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PSYCHOLOGICAL STATUS INFLUENCE
ON THE INTIMA-MEDIA COMPLEX THICKNESS AND TUMOR NECROSIS FACTOR-ALPHA IN YOUNG MEN 18–25 YEARS OLD

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The purpose of the study was to investigate the influence of psycho-emotional status on carotid artery wall characteristics, plasma levels of C-reactive protein and tumor necrosis factor-alpha in men aged 18–25 years. We examined 65 young men (average age 21.9±2.3 years) without cardiovascular pathology and any somatic diseases in the anamnesis. According to the psycho-emotional state (The Spielberger State-Trait Anxiety Inventory), the examined men were divided into 2 groups: main – with high anxiety – 35 people and the control group – 30 people (average age 21.3±2.1 years) without violations of psycho-emotional status. It was found that in the main group there was an increase of carotid intima-media thickness, changes in carotid arterial elasticity according to elasticity and distensibility coefficients, Peterson's and Young's modules in comparison with the control group. It was established that in young aged with high levels of anxiety, an increase in the content of C-reactive protein and tumor necrosis factor-α in blood serum is determined in comparison with the group without psycho-emotional status disorders.

Key words: young men, psycho-emotional disorders, elasticity of arterial wall, tumor necrosis factor-alpha, C-reactive protein.

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ВПЛИВ ПСИХОЛОГІЧНОГО СТАТУСУ
НА СТАН ТОВЩИНИ КОМПЛЕКСУ ІНТИМА-МЕДІА ТА ФАКТОР НЕКРОЗУ ПУХЛИН-АЛЬФА У МОЛОДИХ ЧОЛОВІКІВ 18–25 РОКІВ

Метою роботи було вивчити вплив психоемоційного статусу на стан судинної стінки, вміст С-реактивного протеїну та фактору некрозу пухлин-альфа в крові у чоловіків 18–25 років. Обстежено 65 молодих чоловіків (середній вік 21,9±2,3 роки) без серцево-судинної патології та будь-яких соматичних захворювань в анамнезі. В залежності від психоемоційного стану (опитувальник тривожності Ч.Д. Спілберга) було виділено 2 групи: з високою тривожністю – 35 осіб (основна група) та без порушень психоемоційного статусу – 30 осіб (контрольна група). Встановлено, що в основній групі спостерігалось збільшення товщини комплексу інтима-медіа, зміни еластичності сонних артерій за даними коефіцієнтів еластичності і розтяжності сонних артерій, модулів Петерсона і Юнга в порівнянні з контрольною групою. Визначено, що чоловіків з високим рівнем тривожності молодого віку визначається збільшення вмісту С-реактивного протеїну та фактора некрозу пухлин-α в сироватці крові в порівнянні з групою без порушень психоемоційного статусу.

Ключові слова: молоді чоловіки, психоемоційні порушення, еластичність артеріальної стінки, фактор некрозу пухлин-α, С-реактивний протеїн.

In modern society, a person is less and less exposed to natural biological stressors and is increasingly exposed to the pressure of psychosocial factors, which are caused by economic circumstances, information technologies and interpersonal conflict relations, that, under conditions of low stress resistance, can lead to the earlier development of some diseases or the progression of already existing ones [2]. The data of epidemiological studies made it possible to establish that the level of anxiety, psycho-emotional stress, depression are independent risk factors for arterial hypertension and other cardiovascular diseases [10]. The basis of the development of cardiovascular diseases against the background of chronic stress are molecular and cellular mechanisms, which represent a complex interaction of neuroendocrine, energetic and immune factors and remain not fully understood, that indicates the need for further research in this direction [2]. In addition, the study of pathogenetic mechanisms associated with the influence of psycho-emotional status on arterial wall parameters among healthy young people is relevant, as it will contribute to the development of a strategy of preventive measures aimed at preventing cardiovascular diseases and their progression.

