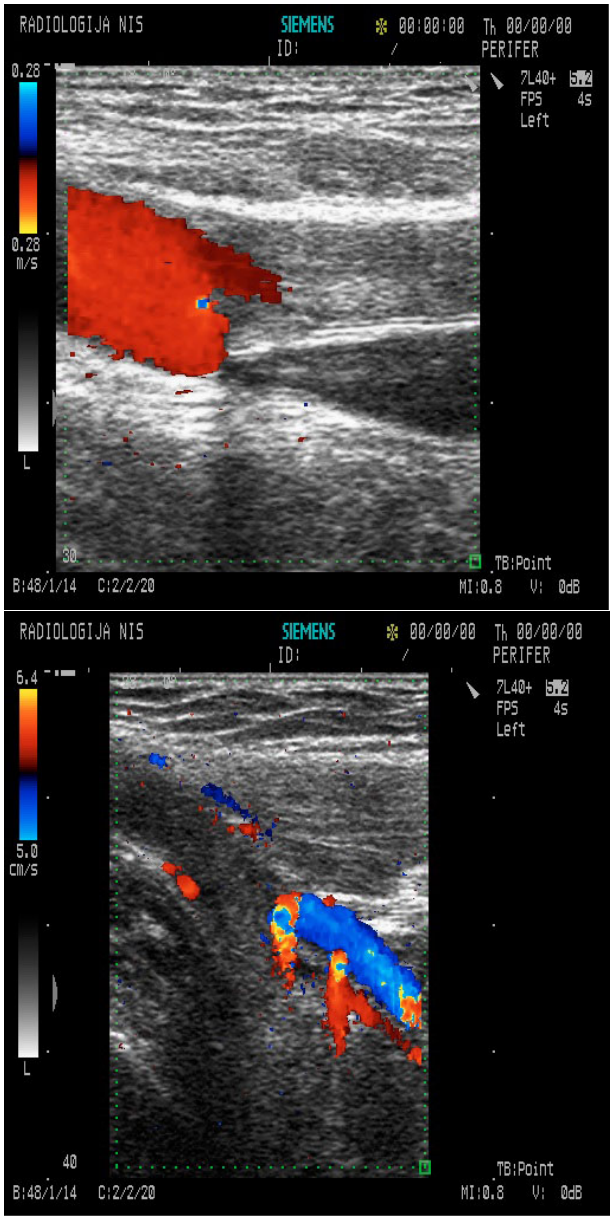


Figure 2. Color Doppler proximal occlusion AFS (left), with reconstruction PoplA. of collaterals (right).Analysis of morphological changes of athero-sclerotic plaque

functional stenosis, and 8 patients (32%) in stage III critical ischemia IV group - total occlusions observed in all 12 patients (48%) in IV stage of critical ischemia (Graph 16, Figure 1, Figure 2).

Analysis of morphological changes of atherosclerotic plaque

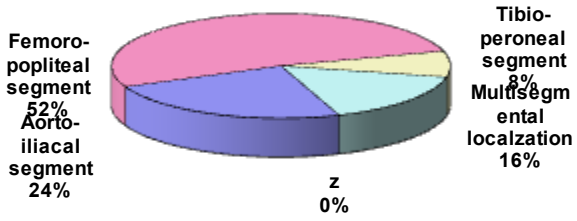
In the group of patients in stages of functional ischemia with atherosclerotic lesions without stenosis and hemodynamic disorders, the most common form was a plaque lipid and fibrolipid in 10 patients (50%-99%). The most common form was the fibrous plaque in the group with subcritical stenosis (20%-49%) in 6 patients (24%) and with a critical stenosis in 8 patients (32 %).The most common form of plaque was a plaque with complete calcification in the group of patients with occlusion of the artery lumen in 7 patients (28%). The most common form werea plaque lipid and fibrolipid in the group of patients in the stages of functional ischemia with atherosclerotic lesions without stenosis and hemodynamic disorders in 10 patients (50%-99%). In the group with subcritical stenosis (20%-49%) in 6 patients (24%) and with a critical stenosis in 8 patients (32%), the most common form was the fibrous plaque. The most common form was a plaque with complete calcification in the group of patients with occlusion of the artery lumen observed in 7 patients (28%) (Graph 17).

