UDC 616.137.83/87-004.6-007.271

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LIPID PROFILE AND HEMORHEOLOGY DYNAMICS IN PATIENTS WITH LOWER EXTREMITY PERIPHERAL ARTERY DISEASE IN THE PREOPERATIVE AND POSTOPERATIVE PERIOD

Abstract

The objective of the study was to evaluate the lipid and hemostatic profile in patients with peripheral artery disease of lower extremities at different levels of lesion and methods of surgery. **Materials and methods.** 330 male patients with peripheral artery disease of lower extremities of II b-III degree were examined: group I consisted of 140 patients with lesions of the femoral-popliteal arterial segment, who underwent femoral-popliteal bypass surgery (58.64 ± 7.73 years), group II — 97 patients with occlusive-stenotic lesions of the aorto-iliac segment, who underwent aorto-femoral bypass surgery (56.82 ± 6.69 years), group III — 93 patients with occlusive stenotic changes of the iliac arteries, who underwent transluminal balloon angioplasty and stenting of the iliac arteries. The examination of patients included general clinical, instrumental and laboratory methods with the assessment of lipid profile fractions and plasma-coagulation level of hemostasis. **Results.** The provided examination showed that patients with peripheral artery disease have disorders of the blood lipid profile, which have significant differences depending on the severity and localization of occlusive-stenotic lesions of the aorta and main arteries. Lipid imbalance persists after correction of arterial blood flow. Significant changes in the hemostatic profile in all groups in the postoperative period were revealed, which were characterized by hypercoagulation in the form of a significant increase in the concentration of fibrinogen, reducing the activity of antithrombin III, shortening of thrombin time in groups I and II and reducing spontaneous fibrinolysis in groups I and II. Thrombin time and spontaneous fibrinolysis in group III increased relative to preoperative values. Open interventions in the volume of femoral-popliteal bypass surgery were accompanied by a more pronounced inhibition of fibrinolysis in comparison with minimally invasive interventions, and in endovascular procedure the anticoagulant potential was more depressed. Open reconstruction of the iliac segment was associated with a large reduction in thrombin time, but less inhibition of anticoagulant potential, compared with endovascular technique, due to large damage to the endothelium. **Conclusion.** It is necessary to monitor the lipid and hemostatic profile both before and after surgery in patients, admitted to the hospital for reconstructive surgery on the aorta and main arteries of the lower extremities, in order to develop an effective personalized drug prevention of lower extremity peripheral artery disease progression and to prevent the development of thrombotic and stenotic complications of the arterial reconstruction zone.

Key words: *peripheral artery disease, lipid profile, hemostatic profile, reconstructive surgery*

For citation: Lazarenko V.A., Bobrovskaya E.A., Belikov L.N. LIPID PROFILE AND HEMORHEOLOGY DYNAMICS IN PATIENTS WITH LOWER EXTREMITY PERIPHERAL ARTERY DISEASE IN THE PREOPERATIVE AND POSTOPERATIVE PERIOD. The Russian Archives of Internal Medicine. 2019; 9(3): 206-212. [In Russian]. DOI: 10.20514/2226-6704-2019-9-3-206-212

DOI: 10.20514/2226-6704-2019-9-3-206-212

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AFB — aorto-femoral bypass, APTT — activated partial thromboplastin time, ATIII-A — antithrombin III activity, AI — atherogenic index, INR — international normalized ratio, LEPAD — lower extremity peripheral artery disease, TC — total cholesterol, PTI — prothrombin index, TBA — transluminal balloon angioplasty, TVT— thrombin time, TG — triglycerides, FG — fibrinogen, HDL-C — high density lipoprotein cholesterol, LDL-C — low density lipoprotein cholesterol

Introduction

According to epidemiological studies, the prevalence of peripheral artery disease of lower extremities (LEPAD) ranges from 2 % to 11 % [1-4]. At the same time, symptomatic lower extremity ischemia requiring active treatment tactics in the Russian Federation reaches 173 883 cases per year [5]. The primary method of treatment of this category of patients is surgical revascularization [3, 6].

