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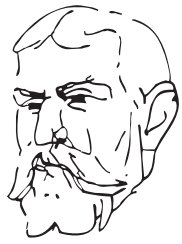

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ORIGINAL ARTICLES

ORIGINAL ARTICLE

NESFATIN-1 ACTIVITY IN THE BLOOD SERUM IN PATIENTS WITH CHRONIC HEART FAILURE OF ISCHEMIC ORIGIN AGAINST THE BACKGROUND OF TYPE 2 DIABETES MELLITUS AND OBESITY

DOI: 10.36740/WLek202305201

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ABSTRACT

The aim: To study the nesfatin-1 activity in the blood serum of patients with chronic heart failure (CHF) of ischemic origin against the background of such metabolic disorders as type 2 diabetes mellitus (T2DM) and obesity.

Materials and methods: 154 patients with CHF were examined, and divided into 4 groups, according to the presence of metabolic disorders. Group 1 included patients with CHF on the background of coronary heart disease (CHD) and T2DM and obesity (n=42). The second group consisted of patients with heart failure on the background of CHD with concomitant T2DM (n=46), the third group - with concomitant obesity (n=36), the fourth group was formed from patients with signs of heart failure of ischemic origin without metabolic disorders (n=30). The control group (CG) included 30 practically healthy persons of comparable age.

Results: The mean level of serum nesfatin-1 was 1.64±0.27 ng/mL in the CHF group, 0.342±0.19 ng/mL in the CHF + T2DM + obesity group, 1.06±0.36 ng/mL in the obese + CHF group, 0.96±0.27 ng/mL in the CHF + T2DM group and 2.98±0.38 ng/mL in the CG. Significant correlation was found between the serum nesfatin-1 level and BMI ($r=-0.34$, $p<0.05$), HOMA ($r=-0.54$, $p<0.05$), insulin ($r=-0.41$, $p<0.05$). No significant correlation was found between the serum nesfatin-1 level and blood glucose level ($r=0.13$, $p=0.65$).

Conclusions: Thus, nesfatin-1 may play a significant role in the pathogenesis of both weight-related abnormalities and type 2 diabetes mellitus in patients with chronic heart failure of ischemic origin.

KEY WORDS: nesfatin-1, chronic heart failure, obesity, type 2 diabetes mellitus

Wiad Lek. 2023;76(5 p.2):1141-1145

INTRODUCTION

In recent years, much attention has been paid to the study of markers of metabolic disorders, including nesfatin-1. Nesfatin-1 has a wide range of predominantly paracrine effects and plays a significant role in various physiological and pathophysiological processes, such as cardiovascular regulation, neuroendocrine control of stress hormone secretion, and participation in the mechanisms of formation of behavioral excitation reactions [1]. The given literary data regarding the biological action of nesfatin-1 provide grounds for the future practical application of the metabolic effects of this adipokine. According to Nikolaos P. E. Kadoglou [2] et al., nesfatin-1 may be useful for clinical practice in terms of two aspects.

Firstly, for the diagnostics of diseases accompanied by obesity, dysglycemia, and dyslipidemia [3-5]. It was established that an increase of nesfatin-1 level in blood serum is accompanied by a blood pressure increase, body weight decrease [6], and a glucose-dependent increase in insulin secretion by β-cells of the pancreas when the blood glucose level increases [7].

Secondly, nesfatin-1 represents a target model for the creation of therapeutic agents for the treatment of obese individuals, because systemic or local administration of drugs based on nesfatin-1 is able to improve the metabolic profile and reduce body weight in patients with obesity and metabolic syndrome [8].

The search for markers of early diagnosis of heart failure and endocrine disorders progression is especially relevant in wartime. After all, since February 24, 2022, most people with chronic diseases have faced considerable difficulties due to the restriction of access to quality drugs and medical care in general. Therefore, today the main goal of scientists and healthcare workers is to develop a qualitative strategy for the progression

and possible complications diagnosis of comorbid cardiovascular pathology.

THE AIM

The aim was to study the nesfatin-1 activity in the blood serum of patients with chronic heart failure (CHF) of ischemic origin against the background of such metabolic disorders as type 2 diabetes mellitus (T2DM) and obesity.

MATERIALS AND METHODS

During 2022 154 patients were examined, who were divided into 4 groups, according to the presence of metabolic disorders. Group 1 included patients with CHF with coronary heart disease (CHD) and T2DM and obesity (n=42). The second group consisted of patients with heart failure on the background of CHD with concomitant T2DM (n=46), the third group - with concomitant obesity (n=36), the fourth group was formed from patients with signs of heart failure of ischemic origin without metabolic disorders (n=30). The control group included 30 practically healthy persons of comparable age.

Pregnant women, patients with acute infectious and autoimmune diseases, diffuse connective tissue diseases, oncological diseases, diseases of the pituitary gland and hypothalamus, chronic renal failure with a decrease of GFR less than 35 ml/min/1.73 m^2, the presence of symptomatic hypertension, acute coronary syndrome, and acute cerebrovascular accident during the last 6 months, exacerbation of chronic or presence of acute inflammatory diseases; patients with a history of alcohol abuse, mental illness; patients who were expected to have a high probability of violating the research protocol and persons who are not citizens of Ukraine were not included in the study. Representatives of vulnerable population groups were also not involved in the project.

The standard method of examining the patient included clinical and laboratory-instrumental research according to the recommendations of the European Society of Cardiology (ESC) in 2021, the American Diabetes Association (ADA) in 2019, and the International Diabetes Federation (IDF) in 2018. Laboratory and instrumental studies were carried out on the basis of the City Clinical Hospital No.27.

The studies were approved by the commission on biomedical ethics of Kharkiv National Medical University (protocol №2, dated 12.10.2022) and conducted in accordance with the written consent of the participants and the principles of bioethics set forth in the Helsinki Declaration "Ethical Principles of Medical Research Involving Humans" and the "Universal Declaration on Bioethics and Human Rights (UNESCO)".

To determine the level of nesfatin-1 (ng/ml), an immunoenzymatic method was used using a set of Human Nesfatin-1 ELISA Kit reagents according to the instructions attached to the kit, on an immunoenzymatic analyzer «Labline-90» (Austria).

A statistical analysis of the data was carried out using the methods of parametric and non-parametric statistics.

Mathematical computer processing of the results was carried out using the software package «Statistica 6.0» (StatSoft Inc, USA). For the comparative analysis of the samples, a standard correlation analysis program was used to calculate the average arithmetic values: the received data is presented as mean value ± standard deviation (SD). Statistical significance was considered to be a discrepancy at $p<0.05$. When analyzing samples not subject to the laws of Gaussian distribution, the Mann-Whitney U-test for independent samples was used. The correlation coefficient (r) was used to assess the degree of relationship between the samples.

More than two groups were compared by one-way ANOVA, using the least significant difference as a post-hoc Tuckey test to compare individual groups. A p-value < 0.05 was considered to be statistically significant. Moreover, receiver operating curve (ROC) analysis was performed to compare the performance of the models.

For the implementation of laboratory and instrumental methods of research, we collaborated with the Central Scientific and Research Laboratory of Kharkiv National Medical University.

RESULTS

General study variables in the four study groups are summarized and compared in Table I. Accordingly, the four groups were comparable in terms of sex and age.

The mean level of serum nesfatin-1 was 1.64±0.27 ng/mL in the CHF group, 0.342±0.19 ng/mL in the CHF + T2DM + obesity group, 1.06±0.36 ng/mL in the obese + CHF group, 0.96±0.27 ng/mL in the CHF + T2DM group and 2.98±0.38 ng/mL in the CG (Fig.1).

The ROC curves of serum nesfatin-1 levels in groups are shown in Figure 2. The corresponding under-the-curve areas in CG, CHF, CHF + T2DM, CHF + obesity, CHF + T2DM + obesity were 0.79 (95% CI, 0.73-0.85, $p<0.001$), 0.81 (95% CI, 0.70-0.92, $p<0.001$), 0.814 (95% CI, 0.71-0.94, $p<0.001$), 0.89 (95% CI, 0.83-0.95, $p<0.001$) and 0.92 (95% CI, 0.86-0.98, $p<0.001$), respectively.

In the present study, the fasting serum nesfatin-1 level was measured in all groups consisting of CG, CHF, CHF + T2DM, CHF + obesity, and CHF + T2DM + obesity. According to our results, the mean level of serum nesfatin-1 was significantly higher in CHF than in CHF

Table I. General study variables in the four study groups (M±SD)

Parameter		CHF, n=30	CHF + T2DM + obesity, n=42	CHF + obesity, n=36	CHF+ T2DM, n=46	CG, n=30
Age		61.37±9.7	60.09±9.4	59.43±6.5	62.34±4.7	58.75±6.3
Sex	Female	17 (56.67)	24 (57.14)	20 (55.56)	26 (56.52)	17 (56.67)
	Male	13 (43.33)	18 (42.86)	16 (44.44)	20 (43.48)	13 (43.33)

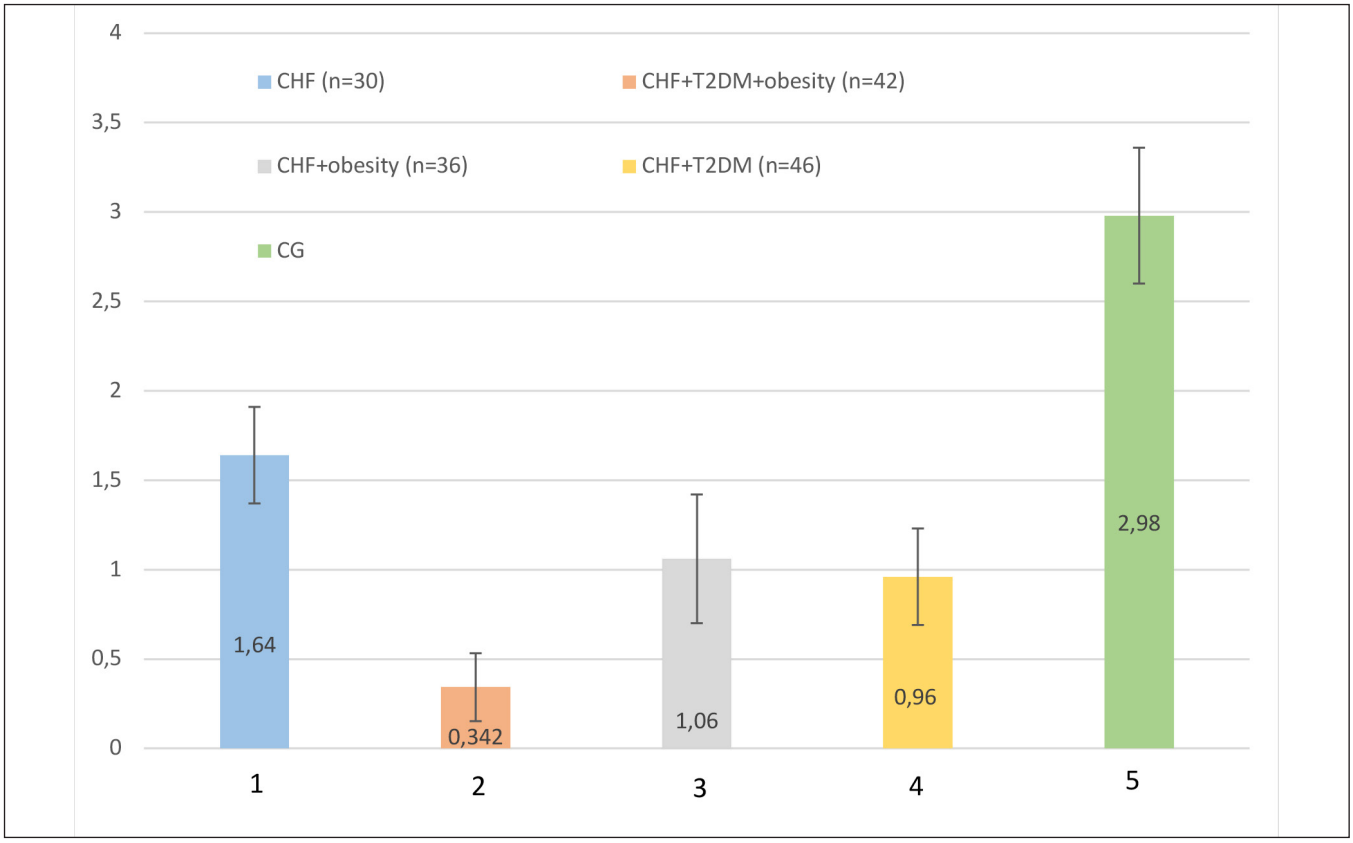

Fig. 1. The mean level of serum nesfatin-1 in the four study groups (M±SD)
Notes: $p_{1-2}<0.001$, $p_{1-3}<0.001$, $p_{1-4}<0.001$, $p_{1-5}<0.001$; $p_{2-3}<0.001$, $p_{2-4}<0.001$, $p_{2-5}<0.001$; $p_{3-4}>0.05$, $p_{3-5}<0.001$; $p_{4-5}<0.001$. Significant at $p < 0.05$

+ T2DM, CHF + obesity, and CHF + T2DM + obesity groups, but significantly lower than that in CG. At the same time, no significant difference was found between the obese and diabetic groups.

A significant correlation was found between the serum nesfatin-1 level and BMI (r=–0.34, p<0.05), HOMA (r=–0.54, p<0.05), and insulin (r=–0.41, p<0.05). No significant correlation was found between the serum nesfatin-1 level and blood glucose level (r=0.13, p=0.65) among all patients involved in the study.

DISCUSSION

A recent study by S. Mirakhor Samani et al. [9], showed that there are significant differences between normal-weight healthy subjects, healthy underweight persons, otherwise healthy obese people, and diabetic patients in terms of serum nesfatin-1 level. The results demonstrated the mean level of serum nesfatin-1 was significantly higher in normal-weight people than in both obese and diabetic groups, but significantly lower than that in underweight patients. At the same time, there was no significant difference between the obese and diabetic groups. In conformity with some previous reports in animal models and rare human studies, this peptide may play a pivotal role in the pathogenesis of both weight-related abnormalities and T2DM.

In a study by Shimizu et al. [5], they showed that nesfatin-1 plays a role in the development of insulin resistance and fat deposition in the liver, independent of effects on energy intake in rats.

The increased content in blood serum of the nesfatin-1 leads to remodeling of myocardium of the left ventricle (LV) in the form of a reduction of the ability of myocardium to a reduction in another report by Shaparenko O. et al. [10], who showed an increase of chambers and the LV sizes and can play a role in pathogenesis arterial hypertension in patients with obesity.

