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Aortoiliac and femoropopliteal lesions in patients with concomitant peripheral arterial disease and medial arterial calcification

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Abstract

Objective: To characterize stenosis and/or occlusion in patients with concomitant peripheral arterial disease (PAD) and medial arterial calcification (MAC). **Patients and methods:** We performed continuous-wave Doppler technique (to measure the ankle-brachial index - ABI) and duplex ultrasonography in 75 consecutive patients at risk for PAD (57 males, age 72.6±6.3 years) admitted to a Medical Clinic between January and March 2006. Group A was composed of 15 subjects with plaques and ABI higher than 1.3 (MAC - 20%). Normal ABI was found in 43 patients (group B - 57.33%). Group C included 17 patients with ABI lower than 0.9 (ischemia - 22.67%). **Results:** Nonsignificant aortoiliac stenosis (less than 50%) was found in 70 subjects (15 in group A, 39 in group B, and 16 in group C - nonsignificant). Significant femoropopliteal stenosis (greater than 50%) was detected in eight patients (five in group A, one in group B, and two in group C – $p<0.001$). Nonsignificant femoropopliteal stenosis was identified in 54 subjects (seven in group A, 42 in group B, and five in group C - $p<0.001$). **Conclusion:** Significant femoropopliteal stenosis significantly correlated with presence of MAC. Nonsignificant femoropopliteal stenosis was identified in patients with normal ABI.

Key words: peripheral arterial disease, medial arterial calcification, ankle-brachial index

Rezumat

Obiectiv: Analiza caracteristicilor stenozei şi/sau ocluziei la pacienţii cu arteriopatie obliterantă periferică şi mediocalcinoză. **Pacienţi şi metodă de lucru:** Am efectuat tehnicile Doppler continuu (pentru determinarea indicelui de presiune sistolică gleznă-braţ – IPS) şi duplex la 75 pacienţi consecutivi cu risc de arteriopatie (57 bărbaţi, vârstă 72,6±6,3 ani) internaţi într-o Clinică Medicală în perioada ianuarie-martie 2006. Cei 15 subiecţi cu plăci şi IPS peste 1,3 (mediocalcinoză) au format grupul A (20%). Grupul B a inclus 43 pacienţi cu IPS normal (57.33%). Grupul C a cuprins 17 pacienţi (22.67%) cu ischemie (IPS sub 0,9). **Rezultate:** Stenoza aortoiliacă nesemnificativă (sub 50%) a fost depistată la 15 pacienţi din grupul A, 39 din grupul B şi 16 din grupul C (nesemnificativ). Stenoza femuropoplitee semnificativă (peste 50%) a fost identificată la opt subiecţi din grupul A, unul din grupul B şi doi din grupul C ($p<0.001$). Stenoza femuropoplitee nesemnificativă a fost diagnosticată la şapte bolnavi din grupul A, 42 din grupul B şi cinci din grupul C ($p<0.001$). **Concluzii:** Stenoza femuropoplitee semnificativă s-a corelat cu prezenţa mediocalcinozei. Stenoza femuropoplitee nesemnificativă a fost diagnosticată la pacienţii cu IPS normal.

Cuvinte cheie: arteriopatie obliterantă periferică, mediocalcinoză, indice de presiune sistolică gleznă-braţ

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Introduction

Peripheral arterial disease (PAD) is characterized by stenosis, occlusion and aneurysm of the aorta, visceral branches, and arteries of the legs due to atherosclerosis and thromboembolism [1]. The results of the Cardiovascular Health Study and of the Atherosclerosis Risk in

Communities Study (ARIC Study) have shown that PAD is increasing cardiovascular morbidity and mortality, and all-cause mortality [2,3]. All risk factors for atherosclerosis (particularly increasing age, current smoking, arterial hypertension, diabetes, and dyslipidemia) are, at the same time, traditional independent risk factors for PAD [4,5]. Therefore, the European Society of Hypertension and the European Society of Cardiology strongly recommend ankle-brachial index (ABI) as a test for the evaluation of patients with hypertension [6]. A value lower than 0.9 is associated with a two- to three-fold increased risk of cardiovascular mortality so that ABI may improve the accuracy of cardiovascular risk prediction, reclassify the Framingham risk categories and modify the treatment recommendations [7,8]. The positive correlation between PAD, coronary artery disease and carotid stenosis is well known [9-11].

