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CD 38, CD 31 lymphocytes in critical ischaemia of the lower extremities

S. S. Dunaevskaya, N. A. Malinovskaya, A. T. Khachatryan

Prof. V. F. Voino-Yasenetsky Krasnoyarsk State Medical University, Krasnoyarsk 660022, Russian Federation

The aim of the research. To study the interrelations between CD38, CD31 lymphocytes and development of critical ischaemia of the lower extremities.

Material and methods. The 1st group included 75 patients with the IIB degree of ischaemia and the 2nd group included 75 patients with critical ischaemia. The control group consisted of 75 healthy subjects. We measured anklebone arterial blood pressure, the ankle-brachial index, toe arterial blood pressure, the transcutaneous tension of oxygen, used ultrasonic Doppler sonography and the CT-angiography. The CD38, CD31 level was determined using immunofluorescence. The data are presented as median and quartiles – Me (LQ, UQ).

Results. The anklebone arterial blood pressure in the 1st group did not differ from the controls while it was 56 [34; 69] mmHg in patients with critical ischaemia. The toe arterial blood pressure in patients of the1st group did not differ from the controls, and in the 2nd group, this index was significantly below 41 [33; 46] mmHg. Transcutaneous tension of oxygen in the 1st group was normal, in the 2nd group it was 38 [28; 53] mmHg, (p2<0.001). The damage to arteries was multifocal. The most expressed stenosis up to full occlusion was revealed in shin arteries. CD31 in the 1st group was 31.53 [29.11; 45.74] %, and in the 2nd group it was 68.14 [57.55; 79.64 %] (p2<0.001)

Conclusion. High and average correlations have been found between CD31, CD38 and ischaemia, high and very high correlations were revealed between CD31 and the arterial blood flow parameters in the lower extremities, and the preserved lumen of arteries.

Key words: ischaemia, atherosclerosis, CD38, CD31, lymphocyte, pathogenesis.

Conflict of interest. The authors declare the absence of obvious and potential conflicts of interest associated with the publication of this article.

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Great scientific interest to problems of arteriosclerosis obliterans (ASO) of vessels of the lower extremities is based on the increase in the incidence of this pathology and multidisciplinary approach in diagnostics and treatment [1]. Progression of the pathological process and development of critical ischaemia are the most urgent problems of modern vascular surgery [2]. Development of atherosclerotic damage of arteries depends on a set of factors, among which damage to endothelium is the leading one [3]. CD38 is a bifunctional enzyme responsible for intracellular and intercellular communication. CD38 expresses on various cells of the organism: blood cells, in particular, lymphocytes, cardiomyocytes, cells of the central nervous system [4]. The platelet and endothelial molecule of type I adhesion (CD31) is a transmembrane glycoprotein related to the immunoglobulin superfamily. CD31 expresses on a cellular surface of endotheliocytes, thrombocytes, lymphocytes, neutrophils, monocytes and megakaryocytes. Its level is regulated by the vascular and endothelial growth factor (VEGF) and the macrophage-colony stimulating factor. [5, 6, 7]. The main CD31 function is regulation of adhesion and selective transendothelial migration of various immune cells. It is established that, at first, migration of neutrophils and monocytes is present with later migration of lymphocytes, eosinophils, etc. Also, CD31 participates in processes of apoptosis, angiogenesis, aggregation of thrombocytes, etc. [8, 9]. The processes caused by activation of these molecules can play an important role in development of ASO and critical ischaemia, as the source of damage to the endothelium. Thus, a research of an expression CD38, CD31 as pathogenetic marker of ASO can be of interest at different stages of the disease. The aim of the research was to study the interrelations between CD38, CD31 lymphocytes and development of critical ischaemia of the lower extremities.

Material and Methods

The study was a cohort prospective research. Included patients with ASO undergoing treatment at the Krasnoyarsk Interdistrict Clinical Hospital № 7 from 2019 to 2021. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The research was approved by the Ethics Committee of the Prof. V.F. Voino-Yasenetsky Krasnoyarsk State Medical University, protocol 57/2019 dated 27.10.2019.