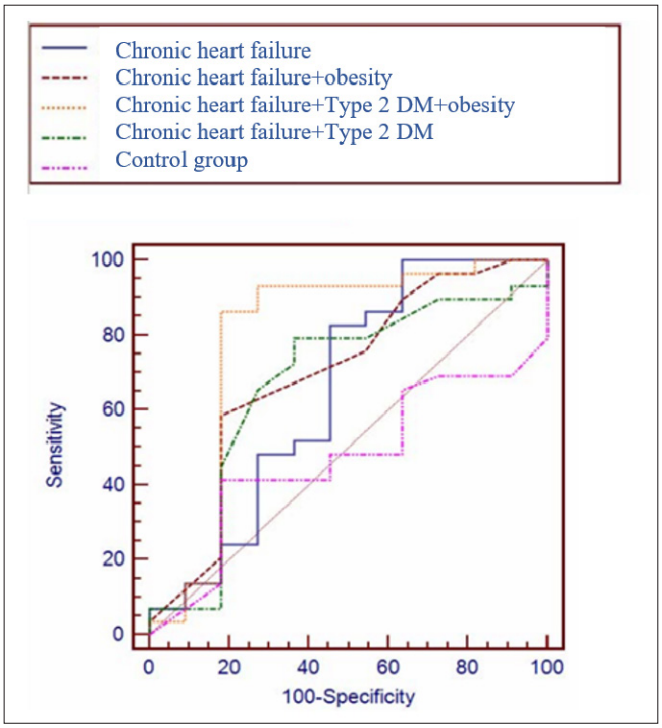

Fig. 2. Receiver operator characteristics curves of the mean serum nesfatin-1 levels in groups.

In recent research, Huang K. et al. [11] demonstrated serum nesfatin-1 as an important factor influencing insulin secretion in the development of T2DM, which may provide new insights for prospective research on the role of these factors in the pathogenesis of T2DM, as well as for active prediction and prevention of prediabetes before it develops into T2DM manifestation.

In another study, by Zhou et al., nesfatin-1 levels were measured in 50 CHF patients with T2DM and 50 CHF patients without T2DM. The results showed that nesfatin-1 levels were significantly higher in CHF patients with T2DM than in those without T2DM, and that nesfatin-1 levels were positively correlated with BMI, fasting glucose levels, and HbA1c levels. The authors suggested that increased nesfatin-1 levels may be a compensatory mechanism in response to T2DM-induced metabolic disturbances [12].

Based on the findings of the study by Luo et al. [13], the authors suggested that nesfatin-1 may play a role in the development of obesity-related cardiovascular complications in patients with chronic heart failure (CHF). They proposed that the elevated levels of nesfatin-1 in CHF patients with obesity may contribute to the pathogenesis of insulin resistance and metabolic dysfunction, which are commonly observed in obese patients with CHF. The authors also suggested that nesfatin-1 could potentially serve as a biomarker for the diagnosis and management of obesity-related cardiovascular disease in CHF patients. Further studies are needed to elucidate the precise mechanisms underlying the relationship between nesfatin-1, obesity, and CHF.

The prospects for the study of this marker also lie in the fact that under the conditions of military events, the number of patients with decompensation of both cardiovascular and metabolic diseases increases significantly. Thus, timely diagnosis aimed at preventing unfavorable consequences of these diseases is a priority for restoring economic stability in the field of medicine.

CONCLUSIONS

This study showed that there are significant differences in serum nesfatin-1 levels between the control group, chronic heart failure group, and chronic heart failure patients on the background of type 2 diabetes mellitus or obesity and with both metabolic disorders. In conformity with some previous reports in animal models and rare human studies, this peptide may play a pivotal role in the pathogenesis of both weight-related abnormalities and type 2 diabetes mellitus. Serum nesfatin-1 levels were negatively correlated with insulin, HOMA, and BMI.

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ORIGINAL ARTICLE

MODIFIED ASSESSMENT OF NEUROLOGICAL AND NEUROPSYCHOLOGICAL DEFICIT IN PATIENTS WITH CHRONIC CEREBRAL ISCHEMIA AND COMORBIDITY

DOI: 10.36740/WLek202305202

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ABSTRACT

The aim: To develop and test the scale of the modified assessment of neurological and neuropsychological deficits (MANND), which would include data on neurological status, higher cortical function disorders, and emotional disorders.

Materials and methods: A clinical-neurological and neuropsychological examination was carried out based on the data of a fragment of a scientific study - a comprehensive study: "Improving patient-oriented approaches to the treatment of patients with cardiovascular and cerebrovascular diseases and comorbid conditions."

Results: The Modified Assessment of Neurological and Neuropsychological Deficits is a neurological symptom assessment scale designed specifically for patients with chronic cerebral ischemia. It takes into account quantitative changes in the neurological status, namely, damage to the pyramidal, sensory, extrapyramidal, coordinating systems, damage to the cranial nerves, and the most common neurological syndromes, such as cephalic, asthenic, and higher cortical function disorders. This scale is a sensitive comprehensive method for assessing the severity of neurological and neuropsychological deficits, in contrast to existing scales for the isolated assessment of focal neurological symptoms (motor deficits, cognitive disorders or disorders of the emotional sphere).

Conclusions: The modified assessment of neurological and neuropsychological deficits can be recommended both for use in clinical practice and for conducting scientific research, as a unique quantitative scale developed taking into account all the features of a wide spectrum of neurological pathology in patients with chronic brain ischemia.

KEY WORDS: chronic brain ischemia, comorbidity, neurological, cognitive disorders, disorders of the emotional sphere

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INTRODUCTION

Cerebrovascular diseases are one of the most important medical and social problems of modern neurology and occupy leading positions in terms of prevalence, mortality and disability rate in almost all countries of the world. According to the WHO, about 5 million people die from cerebrovascular diseases every year. The most common clinical form of cerebrovascular pathology is chronic cerebral ischemia, one of the leading syndromes of which is cognitive impairment. As of 2012, there are 35.6 million people with cognitive impairment worldwide and their number doubles every 20 years [1].

Chronic ischemia of the brain is a slowly progressive dysfunction resulting from a diffuse or small focal lesion of the brain tissue in conditions of long-standing insufficiency of cerebral blood supply. In ICD-10, 3 rubrics are allocated that may correspond to the term: I67.3 - progressive vascular leukoencephalopathy (Binswanger's disease), I67.4 - hypertensive encephalopathy and I67.8 - cerebral ischemia (chronic). The development of neuropsychological disorders is caused by a change in choline-, serotonin-, adrenergic, and glutamatergic activity, which leads to a decrease in cognitive function, a disturbance of memory formation [2]. The predominance of chronic lesions of the brain tissue, the origin of which is mainly multifactorial, differs in the systemic nature of the lesion and comorbidity. This leads to the presence of both cognitive disorders and focal neurological deficits in patients with chronic brain ischemia.

The key diagnostic criterion of the disease is the severity of the neurological disorders observed during the initial examination. Among the scales that are currently used in neurology, the scales that assess the neurological status of a patient after a stroke prevail. Such scales include: the National Institutes of Health Stroke Scale (NIHSS), which is used to objectively assess the condition of a patient with an ischemic stroke during hospitalization, during treatment, on the 21st day of stay in a hospital.

Table I. Characteristics of the stages of atherosclerotic dyscirculatory encephalopathy

Stage	Complaints	Objectively	Social adaptation
Stage I	Rapid fatigue, inattention, deterioration of memory, especially for current events, reduced mental capacity, poor general well-being, headache, tinnitus, non-systemic dizziness, emotional lability, disturbed sleep	Scattered micro-symptomatics of an organic lesion of the nervous system - sluggish or slow pupillary response, asymmetry of cranial innervation, symptoms of oral automatism, tremors of fingers of outstretched hands, etc.	Able to take care of themselves under normal conditions, the difficulty arises only with increased workload
Stage II	Similar to stage I, but more pronounced, some complaints may disappear due to a decrease in criticism	Gross memory disorders, including long-term memory, reduced criticism of one's condition, characteristic overestimation of one's own abilities, excitability, verbosity, frivolity comes to the fore. Intelligence begins to decrease, episodes of dysarthria, impaired coordination are often noted, pathological reflexes appear	Some help is needed in the usual conditions
Stage III	Variable, depending on the leading clinical manifestations and the preservation of criticism	Along with scattered symptoms, there is a predominant damage to certain areas of the brain (subcortical nodes, brainstem, cerebellar systems, etc.). Characteristic amyostatic, pseudobulbar, vestibulocerebellar syndromes, vascular dementia syndrome, drop attacks, «late» epilepsy, global amnesia syndrome.	Some help is needed

The BARHTEL scale, which evaluates the index of activity in daily life, and the Scandinavian stroke scale for the combined assessment of the severity of patients in the acute period of ischemic stroke and the effectiveness of the treatment (SSS; Scandinavian Stroke Study Group) are also widely used. The Rankin scale (Modified Rankin Scale) is quite widely used, which allows to assess the degree of disability after a stroke and covers five ranks [3]. In addition to the scales listed above, a number of scales have also been developed to assess the higher cognitive functions of the patient, in particular, a short scale for assessing the mental status - Mini Mental State Examination - MMSE, Montreal cognitive assessment scale - Montreal Cognitive Assessment - MoCA, frontal dysfunction battery - Frontal Assessment Battery - FAB, the Beck depression scale, the Hamilton anxiety scale and the Hospital Anxiety and Depression Scale - HADS [4].

It should be noted that modern scales do not take into account all aspects of the diverse range of complaints of patients with chronic cerebral ischemia and the data of the primary clinical and neurological examination, since the vast majority of these patients do not have a history of acute cerebrovascular disorders, therefore, accordingly, the use of existing assessment scales, such as NIHSS or SSS, is not warranted for this population. The Modified Rankin Score (mRS) and BARHTEL scales have clinical value, which assesses patients' functional activity and dependence on external assistance, which is especially important for the physical rehabilitation of patients after a stroke, but their use is limited among patients with chronic cerebrovascular disorders, as they usually have moderate degree of neurological deficit.

Higher cortical scales, such as MMSE, MoCA, FAB, Beck Depression Scale, Hamilton Anxiety Scale, and the Hospital Anxiety and Depression Scale, are leading the way in both clinical and research applications in neurology. Their use is justified, given that mild cognitive impairment (MCI) is the leading syndrome of chronic brain ischemia [5, 6]. However, each of these scales gives a limited view of the problem, because it evaluates either cognitive functions or disorders of the emotional sphere in isolation, and does not take into account the data of an objective neurological examination, which also does not provide comprehensive information about the condition of patients with chronic cerebral ischemia.

The only scale that makes it possible to assess the severity of chronic brain ischemia is the characteristic of the stages of dyscirculatory encephalopathy (Table I), which is used in accordance with generally accepted treatment protocols [7].

However, this scale does not provide a detailed point assessment of the degree of severity of neurological and neuropsychological deficits and leading clinical and neurological symptoms, which makes it impossible to use it for the purpose of conducting scientific research and thorough analysis of statistical data.

THE AIM

The aim was to develop and test the scale of the modified assessment of neurological and neuropsychological deficits (MANND), which would include data on neurological status, higher cortical function disorders, and emotional disorders.

Table II. Modified assessment of neurological and neuropsychological deficits

Syndrome	Degree of severity of neurological deficit	Assessment
Reflex pyramidal insufficiency	Two-sided	1
	One-sided	1
Hemiparesis/hemiplegia	Muscle strength is reduced to 3-4	2
	Muscle strength is reduced to 1-2	3
	Muscle strength is reduced to 0	4
Damage to the cranial nerves	Scattered symptomatology on the part of cranial nerves	1
	Scotoma	1
	Quadrant anopsia	2
	Hemianopsia	3
	Anosmia	1
	Weakness of abduction, adduction, convergence	1
	Oculomotor disorders in the form of ptosis, diplopia, convergent/ divergent strabismus, nystagmus	1
	Face hemianesthesia	1
	Peripheral prosoparesis	1
	Central prosoparesis	2
	Sensorineural deafness	1
	Vestibular/cochlear disorders	1
	Elements of bulbar syndrome	2
	Bulbar syndrome	3
	Pseudobulbar syndrome	3
Sensory deficits	Hypoesthesia of the mononeuritic type	1
	Hypoesthesia of the polyneuretic type	2
	Hemianesthesia of deep/superficial sensitivity	3
	Hemianesthesia of all types of sensitivity	3
Damage to the extrapyramidal system	Trembling-rigid syndrome	2
	Akinetic-rigid-tremor syndrome	3
	Choreiform hyperkinesis, torsion dystonia	2
Disturbance of the coordination	Coordination disorders	1
	Vestibule-atactic disorders	2
	Hemiataxia, ataxia	3
Disturbance of higher cortical functions	Elements of motor/sensory aphasia	2
	Motor/sensory aphasia	3
	Total aphasia	4
	Apraxia, agnosia, alexia, acalculia, agraphia	2
	Mnestic decrease	1
	Pronounced cognitive impairment	2
	Dementia	3
Disturbance of the emotional sphere	Anxiety-depressive disorders that do not limit work capacity	1
	Anxiety-depressive disorders that affect the performance of daily tasks	2
	Panic attacks	3
Cephalgic	Headache that does not affect work capacity.	1
	Daily headache that affects the performance of household tasks.	2
Asthenic	General weakness that does not limit working capacity.	1
	General weakness that affects the performance of daily tasks.	2

Table III. Assessment of the severity of neurological and neuropsychological deficits

Total score	Result evaluation
1-3	Mild neurological and neuropsychological deficit
4-7	Moderate neurological and neuropsychological deficit
>7	Pronounced neurological and neuropsychological deficit

Table IV. Characteristics of groups of patients with chronic brain ischemia by age and sex

Characteristics of patients	Group 1	Group 2	Group 3	Total	χ2criteria
Number of persons	34; 34% (25,1%-43,5%)*	39; 39% (29,7%-48,7%)*	27; 27% (18,8%-36,1%)*	100; 100%	p=0,195
Male	14; 41,2% (25,4%-57,9%)*	14; 35,9% (21,8%-51,4%)*	14; 51,9% (33,3%-70,1%)*	42; 42% (32,5%-51,8%)*	p=0,431
Female	20; 58,2% (42,1%-74,6%)*	25; 64,1% (48,6%-78,2%)*	13; 48% (29,9%-66,7%)*	58; 58% (48,2%-67,5%)*	p=0,431
Age	59 (41-75)	63 (33-78)	70,5 (52-84)	63,9 (33-84)	p=0,18

Notes: * – determining 95 % confidence interval, Fisher's turning point.