The purpose of the study was to investigate the influence of psycho-emotional status on carotid artery wall characteristics, plasma levels of C-reactive protein and tumor necrosis factor-alpha in men aged 18–25 years.

Materials and methods. The study included 65 young men aged 18–25 years (average age 21.9±2.3 years) without cardiovascular pathology and any somatic diseases in the anamnesis (Table 1).

Table 1

Clinical characteristics of examined men aged 18–25 years

Parameters	General group (n=65)
Age, years	21.9±2.3
Smoking, n (%)	18 (27.7)
Family history of hypertension, n (%)	28 (43.1)
Family history of early cardiovascular events, n (%)	6 (9.2)
Body mass index (BMI), kg/m²	24.9±0.3
Dyslipidemia, n (%)	12 (18.5)
Glomerular filtration rate CKD-EPI, ml/min/1.73 m²	82.7±1.5

Informed consent for the study was obtained from all the examined persons, which met the ethical norms of the Helsinki Declaration.

Exclusion criteria: cardiovascular diseases (myocarditis, arterial hypertension, heart defects, ischemic heart disease, cardiomyopathies), somatic diseases, excess body weight, dyselectrolyte disorders. The anxiety questionnaire by Ch. D. Spielberg, which contains 40 questions, was used to assess situational and personal anxiety. The result was evaluated as follows: up to 30 – low anxiety, 31–45 – moderate anxiety, 46 and more – high anxiety. Depending on the psycho-emotional state, the examined men were divided into 2 groups: main – with high anxiety – 35 people (average age 22.7±2.5 years) and the control group – 30 people (average age 21.3±2.1 years) without violations of psycho-emotional status. In the main group, the degree of reactive and personal anxiety was (49.8±2.7) and (49.3±2.6) points, respectively, and in the control group – (28.3±1.6) and (28.7±1.5), respectively.

All examinees underwent a general clinical examination, which included a survey to identify risk factors for cardiovascular diseases, an examination, anthropometric measurements, medical physical examination, including measurement of office blood pressure (BP), general blood and urine analysis (with determination of microalbuminuria with a test strip), biochemical blood analysis with determination of fasting glucose, indicators of lipid metabolism, creatinine (calculated GFR according to the CKD-EPI formula), ECG in 12 standard leads on the ECG600G device (Heaco ltd, Great Britain). Ultrasound examination of the brachiocephalic arteries was performed on an ultrasound diagnostic scanner "LOGIQ 5" ("Medical System", Germany) with a 7 MHz linear sensor and Ultima PA (RADMYR, Ukraine) with a 5–12 MHz linear sensor.

The common carotid artery (CCA) was examined in a standard projection. The diameter was assessed at rest (after a 10-minute rest). According to the Consensus of the American Society of Echocardiography (2008), measurements of carotid intima-media thickness (IMT) were carried out, and an individual approach was used to determine normal values, taking into account gender and age: the threshold value of IMT for men under 40 years old – 0.7 mm, 40–50 years old – 0.8 mm, over 50 years old – 0.9 mm, for women under 45 years old – 0.7 mm, 45–60 years old – 0.8 mm, over 60 years old – 0.9 mm. When atherosclerotic plaques were detected, their qualitative and quantitative assessment was carried out.

Calculation criteria were used to assess the stiffness of the vascular wall [9, 15]:

– elasticity coefficient (CC) of the CCA:

$$CC = [(\Delta D/Ds)/2\Delta P] \times \pi Ds2$$

where ΔD is the specific change in the systolic and diastolic diameters of the CCA;

Ds – systolic diameter of the CCA;

ΔP – pulse arterial pressure.

– distensibility coefficient (DC) of the CCA:

$$DC = (2\Delta D/Ds)/\Delta P$$

where – ΔD is the specific change in the systolic and diastolic diameters of the CCA;

Ds – systolic diameter of the CCA;

ΔP – pulse arterial pressure.