Medial artery calcification (MAC) is a non obstructive arterial disease. It produces significant stiffening of the arterial wall heavily calcified and reduces its response to vasodilator stimuli [4,12]. This disease, unrelated to cardiovascular risk factors, is associated with elevated cardiovascular morbidity and mortality in patients with diabetes mellitus and/or end-stage renal failure. Patients with MAC may have falsely elevated ABI (higher than 1.3) due to reduced arterial compliance, so that associated ischemia cannot be diagnosed [7,13,14].

Despite numerous studies, the knowledge of the prevalence of MAC in patients with PAD is limited [13].

Aims

We investigated the localization of the arterial lesions (stenosis and occlusion) and the degree of stenosis in patients with concomitant PAD and MAC.

Patients and methods

The study was conducted at the Department of Internal Medicine, Municipal Hospital, 5th Medical Clinic, „Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Romania between January and March 2006.

There were three inclusion criteria related to the indication for performing ABI: patients with arterial hypertension - ABI is recommended by the European Task Force for the Management of Arterial Hypertension [6] or with diabetes mellitus – the guidelines recommend that the test should be used as screening for hemodynamically significant disease [16] or subjects at risk for PAD [1]. There are six criteria for the risk diagnosis for PAD: age less than 50 years with diabetes and other risk factors (smoking, dyslipidemia, or hypertension) or age 50 to 69 years and history of smoking or diabetes or age over 70 years or leg symptoms (claudication, rest pain) or modified leg pulses or known artery disease (coronary, carotid, or renal) [1]. We used a continuous Doppler machine Kranzbühler Digidop 2.

A total of 75 consecutive patients met the criteria for inclusion in this study. Depending on the value of ABI, patients were divided into three groups: A (ABI higher than 1.3 - MAC), B (normal value of ABI: 0.9-1.3), and C (resting ischemia defined by ABI lower than 0.9).

Duplex ultrasonography was performed in all patients irrespective of ABI and served to analyze the arterial wall (plaques with stenosis lower or more than 50%) and the lumen (occlusion). The arterial circulation of the lower extremity was divided into three segments – aortoiliac, femoropopliteal, and tibioperoneal. All patients had stenoses and/or occlusion. We used, as duplex machines, the Aloka Prosound SSD-400 and General Electric Logiq 500.

The following parameters were analyzed in all patients: demographic data (gender, age), clinical data (intermittent claudication, rest pain, skin changes – color, temperature, trophic lesions, absent or diminished pulses, femoral bruits, Fontaine's stages, history of smoking, diabetes, hypertension, or dyslipidemia, body mass index, abdominal circumference), morphological data (stenosis, occlusion, wall echogenicity, acoustic shadow), hematologic tests (complete blood count, coagulation), biochemical tests (fasting blood glucose and lipid profile, serum creatinine, proteinuria), resting electrocardiogram and echocardiogram, carotid duplex scan, and fundoscopy. We did not perform toe pressure measurement in patients with MAC.

Statistical analysis was performed using the Epi Info computer package, version 3.3.2. We calculated percents for categorical variables and means and standard deviations for continuous variables. Comparative analysis of qualitative variables was made using $\chi 2$ test. The ANOVA test was used to compare the differences between the mean values and to calculate standard deviations. A P value less than 0.05 was considered the level of statistical significance.

Results

All background characteristics of the sample are presented in Table 1.

All the 75 patients included in the study had nonsignificant arterial lesions (aortoiliac and/or femoropopliteal stenosis less than 50%). A total of 24 patients (32%) had, in addition, hemodynamically significant arterial lesions

Table 1. Characteristics of patients with PAD

Parameters		**Number of patients 75**
Demographic data	Men	45 (60%)
	Age (mean ± standard deviation; range)	72.60 ± 6.3 years (44-79)
Clinical data	Stage I	53 (70.67%)
	Stage II	19 (25.33%)
	Stages III and IV	3 (4%)
ABI	>1.30	15 (20%)
	0.91-1.30	43 (57.33%)
	<0.90	17 (22.67%)
Arterial lesions	Aortoiliac stenosis <50%	70 (93.33%)
	Femoropopliteal stenosis <50%	54 (72%)
	Femoropopliteal occlusion	14 (18.66%)
	Femoropopliteal stenosis >50%	8 (10.66%)
	Tibioperoneal stenosis	6 (8%)
	Aortoiliac stenosis > 50%	1 (1.33%)
	Aortoiliac occlusion	1 (1.33%)
Risk factors for atherosclerosis	Hypercholesterolemia	60 (80%)
	Hypertension	53 (70.66%)
	Smoking	46 (61.33%)
	Hypo HDL-cholesterol	41 (54.66%)
	Abdominal obesity	18 (24%)
	Diabetes	9 (12%)
Comorbidities	Coronary artery disease	72 (96%)
	Carotid artery disease	66 (88%)

(aortoiliac and/or femoropopliteal stenosis greater than 50%, tibioperoneal stenoses, aortoiliac or femoropopliteal occlusion).