Analysis of the localization of stenotic-occlusive lesion

The color Doppler duplex scan ultrasonography was used to determine the localization of stenotic-occlusive lesion in the study group of patients in the stage of functional ischemia and it showed that the most frequent involvement was the femoro-popliteal segment disclosed in 12 patients (48%), multisegmental localization was revealed in 7 patients (28%), the aortoiliac segment in 5 patients (20%), and the tibio-peroneal segment was seen in one patient (4%). In the studied group of patients in the stage of critical ischemia, color Doppler imaging showed that the most frequent involvement was the femoro-popliteal segment shown in 13 (52%) patients, the aortoiliac segment in 6 (24%), multisegment localization in 7 (28%) and the tibio-peroneal segment in 2 patients (8%) (Graph 18). Fisher's exact test shows that the difference in the localization of stenotic-occlusive lesion in the stages of functional and critical ischemia is statistically significant ($p < 0.05$).

Discussion

PAD is characterized by a gradual reduction in blood flow in 1 or more limbs secondary to atherosclerosis. PAD most often affects the arteries that supply the legs and can result in poor perfusion of the muscles and skin of the lower ex-



Graph 19. The distribution of patients according to the localization of stenotic-occlusive lesion of segment arterie of the lower extremities

tremity. As a result, PAD is a major risk factor for lower extremity amputation, especially in patients with diabetes. Patients with PAD often have a coexisting systemic vascular disease involving coronary, cerebral, and renal vessels, leading to significant morbidity and reduced life expectancy (7). Patients with PAD have traditionally been classified according to severity of symptoms into Fontaine levels from I to IV (8). In 1954, Fontaine et al. proposed a simple clinical classification of patients with ischaemic rest pain but with no skin lesions as seen in stage III PAD and patients who had skin lesions as in stage IV PAD. CLIcan be used simply as a collective term for these patients. CLI is also equivalent to the clinical description of grades II and III, which includes categories 4, 5, and 6 of the North American recommendations for reporting standards (9). CLI may be defined as acute or chronic ischemic rest pain, or chronic ulceration and/or gangrene, attributable to objectively proven arterial occlusive disease.The incidence of CLI has been calculated to be in the order of 1 per 2,000 individuals per year, out of which up to 30% have diabetes. Approximately 5%–10% of patients identified from a medical center with PAD have CLI. Assessing quality of life and functional status in this group is especially challenging since symptoms may change rapidly (8).

The greatest challenge in the treatment of patients with PAD and diabetic foot syndrome (DFS) is avoiding major amputation. CLI and DFS are the only confirmed indications for crural and pedal revascularization, and the decision to undertake such treatment should be arrived at jointly by angiologists, radiologists, and vascular surgeons. Apart from determination of the appropriate technique for revascularization—surgical or interventional the timing is crucial: soon after failure of conservative treatment, not when advanced infection and spreading of foot necrosis already make amputation unavoidable (10).

PAD is a major risk factor for lower extremity amputation. A peculiar feature of arteriopathy in diabetics is that vascular disease extends into the infrapopliteal axis. In nondiabetic individuals, obstructive plaques are generally localized

in the femoral axis and cause small-artery obstructions. In diabetic patients, the rate of proximal obstructions in the absence of small-artery obstructions is very low: our experience indicates a prevalence rate of 5%. In approximately 30% of individuals, the obstructive disease only affects the subpopliteal axis, whereas in 60% of patients, the disease extends to the femoro-popliteal and infrapopliteal axes. The higher prevalence of occlusions as compared with stenoses was confirmed at the level of tibial arteries. Such anatomical features, along with the difficulties in the diagnostic approach, account for the fundamental role of CLI as the main prognostic indicator for major amputation (above the ankle). It is believed that the true incidence and prevalence of PAD may be greatly underestimated because it is often asymptomatic during the early phases and may therefore remain undiagnosed: more than two thirds of the population aged 60 years and more with PAD in the United States are asymptomatic. This percentage is likely to be greater in the diabetic population because the presence of sensitive neuropathy may attenuate or cancel the sensation of pain at rest or during exercise (11).

CLI occurs when arterial stenoses or occlusions impair blood flow to such an extent that despite compensatory mechanisms such as collateral formation, the nutritive requirements of the peripheral microcirculation cannot be met. This is usually caused by multilevel disease." In some cases, the hemodynamic consequences of arterial lesions may be compounded by chronic venous insufficiency or decreased cardiac output. In contrast to the early stages of PAD, in which compromised skeletal muscle blood flow causes intermittent claudication, rest pain and trophic changes associated with CLI are predominantly attributable to a critical reduction in skin microcirculation. The skin microcirculation is atypical in many ways, most notably that nutritional capillary blood flow only represents approximately 15% of the normal total blood flow in the foot, the remainder having a thermoregulatory function only (7).