Peterson's modulus of elasticity (Ep):

$$Ep = (\Delta P/\Delta D) \times (Ds-Dd)$$

where – ΔD is the specific change in the systolic and diastolic diameters of the CCA;

Dd – diastolic diameters of the CCA;

Ds – systolic diameter of the CCA;

ΔP – pulse arterial pressure.

Young's modulus (YM) of elasticity includes the thickness of the artery wall, which allows considering this indicator of arterial elasticity as independent of the size of the vascular wall. It is calculated according to the formula:

YM = (ΔP/ΔD) × [(Ds-Dd) /h]

where – ΔD is the specific change in the systolic and diastolic diameters of the CCA;

– Dd – diastolic diameters of the CCA;

– Ds – systolic diameter of the CCA;

– h – wall thickness of the CCA;

– ΔP – pulse arterial pressure.

These indices reflect different aspects of arterial elasticity, so they are all used in calculations to determine the structure of the vessel.

Immunoenzymatic analysis was used to determine the concentration of C-reactive protein (CRP) and tumor necrosis factor- α (TNF-α) using diagnostic kits of the company "DRG" (USA) on the enzyme immunoassayer "LabLine-90" (Austria), according to corresponding instructions for sets.

Statistical processing of the results was carried out using Statistica 10.0 statistical programs. For quantitative indicators measured on an interval scale, the average value, standard deviation and error of the average were calculated. For "qualitative" and "ordinal" indicators, the frequency of detection of the indicator in percentages or the frequency of registration of different rank evaluations of the index were determined, respectively. When analyzing intergroup differences in indicators, the value of Student's t-test was calculated. In the case of indicators measured on a nominal scale, the reliability of differences in the frequency of detection of the indicator in the two compared groups was a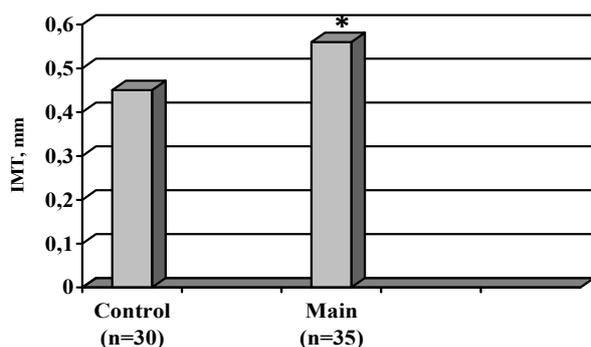ssessed by the Student's t-test using Fisher's transformation, and linear and rank correlation coefficients were also calculated. Differences in mean values and correlations were considered reliable at the significance level of p<0.05.

Fig.1. The thickness of the IMT of the CCA in the examined persons. Note. * – reliability of differences between groups (p<0.05).

Results of the study and their discussion. At the same time, the study of the thickness of the IMT of the CCA revealed early structural changes in the vessel wall in the form of its thickening. Thus, the lowest values of parameters were in the group without violations of psychological status. At the same time, in persons with high anxiety there was a significant increase in the thickness of the IMT by 24.4 % (Fig. 1).

This corresponded to a violation of the elastic properties of arteries, which was evidenced by a decrease in carotid distensibility coefficient (DC) (by 25 %; p<0.05) and elasticity coefficient (CC) of the CCA (by 19.4 %; p<0.05), an increase in Young's module (by 14.3 %; p<0.05)) and Peterson's module of the CCA (by 15.5 %; p<0.05) in comparison with the group of people without violations of psychological status (Fig. 2–4).
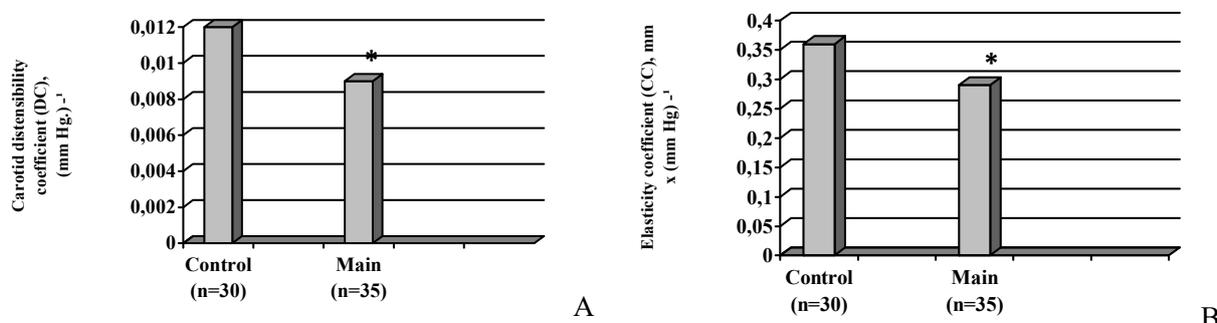