Study Design. Two study groups were formed: the 1st group included 75 patients with the IIB degree of ischaemia according to the classification by Leriche-Fontaine. The 2nd group included 75 patients with clinical manifestations of critical ischaemia. Distribution of patients between the groups was based on the Clinical

recommendations for "arterial diseases of the lower limbs" of the Ministry of Health of the Russian Federation (2020). IIb degree ischaemia means symptoms of alternating lameness when passing a distance of less than 200 meters and the absence of pain at rest. Critical ischaemia of an extremity is a syndrome of a decompensated chronic arterial insufficiency of an extremity due to ASO, the main clinical signs of which are the pain at rest which is not stopped by narcotic analgesics and (or) existence of ulcer and necrotic process of foot. The criteria of non-inclusion into the research were: diabetes mellitus and other endocrine, autoimmune, infectious and oncological diseases in anamnesis; presence of severe accompanying cardiovascular pathology, heart failure 2A and above, 2 or a higher functional class according to the NYHA; medical history of allergic reactions and intolerance to contrast agents, intake of indirect anticoagulants, drugs of prostaglandin E, statins at the outpatient stage of treatment and smoking. Besides, the control group was constituted by 75 apparently healthy subjects did not have symptoms of obliterating diseases of vessels of the lower extremities.

Methods. For objectification of ischaemia degree assessment, we measured the anklebone arterial blood pressure, the ankle-brachial index, toe arterial blood pressure, transcutaneous tension of oxygen in foot fingers. For blood flow assessment in arteries of the lower extremities, we used ultrasonic Doppler sonography of arteries of the lower extremities and the CT-angiography. The groups were comparable by age and sex composition. All patients in both groups of clinical observation and participants of the control group were male. The age was 65 [53; 76] years in the control group, 67 [52; 75] years in the 1st group, 66 [54; 77] years in the 2nd group. The content of CD38, CD31 lymphocytes in peripheral blood was defined in Scientific Research Institute of Molecular Medicine and Pathological Biochemistry of Prof. V.F. Voino-Yasenetsky Krasnoyarsk State Medical University. The research was conducted upon arrival of the patient at the hospital prior to therapy. The maintenance of CD38, CD31 of lymphocytes in peripheral blood was determined by the method of an indirect immunofluorescence by mouse monoclonal antibodies to molecules of various CD polymeric receptors of lymphocytes, also DAPI staining (4′,6-diamidino-2-phenylindole) was carried out. Fluorescent microscopy (magnification h80) was performed with light filters for FITC-tag and for DAPI using a universal microscope Olympus BX-41 "Olympus" (Japan); no less than 30 fields of sight were analysed. The percentage of lymphocytes, CD38 or CD31 was calculated from the total number of lymphocytes, the nuclei of which were stained with high DAPI.

The data are presented as median with lower and upper quartiles – Me (LQ, UQ). For assessment of the nature of distribution, the Shapiro-Wilk test was used. The studied sizes did not comply with normal distribution. The non-parametric Mann-Whitney U-test was used for pairwise comparison in the groups. The critical level of statistical significance when testing the null hypothesis was set at 0.05.

The bonds between separate signs were described by means of the Spearman's rank correlation coefficient (rS).

Results

Anklebone arterial blood pressure in patients of the 1st group did not differ from indicators of the control group (p1=0.328). In development of critical ischaemia this indicator differed significantly and equalled 56 [34; 69] mmHg, (p1<0.001, p2<0.001). It was reflected in the change of the ankle-brachial index in patients with arteriosclerosis obliterans. Thus, this index was 0.64 [0.56; 0.75] (p1=0.002) in the 1st group and 0.33 [0.26; 0.42] (p1<0.001, p2=0.001) in the 2nd group. Toe arterial blood pressure in patients of the 1st group did not differ from values of the control group, and in the 2nd group was significant below and was 41 [33; 46] (p1<0.001, p2<0.001). Transcutaneous tension of oxygen is one of the main criteria of perfusion adequacy. In the 1st group, this indicator did not differ from normal values, in the 2nd group it was reduced to 38 [28; 53] mmHg, (p1<0.001, p2<0.001) (Table 1).

Table 1

Assessment of blood flow parameters in the studied groups (Me [LQ, UQ])

	Control group (n=75)	The 1st group (n=75)	The 2nd group (n=75)
Anklebone arterial blood pressure, mmHg.	138 [124; 152]	120 [108; 135], p_1=0.328	56 [34; 69] p_1<0.001, p_2<0.001
Ankle-brachial index	1.12 [0,96; 1,27]	0.64 [0,56; 0,75] p_1=0.002	0,33 [0,26; 0,42] p_1<0.001, p_2=0.001
Toe arterial blood pressure, mmHg.	125 [116; 147]	118 [111; 133] p_1=0.601	41 [33; 46] p_1<0.001, p_2<0.001
Transcutaneous tension of oxygen, mmHg.	97 [93; 98]	88 [81; 97] p_1=0.904	38 [28; 53] p_1<0.001, p_2<0.001

Note: p_1 – the importance of distinctions of group in comparison with control (Mann-Whitney U-criterion), p_2 – the importance of differences between the 1st and 2nd groups (Mann-Whitney U-criterion).