Table V. Results of the analysis of the influence of comorbidity on the degree of severity of neurological and neuropsychological deficits

The studied groups	CIRS-G	MANND	Correlation coefficient	Criterion
Group 1	4,9 (1-8)*	2,4 (1-3)*	0,642**	p<0,001
Group 2	6,9 (2-11)*	4,5 (4-6)*	0,466**	p<0,003
Group 3	10,6 (5-16)*	8,4 (7-12)*	0,808**	p<0,1
Total	7,2 (1-16)*	4,9 (1-12)*	0,707**	p<0,001

Notes: * - determination of bivariate correlation (% PCC), ** - Pearson's correlation coefficient.

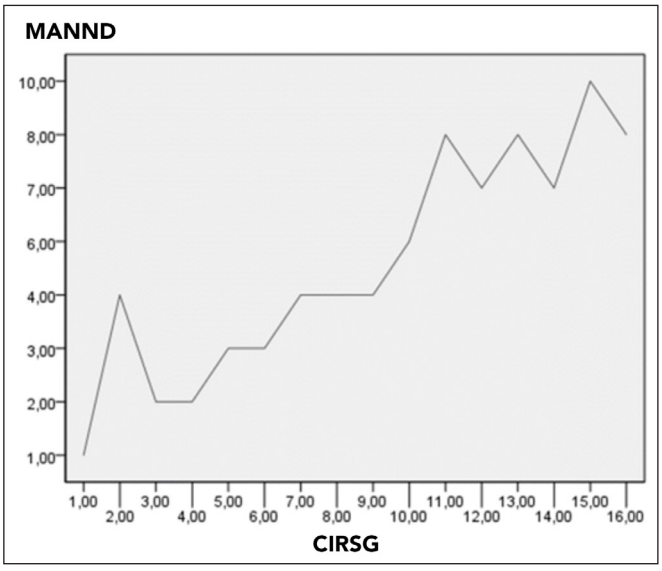

Fig.1. Modified assessment of neurological and neuropsychological deficits in patients with chronic cerebral ischemia. A stable positive correlation between the number of comorbidity scores on the CIRS-G scale and MANND

MATERIALS AND METHODS

A clinical-neurological and neuropsychological examination was carried out based on the data of a fragment of a comprehensive study: "Improving patient-oriented approaches to the treatment of patients with cardiovascular and cerebrovascular diseases and comorbid conditions."

As part of the study, 100 patients aged 33 to 84 years with comorbid pathology and a diagnosis of chronic cerebral ischemia were examined. The diagnosis was confirmed by the data of general clinical, clinical-neurological, laboratory, instrumental examination and neuropsychological examination.

The criteria included in the study are the expanded criteria for diagnosing chronic cerebral ischemia caused by atherosclerosis and hypertension, namely: 1) symptoms and a clinical picture (quick fatigue, inattention, deterioration of memory, especially for current events, reduced mental capacity, poor general well-being, headache, tinnitus, non-systemic dizziness, emotional instability, disturbed sleep, sudden impairment of vision, coordination, speech, sensitivity, etc.); 2) signs of damage to the cerebrovascular channel (stenotic (occlusive) processes or functional disorders of blood circulation (asymmetry of blood flow, changes in the range of cerebrovascular reactivity)); 3) signs of morphological changes in the brain substance according to neuroimaging data (MRI, CT scan); 4) signs of cardiovascular diseases, lung diseases, etc. (pain behind the sternum (angina), shortness of breath, general weakness, increased tiredness, swelling of the lower extremities,

fainting, dizziness, pounding heart, pain or tiredness in the legs when walking (intermittent claudication), skin discoloration, skin ulcers, etc.); 5) laboratory data on changes in blood composition (disorders of lipid metabolism, rheological properties of blood).

The diagnosis can be established in the presence of at least 3 of the 5 signs listed above and a causal relationship between them.

Exclusion criteria from the study are the presence of concomitant uncompensated diseases or acute conditions that could significantly affect the results of the study.

Statistical processing of the research results was carried out on a PC using the Microsoft Excel software package. Mathematical processing was performed using standard statistical packages (STATISTICA 6.0). Used methods of nonparametric biostatistics, Fisher's turning point, Pearson's correlation coefficient.

RESULTS

Data from the patients' history and neurological examination were evaluated using the scale of the modified assessment of neurological and neuropsychological deficits (MANND), developed by us empirically – Table II.

Assessment of the severity of neurological and neuropsychological deficits is presented in Table III.

This scale is designed specifically for patients with chronic cerebral ischemia. It takes into account quantitative changes in the neurological status, namely, damage to the pyramidal, sensitive, extrapyramidal, coordinating systems, damage to the cranial nerves, and the most common neurological syndromes, such as cephalic, asthenic, and higher cortical function disorders. When creating this scale, it was assumed that the basic assessment of neuropsychological deficit is the neuropsychological factor - the main concept of neuropsychology. It is a fundamental concept that is used to develop a methodology for neuropsychological diagnosis, a methodology for analyzing disorders of higher mental functions in the case of local brain lesions [8]. Assessment of neuropsychological deficits was carried out on the basis of the performance and comprehensive assessment of psychometric tests: MMSE, DASS-21, the results of which comprehensively reflected both the degree of disturbance of higher mental functions and the severity of disturbances in the emotional sphere.

This scale is a sensitive comprehensive method for assessing the expressiveness of neurological and neuropsychological deficits, in contrast to existing scales for the isolated assessment of motor deficits, cognitive disorders or disorders of the emotional sphere.

As a result of an examination of 100 patients with comorbid pathology and a diagnosis of chronic cerebral ischemia using the scale of the modified assessment of neurological and neuropsychological deficits, a quantitative characteristic of the degree of severity of chronic cerebral ischemia was established. Patients were divided into 3 groups according to the severity of neurological and neuropsychological deficits based on the total number of MANND points. The first group included 34 patients with a score of 1-3, which was equal to mild neurological and neuropsychological deficits. The second group consisted of 39 patients with a total score of 4-7, which corresponds to a moderate neurological and neuropsychological deficit. In the third group, there were 27 patients with a pronounced deficiency with a score >7 according to MANND. The distribution of patients by gender and age is shown in Table IV.

In addition, the history of chronic diseases of each patient was retrospectively analyzed. In order to study the relationship between the degree of severity of neurological and neuropsychological deficits and the comorbid background, CIRS-G scale was chosen (Cumulative Illness Rating Scale for Geriatrics) [9].

The predominance of cerebrovascular pathology in the structure of chronic diseases, the genesis of which is mainly multifactorial in nature, differs in the systemic nature of the lesion and comorbidity. The unity of pathophysiological processes leading to the development and progression of cerebrovascular diseases, is confirmed by the risk factors that are unique to them, such as arterial hypertension, atherogenic dyslipidemia, hyperglycemia and diabetes mellitus, obesity, metabolic syndrome, insulin resistance, chronic kidney disease, as well as smoking and hypodynamia. As can be seen from the presented risk factors, many of them are already independent diseases that lead to the development or deterioration of the prognosis of existing diseases.

A stable positive correlation was found between the number of CIRS-G comorbidity scores and the MANND score (Fig.1). According to correlation analysis, the Pearson coefficient is 0.707 ($p<0.001$) for the total sample of patients. Also, the expressed positive correlation coefficient for the 1st and 2nd groups remained at 0.642 ($p<0.001$) and 0.466 ($p<0.003$), respectively. The relationship between comorbidity and neurological symptoms was found to be somewhat higher in the 3rd group – 0,808 ($p<0,1$), but these data are not reliable, due to two factors, namely: a smaller sample size, since most patients with chronic cerebral ischemia have mild to moderate neurological deficits, and significant maximum CIRS-G values (Table V).

According to the conducted studies, it is possible to conclude that the use of a modified assessment of neurological and neuropsychological deficits is a sufficiently sensitive method that takes into account both the data of the neurological and psychological status, as well as the most common complaints of patients with chronic brain isch-

emia. The identified relationship with comorbidity proves that the use of this scale is justified. Thus, the modified assessment of neurological and neuropsychological deficits can be recommended both for use in clinical practice and for conducting scientific research, as a unique quantitative scale developed taking into account all the features of a wide spectrum of neurological pathology and mental complications in patients with chronic cerebral ischemia.

DISCUSSION

Chronic cerebral ischemia is considered as a syndrome that develops as a result of a slowly progressive disorder of cerebral circulation, resulting from the gradual accumulation of ischemic and secondary degenerative changes in the brain, which are caused by repeated ischemic episodes due to the development of the atherosclerotic process and arterial hypertension, manifested by progressive neurological, neuropsychological and mental disorders [10].

Depending on the degree of severity, cognitive disorders are classified as mild, moderate, and severe. In most cases, moderate cognitive disorders progress and later transform into dementia [11].

However, the characterization of the stages of dyscirculatory encephalopathy is based on the assessment of complaints, the presence of objective symptoms, and the level of social adaptation. The developed scale is a sensitive comprehensive method for assessing the expressiveness of neurological and neuropsychological deficits, in contrast to existing scales for the isolated assessment of focal neurological symptoms (motor deficits, cognitive disorders or disorders of the emotional-volitional sphere) and provides an objective quantitative assessment of the expressiveness of neurological, neuropsychological and mental violations.

The unity of the pathophysiological processes leading to the development and progression of cerebrovascular diseases and cardiovascular diseases is confirmed by the unique risk factors for them, characterized by systemic damage and comorbidity. Therefore, a stable positive correlation was found between the number of CIRS-G comorbidity assessment points and the MANND score.

Timely diagnosis of vascular pre-demented cognitive disorders is of great practical importance for ensuring the quality of life and preserving the working capacity of patients [12].

Therefore, at the initial stages of the development of cognitive disorders, when there are often difficulties in their objectification and control over the effectiveness of the treatment, the developed scale can be very useful.

CONCLUSIONS

1. Modified assessment of neurological and neuropsychological deficits is a scale for assessing neurological symptoms and psychological status, which was developed specifically for patients with chronic cerebral ischemia.
2. Modified assessment of neurological and neuropsychological deficits gives a quantitative result of the severity of changes in the neurological status, namely, damage to the pyramidal, sensory, extrapyramidal, coordinating systems, damage to the cranial nerves, and also takes into account the most common neurological syndromes, such as cephalic, asthenic and disorders of higher cortical functions.
3. Modified assessment of neurological and neuropsychological deficits is a comprehensive method, in contrast to existing scales for the isolated assessment of motor deficits, cognitive disorders or disorders of the emotional sphere, and has a stable positive correlation (0.707 ($p<0.001$)) between the number of comorbidity assessment scores according to the CIRS-G scale and the MANND score.

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Compliance with ethical standards. The authors adhere to the standards of the Helsinki Declaration of the World Health Organization association, as well as Interdisciplinary norms and regulations on the use of animals in research, testing and educational programs, which are published by the appropriate committee dealing with animal research at the Academy of Sciences in the city of New York. The submitted manuscripts relate to the work patients and are prepared in accordance with ethical standards. The study was conducted as a fragment of the complex scientific project of the Scientific Department of Internal Medicine (State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department) «Improvement of patient-oriented approaches to the management of patients with cardiovascular and cerebrovascular diseases with comorbid conditions, in particular in those suffered from COVID-19» (state registration number 0122U000234; term: 2022-2024).

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ORIGINAL ARTICLE

THE MORBIDITY RATE OF GENITOURINARY DISEASES ACCORDING TO THE DATA ON POPULATION RECEIVING MEDICAL CARE IN A MULTIFUNCTIONAL HEALTH CARE FACILITY

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ABSTRACT

The aim: Establishing the characteristic features and morbidity rate of genitourinary diseases in order to substantiate the need for health care services.

Materials and methods: The article uses bibliographic, medical, statistical and content analysis, as well as analytical methods. We have analyzed the sex-age characteristics of the morbidity rate of genitourinary diseases, with the morbidity rates among different sex-age groups of the population in 2015-2022 evaluated.

Results: Diseases of the genitourinary system constitute a significant share in the overall structure of the morbidity rate (7.3%-10.6%) and disease prevalence (6.1%-7.3%) among adults.

In 2015-2022, the dynamics of the morbidity rate of genitourinary diseases and their prevalence were characterized by a constant increase until 2019, with a subsequent decrease until 2022. Such trends in the morbidity rate and prevalence of genitourinary diseases among people may be related to the impact of the COVID-19 pandemic, which led to the restricted access to health care services as a result of taking measures to prevent the spread of infection, excessive load on the network of health care facilities within the pandemic period, etc.

The features of prevalence and dynamics of the incidence of genitourinary diseases in adolescents, adults, and persons of older age groups are determined.

Conclusions: The identified sex-age characteristics of the morbidity rate of genitourinary diseases, prevailing nosologies in certain age and sex groups will become the basis for substantiating measures to improve the quality of medical care, taking into account the principle of patient centricity and integration of care.

KEY WORDS: morbidity; prevalence of diseases; diseases of the genitourinary system; gender and age characteristics

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INTRODUCTION

Health and well-being of the population are important conditions for the social development and progress of humanity in various spheres of life. The principal goal of achieving a high level of health and well-being requires solving many socio-economic, medical and organizational tasks with the priority of the universal coverage of health care services. The specified direction of health care sector development is determined by a number of international documents adopted by the UN and the WHO. The Sustainable Development Goals of the UN provide for ensuring universal health coverage [1].

A resolution adopted by the UN General Assembly in 2017 declared the 12th of December as the International Universal Health Coverage Day. According to national priorities, it is recommended to perform educative activities and organize events to raise awareness of the need for a reliable and sustainable health care system and universal health coverage [2]. The WHO twice dedicated World Health Day to the issue of universal health coverage [3-4].

The issue of universal health coverage is defined as a priority in the programme documents of the WHO/Europe Health-2020: Foundations of European Policy in Support of the Actions of the Entire State and Society in the Interests of Health and Well-being and Priority Tasks in the Field of Improving Health Care Systems in the WHO European Region for 2015-2020 [5-6].

In the European Agenda for Action 2020–2025: United Action for Better Health, the WHO guides Member States' efforts to build stable, sustainable, and evidence-based health systems by five areas of activity [7].

Universal health coverage is known to assume that all people receive necessary services without financial dif-

ficulties caused by their payment. This principle requires ensuring access to the entire range of basic services, including health promotion, prevention, diagnosis, treatment, rehabilitation and palliative care. Methods of ensuring general health coverage at the national level shall be determined, taking into account the specific needs of the population and available resources [8-9].