At the same time, the problem of thrombotic occlusions and stenosis in the arterial reconstruction area remains relevant and significantly limits the widespread introduction of surgical methods. A very important role in the development of these complications is played by risk factors associated with atherosclerosis, which are well known and described in many works [7–14]. Unsatisfactory long-term results of treatment are associated primarily with a high degree of activity of the atherosclerotic process, especially in young patients. Yu.I. Kazakov et al. proved that in patients under the age of 50 years, there are gross changes in the lipid spectrum of blood, mainly phospholipid fractions, manifested by a decrease in the amount of sphingomyelin and phosphotidylcholine by 2.5 % and 4.4 %, and an increase in the content of lysophosphotidyl-ethanolamine and phosphotidylinositol fractions by 4.5 % and 9.7 % compared to persons aged over 50 years [15]. Dyslipoproteinemia, as a risk factor for the development and progression of atherosclerosis, occurs in 73.3 % of patients with surgical correction of lower limb vessels, among which hypercholesterolemia with increased low-density lipoprotein cholesterol (LDL-C) in 61.7 % and hypertriglyceridemia in 35 % [16] which are the most often diagnosed These risk factors are the independent predictors of reducing the primary patency of shunts [17]. At the same time, after successful surgical correction of LEPAD patients fall out of the field of vision of local therapists as patients at very high cardiovascular risk and do not receive appropriate lipid-lowering therapy; the frequency of achieving the target values of LDL-C in such patients is only 15–18 % [18]. Active use of effective doses of statins improves long-term prognosis in such patients [19].

On the other hand, a number of Russian studies have revealed the presence of disorders in the hemostatic system in such patients, which is manifested by a decrease in the activity of fibrinolysis and natural anticoagulants [1, 20–23]. According to some authors [24], when evaluating the hemostatic potential in patients with LEPAD and the phenomena of chronic ischemia of the lower extremities, such factors as the activity of antithrombin III (at III), activated partial thromboplastin time (APTT), prothrombin index (PTI), thrombin time (TT) remained in the normal range. However, despite the extreme importance of assessing the lipid spectrum of blood and the state of homeostasis in patients with LEPAD who underwent surgery, in order to develop tactics of drug prevention of stenotic and thrombotic complications, studies in this area are few and are preliminary in nature [25].

In this regard, the aim of the study was to assess the lipid and hemostatic profile in patients with peripheral artery disease of the lower extremities with different levels of damage and methods of surgery.

Material and methods

The study included 330 male patients, having LEPAD of the II B-III degree according to the classification of R.Fontaine — A.V.Pokrovskiy. All patients signed an informed consent to participate in the study, which was approved by the Ethical Committee of Kursk State Medical University.

Inclusion criteria: male patients, having peripheral artery disease of lower extremities of the II B-III degree to the classification of R. Fontaine — A.V. Pokrovskiy.

Exclusion criteria: patients with autoimmune diseases, acute and chronic pathology in the acute stage, foci of inflammation of any localization, liver or blood system diseases, diabetes, cancer at the time of examination or in history, decompensated cardiovascular diseases, degenerative diseases of the nervous system, patients who underwent reconstructive interventions of coronary and peripheral arteries in history.

Surgical intervention was determined according to generally recognized guidelines in vascular surgery [26]. Depending on the localization of the lesion and the method of revascularization, the patients were divided into three randomized groups (stratification criterion — localization of occlusive stenotic lesion): The first (I) group of the study (n = 140) consisted of patients with lesions of the femoral-popliteal arterial segment who underwent femoral-popliteal bypass surgery (FPB) (mean age 58.64 ± 7.73). The second (II) study group (n = 97) consisted of patients with occlusive stenotic lesions of the aorto-iliac segment who underwent aorto-femoral bypass surgery (AFB) (mean age 56.82 ± 6.69). The third (III) of the study (n = 93) included patients with occlusive stenotic changes of the iliac arteries who underwent transluminal balloon angioplasty (TBA) and stenting of the iliac arteries.