Table 2

Visualised lumen of arteries of the lower extremities using ultrasonic dopplerography (Me [LQ, UQ])

	Control group (n=75)	The 1st group (n=75)	The 2nd group (n=75)
CFA, %	88.9 [87.7; 94.2]	67.8 [64.5; 71.4], p_1=0,003	50.2 [47.3; 54.4], p_1<0.001, p_2=0.011
SFA, %	72.2 [68.4; 74.4]	32.7 [29.8; 41.4], p_1<0.001	20.8 [16.4; 22.8], p_1<0.001, p_2=0.003
DFA, %	83.7 [79.4; 92.0]	69.2 [66.3; 79.4], p_1=0.238	51.2 [38.5; 55.1], p_1<0.001, p_2=0.014
PA, %	76.5 [72.1; 88.5]	30.8 [22.5; 38.6], p_1<0.001	16.2 [11.3; 19.5], p_1<0.001, p_2=0.002
PTA, %	87.2 [64.6; 91.3]	23.5 [20.6; 38.7], p_1<0.001	10.7 [5.5; 18.6], p_1<0.001, p_2=0.021
ATA, %	89.8 [78.5; 93.4]	22.2 [18.3; 36.6], p_1<0.001	9.4 [3.3; 12.7], p_1<0.001, p_2=0.013

Note: CFA – common femoral artery, SFA – superficial femoral artery, DFA – deep femoral artery, PA – a popliteal artery, PTA – posterior tibial artery, ATA – anterior tibial artery, p_1 – the significance of differences in the groups in comparison with the controls (Mann-Whitney U-test), p_2 – the significance of differences between the 1st and the 2nd groups (Mann-Whitney U-test)

Table 3

The content of CD38, CD31 lymphocytes in peripheral blood (Me [LQ, UQ])

	Control group (n=75)	The 1st group (n=75)	The 2nd group (n=75)
CD38 lymphocytes, %	11.80 [9.50; 15.70]	25.52 [23.70; 30.65], p_1<0.001	55.82 [50.12; 65.72], p_1<0.001, p_2<0.001
CD31 lymphocytes, %	8.12 [6.31; 9.05]	31.53 [29.11; 45.74], p_1<0.001	68.14 [57.55; 79.64], p_1<0.001, p_2<0.001

Note: p_1 – the significance of differences in the groups in comparison with the controls (Mann-Whitney U-test), p_2 – the significance of differences between the 1st and the 2nd groups (Mann-Whitney U-test).

Damage to arteries of the lower extremities in patients of both groups had multifocal character. The preserved lumen of vessels in patients with ASO in all cases differed from indicators of almost healthy subjects of the control group. The lumen of the common femoral artery (CFA) in the 1st group was 67.8 % [64.5; 71.4], (p_1=0,003), in the 2nd group it was slightly lower than 50.2 % [47.3; 54.4], (p_1<0.001, p_2=0.011). In patients of both groups, the lumen of the superficial femoral artery (SFA) decreased to 32.7 % [29.8; 41.4] in the 1st group, (p_1<0.001) and to 20.8 % [16.4; 22.8] in the 2nd group was revealed (p_1<0.001, p_2=0.003). It should be noted that a significant decrease in the lumen of the deep femoral artery (DFA) 69.2 % [66.3; 79.4], (p_1=0.238) was not revealed in the 1st group while this indicator was much lower in the 2nd group: 51.2 % [38.5; 55.1], (p_1<0.001, p_2=0.014). The lumen of the popliteal artery (PA) was considerably narrowed in both groups. The most expressed stenosis up to full occlusion was observed in shin arteries (table 2).