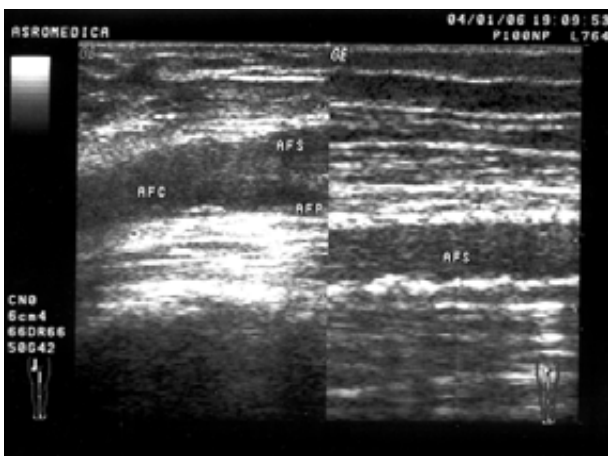

Figure 1. Long-axis view of the right common and superficial femoral arteries. Heterogenous plaques with irregular surface on the posterior wall. AFC: common femoral artery. AFS: superficial femoral artery. AFP: deep femoral artery

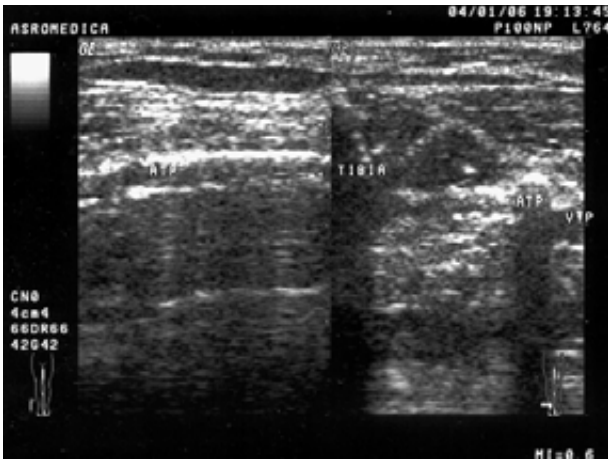

Figure 2. Longitudinal and transverse images of the right posterior tibial artery. Hyperechoic arterial wall with acoustic shadow. ATP: posterior tibial artery. VTP: posterior tibial vein

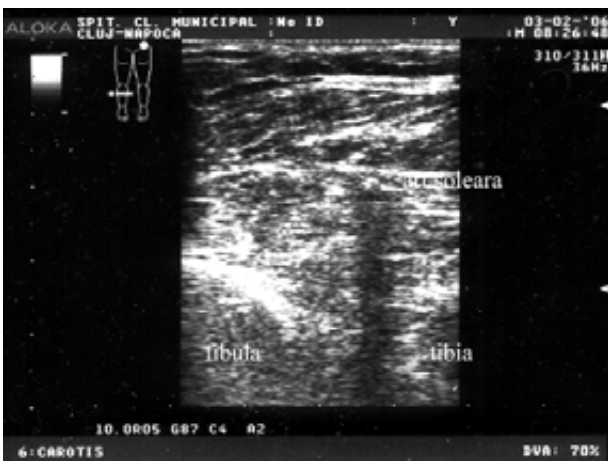

Figure 3. Short-axis view of the left calf. Prone position. Soleal artery with hyperechoic wall with shadowing. Art soleara: soleal artery.

Concomitant aortoiliac and femoropopliteal involvement was encountered in 58 patients (77.32%). A total of 6 patients had simultaneous aortoiliac and tibioperoneal lesions. Only two subjects had femoropopliteal and tibioperoneal involvement. Two patients had impaired circulation of the three segments of the legs (aortoiliac, femoropopliteal, and tibioperoneal).

Femoral stenoses less than 50% were frequent (fig 1).

All patients with MAC had hyperechoic tibial arteries with shadowing (fig 2).