All patients underwent ultrasound diagnosis of the abdominal aorta and main arteries of the lower extremities (LOGIQ 5 Expert, GE, Medicalsystems, Inc (USA)) with measurement of the ankle-brachial index, angiographic study (mobile angiographic complex GE OEC 9800, Medicalsystems, Inc (USA). Routine tests were carried out: complete blood count, urinalysis, blood chemistry with the assessment of creatinine, liver transaminases, serum electrolytes before and after surgery. The study of lipid profile fractions included determination of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C), triglycerides (TG) with the calculation of atherogenic index (AI = (total cholesterol — HDL-C)/HDL-C. Blood lipid spectrum parameters were evaluated by enzymatic colorimetric method using biochemical automatic analyzer vitalab Fexor XL (Netherlands).

To assess the plasma coagulation level of hemostasis, the following tests were determined: APTT, PTI, international normalized ratio (INR), fibrinogen level (FG), thrombin time (TT), spontaneous fibrinolysis, antithrombin activity III (ATIII-A). The study was carried out on the automatic hemostasis analyzer, STA-compact Diagnostics Stago (France). Blood for analysis of these parameters was taken from the ulnar vein of each patient on an empty stomach in the morning, 5 days before the surgery and 5 days after the surgery. Patients took their last meal at least 12 hours before the study; also on the day of the study physical activity and stressful situations were avoided. All patients in the postoperative period received traditional conservative therapy according to the National recommendations for the management of patients with lower extremity artery disease [26].

Statistical processing of the obtained results was carried out by calculating the arithmetic means (M), mean errors (m) and the standard deviation of the characteristic (σ). The significance of the difference in mean values was assessed using the Student's parametric t-test. Differences between the groups were considered statistically significant at the significance level $p < 0.05$.

Results of the study and their discussion

The study of lipid profile fractions in the groups before and after surgery is presented in Table 1.

All patients who were supposed to undergo revascularization surgery had high blood atherogenicity exceeding the optimal values of lipid parameters, which is consistent with the literature data [27, 28]. In patients of group II, the initial preoperative level of TG was significantly higher than in group I (by 12.25 %, $p = 0.015$), and the level of LDL cholesterol, on the contrary, was lower (by 7.42 %, $p = 0.046$). Compared with patients of group III, in group II of the study, HDL-C level was significantly higher (by 9.19 %, $p = 0.03$), which positively affected the lower value of the atherogenicity index in this group (by 24.31 %, $p = 0.02$). In the comparative analysis of groups I and III, significant initial differences in the level of blood lipids were observed with respect to TG, HDL-C and LDL-C. So in group III, increased TG concentration (24.68 %, $p = 0.0000$), decreased HDL-C (9.34 %, $p = 0.014$) and LDL-C (8.25 %, $p = 0.02$) with increased AI (26.65 %, $p = 0.003$) were detected, while the TC level did not differ significantly between groups.

In group I of the study significant changes in the lipid changes during postoperative period were not detected.

In group II in the postoperative period there was a slight decrease in the level of TC from baseline (by 7.01 %, $p = 0.003$) without significant changes in the remaining fractions, which did not affect the change in AI.

Important data are presented, which show that in group III of patients there were changes characterized by an increased HDL-C level (by 10.56 %, $p = 0.03$) and a decreased LDL-C level (by 7.66 %, $p = 0.055$) with a significant decrease in AI (by 21.82 %, $p = 0.01$) in the postoperative period from baseline.

In comparative analysis of blood lipid concentration in groups I and II during postoperative period, patients of group II showed significantly low LDL-C (by 8.25 %, $p = 0.019$) and TC (by 6.93 %, $p = 0.008$). Also significantly lower LDL-C level in the postoperative period was found in group III compared to group I (by 10.41 %, $p = 0.003$).

There were no significant postoperative differences between the lipid spectrum in groups II and III.

Changes in coagulation parameters over time in the groups before and after surgery are presented in Table 2.

As it can be seen from table 2, the comparative analysis of coagulation parameters between groups I and II before surgery revealed no significant differences.