Fig. 2. Carotid Distensibility coefficient (DC) (A) and elasticity coefficient (CC) of the CCA (B) in the examined persons. Note: * – reliability of differences between groups (p<0.05).

The obtained data indicate that in young men with high anxiety, there were signs of structural and functional changes in the carotid arteries in the form of an increase in the IMT and changes in the elasticity of the wall in comparison with the group without violations of the psychological status.
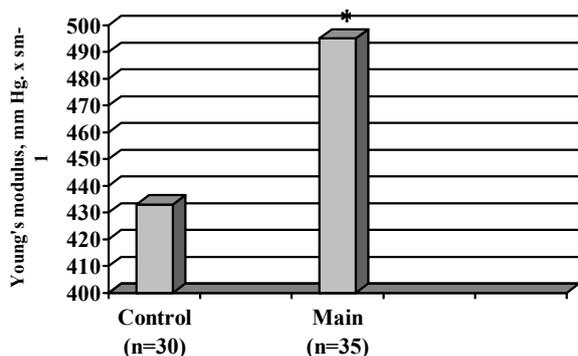
Fig. 3. Young's modulus (Eu) of CCA in examined persons.

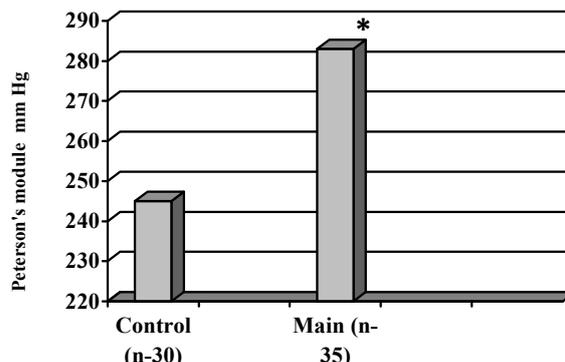Note: * – reliability of differences between groups (p<0.05).

Fig. 4. Peterson's module (Ep) of the CCA in the examined patients.

Note: * – reliability of differences between groups (p<0.05).

The analysis of the TNF-α content in the groups of subjects allowed us to establish that in young men with high anxiety, this parameter was 1.6 times significantly higher, in contrast to the data of the group without violations of psychological status (p<0.001) (Table 2).

Table 2

The content of the pro-inflammatory cytokine TNF-α and CRP in the blood of the examined persons

Parameters	Control group (n=30)	Main group (n=35)
TNF-α, pg/ml	59.3±5.25	97.5±8.71*
CRP, mg/l	1.08±0.10	3.62±0.41*

Note: * – p<0.001 difference is probable between the main and control groups.

CRP was characterized by similar changes in levels in the study groups, as was TNF-α. Thus, in young men with high anxiety, significantly higher CRP values were found compared to the control group (p<0.001).