An indisputable condition for achieving universal health coverage is an effective system of primary health care, oriented to people's needs. Thus, it is necessary to reorient national health care systems to primary health care as a solid foundation for ensuring universal health coverage [10].

According to the WHO, the health coverage index increased from 45 to 67 in 2000-2019. However, despite the progress, 30% of the world's population still does not have access to basic health services. Nearly 2 billion people face disastrous or devastating health care costs. The COVID-19 pandemic has become a new obstacle to universal health coverage. [11].

Achieving universal health coverage requires, inter alia, determining the needs for these services, which, in turn, are determined by the state of health of the population. Therefore, monitoring health and determining the needs of the population is an integral part of measures to achieve universal health coverage.

Important population health monitoring is protected by the Law of Ukraine On the Public Health System. Its provisions ensure establishing and functioning of a monitoring and evaluation system in the field of public health; establishing a public health information fund, in other words, a state information resource which contains data on the state of health, sanitary and epidemic well-being of the population, as well as indicators of the living environment [12].

Among the numerous components of population health monitoring, an important role is played by collection and analysis of data on the morbidity rate of diseases of the genitourinary system with regard to prevalence of pathology among the population, its contribution to the formation of the health burden, as well as negative medical and social effects, etc.

THE AIM

Establishing the characteristic features and morbidity rate of genitourinary diseases in order to substantiate the needs for health care services.

MATERIALS AND METHODS

The article uses bibliographic, medical, statistical and content analysis, as well as analytical methods. We have studied statistical data on the population receiving medical care in a multifunctional health care facility with regard to genitourinary diseases. For this purpose, data on seeking medical care have been taken from the statistical reporting form No. 12. We have analyzed the sex-age characteristics of morbidity rate of genitourinary diseases separately for teenagers, adults and people above the working age, with the morbidity rates among different sex-age groups of the population in 2015-2022 evaluated.

RESULTS

Studying the morbidity rate among adults, served in a multifunctional health care institution, has shown that pathology of the genitourinary system is quite common. A relative share of genitourinary diseases in the overall morbidity rate of the population served was 7.3-10.6% in 2015-2022. The share of this pathology in the structure of the prevalence of diseases was also significant and amounted in different years of the study 6.1% - 7.3%.

The analysis of the morbidity rate of genitourinary diseases among adults had a clear upward tendency in 2015-2019. During the period specified, it increased from 3,558.5 cases to 4,831.5 cases per 100,000 adults, i.e. 35.8%. In the following years, the morbidity rate of genitourinary diseases decreased to 3,517.0 cases in 2020, 3,397.8 cases in 2021, and 2,580.5 cases per 100,000 adults in 2022 (Fig. 1).

The basic nosological forms of genitourinary diseases include diseases of the prostate gland, kidney and ureteral stones, cystitis, kidney infections, inflammatory and non-inflammatory diseases of the uterine cervix, pathologic menopause and postmenopausal disorders, etc. Most of them are characterized by a higher morbidity rate in 2015-2019, followed by a decline. Thus, the morbidity rate of prostate diseases among people receiving medical care increased from 659.3 cases in 2015 to 1055.0 cases per 100,000 adults in 2019, or by 60%, with a subsequent decrease to 295.7 per 100,000 of the corresponding population in 2022.

Trends to a significant increase of the morbidity rate of adults in 2015-2019 were typical for salpingitis, oophoritis (by 4.5 times), inflammatory diseases of the uterine cervix (by 6.5 times), and menstrual disturbance (by 4.8 times).

In general, the genitourinary disease prevalence increased in 2015-2019 from 21,006.6 cases to 24,530.5 cases per 100,000 adults, i.e. by 16.8%. In the following years, there was a gradual decrease in the prevalence of this pathology to 21,040.2 cases per 100,000, or almost to the initial level of 2015.

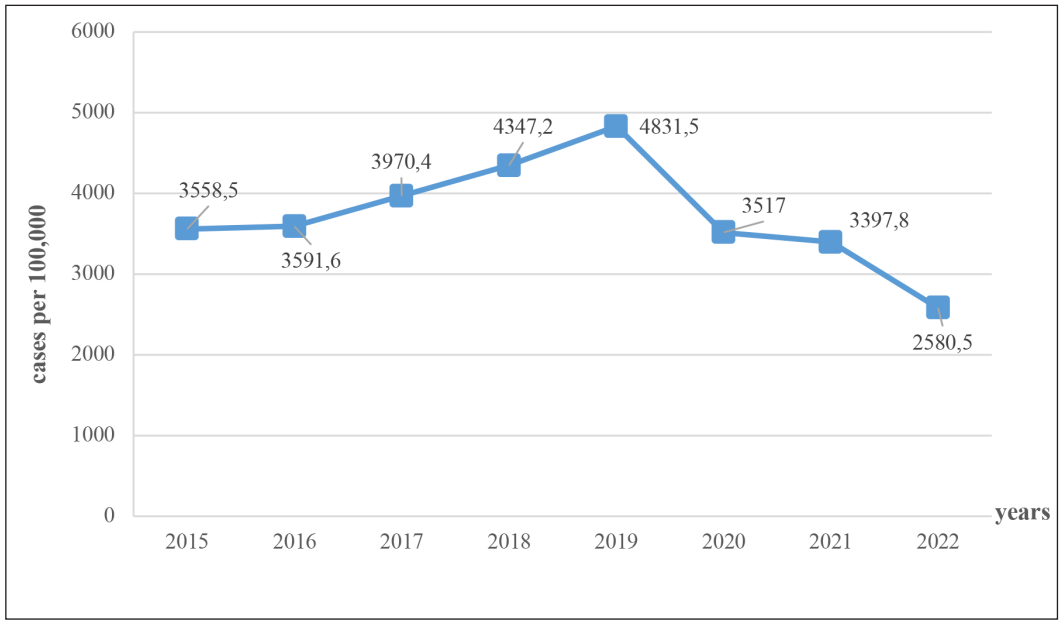

Fig. 1. Morbidity rates of genitourinary diseases among adults seeking medical care in a multifunctional health care facility in 2015-2022 (per 100,000)

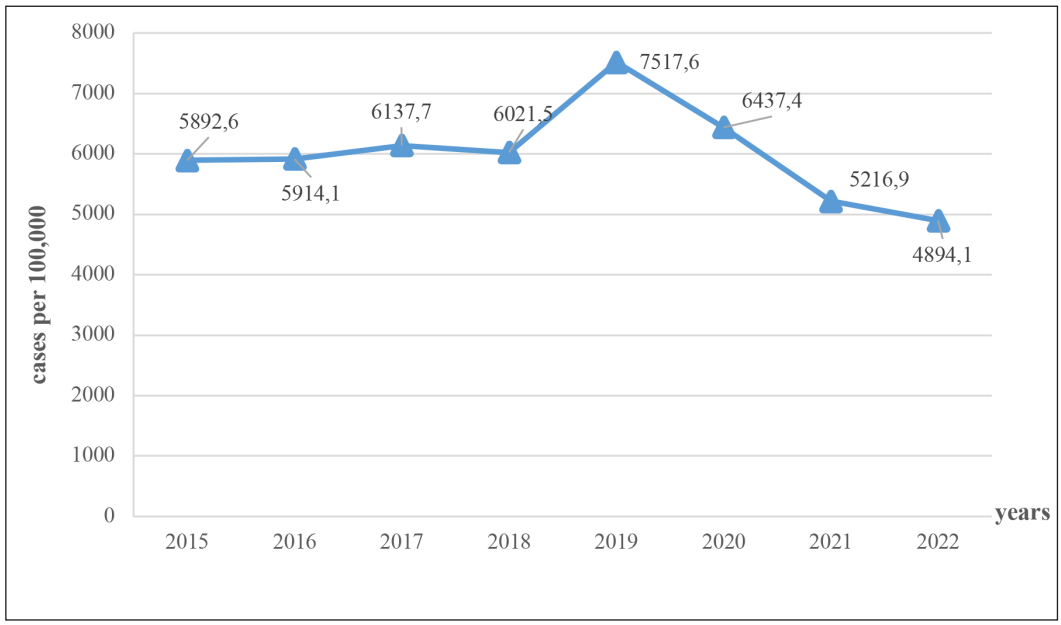

Fig. 2. Prevalence of prostate diseases among adults receiving medical care in a multifunctional health care facility in 2015-2022 (per 100,000).

Among individual nosological forms of genitourinary diseases, the rapid rates of increase in prevalence in 2015-2019 were characteristic of diseases of the prostate gland (+27.6%). The gradual decrease in the prevalence of this pathology in subsequent years of studying reached the level of 4,894.1 cases per 100,000 adults in 2022, which is 16.9% less than the initial level of 2015 (Fig. 2).

In 2015-2019, the increase in the prevalence of kidney and ureteral stones (+21.6%), cystitis (+59.0%), and cervical inflammatory diseases among adults visiting a multifunctional health care facility was observed (+11 times), pathologic menopause and postmenopausal disorders (+5.8%). At the same time, the prevalence of salpingitis, oophoritis, endometriosis, and non-inflammatory diseases of the uterine cervix tended to decrease.

The analysis of the age-related aspects of disease prevalence of the genitourinary system in 2022 has shown that the highest prevalence rates of this pathology are characteristic of adults (21,040.2 cases per 100,000), the lowest – of adolescents (1,106.5 cases per 100,000). The same regularity is observed for the morbidity rate of diseases of the genitourinary system (Fig. 3).

In 2022, the most frequent genitourinary disease of teenagers was cystitis (553.3 cases per 100,000), of adults – diseases of the prostate gland (295.7 cases per 100,000), kidney and ureteral stones (123.4 cases per 100,000), cystitis (155.0 cases per 100,000), kidney infections (40.2 cases per 100,000), etc., of people above working age – prostate gland hyperplasia (244.6 cases per 100,000)), cystitis (134.3 cases per 100,000), kidney

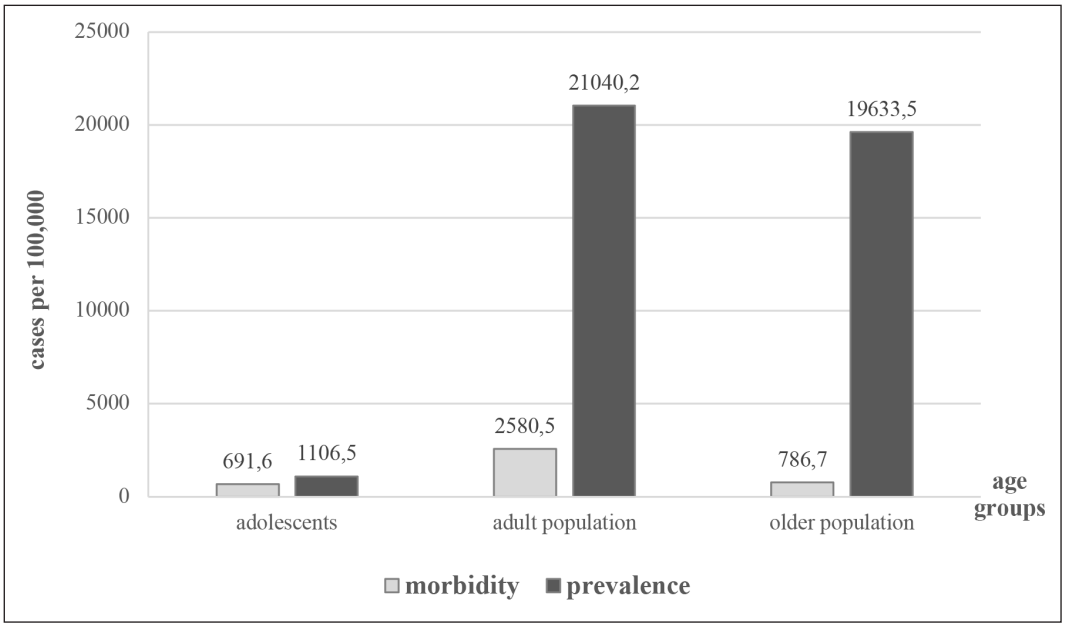

Fig. 3. Morbidity and prevalence rates of genitourinary diseases in 2022 (per 100,000) in various age groups seeking medical care in a multifunctional health care facility

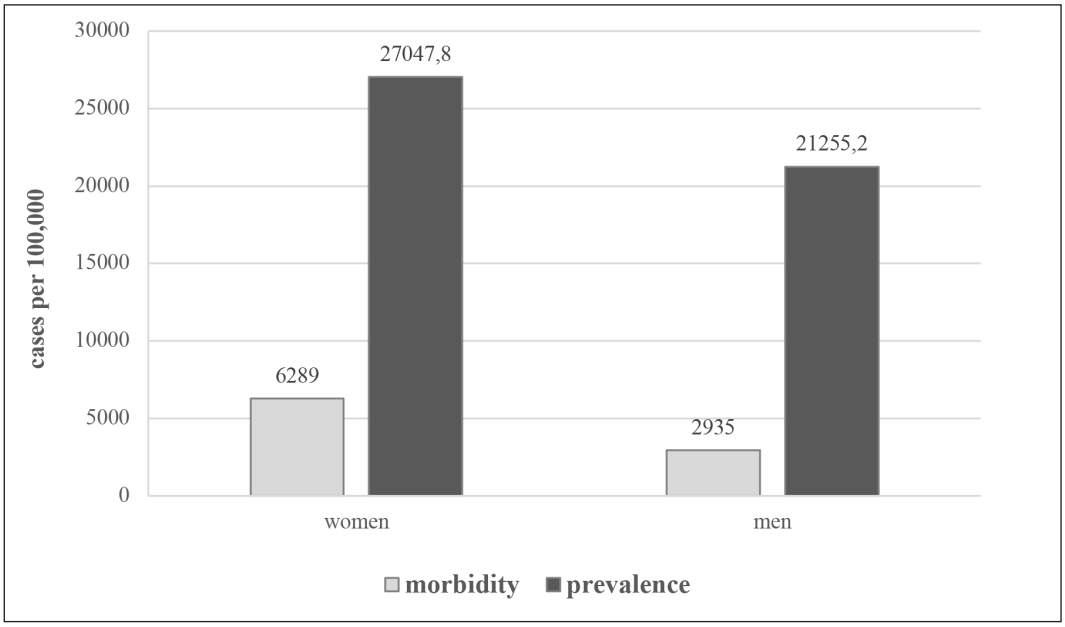

Fig. 4. Morbidity and prevalence of genitourinary diseases among men and women receiving medical care in a multifunctional healthcare facility in 2019 (per 100,000)

and ureteral stones (76.7 cases per 100,000), kidney infections (14.4 cases per 100,000).