Some of the subjects had also strong echogenicity of the muscular and superficial femoral arteries (fig 3, fig 4).

All data of patients from the three groups (A, B, and C) are presented in Table 2.

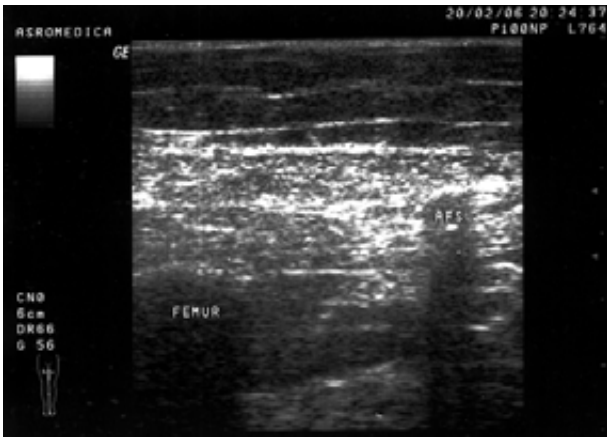

Figure 4. Transverse view of the right superficial femoral artery. Strong echogenicity arterial wall with shadowing. AFS: superficial femoral artery.

Table 2. Characteristics of patients from groups A, B, and C

Parameters	Group A N=15	Group B N=43	Group C N=17	p
Men	12	20	13	0.021
Age (mean ± standard deviation; range)	74.9±2.4 70-78	72.2±5.6 55-79	71.8±9.7 44-79	0.15
Stage I	6	43	4	<0.0001
Stage II	8	0	11	<0.0001
Stages III and IV	1	0	2	0.09
Aortoiliac stenosis <50%	15	39	17	0.21
Femoropopliteal stenosis <50%	12	43	7	<0.0001
Femoropopliteal occlusion	1	0	7	<0.0001
Femoropopliteal stenosis >50%	5	1	2	0.004
Tibioperoneal stenosis	0	0	6	<0.0001
Aortoiliac stenosis > 50%	0	0	1	0.18
Aortoiliac occlusion	0	0	1	0.18
Hypercholesterolemia	11	35	14	0.77
Hypertension	12	30	11	0.62
Smoking	12	22	12	0.09
Hypo HDL-cholesterol	14	16	11	0.0005
Abdominal obesity	7	8	3	0.07
Diabetes	4	4	1	0.14
Coronary artery disease	15	42	15	0.16
Carotid artery disease	15	36	16	0.16

Discussion

Of the 75 patients included in the study, 40 were men. The male-to-female ratio was 1.5. This value is little different from the sex ratio found in recent large studies. There are no clear differences between men and women in the prevalence of PAD diagnosed based on ABI. The male-to-female ratio found in the Framingham Offspring Study and in the Rotterdam Study was 1.18 and 0.82, respectively [17,18]. When only group B was taken into consideration, the male-to-female ratio was 0.86.

Over two thirds of patients had no pain. All patients included in group B had Fontaine stage I. Without duplex technique, hemodynamically nonsignificant arterial lesions remain undiagnosed. Only 25% of patients had intermittent claudication (they were part of groups A and C). In the Rotterdam Study, 6.3% of patients with PAD (8.7% of men and 4.9% of women) reported intermittent claudication [18]. McDermott *et al.* reported that only 10% to 30% of patients with ABI below 0.90 have this type of pain [7]. Fontaine stages III and IV were encountered only in three patients because, in general, patients with chronic critical ischemia are admitted into surgical clinics for revascularization or amputation.

Over half of the patients had normal ABI. Unfortunately we could not perform the treadmill exercise. This test could have been important in the alteration of the number of patients in groups B and C because ABI could fall by at least 0.10 post exercise in patients with hemodynamically nonsignificant plaques at rest [19,20].

Approximately 33% of patients with nonsignificant arterial disease had also hemodynamically significant lesions (stenosis greater than 50% or occlusion). The patients included in group C had the most important lesions. Sacks *et al.* showed that the decrease of ABI correlates with the severity of arterial disease [15]. All patients from group B had at least nonsignificant femoropopliteal stenosis ($p<0.0001$).