The content of CD38 lymphocytes in patients of the1st group was 25.52 % [23.70; 30.65] (p_1<0.001) while in the 2nd group it was 55.82 % [50.12; 65.72], (p_1<0.001, p_2<0.001), which was much higher than contents of lymphocytes in the control group. The CD31 lymphocytes in patients of the 1st group was 31.53 % [29.11; 45.74], (p_1<0.001) and 68.14 % [57.55; 79.64] in the 2nd group (p_1<0.001, p_2<0.001) (see Table 3).

The correlation coefficient between CD38 and anklebone arterial blood pressure was rS=-0.68, (p=0.007) that corresponded to average negative correlation. The correlation between the ankle-brachial index and peripheral blood CD 38 lymphocytes was equal, rS= -0.71, (p=0.008), i.e. high negative correlation. The correlation coefficient between CD38 and transcutaneous tension of oxygen was rS=-0.73, (p=0.014): high negative correlation. The correlation coefficient between CD31 lymphocytes and anklebone arterial blood pressure was rS=-0.82, (p=0.003) that corresponded to high negative correlation. The correlation between the ankle-brachial index and CD31 was equal to rS=-0.92, (p<0.001), which is very high negative correlation. Toe arterial blood pressure had average force negative correlation with CD31. The transcutaneous tension of oxygen and CD31 had a correlation coefficient of rS=-0.89, (p=0.002) that corresponded to high negative correlation (Table 4).

Negative correlations between CD38 and the lumen of PA at rS=-0.74, (p=0.002), and the lumen of PTA at rS=-0.76, (p<0.001) were high. Additionally, high negative correlation coefficient was established between the lumen of ATA and CD38 at rS=-0.89, (p=0.003). The correlation coefficient between the visualised lumen of CFA and CD31 was rS=-0.42, (p=0.015), which corresponded to weak negative correlation. A correlation coefficient between the lumen of SFA and the CD31 was rS=-0.66,

Table 4

Correlation coefficients between indicators of the blood flow condition and the content of peripheral blood CD38, CD31 lymphocytes

	Spearman's rank correlation coefficient with CD38	Spearman's rank correlation coefficient with CD31
Anklebone arterial blood pressure, mmHg.	rS= -0.68, p=0.007	rS= -0.82, p=0.003
Ankle-brachial index	rS= -0.71, p=0.008	rS= -0.92, p<0.001
Toe arterial blood pressure, mmHg.	rS= -0.51, p=0.012	rS= -0.69, p<0.001
Transcutaneous tension of oxygen, mmHg.	rS= -0.73, p=0.014	rS= -0.89, p=0.002

Note: rS – Spearman's rank correlation coefficient, p – bilateral significance of Spearman's rank correlation coefficient considered reliable at p≤0.01.

(p=0.002), which corresponded to negative correlation of average force. Negative correlations between CD31 and the lumen of PA at rS= -0.78, (p<0.001), and the lumen of PTA rS= -0.88, p<0.001 were high. Very high negative correlation coefficient was received between lumen of ATA and CD31 rS= -0.93, (p=0.002) (Table 5).

Table 5

Correlation coefficients between the visualised artery lumens and the content of CD38, CD31 lymphocytes in peripheral blood

	Spearman's rank correlation coefficient with CD38	Spearman's rank correlation coefficient with CD31
CFA, %	rS= -0.35, p=0.013	rS= -0.42, p=0.015
SFA,%	rS= -0.57, p=0.003	rS= -0.66, p=0.002
DFA,%	rS= -0.36, p=0.015	rS= -0.47, p=0.008
PA,%	rS= -0.74, p=0.002	rS= -0.78, p<0.001
PTA,%	rS= -0.76, p<0.001	rS= -0.88, p<0.001
ATA,%	rS= -0.89, p=0.003	rS= -0.93, p=0.002

Note: CFA – common femoral artery, SFA – superficial femoral artery, DFA – deep femoral artery, PA – a popliteal artery, PTA – posterior tibial artery, ATA – anterior tibial artery, rS – Spearman's rank correlation coefficient, p – bilateral significance of Spearman's rank correlation coefficient considered reliable at p≤0.01.

Discussion

CD38 is involved in cell activation, differentiation, apoptosis, and proliferation. The biochemical changes induced by it include intracellular calcium release, phosphorylation of substrates, and increased expression of molecules involved in proliferation or apoptosis [10]. CD38 activation in the endothelium is an important cause of post-ischaemic endothelial dysfunction [11, 12].