In 2022, among the most common pathologies of the genitourinary system of teenagers were kidney and ureteral stones (553.3 cases per 100,000), chronic glomerulonephritis (138.3 cases per 100,000), and of adults – diseases of the prostate gland (4,894, 1 case per 100,000), kidney and ureteral stones (800.8 cases per 100,000), cystitis (473.6 cases per 100,000), kidney infections (86.1 per 100,000), of people above working age – prostate gland hyperplasia (3458.5 cases per 100,000), kidney and ureteral stones (719.5 cases per 100,000), cystitis (561.2 cases per 100,000), kidney infections (177.5 cases per 100,000).

In 2015-2019, the speed of growth in morbidity rates of genitourinary diseases was the highest among teenagers (+200.9%), and the lowest among the elderly (28.8%). The genitourinary disease prevalence grew at the fastest rate among adults (16.7%), with the lowest one among teenagers (+9.4%).

The study has analyzed the peculiarities of the morbidity rate of genitourinary diseases depending on gender of people, receiving medical care in a multifunctional health care facility. In 2019, the morbidity rate of genitourinary diseases of men was 2,935.0 cases per 100,000, and of women – 6,289.0 cases per 100,000, respectively. In 2019, prevalence of genitourinary diseases among men reached 21,255.2 cases per 100,000, among women – 27,047.8 cases per 100,000 (Fig. 4).

As the above data show, a higher morbidity rate of genitourinary diseases is characteristic of women, compared to that of men. This is due to a higher

morbidity rate of kidney infections (by 79.3%), cystitis (by 32 times) of women than that of men, as well as a high morbidity rate of salpingitis, oophoritis, inflammatory and non-inflammatory diseases of the uterine cervix, pathologic menopause and postmenopausal disorders. Among men, compared to women, higher morbidity rates of kidney and ureteral stones were revealed (3.2 times), as well as high morbidity rates of prostate gland diseases.

Diseases of the genitourinary system are known to cause a number of medical and social problems, including suffering, deterioration of the quality of life, loss of working capacity, disability and death. Malignant diseases of the genitourinary organs make a significant contribution to the health burden. While analyzing the morbidity rate of genitourinary cancer of people receiving medical care in multifunctional healthcare facilities in 2015-2022, we have revealed a decreased rate from 43 to 20 cases per 10,000 people, or by 53.4%. Within this period, there was a significant decrease in the morbidity rate of kidney, bladder and prostate cancer. At the same time, we have revealed an increase in prevalence of malignant neoplasms of the genitourinary system among people served by 5.1%, and prostate cancer by 13.1%. In 2015-2022, the morbidity rates of kidney and bladder cancer, as well other types of cancer of the genitourinary system, remained high.

In 2015-2022, the share of deaths from cancer of the genitourinary system in the overall population mortality structure ranged from 8.5% to 16.3%. At the same time, we have not revealed a stable trend in the dynamics of mortality rates from cancer of the genitourinary system over the years of studying.

DISCUSSION

Analysis and evaluation of the frequency and dynamics of the morbidity rate of genitourinary diseases of people receiving medical care in a multifunctional health care facility enabled identifying some features and patterns of prevalence of this pathology, depending on age, sex, nosological form, etc. It is important to note that the genitourinary pathology constitutes a significant share in the overall structure of the morbidity rate (7.3%-10.6%) and prevalence of diseases (6.1%-7.3%) among adults.

The general trend is an increased morbidity rate of genitourinary diseases among adults from 2015 to 2019 (by 35.8%) and genitourinary disease prevalence (by 16.8%), with a further decrease of these indicators until 2022 (by 46.6 % and 14.2%). This trend may be due to the influence of such an important confounder as the COVID-19 pandemic and the quarantine restrictions caused by it. These factors have led to a lower number of visits to health care facilities and a decreased availability of medical services. This trend has been noted in the works of other researchers. In particular, the analytical review *Health and Education: How the COVID-19 Pandemic Affected Access to Public Services in Ukraine* has stated that access to public health care services was limited during the pandemic. The lockdown introduction in order to reduce the scale of the COVID-19 pandemic, the significant burden on the network of the health care facilities and the re-orientation of part of the health care facilities to the preferential service of patients with COVID-19 and urgent patients have led to restrictions in providing services to people, search for alternative ways of receiving services or refusal of receiving services [13].

This problem is global, as the diversion of health care system resources to combating COVID-19 has caused long-term irregularities in providing basic types of medical care to people in many countries around the world. The WHO experts indicate that new obstacles to meeting the demand for medical services, such as restrictions on movement, reduced ability to pay, as well as fear of infection, have created additional unprecedented problems in achieving universal health coverage [14].

An important result of the study is establishing the structure of the morbidity rate of genitourinary diseases of people receiving medical care in a multifunctional health care facility, within the context of determining the needs for medical care and the resources required. Considering the frequency of diseases and the negative dynamics, priority should be given to prevention, diagnosis and treatment of diseases of the prostate gland, kidney and ureteral stones, cystitis, kidney infections, inflammatory and non-inflammatory diseases of the uterine cervix, pathologic menopause and postmenopausal disorders. These data are consistent with the data of other researchers with regard to the medical and social significance of the genitourinary pathology and its trends [15-16].

The age-related characteristics of the prevalence of genitourinary diseases indicate high rates among adults compared to teenagers, which is natural given the decrease in the body resistance with age, the influence of numerous adverse factors of production and environmental nature, etc. throughout life. The data revealed during the study on the peculiarities of the morbidity rate of each age group and its dynamic changes are an important basis for determining the priority of preventive, diagnostic and therapeutic measures for different age groups.

The gender aspects of the morbidity rate of diseases of the genitourinary system raise an important issue of preserving and strengthening reproductive health, indicate the priority of prevention and treatment of salpingitis, oophoritis, inflammatory and non-inflammatory diseases of the uterine cervix. This approach is consistent with the Sexual and Reproductive Health Action Plan in support of implementing the Sustainable Development Agenda for the Period up to 2030 in Europe – No One Left Behind [17]. At the same time, in terms of ensuring healthy aging, the issues of medical care for women with pathologic menopause and postmenopausal disorders and men with prostate diseases require special attention.

Particular attention should be paid to the identified problems of an increased prevalence of malignant neoplasms of the genitourinary system among people in 2015-2022 by 5.1%, including prostate cancer by 13.1%; high prevalence rates of kidney and bladder cancer, and other types of genitourinary cancer with no declining trends and persistent genitourinary cancer mortality rates. These data are consistent with the data of other researchers, which indicates the global nature of the problem of combating malignant neoplasms of the genitourinary system [18].

The features and trends in the morbidity rate of genitourinary diseases of people receiving medical care in a multifunctional health care facility enable determining the needs for medical care and the priorities of preventive, therapeutic and diagnostic activities.

CONCLUSIONS

Diseases of the genitourinary system constitute a significant share in the overall structure of the morbidity rate (7.3%-10.6%) and disease prevalence (6.1%-7.3%) among adults.

In 2015-2022, the dynamics of the morbidity rate of genitourinary diseases and their prevalence were characterized by a constant increase until 2019, with a subsequent decrease until 2022. Such trends in the morbidity rate and prevalence of genitourinary diseases among people may be related to the impact of the COVID-19 pandemic, which led to the restricted access to health care services as a result of taking measures to prevent the spread of infection, excessive load on the network of health care facilities within the pandemic period, etc. The issue requires in-depth study, clarification of the reasons and justification of the relevant organizational and management decisions.

Priority, in terms of improving medical care in accordance with needs, should be given to prevention, diagnosis and treatment of diseases of the prostate gland, kidney and ureteral stones, cystitis, kidney infection, inflammatory and non-inflammatory diseases of the uterine cervix, pathologic menopause and postmenopausal disorders, given the significant prevalence of these nosological forms and negative growth trends.

The identified sex-age characteristics of the morbidity rate of genitourinary diseases, prevailing nosologies in certain age and sex groups will become the basis for substantiating measures to improve the quality of medical care, taking into account the principle of patient centricity and integration of care.

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ORIGINAL ARTICLE

DETERMINATION OF SOMATIC, NEUROLOGICAL AND PSYCHO-EMOTIONAL MANIFESTATIONS OF THE ACUTE AND POSTCOVID PERIOD IN PATIENTS WITH A MILD COURSE OF COVID-19 IN WARTIME

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ABSTRACT

The aim: To analyze the typical symptom complex at the stage of COVID-19 acute phase in the systemic relationship with somatic, psychosomatic, and neurological manifestations.

Materials and methods: The collection of primary material was performed by clinical-anamnestic method, laboratory, and sociological examination of patients treated out patiently. Summarizing of the results was performed according to the analysis of 100 completed cases of COVID-19 in patients aged 35-45 years (50 men and 50 women) who had no concomitant chronic pathology, and patients did not receive any vaccine dose before the disease (acute COVID-19) and during the next follow-up period (6 months).

Results: The data of the analysis allowed us to make a grounded conclusion about the syndromic heterogeneity of COVID 19 in a standardized patients group with a mild course.

Conclusions: the highest number of symptoms in the postcovid period by frequency, polymorphism, and life quality impact was found in the group of patients with subjectively tolerate acute COVID-19 most easily. Patients whose acute episode meets the mild criteria have pronounced neurological and psychoemotional manifestations during the postcovid period.

KEY WORDS: COVID-19, POST-COVID syndrome, depression, anxiety, cognitive deficits, somatic manifestations

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INTRODUCTION

The COVID-19 pandemic has led to an increase in mental health problems and the prevalence of mental illness. Many studies confirm the development of such negative manifestations when suffering from COVID-19, such as anxiety (about 40.0%), fear (13.0%), uncertainty (6.0%), feelings of grief (5.0%), and anger (3.0%) [1]. These negative manifestations are also significantly characteristic of persons who feel the impact of the introduction of active hostilities both among the civilian population and among the military. With the simultaneous emergence and development of the covid syndrome and the impact of extremely intense psychological overloads, which are noted in persons who are in the zone of active hostilities, these effects on mental health are potentiated and can cause quite significant disorders and diseases, which will be noted by a wide spectrum of corresponding psychopathological symptoms. Therefore, the study of the peculiarities of the course of the covid syndrome and the post-covid period and the prevention of the possible development of various psychopathological changes is a very relevant and significant problem against the background of active hostilities in Ukraine.

In the context of the COVID-19 pandemic, health professionals and scientists in various fields have faced a number of new challenges, including the so-called "postcovid" syndrome [2]. In patients with acute disease, symptoms may persist for a long time and affect the quality of life and performance [3]. This determines the social significance of this disease and requires dynamic monitoring of patients, as well as the development of rehabilitation programs [4]. At the beginning of the COVID-19 pandemic, the main attention of researchers

was focused on the study of acute manifestations of the disease [5], the picture of the clinical course [6], risk factors for the severe course, and the development of treatment algorithms [4, 7]. Today the problem of algorithmization of medical and preventive care for patients after an acute case has become relevant [4, 8].

According to the literature, neurological and psychoneurological manifestations of varying severity are present in 100% of acute COVID patients (minimal – even if asymptomatic course) and almost in 90% of patients in the post-COVID period [2, 6, 8]. Among the neurological symptoms general weakness, dizziness, and anosmia was noted [3, 9]. Such neurological signs as encephalitis, meningoencephalitis, acute hemorrhagic necrotizing encephalopathy, acute cerebrovascular disorders, microhemorrhages, diffuse leukoencephalopathy, Guillain-Barré syndrome, myoclonus, Miller-Fischer syndrome, polyneuritis with cranial nerve damage, and skeletal muscle damage also described [7, 10].

With certain respect to the problem of medical care to acute patients with severe and extremely severe courses [11], it should be emphasized that most people tolerate COVID-19 in mild or moderate WHO criteria and are treated out-patiently. [12]. Such patients formally recovered (after completion of an acute case) are often overlooked not only by health professionals but also by scientific research [13]. At the same time, their health condition requires correction and coverage and systematic justification of ways to solve it.

THE AIM

The aim was to analyze the typical symptom complex at the stage of COVID-19 acute phase in the systemic relationship with somatic, psychosomatic, and neurological manifestations during 6 months of dynamic follow-up after the episode and to establish ways to improve treatment of patients with neurological and somatic complications.

MATERIALS AND METHODS

On the basis of typical clinical signs generalization during the next 6 months of clinical support after the acute COVID-19 the features of the somatic and psychoneurological symptoms evolution, the most influential clinical and medical-social factors identified at the outpatient stage. The study was conducted for the period 2021-2023.

This article highlights the preliminary results of generalizing the factors of the typical clinical course of acute COVID-19 and the next 6 months after the disease with an emphasis on neuro vegetative and psychoneurological manifestations.

The collection of primary material was performed by clinical-anamnestic method, laboratory, and sociological examination of patients treated out patiently. COVID-19 was confirmed by two types of laboratory tests (positive PCR test on the 3rd-10th day of acute disease and the presence of IgG antibodies in diagnostically significant titers after 8 weeks).

Summarizing of the results was performed according to the analysis of 100 completed cases of COVID-19 with a mild course according to WHO criteria [14–16] in patients aged 35–45 years (50 men and 50 women) who had no concomitant chronic pathology, and patients did not receive any vaccine dose before the disease (acute COVID-19) and during the next follow-up period (6 months).

The examination program consisted of several fragments: study and analysis of the somatic, neurological, and mental status of patients in the acute phase and for six months after the disease, a sociological survey of patients and their relatives, and retrospective analysis of major symptoms and syndromes. Patients examination was carried out in accordance with the requirements of current medical and technological documents of the Ministry of Health of Ukraine [15, 16]. All patients were tested for anxiety (Hospital Anxiety and Depression Scale (HADS), Spielberger The State-Trait Anxiety Inventory (STAI)), depression (HADS, modified Beck scale), cognitive impairment (Mini-Mental Scale Examination (MMSE)). Data were entered into a unified patient observation card developed by the authors taking into account the objectives of the study, with a certain periodicity: twice a day for the first 14 days of illness (or until the end of the episode), once a week from 15 to 45 days of observation, once a month (in the absence of patient complaints) from 46 to 180 days of observation.

To conduct a comprehensive sociological survey a standardized program for collecting and developing material was worked out. Sampling type – target. The author's methodology is based on the study of the respondents' assessment of the structural components of medical care quality for patients with COVID-19 and postcovid syndrome provided at the outpatient stage.

All respondents were guaranteed complete anonymity and confidentiality. The information was used by researchers only in generalized form.