Pulse palpation is an essential screening tool in assessing for the presence of PAD. The 2006 guidelines recommend defining a pulse as abnormal, diminished, or absent. In the literature, grading of pulse palpation is strongly examiner-dependent and thus prone to variability. According to the 2003 American Diabetes Association (ADA) report, the pedal pulse is absent in 8.1% of healthy individuals, and the posterior tibial pulse is absent in 2% of the healthy population. Other reports indicate that abnormalities of the dorsalis pedis pulse may be detected in up to 30% of cases. The absence of the posterior tibial pulse seems to be a more sensitive and specific indicator than the absence of the pedal pulse (11). The mechanisms underlying the regulation of blood flow to the lower limbs might also play a role in the development of intermittent claudication independently of the burden of peripheral artery atherosclerosis (12).

The prevalence of exertional leg symptoms other than claudication varies from approximately 30% to 45% among patients with PAD. The classical symptom of intermittent claudication is exertional calf pain that resolves within 10 minutes of rest. Nineteen percent of WALCS participants with PAD had exertional leg pain that sometimes began at rest (pain on exertion and rest), 9% had exertional leg symptoms that did not cause them to stop walking (atypical leg pain/carry on), and 20% had other exertional leg pain that was not consistent with classical claudication (atypical exertional leg pain/stop) (8). Claudication affects a certain group of muscles according to the level of occlusion: in aortoiliac occlusion, the pain affects the gluteal muscles; in femoro-popliteal occlusion, the pain affects the calf muscle; and in more distal occlusion, the pain affects the foot muscle. Pain may be ambiguous because patients with claudication may have cramping or fatigue occurring in only one leg. Radiculopathy may be confused with claudication. Although claudication has low diagnostic sensitivity for PAD, it has a very high specificity. Diabetes is regarded as a major risk factor for progress of claudication to CLI. Therefore, medical treatment and reduction of the above-mentioned risk factors are of the utmost importance in claudicating patients (11).

Weinberg et al. (3) indicates that regional neuropathy is commonly associated with chronic ischemia and CLI. Understanding of physiology can allow a clinician to locate the site of arterial occlusion based on the location of the symptoms. For example, pain or discomfort in the calf, ankle, or foot could indicate an obstruction/occlusion in the popliteal or superficial femoral arteries. Symptoms located primarily in the calf or thigh could indicate involvement of the femoral arteries or their branches, whereas symptoms in the buttock, hip, and thigh indicate higher disease in the aorta or iliac artery (13).

Patients may also present with nonhealing ulcers or regions of gangrene on the distal aspect of the leg, foot, or toes, which is a more obvious manifestation of peripheral vascular disease. In diabetic patients, the combination of lower extremity neuropathy and ischemia secondary to atherosclerosis can lead to pressure necrosis, ulceration, and microbial infection. If these problems are unrecognized and therefore not managed, they can lead to gangrene and ultimately limb loss. Ischemia is accompanied by infection in more than 50% of diabetic patients and that most of these patients will have some element of peripheral neuropathy as well. Although it is important to focus on restoration of arterial flow to the foot, it is necessary for the vascular team to simultaneously address the issues of infection and neuropathy as well as to achieve limb salvage (7). Claudication defined as a painful, aching, cramping, or a feeling of tiredness in the calves that occurs during walking, does not begin at rest, does not subside if walking continues, and is relieved within

10 minutes or less when activity ceases. Classic claudication, as measured by a variety of questionnaires, is only reported in 7.5%to 33% of PAD patients. Higher prevalence has been reported in smaller populations (43.8%) and specific populations including only individuals complaining of leg pain (78.8%), or excluding individuals who have non-compressible arteries, CLI, or a history of revascularization (43.6%) (13). Imaging is necessary for planning interventions in patients with lower extremity PAD. Noninvasive imaging modalities, including duplex ultrasonography is available for grading lower extremity arterial disease. Ultrasound is easily accessible and does not require radiation or contrast agents (14). Doppler ultrasound based flow studies are routinely used in clinical practice for the assessment of arterial stenosis in symptomatic patients to identify those who would benefit from surgical intervention. With recent improvements in image quality and built-in automation, perhaps ultrasound can similarly be deployed to assess subclinical atherosclerosis in the asymptomatic population to identify subjects who would benefit from prophylactic medical intervention. Automation in ultrasound imaging technoogy allows users to evaluate the presence of subclinical atherosclerosis. Detection of subclinical disease is further enhanced by inclusion of the iliofemoral artery examination. The resulting pla-que quantification may become clinically relevant for monitoring response to medical intervention (15).