It is known that a stressogenic factor leads to the activation of the sympathetic nervous system and the secretion of catecholamines and the hypothalamic-pituitary-adrenal system with a significant increase in the level of cortisol. Next, a cascade of behavioral, cardiovascular, endocrine and metabolic changes is launched, which adapts the body to the changing conditions of the external environment. At the same time, the impact of a stressor does not always end with successful adaptation. It should be emphasized that stress-induced diseases (myocardial infarction, peptic ulcer disease, etc.) develop not in everyone, but only in people who have low resistance to stress. There is strong evidence that a number of psychosocial factors are independent risk factors for cardiovascular disease, adverse outcomes, and death from cardiovascular disease [14]. In addition, the studied groups included older persons who already had signs of manifestations of cardiovascular diseases [13].

Our study, which included healthy men aged 18–25, was aimed at studying the influence of psycho-emotional factors on early structural changes of the arterial wall based on the data of the IMT thickness index of the carotid arteries. IMT is known to be a well-accepted marker of atherosclerosis risk, and although its use is not recommended in clinical guidelines for risk stratification, it has been shown to predict future cardiovascular events independent of traditional risk factors in adults [5].

Previously, it was shown that the IMT thickness of the carotid arteries is primarily associated with traditional cardiovascular risk factors, such as age, gender, race, smoking, alcohol use, lack of physical activity, high blood pressure, hypercholesterolemia, poor diet, and diabetes [1]. The measurement of this parameter has received considerable attention because it is closely correlated with coronary heart disease and cerebral disease and is a predictor of both vascular events. Current evidence considers carotid IMT as a marker of arterial damage and a predictor of adverse outcomes such as myocardial infarction [13].

The data of many studies indicate the impact of psycho-emotional stress on the immune system [5]. The occurrence of systemic inflammation is considered as a possible mechanism that combines chronic stress with the development of cardiovascular diseases. It has been established that stress at work, especially high demands and insufficient social support, is associated with an increase in the levels of immunological markers, namely an increase in the concentration of CRP in the blood [4].

Analyzing the parameters of the duplex examination of the vessels of the neck, it was noted that the values of the IMT in the studied groups were within normal limits (0.9 mm), which did not exceed the accepted value as a criterion for vessel damage as a target organ [8].

We found that men aged 18–25 with high anxiety have high levels of CRP in the blood, which confirms previously obtained data in people of an older age group [12]. The peculiarity of the inflammatory process is reflected not only by the content of CRP, but also by the state of pro-inflammatory cytokines, including TNF-α, which takes part in the regulation of CRP production. We found a significant increase in TNF-α content in the blood of people with high anxiety. It was previously noted that TNF-α can be considered as a factor in damage to the vascular endothelium [7]. It is known that TNF-α contributes to the increase in the generation of free radicals and can cause the intensification of the processes of apoptosis of the vascular endothelium and inactivation of nitric oxide [3]. It has been shown that TNF-α stimulates the proliferation of endotheliocytes, increases the synthesis of collagen by fibroblasts [6]. These processes can contribute to changes in the vascular structure and increase in the intima-media complex, and the content of TNF-α in the blood can potentially be considered as a biomarker of susceptibility to IMT thickening of the CCA.

Conclusions

1. In men aged 18–25 without cardiovascular pathology and any somatic diseases in the anamnesis with high anxiety (The Spielberger State-Trait Anxiety Inventory), the criteria for carotid artery remodeling are determined: an increase in the thickness of the intima-media complex, changes in the elasticity of the carotid arteries (a decrease in elasticity coefficient (CC) and distensibility coefficient (DC), an increase in Peterson's modulus and Young's modulus) in comparison with young men without violations of the psycho-emotional status.

2. It was established that in men aged 18–25 years without cardiovascular pathology and any somatic diseases in the anamnesis with high anxiety, an increase in the content of C-reactive protein and tumor necrosis factor-alpha in blood serum are determined in comparison with young men without psycho-emotional status disorders. The observed changes in immunological parameters reflect subclinical inflammation processes that contribute to morphological changes and vessel wall remodeling.