A total of 5 subjects in group A (33.33%) had also femoropopliteal stenosis greater than 50% ($p=0.004$). We found no explanation in the medical literature. The association between nonsignificant and/or significant aortoiliac and femoropopliteal diseases, found in 58 patients (77.32%) was the most common combination of segmental lesions. Vogt *et al.* (1993) found this two-segment disease in 18% of men and 22% of women [21]. Two patients had three-segment disease (aortoiliac, femoropopliteal, and tibioperoneal disease). Vogt's study showed that 2% of men and 3% of women had this kind of disease [21].

There were no statistically significant differences between the three groups concerning the frequency of hypertension, hypercholesterolemia, current smoking,

abdominal obesity, and diabetes. Diabetes was diagnosed in 9 patients with PAD (12%) and in 4 subjects with PAD and MAC (p=0.15). It is known that MAC is associated with diabetes mellitus, chronic renal insufficiency, and older age [13,14].

Some data from the literature are inconclusive. In the Rotterdam Study, current smoking and hypertension were more frequent in persons with ABI lower than 0.90 than in subjects with normal or higher ABI [18]. A total of 4393 American Indians were included in the Strong Heart Study and followed up for 8.3±2.2 years. Diabetes was found in 60.2% of patients with ABI lower than 0.90 and in 67.8% of subjects with ABI greater than 1.30 (nonsignificant). The prevalence of hypertension in the two groups was 50.1% and 45.1%, respectively [22]. Vogt et al.(1993) found that diabetes was significantly associated with tibioperoneal disease. Aortoiliac lesions and femoropopliteal disease was associated with a high frequency of current smoking and hypertension [21]. Nosenko et al. (2003) examined 68 patients (40 of them were diabetics). There were no significant difference concerning the frequency of aortoiliac and popliteal disease between patients with and without diabetes [23]. Kröger *et al.* (2006) presented their study on 4735 German subjects aged 45-75 years. Patients were followed up for four years. In contrast with PAD, the prevalence of MAC did not increase with age [24].

The highest frequency of hypo HDL – cholesterolemia was encountered in 14 out of 15 patients in group A (93.33%). We found no explanation in the literature.

Ischemic heart disease and asymptomatic carotid artery disease were very frequent (96% and 88%, respectively) without differences between groups. It is known that patients with PAD are more likely to have other atherosclerotic disorders [25]. In fact The American Society of Neuroimaging and the Society of Vascular and Interventional Neurology recommend screening for asymptomatic carotid artery stenosis in patients with PAD and/or hypertension [26].

Limitations

We did not perform some investigations (the estimated glomerular filtration rate, microalbuminuria, provoked – hyperglycemia test, treadmill exercise, and toe-brachial index).

Conclusion

Significant femoropopliteal stenosis and hypo HDL–cholesterolemia significantly correlated with the presence of MAC. Nonsignificant femoropopliteal stenosis was identified in patients with normal ABI.

References

1. Hirsch AT, Haskal ZJ, Hertzer NR, et al. ACC/AHA Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary: a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients with Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic). J Am Coll Cardiol 2006;47:e1-e192. (http://content.onlinejacc.org/cgi/content/full/47/6/e1)
2. Weatherley BD, Nelson JJ, Heiss G, et al. The association of the ankle-brachial index with incident coronary heart disease. The Atherosclerosis Risk In Communities (ARIC) Study, 1987-2001. BMC Cardiovascular disorders 2007;7:3. (http://www.biomedcentral.com/1471-2261/7/3).
3. Aronow WS, Ahmed MI, Ekundayo OJ, Allman RM, Ahmed A. A propensity-matched study of the association of peripheral arterial disease with cardiovascular outcomes in community-dwelling older adults. Am J Cardiol 2009;103:130-135.
4. Soor GS, Vukin I, Leong SW, Oreopoulos G, Butany J. Peripehral vascular disease: who gets it and why? A histomorphological analysis of 261 arterial segments from 58 cases. Pathology 2008;40:385-391.
5. Aboyans V, Ho E, Denenberg JO, Ho LP, Natarajan L, Criqui MH. The association between elevated ankle systolic pressures and peripheral occlusive arterial disease in diabetic and nondiabetic subjects. J Vasc Surg 2008;48:1197-1203.
6. Mancia G, De Backer G, Dominiczak A, et al. 2007 Guidelines for the management of arterial hypertension. The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2007;28:1462-1536.
7. McDermott MM. The magnitude of the problem of peripheral arterial disease: epidemiology and clinical significance. Cleve Clin J Med 2006; 73 Suppl 4: S2-S7.
8. Fowkes FG, Murray GD, Butcher I, et al. Ankle brachial index combined with Framingham risk score to predict cardiovascular events and mortality. A meta-analysis. JAMA 2008;300:197-208.
9. Mullenix PS, Steele SR, Martin MJ, Starnes BW, Andersen CA. C-reactive protein level and traditional vascular risk factors in the prediction of carotid stenoses. Arch Surg 2007; 42:1066-1071.
10. Sobel M, Verhaeghe R. Antithrombotic therapy for peripheral artery occlusive disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133(6 Suppl):815S-843S.
11. Bosevski M, Georgievska-Ismail Lj, Tosev S, Borozanov V. Risk factors for development of peripheral and carotid