PAD participants who were asymptomatic had smaller mean and maximum plaque area and greater mean and minimum percent lumen area as compared with PAD participants with intermittent claudication. PAD participants with atypical leg pain had smaller normalized maximum plaque area than PAD participants with intermit-tent claudication. Direct measurement of atherosclerotic plaque in the superficial femoral artery (SFA) may better assess progression or regression of plaque. Asymptomatic PAD participants have less atherosclerotic plaque in the proximal SFA than PAD participants with intermittent claudication. Asymptomatic PAD participants may consist of a heterogeneous group of individuals, including individuals with mild PAD and those with more severe disease who have limited their walking speed or slowed down their activity to avoid leg symptoms (4).

Conclusion

Although non-invasive ultrasound imaging technology seems to bring reliable information on underlying atherosclerosis and direct plaque visualization, physical objective examination of the lower limbs provides valuable information on the presence of stage of CLI and subclinical atherosclerosis. Early detection of PAD is crucial for the timely treatment and prevention of amputation, heart attack, stroke, and death.

References

1. Farhan J, Khawaja J, Iftikhar J,Kullo. Novel markers of peripheral arterial disease. Vascular Medicine 2009; 14: 381–92. [CrossRef] [PubMed]
2. Kosmas I,Paraskevas KI, Mukherjee D, Whayne Jr TF. Peripheral arterial disease: implications beyond the peripheral circulation.Angiology 2012; 64(8): 569-71.
3. Weinberg DH, Simovic D, Isner J, et al. Chronic ischemic monomelic neuropathy from critical limb ischemia. Neurology 2001; 57: 1008–12. [CrossRef][PubMed]
4. McDermott MM, Kiang Liu K, Carr J, Criqui MH, Tian L et al. Superficial femoral artery plaque, the ankle-brachial index, and leg symptoms in peripheral arterial disease the walking and leg circulation study (WALCS) III. CircCardiovasc Imaging 2011; 4: 246-52.[CrossRef][PubMed]
5. Wain RA, Berdejo GL, Delvalle WN, Lyon RT, Sanchez LA, Suggs WD et al. Can duplex scan arterial mapping replace contrast arteriography as the test of choice before infrainguinal revascu larization? J VascSurg 1999;29(1):100e7.
6. Eiberg JP, Hansen MA, Jorgensen LG, Rasmussen JB, Jensen F, Schroeder TV. In-situ bypass surgery on arteriographically invisible vessels detected by Doppler-ultrasound for limb salvage. J CardiovascSurg2004;45(4):375e9.
7. Dinh T, Scovell S, Veves A.Peripheral arterial disease and diabetes: a clinical update. The International Journal of Lower Extremity Wounds 2009; 8 (2): 75-8. [CrossRef][PubMed]
8. Nehlera MR, McDermottb MM, Treat-Jacobsonc D,ChetterdI,Regensteiner JG. Functional outcomes and quality of life in peripheral arterial disease: current statusVascular Medicine2003; 8: 115–26. [CrossRef]
9. [No authors listed]. Chronic critical limb ishemia. Eur J Vase EndovascSurg 2000; 19, 514-1-5243.
10. Dohmen A, Eder S, Euringer W, Zeller T, Beyersdorf F. Chronic critical limb ischemia. DtschArzteblInt 2012; 109(6): 95–101.[PubMed]
11. Faglia E. Characteristics of peripheral arterial disease and its relevance to the diabetic population. The International Journal of Lower Extremity Wounds 2011; 10(3) 152–66. [CrossRef][PubMed]
12. Thais Coutinho, Thom W Rooke and Iftikhar J Kullo.Arterial dysfunction and functional perfor mance in patients with peripheral artery disease:

A review. Vascular Medicine 16(3) 203–11. [CrossRef][PubMed]
13. Schorr EN, Treat-Jacobson D.Methods of symptom evaluation and their impact on peripheral artery disease (PAD) symptom prevalence: A review.Vascular Medicine 2013;18(2): 95–111. [CrossRef][PubMed]
14. Rosemarie Met, Bipat S, Legemate DA, Reekers JA, Koelemay MJW. Diagnostic performance of computed tomography angiography in peripheral arterial disease a systematic review and meta-analysis. JAMA 2009; 301(4): 415-24. [CrossRef] [PubMed]
15. Bedi R, Nagray A, Fukumotoz T, Lynumz S, Senguptax P, Awk J. Detection of subclinical atherosclerosis in peripheral arterial beds with b-mode ultrasound a proposal for guiding the decision for medical intervention and an artifact-corrected volumetric scoring index. Global heart 2014; 9 (4): 367-78. [CrossRef][PubMed]