The assessment of secretion of adhesive molecules in patients with stenosis of carotid arteries after carotid endarterectomy is carried out. It is revealed that indicators of sPECAM-1 decrease on the 1st day after surgery. Nevertheless, half a year later, the level of secretion of this molecule was comparable to reference values [13]. It can be considered a marker of endothelium impairment against the background of ischaemia. Some authors consider CD31 microparticles as a predictive marker of intensity of endothelial cells apoptosis [14]. These are of great predictive value for nonfatal myocardial infarction in comparison with other molecules of intercellular adhesion, sPECAM-1 and endothelin-1 [15]. The increased sPECAM-1 level in blood plasma is associated with risk of development of an atherosclerotic cerebral infarction [16].

Data on the content of CD31 and CD38 in peripheral blood of the patients with non-coronary atherosclerosis have been obtained for the first time. Additionally, regularities between the content of these markers and key indicators characterising the damage to peripheral arteries and ischaemia severity have been revealed. It allows suggesting a role of activation of lymphocytes in ASO pathogeny. However, it has not been possible to establish which process is primary: the damage to endothelium in response to activation of lymphocytes or activation of lymphocytes in response to damage to endothelium.

Research limitations. Many important factors affecting arterial circulation were chosen as criteria for non-inclusion in the research. The data obtained are correct for non-smoking patients, without clinically significant manifestations of coronary atherosclerosis and heart failure. The role of drugs for treatment of arterial diseases of the lower limbs on an expression of CD31 and CD38 is not known as patients in our research did not receive these drugs at a stage of outpatient treatment.

Conclusion

High and very high correlation bonds between the content of CD31 of lymphocytes and high and average force correlation bonds between the content of CD38 of lymphocytes in peripheral blood are both indicators of the condition of arterial blood flow in the lower extremities, and the retained lumens of arteries of the lower extremities have been revealed.

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References

1. Lichtenberg M, Schreve MA, Ferraresi R, van den Heuvel DAF, Ünlü Ç, Cabane V, Kum S. Surgical and endovascular venous arterialization for treatment of critical limb ischaemia. *Vasa.* 2018;47(1):17-22. DOI: 10.1024/0301-1526/a000669

2. Kalinin RE, Suchkov IA, Chobanian AA, Nikiforov AA, Dmitrieva MN, Isakov SA. Markers of the course of obliterating atherosclerosis of lower limb arteries. *Angiology and Vascular Surgery.* 2021; 27(2):17-24. DOI: 10.33529/ANGIO2021203

3. Topaz G, Yehezkel E, Benchetrit S, Korzets Z, Arnson Y, Kitay-Cohen Y, Pereg D, Cohen-Hagai K. Non-coronary cardiac calcifications and outcomes in patients with heart failure. *Journal of Cardiology.* 2021;77(1):83-87. DOI: 10.1016/j.jjcc.2020.07.019

4. Piedra-Quintero ZL, Wilson Z, Nava P, Guerau-de-Arellano M. CD38: An Immunomodulatory Molecule in Inflammation and Autoimmunity. *Frontiers in immunology.* 2020;(11):597959. DOI: 10.3389/fimmu.2020.597959. eCollection 2020

5. Bartosch AMW, Mathews R, Mahmoud MM, Cancel LM, Haq ZS, Tarbell JM. Heparan sulfate proteoglycan glypican-1 and PECAM-1 cooperate in shear-induced endothelial nitric oxide production. *Scientific Reports.* 2021;11(1):11386. DOI: 10.1038/s41598-021-90941-w.

6. Winneberger J, Schöls S, Lessmann K, Rández-Garbayo J, Bauer AT, Mohamud Yusuf A, Hermann DM, Gunzer M, Schneider SW, Fiehler J, Gerloff C, Gelderblom M, Ludewig P, Magnus T. Platelet endothelial cell adhesion molecule-1 is a gatekeeper of neutrophil transendothelial migration in ischemic stroke. *Brain, Behavior, and Immunity.* 2021;(93):277-287. DOI: 10.1016/j.bbi.2020.12.026

7. Xie X, Wang F, Zhu L, Yang H, Pan D, Liu Y, Qu X, Gu Y, Li X, Chen S. Low shear stress induces endothelial cell apoptosis and monocyte adhesion by upregulating PECAM-1 expression. *Molecular Medicine Reports.* 2020;21(6):2580-2588. DOI: 10.3892/mmr.2020.11060