Statistical and informational methods were used in the study: retrospective quantitative analysis, variation statistics, probability distribution of characteristics with an assessment of the reliability of the results, correlation (rank method and linear correlation method), and regression (multiple regression method) analysis. Taking into account the number of reliable ($p < 0,05$) relationships and the average strength of these relationships

(r_{XY}) for each of the analyzed factors, the coefficients of system formation (C_s) are determined, which in general characterize the most influential factors of the system. The degree of probability of an impact was determined using the standard value of Fisher's criterion (probable at $F \geq 2,2$).

The medical-statistical calculation of the obtained research results was performed using a package of application programs: Microsoft Excel 2016, Statsoft Statistica 10.0 for Windows, IBM SPSS 25.0 for Windows, etc. When characterizing the central tendency and variability of quantitative (continuous or interval) traits, the mean value (M) and standard deviation (SD) were determined. The probability of differences in the obtained quantitative characteristics in two mutually independent groups was determined using the Mann-Whitney U-test and in mutually dependent groups - the Wilcoxon matched-pairs signed-ranks T-test.

RESULTS

The analysis data allowed to draw a reasonable conclusion about the syndromic heterogeneity of COVID-19 in a standardized group of patients with mild course. Based on the most common symptoms and the power of their systemic relationships, we have conditionally identified three variants of the typical course: "anosmic", "hyperthermic with a cough" and "cephalgic".

The first variant ("anosmic") was demonstrated by 32 patients, including 22 women and 10 men. The pathognomonic sign of the acute episode in this subgroup of patients was loss of smell (P = 100%, $C_S = 0.319 \pm 0.021$), absolute anosmia was observed for 12.5 ± 2.1 days, and various types of dysosmia persisted 72,1 ± 15.1 days. It should be emphasized that for such patients was typical partial ageusia lasting 10.1 ± 1.9 days with a gradual restoration of taste sensation.

Another characteristic feature of acute COVID-19 in these individuals is the so-called hyper-hypothermic syndrome (P = 96.8 ± 5.6%, $C_S = 0.309 \pm 0.013$), which was manifested by temperature increase in the first days of the disease to subfebrile values (37,5 ± 0.9°C), lasting 3.0 ± 0.7 days, after which the temperature decreased to 35.7 ± 0.4°C and gradually over 10.5 ± 3.5 days set at normal levels.

The third most frequent complaint in patients of this subgroup was astheno-vegetative syndrome (P = 90.1 ± 9.8%, $C_S = 0.305 \pm 0.018$), which was manifested by a general weakness that affected daily life and work capacity (average weakness score on a ten-point scale – is 7.1 ± 2.7 points, lasting 16.3 ± 4.3 days), by tachycardia (heart rate – 90.5 ± 15.3 beats per minute, symptom duration – 24.0 ± 4.3 days) and by sweating.

A typical complaint for such patients is also back pain of muscular-tonic nature: the symptom frequency in the group – 84.3 ± 7.0%, $C_S = 0.303 \pm 0.015$, the average intensity on pain assessment scale – 5.1 ± 1,3 scores, duration – 7.5 ± 2.5 days. We also found a pathognomonic laboratory phenomenon in patients in which acute COVID-19 flows with olfactory loss (P = 90.1 ± 9.8%) – low white blood cell count ($4.0 \pm 1.1 * 10^9$/l – control on the 8th day from the case beginning). Other deviations of laboratory parameters recommended for control were not pathognomonic for this subgroup of patients.

Over the next 6 months of follow-up for patients of this group, the following signs were typical (with a frequency higher than 75.0%): the tendency to lose weight (-3.5% ± 1.1%), myalgia, pustular skin lesions, frequent (nontypical in the past for the patient) herpes infection exacerbation, candidiasis.

Sleep disorders in patients of this subgroup deserve special attention. Patients (P = 87.5 ± 11.0%, $C_S = 0.289 \pm 0.025$) complained of waking up in the second half of the night and difficulty falling asleep. This type of insomnia was determined after 18.1 ± 4.1 days from the acute case beginning and lasted until 150.8 ± 35.1 days of observation.

Interesting is the fact of gradual severity increase of anxiety and depression in patients from this subgroup – from negligible at the end of acute COVID-19, with a gradual growth up to significant after 6 months (Table I).

Patients in this subgroup expressed a positive attitude to vaccination and planned it in the near future (78.1 ± 10.2%), but the motives (62.5 ± 7.2%) were called administrative restrictions, not fear of getting sick again. At the same time, patients adequately perceived the fact of the disease, characterized the course as "mild", and strictly followed the doctor's prescription (compliance level according to the survey – 78.5 ± 10.4%).

The second variant of the course according to the main symptoms of an acute case was conditionally defined as "hyperthermic with a cough". We found this type in 39 patients, including 27 men and 12 women.

At the beginning of the acute episode, all patients had a specific hyperthermic syndrome (pathognomonic 100%, $C_S = 0.318 \pm 0.021$), which was manifested by a sudden temperature increase to high values (39.5 ± 0.8°C), duration 6.1 ± 1,8 days, then during the next 5.8 ± 1.6 days there were observed temperature fluctuations with morning normothermia and evening subfebrile. From the first to the last days, the temperature was well reduced with paracetamol or ibuprofen in the recommended dosages.

At the same time, at the first stage (high constant numbers) hyperthermia is accompanied by severe chills (frequency of 100%), is debilitating, and subjectively

Table I. Dynamics of anxiety and depression in young patients with a mild course of acute COVID-19 (variant with anosmia)

Term of examination	Anxiety level		Depression level	
	HADS scale	STAI scale	HADS scale	Beck scale
10-th day from the beginning of an acute case	8,1±1,1	68,2±10,5	9,0±2,1	13,2±3,1
1 month after the end of the acute case	11,2±3,1	82,2±9,5	13,0±4,1	15,2±2,2
2 months after the end of the acute case	14,5±2,1	84,2±5,9	14,1±2,2	19,0±6,1
3 months after the end of the acute case	15,1±2,4	86,3±7,9	16,1±2,5	21,1±6,3
4 months after the end of the acute case	15,5±2,3	89,2±5,9	18,1±4,2	22,0±6,4
5 months after the end of the acute case	16,3±4,1	104,2±9,9	19,1±3,2	29,0±7,1
6 months after the end of the acute case	15,9±3,9	110,2±10,9	19,3±4,2	32,0±10,1

Table II. Dynamics of anxiety and depression in young patients with mild course of acute COVID-19 (variant owith cephalgia)

Term of examination	Anxiety level		Depression level	
	HADS scale	STAI scale	HADS scale	Beck scale
10th day from the beginning of an acute case	18,1±4,1	122,2±15,6	14,5±3,1	23,4±3,7
1 month after the end of the acute case	16,4±3,5	124,2±17,9	17,0±4,2	27,2±4,2
2 months after the end of the acute case	19,2±6,8	131,4±25,1	16,1±2,8	25,4 ±7,1
3 months after the end of the acute case	18,6±5,1	129,3±13,4	16,4±2,3	28,5±6,1
4 months after the end of the acute case	16,4±4,0	126,2±21,1	17,2±5,0	29,0±3,7
5 months after the end of the acute case	16,3±2,7	116,4±14,8	18,4±3,9	33,2±7,1
6 months after the end of the acute case	16,9±3,5	119,3±11,5	17,3±2,6	30,1±9,9

difficult to tolerate by the patient ("hell flame"). At the second stage (fluctuations) fever is combined with significant diaphoresis, without chills, but it is characteristic that sweating itself does not lead to temperature decrease and requires antipyretics. It should be noted that in the period of persistent hyperthermia, patients were diagnosed with reversible cognitive impairment (MMSE scale (20.5 ± 4.5 points) with the most pronounced short-term memory deficit and disorientation over time.

Cough (P = 89.7 ± 8.2%, C_S = 0.307 ± 0.018) is persistent, tolerant to therapy, dry paroxysmal, scratchy, more pronounced during the day, intensified by physical or vocal exertion, duration is 22.8 ± 6.8 days.

Typical laboratory changes and other pathognomonic somatic manifestations were not found in patients of this group.

Interestingly, patients subjectively described the acute case of COVID-19 as "severe" or "very severe". The level of anxiety in this subgroup was expressed from the very beginning (HADS – 16.4 ± 3.1 points, STAI – 123.2 ± 19.5 points) and increased with the duration of the acute episode (HADS – 19.3 ± 4.1 points, STAI – 144.2 ± 28.6 points). After lowering the temperature and disappearing the cough, the anxiety of patients in this group decreased sharply (HADS – 8.3 ± 2.9 points, STAI – 53.4 ± 13.8 points) and was low throughout the follow-up period.

The level of depression in this patient's subgroup was low during the acute phase and remained so throughout all observation periods (HADS – 6.9 ± 1.3 points, Beck scale – 10.3 ± 2.2 points).

Patients in the subgroup with hyperthermia and cough expressed a negative attitude towards vaccination and did not plan to be vaccinated against COVID-19 in the near future, citing the fact that they had been already ill and "have sufficient natural defenses" (P = 76.9 ± 12.3%).

In the third group ("cephalgic" variant) we united 29 people, 16 women, and 13 men. The main active patients' complaint (pathognomonicity 100%, C_S = 0.306 ± 0.013) in this subgroup is headache, new, migraine-like, pulsating, intense (7.9 ± 1.3 points on a ten-point scale), holocranial, lasting more than 72 hours, resistant to standard therapy. Attacks of throbbing pain were combined with squeezing and pressing pain in the inter-fall period. At the same time, excluding the so-called "red" and "orange" flags [13], the symptoms persisted for more than 6 weeks, on average (49.1 ± 8.9 days).

A characteristic combination of other somatic syndromes was not found in this subgroup, although these patients had complaints of fever (P = 65.5 ± 33.6%), cough (P = 68.9 ± 19.3 %), rhinitis (P = 34.4 ± 27.9%), sore throat (P = 34.4 ± 27.9%), muscle pain (P = 51.7±23.9%), partial loss of smell (P = 44.8 ± 25.6%), others. In patients of this subgroup, we found high levels of anxiety and depression

from the beginning of the acute case with minor fluctuations throughout the observation period (Table II).

Subjectively, patients considered (P = 79.3 ± 15.3%) the course of the acute COVID-19 "mild" or "moderate", and they singled out a symptom of "unbearable headache", which drank to the daily life and reduced efficiency.

Patients in this subgroup also showed (P = 86.2 ± 12.8%, C_S = 0.272 ± 0.016) moderate cognitive impairment during the acute episode (MMSE scale (22.4±4.5) points) with the gradual recovery of function during the next 6 months. In particular, throughout the follow-up period, these patients had a decrease in memory and attention, which hindered or made difficult the performance of their daily duties.

A typical attitude towards COVID-19 vaccination was not found in this subgroup: most patients expressed doubts about its need (P = 62.1 ± 21.3%), but did not completely rule out the possibility of vaccination in the near future.

Please note that patients from all three subgroups had other symptoms of acute disease (rhinitis – 48.0±7.2%, dizziness – 78.0 ± 4.7%, diarrhea – 23.0 ± 8.8%, abdominal pain – 24.0 ± 8.7%, heart pain – 51.0 ± 7.0%, liver dysfunction – 54.0 ± 6.8%, other) and complaints in the postcovid period (diffuse alopecia – 43.0 ± 7.5%, allergic skin lesions – 22.0 ± 8.8%, muscle pain – 61.0 ± 6.2%, sleep disorders – 76.0 ± 4.9%, others), but these complaints were not pathognomonic for a particular subgroup of observations and did not have a probable systemic influence on the disease course, and therefore were not discussed by the authors as typical.

Analysis of the systemic relationships of typical somatic, neurovegetative and psychoneurological manifestations revealed that the most significant factor influencing the development of depressive states is olfactory loss (r_{XY} = +0.701), second place occupied by headache (r_{XY} = +0.692), third place – body temperature below 36.0 (r_{XY} = +0.683), on the fourth - cough (r_{XY} = +0.652). It can be argued that anxiety in the observation group is formed under the influence of hyperthermia (r_{XY} =+0.801), headache (r_{XY} = +0.743), cough (r_{XY} = +0.694), and asthenic syndrome (r_{XY} = +0.622).

DISCUSSION

Our results were in terms of expressiveness neurological and psychoemotional manifestations during the postcovid period also proven by other studies. Thus, Zolotovskaia I. A. et al. based on the results of MMSE data analysis, significant declines in cognitive functions were established after COVID-19 [17]. The authors installed that MMSE scores were 24.61 ± 1.5 points in the study group and 24.88 ± 0.75 points in the reference group (p = 0.754). The authors brought up that, low MMSE scores in patients whose age is not associated with any significant cognitive disorders, is linked with pseudocognitive defi cits on the background of severe asthenic syndrome at COVID-19.

Research by Boiko D. [18] determined the presence of anxiety disorders in 67.0% of convalescents. The authors found that anxiety disorders during the first 6 months after experiencing COVID-19 develop more often than in those who did not suffer from this disease during the last six months. They determined that patients who contracted COVID-19 in recent weeks were at increased risk of post-epidemic anxiety disorders, requiring close medical supervision and adequate awareness of possible symptoms. People have reported autonomic symptoms, including increased sweating and tachycardia, feelings of inner emptiness, and circadian rhythm disturbances such as difficulty falling asleep and waking up at the right time. The authors found that among those who underwent COVID-19, anxiety symptoms were noted by 63% of people (in the period from 5 to 12 weeks) and 37% of people (from 12 to 24 weeks). It was found at COVID-19 the frequency of anxiety is higher ($\chi 2$ = 4.54, p = 0.34). For people with COVID-19 the risk of developing anxiety disorders is 1.24 times higher (RR=1.243, 95% CI 1.06-1.49, p=0.036). For people with COVID-19, there were complaints of pathological fatigue (89%), constant feeling of danger (85%), difficulties in falling asleep (76%) and waking up (72%), excessive sweating (63%), tachycardia (59%) and feelings of inner emptiness (54%).

Other conducted studies also determined a high frequency of the occurrence of post-COVID stress disorders, which develop in different periods after the illness: 1 month after the disease in 42.0% of patients (studies Huang C. et al. [19]) and after 6 months in 23.0% (studies Sher L. [20]).

CONCLUSIONS

The data of the analysis allowed to make a grounded conclusion about the syndromic heterogeneity of COVID 19 in a standardized patients group with mild course, which requires a differentiated approach to medical and preventive care for such patients.

The highest number of symptoms in the postcovid period by frequency, polymorphism and life quality impact was found in the group of patients with loss of smell, i.e. in patients who subjectively tolerate acute COVID-19 most easily. This requires a more detailed study of the condition and the development of specific treatment and rehabilitation measures.