Table 1. *Lipid profile fractions in the study groups (M ± m)*

Parameters \ Groups	I group		II group		III group	
	before surgery	after surgery	before surgery	after surgery	before surgery	after surgery
TG, mmol/L	1.47 ± 0.04	1.56 ± 0.04	1.65 ± 0.07*	1.67 ± 0.07	1.83 ± 0.09**	1.62 ± 0.07
HDL-C, mmol/L	1.54 ± 0.03	1.53 ± 0.036	1.537 ± 0.04	1.53 ± 0.04	1.39 ± 0.05*****	1.54 ± 0.05$^{\#}$
LDL-C, mmol/L	4.34 ± 0.09	4.103 ± 0.09	4.02 ± 0.14*	3.76 ± 0.1*	3.98 ± 0.12**	3.68 ± 0.10**
TC, mmol/L	5.76 ± 0.09	5.68 ± 0.1	5.69 ± 0.09	5.29 ± 0,1$^{\# *}$	5.75 ± 0.13	5.49 ± 0.11
Atherogenic index	3.02 ± 0.13	3.002 ± 0.12	3.08 ± 0.18	2.8 ± 0.16	3.83 ± 0.27*****	2.99 ± 0.18$^{\#}$

Note: *I–II p <0.05; **I–III p <0.05; ***II–III p <0.05 differences in indicators in the study groups; #p <0.05 differences relative to the data before the operation

Table 2. *Coagulation parameters in the study groups (M ± m)*

Parameters	Before/after surgery	I group	II group	III group
APTT, sec	before	34.19 ± 0.47	32.78 ± 0.85	32.64 ± 0.53**
	after	43.74 ± 1.31$^{\#}$	41.16 ± 1.50$^{\#}$	41.06 ± 0.97$^{\#}$
PT, %	before	99.43 ± 1.02	101.44 ± 1.23	99.1 ± 1.02
	after	94.87 ± 0.95$^{\#}$	98.06 ± 1.05$^{\# *}$	97.88 ± 0.82**
INR	before	1.02 ± 0.01	0.99 ± 0.01	1.04 ± 0.01***
	after	1.05 ± 0.01	1.02 ± 0.01*	1.04 ± 0.01
Fibrinogen, g/l	before	4.33 ± 0.09	4.35 ± 0.12	4.06 ± 0.08**
	after	5.14 ± 0.11$^{\#}$	4.85 ± 0.12$^{\#}$	5.08 ± 0.11$^{\#}$
Thrombin time, sec	before	18.28 ± 0.16	18.53 ± 0.37	18.17 ± 0.35
	after	17.19 ± 0.26$^{\#}$	17.06 ± 0.34$^{\#}$	21.66 ± 1.07$^{\# ** ***}$
Spontaneous fibrinolysis, %	before	10.95 ± 0,46	12.16 ± 0.57	8.10 ± 0.25$^{** ***}$
	after	8.92 ± 0.42$^{\#}$	10.15 ± 0.40$^{\# *}$	10.44 ± 0.26$^{\# **}$
Antithrombin III, %	before	102.36 ± 0.79	100.25 ± 0.90	103.96 ± 0.66***
	after	97.01 ± 0.88$^{\#}$	96.39 ± 0.95$^{\#}$	93.74 ± 0.73$^{\# ** ***}$

Note: *I–II p <0.05; **I–III p <0.05; ***II–III p <0.05 differences in indicators in the study groups; #p <0.05 differences relative to the data before the operation

When comparing the baseline coagulation parameters in groups I and III, differences in APTT, FG, spontaneous fibrinolysis were revealed: in group I, APTT values were higher (by 4.54 %, ρ = 0.03), and FG level (by 6.23 %, ρ = 0.038) and spontaneous fibrinolysis (by 25.99 %, ρ = 0.0000) were also higher than in group III.

Between groups II and III initially significant changes were found in the level of INR, spontaneous fibrinolysis and ATIII. In group III, the value of INR was higher (by 4.2 %, ρ = 0.008), spontaneous fibrinolysis was lower (by 33.39 %, ρ = 0.0000), and baseline activity of AT III was higher (by 3.7 %, ρ = 0.001) compared with group II.