Originalni rad **UDC: 616.13-008.64-07**
doi:10.5633/amm.2016.0307

ODNOS SUBJEKTIVNIH TEGOBA I EVALUACIJA DIJAGNOSTICKIH PROCEDURA ZASNOVAN NA ODREĐIVANJU STADIJUMA HRONIČNE ARTERIJSKE INSUFICIJENCIJE DONJIH EKSTREMITETA

Nebojša Ignjatović[1,2], Miroslav Stojanović[1,2], Goran Stanojević[1,2], Aleksandar Karanikolić[1,2], Milan Radojković[1,2], Saša Živić[2,3], Dragan Stojanov[2,4], Miodrag Đorđević[2], Jelena Ignjatović[4], Daniela Benedeto-Stojanov[2,5], Bobana Milojković[1,2]

Klinika za opštu hirurgiju, Klinički centar Niš, Niš, Srbija[1]
Univerzitet u Nišu, Medicinskifakultet, Niš, Srbija[2]
Klinika zakardiovaskularnu i transplantacionu hirurgiju, Klinički centar Niš, Niš, Srbija[3]
Institut za radiologiju, Klinički centar Niš, Niš, Srbija[4]
Klinika za gastroenterologiju, Klinički centar Niš, Niš, Srbija[5]

Kontakt: Nebojša Ignjatović
Mokranjčeva 29/13, 18000 Niš
e-mail: n.ignjat@gmail.com

Periferna arterijska bolest (PAB) donjih ekstremiteta predstavljaja grupu poremećaja koju karakteriše sužavanje ili okluzija arterija koja dovodi do postepenog smanjenja dotoka krvi u ekstremitete. Cilj ovog rada bio je da se ispita predominantna subjektivna nelagodnost, objektivni klinički nalaz i predominantna lokalizacija stenozno-okluzivnih lezija kod bolesnika u stadijumima funkcionalne i kritične ishemije hronične arterijske insuficijencije donjih ekstremiteta. Prospektivnom studijom analizirali smo grupu od 50 bolesnika, lečenih na Odeljenju za vaskularnu hirurgiju Hirurške klinike u Nišu u periodu od septembra 2000. do oktobra 2001. godine sa jasnim simptomima i znacima različitih stadijuma hronične arterijske insuficijencije donjih ekstremiteta, prethodno verifikovanih kolor doplerom i objektivnim kliničkim pregledom. Kritična ishemija je češće povezana sa promenom boje kože ($p<0,05$), atrofičnim promenama ($p<0,001$), odsustvom pulzacija ($p<0,01$), pojavom mišićne atrofije ($p<0,01$), gangrene ($p<0,05$). Gangrena je klinički domi-nantno prisutna sa pojavom ulceracija ($p <0,05$) u stadijumu kritične ishemije. U stadijumu funkcionalne ishemije, kao signifikantan znak često se pojavljuje bledilo ($p<0,01$) i očuvana pulzacija a.politealisa ($p<0,01$). Asimtomatske stenozano-okluzivne lezije sa stenozom od 1-19% bile su predominantne kod bolesnika u stadijumu I funkcionalne ishemije. Subkritična stenoza, koja je iznosila od 20-49%, bila karakteristična za bolesnike u stadijumu IIa, dok je kritična stenoza od 50-99% bila prisutna kod bolesnika u IIb i III stadijumu kritične ishemije. Bolesnici u IV stadijumu kritične ishemije imali su totalnu okliziju distalnih arterija donjih ekstremiteta. U stadijumima kritične ishemije, najčešći stenozno-okluzivni proces bio je lokalizovan na femoro-poplitealnom segmentu (a. femoralis superficialis). Rano otkrivanje periferne arterijske bolesti donjih ekstremiteta je od ključnog značaja za pravovremeno lečenje i prevenciju amputacija, infarkta srca, moždanog udara i smrti bolesnika. *Acta Medica Medianae 2016;55(3):44-56.*

Ključne reči: *hronična arterijska insuficijencija, fukcionalna ishemija, kritična ishemija*