Patients whose acute episode meets the mild criteria, have pronounced neurological and psychoemotional manifestations during the postcovid period and may require the involvement of a specialist in rehabilitation and treatment regimens.

An important promising study area of the determinants of acute COVID-19 and postcovid period is searching for objective signs sensitive to the dynamic processes in patients with COVID-19; that is what determines the relevance of further research in this field for scientists and physicians of various clinical specialties.

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ORIGINAL ARTICLE

TREATMENT OF COMBAT GUNSHOT SHRAPNEL TRAUMA OF LARGE DEFECTS OF THE SOFT TISSUES OF THE LOWER EXTREMITIES WITH PLASTIC SURGERY IN COMBINATION WITH VACUUM ASSISTED WOUND CLOSURE (VAC)

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ABSTRACT

The aim: To evaluate efficacy of the tissue defect closure techniques in combination with VAC in the treatment of battle casualities of the lower extremities.
Materials and methods: The results of wound healing until complete wound closure, of 62 patients with shrapnel defects of the lower extremities where assessed.
Results: Treatment of patients with soft tissue defects of the lower extremities using rotational flaps on the vascular pedicle and VAC significantly reduces the incidence of infectious complications (18.75% in the main group vs. 30% in the control group ($p<0.05$)), reduces the intensity of pain according to the VAS scale during the first week of treatment in the main group to 5 ± 0.5 versus 7 ± 0.8 in the control group ($p<0.05$) and reduces the length of hospital stay by 7 days.
Conclusions: The use of rotational flaps on the vascular pedicle and local tissue closure techniques in combination with VAC is an effective method of treating patients with combat gunshot wounds of the soft tissues of the lower extremities

KEY WORDS: war casualties, soft tissue reconstruction, rotational flap, vacuum-assisted closure, wound management

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INTRODUCTION

Today, the treatment of mine-blast trauma is a significant challenge for all surgeons in Ukraine. While surgeons had some treatment for small bullet or shrapnel gunshot wounds in civilian life, with massive mine-blast injuries to the extremities since the beginning of the Russian military aggression against Ukraine have presented considerable difficulties for the Ukrainian surgical community in treating and reconstructing these defects. This applies to the provision of primary premedical and medical care, evacuation, and highly specialized surgical treatment with reconstruction of soft tissue defects of the limbs. Since the beginning of the full-scale invasion of Ukraine by Russian troops, the frequency of limb injuries among soldiers has increased significantly [1-7].

Today, the use of local flaps on perforating arteries is probably the best way to reconstruct complex soft tissue defects of the lower extremities. First time possibility of rotational flaps was described by Taylor G I, Palmer J H. [8]. The so-called «workhorses» of surgery of significant defects of the lower extremities have become the methods of rotational flap ALT (anterior-lateral tibial flap), PRSF (reverse sural flap on the leg). Simplicity of performance, better graft survival rate, better cosmetic results, and greater safety for patients are the main advantages of this technique. In case of smaller defects, plastic surgery with the Keystone rotary flap and local closure of defects with surrounding tissues are also used [2; 9].

The treatment of large soft tissue wounds is time-consuming, accompanied by significant difficulties in performing surgical wound care in the form of daily dressings, severe pain and numerous anesthetic support, purulent and inflammatory complications, and the cost of material support for treatment [10].

Vacuum-assisted wound closure (V.A.C.) was first proposed by Argenta in 1997. The use of NPWT for war trauma first time was proposed at 2004 by Burris et al. at 2004. A number of authors also use the term Negative pressure wound therapy (NPWT). According to Argenta's original method, the application of subatmospheric

pressure of 125 mmHg to wounds favorably affected the growth of granulations, and closure of wound cavities, which were subsequently closed either with a split skin graft or a rotational flap. The use of this technique allows to improve and accelerate wound healing through effective debridement, improved microcirculation, and reduced microbial contamination. It also reduces the number of painful dressings and anesthetic loads [1, 11, 10].

Today, V.A.C. assisted wound closure has been widely implemented in various fields of surgery: treatment of traumatic wounds, purulent wounds, orthopedics, treatment of peritonitis, burns, skin flaps, etc. For the plastic surgery of large and deep soft tissue defects of the extremities, skin flaps on perforated vessels are often used [2].

THE AIM

The aim was to improve the effectiveness of wound healing in the local tissue defects treatment after battle casualties of the lower extremities by using ALT (anterior-lateral tibial flap), PRSF (reverse sural flap on the leg), Keystone rotation flap repair, local tissue defect closure techniques in combination with vacuum-assisted wound closure.

MATERIALS AND METHODS

A clinical examination of patients was carried out as part of a scientific study titled "Development of optimal methods of surgical treatment and prevention of postoperative complications in patients with diseases of the abdominal and thoracic cavity using minimally invasive technologies" (No. 0113U007692). A total of 62 patients with multiple gunshot shrapnel defects of the lower extremities were examined between 2022 and 2023. At the initial stages of treatment, all patients underwent surgical debridement of wounds, followed by negative pressure wound therapy (NPWT) using a white foam sponge for a period of 6 to 17 days with dressing changes every 3 days. Antibiotic therapy was performed for all patients according to local protocols and the hospital's bacterial passport. The study was performed in accordance with all bioethical rules. Informed written consent for data processing was obtained from all patients. The main group consisted of 32 patients with wound defects repaired by the following methods: 9 - with a rotational flap on the perforating artery "propeller flap" ALT (anterior lateral thigh), 7 - with a displaced flap on the pedicled reverse sural flap (PRSF), 6 - with a mobilized "keystone" flap, 10 - with wound closure with mobilization of wound edges and subsequent vacuum-assisted wound treatment. The control group consisted of 30 patients with the following methods of wound defect repair 8 - rotational flap on the perforating artery "propeller flap" ALT, 6 - rotated flap on the pedicle PRSF, 7 - mobilized flap "keystone", 9 - wound closure with mobilization of wound edges with wound treatment under a mesh petroleum jelly dressing. The type of soft tissue defect plastic surgery was chosen individually, taking into account the type and extent of the wound, the condition of the tissues around the wound, the presence of a bone fracture, the installation of an external fixation apparatus (EFA), other wounds of the same limb, infection, internal organ injuries, and the patient's general condition. Patients with wound closure with a split skin flap and with damage or plastic surgery of the great vessels of the lower extremities were not included in this study.

Patients underwent a daily clinical examination, a study of the intensity of postoperative pain was performed according to the Visual Analog Pain Scale (VAS, Huskisson 1974), general laboratory methods, ultrasonographic examination of flaps and wounds to diagnose fluid accumulation, and Doppler ultrasonography to assess the blood supply to the flaps. The presence of postoperative complications was clinically determined: wound infection, flap necrosis, and the need for repeated wound revisions.

Statistical data collection of the research results was carried out on a PC using Microsoft Excel software. Mathematical processing was performed using standard statistical packages (SPSS version 12). Having a normal distribution of parameter values, the arithmetic mean value (M) and its standard error (m) were determined. The significance of the differences in parametric data was assessed using the Student's test (t). For all types of analysis, the critical level of significance (p) was $<0,05$.

Our study was performed in accordance with the World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, the Council of Europe Convention on Human Rights and Biomedicine, relevant laws, and orders of the Ministry of Health of Ukraine. Each patient of the study signed a detailed form of written informed consent to participate in this research.

RESULTS

All patients of both study groups were males aged 18-58 years with an average age of 32±2.1 years. According to the localization of the wounds, both groups were comparable: thigh wounds, lower leg wounds, and foot wounds (Fig. 1).

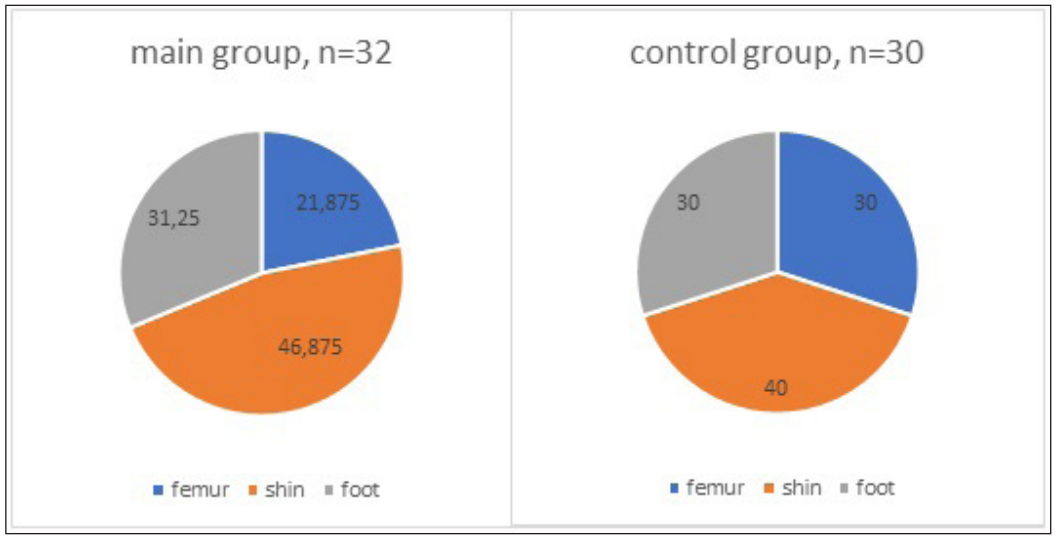

Fig. 1. Distribution of injuries to the lower extremities according to localization (%).

Fig. 2. Patient S., the main group of rotational flap repair on the perforating artery (ALT) at the time of admission (A), intermediate treatment result (B) and the appearance of the limb at the time of transfer to the rehabilitation department (C).

In 36% of patients, soft tissue wounds of the lower extremities were combined with bone fractures. In the structure of fractures, 9% were femur fractures, 31% were shin bones, and 60% were foot bones.

16% of patients in the main group with rotational flaps had the following complications: 6 - wound infection, 1 - flap necrosis with its removal and re-plasty, 1 marginal flap necrosis, 1 - wound edge divergence. In the control group it was noted: 8 - wound infection, 2 - flap necrosis with its removal and repeated plastic surgery, 5 - marginal flap necrosis, 4 - wound edge discontinuity. All complications required repeated revisions of the wound and debridement.

The treatment terms for patients in both groups depended on the type of wound, and concomitant pathology caused by gunshot blast injury and ranged from 14 to 90 days. Days for the treatment of wounds of the soft extremities after plastic surgery were 18.1±1.12 in the main group and 24.9±2.9 in the control group ($p<0.05$).

Patients of both groups complained of pain in the wound area and required pain relief according to local protocols. The intensity of the pain syndrome according to the VAS during the first week of treatment in the main group was 5±0.5, which was significantly less than in patients of the control group 7±0.8 ($p<0.05$). In the main group, there was better dynamics of pain reduction.

The total number of wound complications in the main group - 6 patients (18.75%) was significantly less than in the control group - 9 patients (30%). In both groups, the same frequency of infection of gunshot wounds during treatment was noted, in 3 cases with multidrug-resistant microorganisms (MDROs). In patients of the main ALT group, a significant decrease in the number of complications was noted in the absence of wound edge discontinuity and flap necrosis (Fig. 2). In the main PRSF group, only one case of flap necrosis was noted, in contrast to the comparison group (2 cases), the need for its removal was confirmed by Doppler ultrasonography, and the wound was closed with a split skin flap. «Keystone» plasty did not have a significant difference in the amount of wound suppuration. We did not observe any differences in wound edges and flap necrosis in this study. Plastic surgery of soft tissue defects with own tissues using vacuum-assisted wound treatment significantly had fewer complications due to a decrease in the number of wound edge dehiscerence, in contrast to the comparison group (Fig. 3). No wound edge necrosis was observed in patients with defect repair using their own tissues.

The dynamics of laboratory parameters did not differ significantly in both study groups.

Table I. Distribution of wounded in the main and control groups according to the localization of wounds and types of plastic closure of soft tissue defects of the lower extremities.

Parameters	Main group, n	%	Infection	Dehiscerence of the wound edges	Flap necrosis	Control group, n	%	Infection	Dehiscerence of the wound edges	Flap necrosis	In total	p
ALT	9	28,1	1	-	-	8	26,7	2	1	2	17	<0,05
PRSF	7	21,9	1	-	1	6	20	2	1	2	13	<0,05
«Keystone»	6	18,8	2	-	-	7	23,3	1	-	-	13	NS
Plastics with own tissues	10	31,2	2	1	-	9	30	3	4	-	19	<0,05
In total	32	100	6	1	1	30	100	8	7	4	62	p<0,05

Note: NS – non-significant

Fig. 3. Patient B., control group of PRSF pedicle flap repair at the time of admission (A) and at the time of transfer to the rehabilitation department (B).

The average number of revisions after defect plastic surgery in the main group was 2.6±0.7 and in the control group - 5.2±1.2 (p<0.05).

DISCUSSION

Of the 9 articles published between 2000 and 2021 it was found in four retrospective studies and five case series that NPWT was applied superficially to 56 free flaps, and 54 had successful outcomes [12]. Our study also has shown much better results of flaps healing with significantly less necrosis rate with VAC therapy usage.

Rates of graft loss in our study also are lower when VAC is used which is comparable with data from Webster J. However, in contrast to the results of this review, we obtained a significant reduction in the number of postoperative wound graft infection complications and the need for wound revisions. [3]

In comparison to clean wounds treatment with prophylactically VAC usage after surgery fewer SSIs (8.7%) of participants than people treated with standard dressings (11.75%). A 39 clinical studies analysis has shown that NPWT probably results in fewer SSI (8.8% of participants) than treatment with standard dressings (13.0% of participants) after surgery [13]. In our study, we got the same positive tendention for battle casualties wounds SSIs rate (18.75% in the main group with VAC against 30% in the comparison group (p<0.05)).

Slide-swing plasty in combination with VAC has shown better wound treatment results and minimal morbidity to patients with pilonidal cyst surgery with no VAC as in our study, but has shown elongated hospitalization time and more frequent interventions in opposite to our results with less hospitalization time and less interventions amount to flap reconstruction after battle casualties repair using VAC therapy [14].

Better results of treatment using vacuum-assisted wound closure in patients with skin flaps may be due to antibacterial action and effective drainage, improved microcirculation at the edges of the flaps due to the action of the VAC pump [2]. Better treatment results in plastic surgery with own tissues may be due to a decrease in the tension of sutured tissues, stable tissue approximation, drainage, and antibacterial effect. These claims require further research.