References

1. Abeysuriya V, Perera BPR, Wickremasinghe AR. Regional and demographic variations of Carotid artery Intima and Media Thickness (CIMT): A Systematic review and meta-analysis. PLoS ONE. 2022;17:e0268716.
2. Alwani AA, Singh U, Sankhyan S, Chandra A, Rai SK, Nongkynrih B. Hypertension-related distress and its associated factors: findings from an urban primary health centre of South Delhi, India. J Family Med Prim Care. 2023;12(9):1885–1892. doi: 10.4103/jfmpc.jfmpc.
3 Chen JX, Huang XY, Wang P, Lin WT, Xu WX, Zeng M. Effects and mechanism of arachidonic acid against TNF-α induced apoptosis of endothelial cells. Clin Hemorheol Microcirc. 2021;77(3):259–265. doi: 10.3233/CH-200946.
4. Haybar H, Bandar B, Torfi E, Mohebbi A, Saki N. Cytokines and their role in cardiovascular diseases. Cytokine. 2023; 169:156261. doi: 10.1016/j.cyto.2023.156261.
5. Henein MY, Vancheri S, Longo G, Vancheri F. The Impact of Mental Stress on Cardiovascular Health-Part II. J Clin Med. 2022;11(15):4405. doi: 10.3390/jcm11154405.
6. Hu H, Huang J, Zhang S, Zhang B, Li W, Sun K. Tumor necrosis factor-α stimulation endothelial-to-mesenchymal transition during cardiac fibrosis via endothelin-1 signaling. J Biochem Mol Toxicol. 2023;37(9):e23411. doi: 10.1002/jbt.23411.
7. Luk C, Haywood NJ, Bridge KI, Kearney MT. Paracrine Role of the Endothelium in Metabolic Homeostasis in Health and Nutrient Excess. Front Cardiovasc Med. 2022 Apr 26; 9:882923. doi: 10.3389/fcvm.2022.882923.
8. Mancia G, Kreutz R, Brunstrom M, Burnier M, Grassi G, Januszewicz A, et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). J. Hypertens. 2023; 41:1874–2071.
9. Meinders JM, Kornet L, Brands PJ, Hoeks AP. Assessment of local pulse wave velocity in arteries using 2D distension waveforms. Ultrason Imageing. 2001; 23:199–215.
10. Richards SH, Anderson L, Jenkinson CE, Whalley B, Rees K, Davies P, et al. Psychological interventions for coronary heart disease: Cochrane systematic review and meta-analysis. Eur J Prev Cardiol. 2018;25(3):247–259. doi: 10.1177/2047487317739978.
11. Rustamian ST, Katerenchuk IP, Yarmola TI, Pustovoyt HL, Tkachenko LA, Ovcharenko LK. Relationship between indicators of depression, quality of life, compliance and blood pressure in patients undergoing renal replacement therapy // World of Medicine and Biology. 2023;2 (84):134–138. doi: 10.26724/2079-8334-2023-2-84-134-138.
12. Sanchez-Carro Y, de la Torre-Luque A, Vassou C, Lopez-Garcia P, Georgousopoulou E, Pitsavos C, et al. Effects of elevated emotional symptoms on metabolic disease development: a 10-year follow-up study. Front Psychiatry. 2023;14:1148643. doi: 10.3389/fpsyt.2023.1148643.
13. Spence JD. IMT is not atherosclerosis. Atherosclerosis. 2020 Nov; 312:117–118. doi: 10.1016/j.atherosclerosis.2020.09.016.
14. van den Munckhof ICL, Jones H, Hopman MTE, de Graaf J, Nyakayiru J, van Dijk B, et al. Relation between age and carotid artery intima-medial thickness: a systematic review. Clin Cardiol. 2018;41(5):698–704. doi: 10.1002/clc.22934.
15. Xu L, Wang P, Xia P, Wu P, Chen X, Du L. et al. A Flexible Ultrasound Array for Local Pulse Wave Velocity Monitoring. Biosensors (Basel). 2022;12(7):479. doi: 10.3390/bios12070479.