artery disease among type 2 diabetic patients. Prilozi 2009; 30:81-90 (http://e20.manu.edu.mk/prilozi/5bm.pdf)
12. Kerr PG, Guerin AP. Arterial calcification and stiffness in chronic kidney disease. Clin Exp Pharmacol Physiol 2007;34:683-687.
13. Leskinen Y, Salenius JP, Lehtimäki T, Huhtala H, Saha H. The prevalence of peripheral arterial disease and medial arterial calcification in patients with chronic renal failure: requirements for diagnostics. Am J Kidney Dis 2002;40:472-479.
14. Bonham PA. Get the LEAD out: noninvasive assessment for lower extremity arterial disease using ankle brachial index and toe brachial index measurements. J Wound Ostomy Continence Nurs 2006;33:30-41.
15. Sacks D, Bakal CW, Beatty PT, et al. Position statement on the use of the ankle brachial index in evaluation of patients with peripheral vascular disease. A consensus statement developed by the Standards Division of the Society of Interventional Radiology. J Vasc Interv radiol 2003; 14(9Pt2): S389.
16. Wisconsin Diabetes Advisory Group. Wisconsin diabetes mellitus essential care guidelines. Madison (Wi): Wisconsin Diabetes Prevention and Control Program. 2008. http://dhs.wisconsin.gov/health/diabetes/guidelines.htm
17. Murabito JM, Evans JC, Nieto K, Larson MG, Levy D, Wilson PW. Prevalence and clinical correlates of peripheral arterial disease in the Framingham Offspring Study. Am Heart J 2002;143:961-965.
18. Meijer WT, Hoes AW, Rutgers D, Bots ML, Hofman A, Grobbee DE. Peripheral arterial disease in the elderly: The Rotterdam Study. Arterioscler Thromb Vasc Biol 1998;18:185-192.
19. Beckman JA, Creager MA. Peripheral arterial disease: clinical evaluation. In: Creager MA, Dzau VJ, Loscalzo J (eds). Vascular Medicine: a companion to Braunwald´s Heart Disease. Saunders Elsevier Philadelphia 2006:255-269.
20. van Langen H, van Gurp J, Rubbens L. Interobserver variability of ankle-brachial index measurements at rest and post exercise in patients with intermittent claudication. Vasc Med 2009;14:221-226.
21. Vogt MT, Wolfson SK, Kuller LH. Segmental arterial disease in the lower extremities: correlates of disease and relationship to mortality. J Clin Epidemiol 1993;46:1267-1276.
22. Resnick HE, Lindsay RS, McGrae McDermott M, et al. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality. The Strong Heart Study. Circulation 2004;109:733-739.
23. Nosenko EM, Sidorenko BA, Koshkin VM, Dadova LV, Gracheva OA, Koshkina IV. Clinical manifestations and characteristics of vascular bed involvement in atherosclerosis of lower extremities in patients with type 2 diabetes. Kardiologiia 2003;43:36-42.
24. Kröger K, Stang A, Kondratieva J, et al. Prevalence of peripheral arterial disease-results of the Heinz Nixdorf recall study. Eur J Epidemiol 2006;21:279-285.
25. Criqui MH, Ninomyia J. The eEpidemiology of peripheral arterial disease. In: Creager MA, Dzau VJ, Loscalzo J (eds). Vascular Medicine: a companion to Braunwald´s Heart Disease. Saunders Elsevier Philadelphia 2006:223-238.
26. Qureshi AI, Alexandrov AV, Tegeler CH, Hobson RW, Baker JD, Hopkins LN. Guidelines for screening of extracranial carotid artery disease: a statement for healthcare professionals from the Multidisciplinary Practice Guidelines Committee of the American Society of Neuroimaging. J Neuroimaging 2007;17:19-47.