8. Liao D, Sundlov J, Zhu J, Mei H, Hu Y, Newman DK, Newman PJ. Atomic Level Dissection of the Platelet Endothelial Cell Adhesion Molecule 1 (PECAM-1) Homophilic Binding Interface: Implications for Endothelial Cell Barrier Function. *Arteriosclerosis, Thrombosis, and Vascular Biology.* 2022;42(2):193-204. DOI: 10.1161/ATVBAHA.121.316668

9. Wimmer I, Tietz S, Nishihara H, Deutsch U, Sallusto F, Gosselet F, Lyck R, Muller WA, Lassmann H, Engelhardt B. PECAM-1 Stabilizes Blood-Brain Barrier Integrity and Favors Paracellular T-Cell Diapedesis Across the Blood-Brain Barrier During Neuroinflammation. *Frontiers in Immunology.* 2019;(10):711. DOI: 10.3389/fimmu.2019.00711

10. Ahn Y, An JH, Yang HJ, Lee DG, Kim J, Koh H, Park YH, Song BS, Sim BW, Lee HJ, Lee JH, Kim SU. Human Blood Vessel Organoids Penetrate Human Cerebral Organoids and Form a Vessel-Like System. *Cells.* 2021;10(8):2036. DOI: 10.3390/cells10082036

11. Guerreiro S, Privat AL, Bressac L, Toulorge D. CD38 in Neurodegeneration and Neuroinflammation. *Cells.* 2020;9(2):471. DOI: 10.3390/cells9020471

12. Herrmann H, Sadovnik I, Eisenwort G, Rülicke T, Blatt K, Herndlhofer S, Willmann M, Stefanzl G, Baumgartner S, Greiner G, Schulenburg A, Mueller N, Rabitsch W, Bilban M, Hoermann G, Streubel B, Vallera DA, Sperr WR, Valent P. Delineation of target expression profiles in CD34+/CD38- and CD34+/CD38+ stem and progenitor cells in AML and CML. *Blood Advances.* 2020;4(20):5118-5132. DOI: 10.1182/bloodadvances.2020001742

13. Costa F, Dalla Palma B, Giuliani N. CD38 Expression by Myeloma Cells and Its Role in the Context of Bone Marrow Microenvironment: Modulation by Therapeutic Agents. *Cells.* 2019;8(12):1632. DOI: 10.3390/cells8121632

14. Atiakshin D, Samoilova V, Buchwalow I, Tiemann M. Expression of CD38 in Mast Cells: Cytological and Histotopographic Features. *Cells.* 2021;10(10):2511. DOI: 10.3390/cells10102511

15. Guan XH, Hong X, Zhao N, Liu XH, Xiao YF, Chen TT, Deng LB, Wang XL, Wang JB, Ji GJ, Fu M, Deng KY, Xin HB. CD38 promotes angiotensin II-induced cardiac hypertrophy. *Journal of Cellular and Molecular Medicine.* 2017;21(8):1492-1502. DOI: 10.1111/jcmm.13076

16. Burns M, Ostendorf L, Biesen R, Grützkau A, Hiepe F, Mei HE, Alexander T. Dysregulated CD38 Expression on Peripheral Blood Immune Cell Subsets in SLE. *International Journal of Molecular Medical Science.* 2021;22(5):2424. DOI: 10.3390/ijms22052424

Author information

Svetlana S. Dunaevskaya, Dr. Med. Sci., Professor, Prof. V.F. Voino-Yasenetsky Krasnoyarsk State Medical University; Address: 1, Partizan Zheleznyak Str., Krasnoyarsk, Russian Federation 660022; Phone: +7(905)0873585; e-mail: vikto-potapenk@yandex.ru, http://orcid.org/0000-0003-2820-4737

Natalia A. Malinovskaya, Dr.Med.Sci., head of the department, Prof. V.F. Voino-Yasenetsky Krasnoyarsk State Medical University; Address: 1, Partizan Zheleznyak Str., Krasnoyarsk, Russian Federation 660022; Phone: +7(983)3637925; e-mail: malinovskaya-na@mail.ru, http://orcid.org/0000-0002-0033-3804

Aik T. Khachatryan, graduate student, Prof. V.F. Voino-Yasenetsky Krasnoyarsk State Medical University; Address: 1, Partizan Zheleznyak Str., Krasnoyarsk, Russian Federation 660022; Phone:+7(923)3777999, e-mail: hachatryan.na@gmail.com, http://orcid.org/0000-0001-5818-1631

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