In the postoperative period in all groups of the study there was a statistically significant increase in FG concentration: in group I — by 18.71 % (ρ = 0.0000), in group II — by 11.39 % (ρ = 0.004), in group III — by 25.06 % (ρ = 0.0000) compared to the baseline. The reduction of anticoagulant potential in all groups in the postoperative period relative to preoperative values, characterized by a significant decrease in the activity of ATIII, which was more pronounced in group III of the study, was also revealed.

In the postoperative period there was a significant reduction in thrombin time in groups I and II, and in group III, on the contrary, there was an increase compared to baseline values. The decrease in fibrinolytic activity was characterized by a statistically significant decrease in spontaneous fibrinolysis also in groups I and II, and in group III its increase was observed compared to baseline values.

The values of PTI also decreased slightly in the postoperative period compared to the baseline in groups I (by 4.58 %, ρ = 0.001) and II (by 3.33 %, ρ = 0.038), and did not significantly change in group III (ρ = 0.36).

Postoperative INR values characterizing the second phase of coagulation had no significant changes in all groups of the study compared to the preoperative level.

A comparative analysis between the groups after surgery revealed the following changes. After surgery there were significant differences between groups I and II in PTI, INR, spontaneous fibrinolysis: in group II, an increase in PTI (by 3.36 %, ρ = 0.027), a decrease in INR (by 2.71 %, ρ = 0.016), an increase in spontaneous fibrinolysis (by 13.75 %, ρ = 0.045) compared with group I.

There were differences in the levels of PTI, TT, spontaneous fibrinolysis, ATIII-A between group I and group III after surgery. The level of PTI in group I was lower (by 3.18 %, ρ = 0.026), TT was lower (by 25.99 %, ρ = 0.0000), spontaneous fibrinolysis was lower (by 16.97 %, ρ = 0.007), but the level of ATIII-A was higher (by 3.36 %, ρ = 0.009) compared to group III.

There were significant differences in the level of TT and ATIII-A between group II and group III in the postoperative period. In group III, TT was higher (by 26.95 %, ρ = 0.0000), and the level of ATIII-A was lower (by 2.75 %, ρ = 0.028) compared to group II.

Thus, studies of blood lipid spectrum showed that patients with peripheral artery disease had impaired fractions of blood lipid spectrum, which had significant differences depending on the severity and level of atherosclerotic lesions in the main arteries. Lipid imbalance persists after correction of arterial blood flow.

During hemostatic profile assessment, significant changes were found in all groups in the postoperative period, characterized by hypercoagulation orientation in the form of a significant increase in FG concentration, a decrease in anticoagulant potential with a significant decrease in the activity of AT III, shortening of TT in groups I and II and a decrease in spontaneous fibrinolysis in groups I and II. TT and spontaneous fibrinolysis in group III increased relative to preoperative values. Thus, open interventions in the volume of FPB are accompanied by a more pronounced inhibition of fibrinolysis in comparison with minimally invasive interventions, and with endovascular procedure, ATIII is more depressed, possibly due to greater damage to the arterial wall. Open reconstruction of the iliac segment is associated with a greater decrease in TT, but less inhibition of anticoagulant potential, compared with endovascular technique, due to greater damage to the endothelium.

Summarizing the literature data on the effect of angioplasty and open surgical revascularization of the lower extremities on coagulation, fibrinolysis and platelet activation, H.S Rayt et al. noted that percutaneous intervention caused an increase in prothrombotic and impairment in fibrinolytic status, and surgical intervention caused prothrombotic status with a decrease in fibrinolysis and platelet hyperactivity similar to percutaneous intervention, which persists for a significant period after surgery [29].

Conclusion

Patients admitted to the hospital for reconstructive surgery on the aorta and main arteries of the lower extremities need to monitor the lipid profile and hemorheology both before surgery and in the postoperative period in order to develop effective drug prevention and personalized corrective measures to prevent the development of thrombotic and stenotic complications in the arterial reconstruction area.

Conflict of interests

The authors declare no conflict of interests.

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Article received on 28.03.2019
Accepted for publication on 12.04.2019