Thus, the use of rotational flaps on vascular pedicles and the technique of local tissue closure in combination with vacuum assisted wound closure (VAC) is a safe and effective method of treating patients with massive combat gunshot wounds of the soft tissues of the lower extremities.

CONCLUSIONS

Treatment of patients with massive gunshot-shrapnel defects of the lower extremities using rotational flaps on the vascular pedicle in combination with V.A.C. wound closure is an effective method of treating patients with combat gunshot wounds of the soft tissues of the lower extremities and can significantly reduce the number of purulent and inflammatory complications, reduce the intensity of pain, reduce the percentage of wound divergence. It also helps to reduce the number of surgical revisions of wounds in the hospital, accelerate the engraftment of flaps and shorten the length of hospital stay.

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ORIGINAL ARTICLE

VITAMIN D LEVEL AND ITS LINK WITH VISUAL ACUITY AND CONTRAST SENSITIVITY IN PATIENTS WITH AGE-RELATED MACULAR DEGENERATION

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ABSTRACT

The aim: Determination of vitamin D level and its connection with visual functions in patients with age-related macular degeneration, dry form.

Materials and methods: We analyzed the data of studies ($25(OH)D_3$ levels (nmol/l), LogMAR visual acuity and Logarithmic contrast sensitivity) of 2 groups of women of postmenopausal age: 1 group (58 people – 58 eyes) – patients with age-related macular degeneration (dry form) – study group; 2 group (29 people – 29 eyes) – people without ophthalmic pathology – control group.

Results: In the study group, 37 patients (63,8%) had vitamin D deficiency, 21 people (36,2%) had vitamin D insufficiency. In the control group, these figures were 69% and 31%, respectively. These indicators were defined as low (the normal supply of vitamin D is considered to be 100 nmol/l and more).

Visual acuity due to ETDRS chart in the study group was 0,22±0,04 (in patients with vitamin D deficiency) and 0,12±0,03 (in patients with vitamin D insufficiency), in the control group – 0,13±0,04 and 0,05±0,04 respectively.

In the control group, the logarithmic values of contrast sensitivity (log CS) were 1,58±0,04 log CS (in patients with vitamin D deficiency) and 1,62±0,02 log CS (in patients with vitamin D insufficiency). For patients from the study group, these figures were reduced to 0,98±0,1 log CS and 1,10±0,06 log CS respectively.

Conclusions: Patients with age-related macular degeneration, dry form, have low levels of vitamin D, with a predominance of its deficiency. It has been determined that with age-related macular degeneration, functional losses are observed when perceiving objects of low contrast.

KEY WORDS: Age-related macular degeneration, vitamin D, contrast sensitivity test, visual acuity changes

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INTRODUCTION

Age-related macular degeneration (AMD) is a chronic progressive degenerative disease of the retina. It leads to irreversible changes in the macula, which, lead to deterioration or loss of central vision [1]. AMD is the main cause of visual acuity disorders in people over 50 years, the incidence of the disease increases with age [2]. It is known that when AMD is detected in one eye, the second eye is affected in 5 years [3].

Wong and colleagues have estimated that by 2040, nearly 288 million people will suffer from AMD [4,5]. European research data shows that by 2050, 77 million people all around Europe will have AMD. The incidence of new cases will increase by 75% [6]. The sharpest growth will be among people aged 75 and older, increasing from 50 to 58 million cases (15%) [6].

In the USA, vision loss and blindness due to AMD are expected to increase from 620,000 cases in 2020 to approximately 1 million cases in 2050, regardless the widespread vitamin prophylaxis of early stages of AMD and appropriate treatment of neovascular forms of AMD [7].

Nowadays people in Ukraine experience the worst possible situation, that may happen all over the world – war. People live in chronic stress since 24.02.2022.

That is why our citizens may have a higher risk of developing AMD due to various factors such as stress, poor nutrition, and lack of access to medical care. The war has disrupted the healthcare system in Ukraine, making it harder to get the required treatment for conditions such as AMD. Many ophthalmologists have changed their working places (because in their hometowns it is not safe to be present due to rocket attacks, lack of electricity and water supply, destruction of medical equipment and hospitals), some doctors were killed. Thousands of people moved abroad as they are scared to live in their homes. These people abroad do not normally go on annual check-ups due to their pathologies.

Table I. Classification of vitamin D sufficiency and insufficiency (C. Gómez Alonso, 2003).

25(OH)D_3 level, nmol/l	Diagnosis
>100,0-250,0	Normal level
150,0-225,0	Optimal level
75,0-<100,0	Vitamin D hypovitaminosis
50,0-<75,0	Vitamin D insufficiency
<50,0	Vitamin D deficiency
>750,0	Vitamin D hypervitaminosis
>250,0	Guarantee of a wide range of safety

Table II. Comparative assessment of functional parameters in patients of the study and control groups.

	Study group (n=58)	Control group (n=29)	The level of significance of differences between groups, p
LogMAR visual acuity (ETDRS)	0,2±0,06	0,1±0,06	<0,001
Logarithmic contrast sensitivity (log CS)	1,02±0,1	1,6±0,04	<0,001

The comparison revealed a difference in visual acuity in two independent groups (p<0,001).
The comparison revealed a difference in logarithmic indicators of contrast sensitivity in two independent groups (p<0,001).

Table III. Comparative assessment of functional parameters in groups of patients with different levels of vitamin 25(OH)D3 deficiency.

	25(OH)D_3 level, nmol/l	
	up to 50 nmol/l	51-75 nmol/L
LogMAR visual acuity (ETDRS) Study group (n=58)	37 people 0,22±0,04	21 people 0,12±0,03
LogMAR visual acuity (ETDRS) Control group (n=29)	20 people 0,13±0,04	9 people 0,05±0,04
Logarithmic contrast sensitivity (log CS) Study group (n=58)	37 people 0,98±0,1	21 people 1,10±0,06
Logarithmic contrast sensitivity (log CS) Control group (n=29)	20 people 1,58±0,04	9 people 1,62±0,02

Table IV. Comparative assessment of vitamin 25(OH)D3 supplementation (X±σ nmol/l) among patients of study and control groups.

	25(OH)D_3 level, nmol/l	
	up to 50 nmol/l	51-75 nmol/L
Study group (n=58)	37 people 36,1±6,5	21 people 60,4±6,0
Control group (n=29)	20 people 36,6±6,4	9 people 59,4±6,3

They experience mental health issues (depression and anxiety), which can also contribute to the development or progression of AMD.

AMD is a multifactorial disease. The role of vitamin D in the pathogenesis of AMD is actively discussed in the modern literature [8, 9, 10]. The exact mechanism of how vitamin D affects AMD is still unknown. Research data are contradictory.

The issue of vitamin D insufficiency and deficiency is actively studied by specialists in various fields. According to different authors, around 50-80% of the world's population has various degrees of vitamin D deficiency [11].

According to the C. Gómez Alonso (2003) classification, there are different degrees of saturation of the body with vitamin D [12] (Table I).

Vitamin D insufficiency has been found in postmenopausal women in 50% of the population of Thailand and Malaysia, in 75% of the US population, in 90% of the population of Japan and South Korea [13]. Vitamin D deficiency is very common in the countries of Middle East and South Asia, where the average levels of 25(OH) D_3 in the blood are around 10-30 nmol/l [14].

In Ukraine, the issue of vitamin D insufficiency and deficiency also plays a key role among specialists in various fields. According to V.V. Povoroznyuk et al. study (2011),

which included 1575 residents of Ukraine aged 20-95 years who did not have a history of calcium and vitamin D intake for the past 6 months (mostly women – 86,3%, mean age 58,61±0,37 years; age of men – 54,93±1,09 years; p <0,001) [15]:

- in 4,6% the optimal level of vitamin D was found;
- in 13,6% – vitamin D insufficiency;
- in 81,8% – vitamin D deficiency.

Low levels of vitamin D in the blood are associated with an increased risk of severe general pathologies: diseases of the cardiovascular and nervous systems, diabetes, osteoporosis, autoimmune diseases, tumors [16].

An epidemiological study performed by Aksoy et al. (2000) has shown that patients with low levels of vitamin D in the blood have been diagnosed with severe forms of diabetic proliferative retinopathy [17]. While in patients with nonproliferative retinopathy, sufficient levels of vitamin D were observed. Over time, several other similar studies have shown next: the lower levels of supplementation of vitamin D in the body are related to the more severe diabetes and the more severe eye complications [18].

An experimental study of human retinoblastoma cells revealed the presence of vitamin D receptors [19]. Increased apoptosis of cancer cells and slowing of angiogenesis in the tumor have been observed with the addition of vitamin D supplements to the retinoblastoma treatment regimen [20]. Thus, a reduction in tumor size was achieved without significant toxic effects on the body. The optimal levels of vitamin D in the serum for the prevention of cancer, according to research, are 100-150 nmol/l [21].

THE AIM

Determination of vitamin D level and its connection with visual functions in patients with age-related macular degeneration, dry form.

MATERIALS AND METHODS

We analyzed the data of studies of 2 groups of women of postmenopausal age: 1 group (58 people – 58 eyes) – patients with age-related macular degeneration (dry form) – study group; 2 group (29 people – 29 eyes) – people without ophthalmic pathology – control group, who were treated at the clinical bases of the Department of Ophthalmology of Bogomolets National Medical University. During the research, the ethical principles of the World Medical Association Declaration of Helsinki (1964) were followed [22].

There were no differences in gender and age in the groups, the mean age of patients in both groups being 72±10 years.

All examined patients had a reduced level of vitamin D. The degree of vitamin D supplementation was assessed according to the C. Gómez Alonso classification, 2003 (Table I).

Visual acuity was checked subjectively using the ETDRS chart (LogMAR) from a distance of 4 meters [23]. The maximum corrected visual acuity was taken into account.

During the study, the last line, where the patient correctly named all 5 letters, was determined. Next, a logarithmic score was determined for this line (these results are displayed in the fields of the ETDRS test, for example, line 20/25 has a logarithmic score of 0,1). The next step was to subtract 0,02 logarithmic units for each letter that has been correctly identified on the last line, where all letters were named correctly. For example, if the patient reads all the letters in line 20/30 correctly and then 3 letters correctly in line 20/25, the visual acuity index will be calculated as follows:

line 20/30 = 0,20

3 letters X 0,02 log/letter = -0,06

Visual acuity on the ETDRS chart = 0,14

To study the contrast sensitivity "The Mars Numeral Contrast Sensitivity Test" tables were used – portable, size 23×36 cm, designed for the use at a distance of 50 cm [24].

The test system is a set of 3 printed tables for independent testing of the left eye, right eye and both eyes. All tables are identical, except for the sequence of numbers. Each table consists of 48 digits arranged in 8 rows of 6 digits each. The contrast of each digit when read from left to right decreases by a constant factor (0,04 units). The patient names the numbers in rows as in a standard visual acuity test (however, instead of the optotypes decreasing in size, they decrease in contrast).

The contrast of the last digit, after which the patient incorrectly identified two consecutive digits, corrected for the previously incorrect number of responses, determines the contrast sensitivity of the patient.

In order to assess the degree of clouding of the lens, the LOCS III classification (Lens Opacities Classification System, 1993) was used [25]. It is represented by 6 reference images of changes in the color of the nucleus:

1st group – the nucleus is soft, almost transparent;

2nd group – the nucleus has very low density, light gray hue;

3rd group – the nucleus has low density, grayish-yellow or light gray hue;

4th group – the nucleus has medium density with a yellow or gray tinge;

5th group – dense nucleus of amber-yellow color;

6th group – very dense nucleus, amber or black color.

Changes in the nucleus starting from 3rd group and above affect the visual functions.

Criteria for excluding patients from the study were next:

- men;
- women who have not reached the postmenopausal period;
- the presence of concomitant ophthalmic diseases (glaucoma, cataract groups 3-6 according to the LOCS III classification), which can lead to decreased visual acuity and interfere the fundus examination;
- the presence of systemic diseases (diabetes, autoimmune diseases, liver and kidney diseases);
- postponed vitreoretinal operations.

Descriptive statistics methods were used to present the results of the study. Summarizing the analysis of quantitative variables, the results are represented by indicators of mean and standard deviation, to compare the features Student's t-test was used in the case of the normal law of distribution of the quantitative variables; indicators of the median and the first and third quartiles, to compare the features Wilcoxon-Mann-Whitney test was used in the case of a distribution law other than normal. The statistical significance of the results was estimated at a given marginal level of first-order error of not more than 5% ($p<0,05$).

Statistical packages used: MedStat V.5.2. Quantitative changes are presented as mean±standard deviation (SD). The Student's t-test was used to assess the probability of the obtained results. Differences were considered probable at $p<0.05$.

RESULTS

The results of the study show that in the study group, 37 patients (63,8%; 36,1±6,5) had vitamin D deficiency, 21 people (36,2%; 60,4±6,0) had vitamin D insufficiency. In the control group, these figures were 69% (36,6±6,4) and 31% (59,4±6,3), respectively (Table IV).

These indicators were defined as low (a normal supply of vitamin D is considered to be 100 nmol/l and more [12]).

Visual acuity due to ETDRS chart in the study group was 0,2±0,06, and in the control group – 0,1±0,06. The level of the difference between the groups is $p<0,001$ (Table II, III).

In the control group, the logarithmic values of contrast sensitivity (log CS) were 1,6±0,04 log CS. For patients from the study group, this figure was reduced to 1,02±0,1 log CS. The level of the difference between the groups is $p <0,001$ (Table II, III).

DISCUSSION

In a prospective multicenter randomized clinical study dedicated to age-related macular degeneration (AREDS - Age-Related Eye Disease Study) [26], it was found that more than 10% of the population aged 65-74 have symptoms and signs of AMD, while among the population over 75 years of age, this indicator increased significantly (up to 25%), and among people over 85 years of age - more than 30%.

As is well known, the dry form of AMD is seen in 85-90% of all AMD cases worldwide. Despite that, more than 80% of visual loss is caused by wet AMD [27]. Measures that correct pathogenetic changes, thus slowing down the transition from the dry form to the wet, are relevant.

The annual economic cost of visual loss from AMD is estimated to be $4.6 billion in direct medical costs in the USA [28].

The situation with the prevalence of AMD in Ukraine is ambiguous. The latest official statistics are available for 2017 and are not complete. According to them, about 1,5 million adults suffer from eye pathology and its adnexa, about 30% of which are retinal diseases.

The action of vitamin D arouses interest among scientists all over the world. Experimental studies are dedicated to the effects of vitamin D metabolites on AMD in course of experiments.

One of the functions of vitamin D is an anti-inflammatory effect [29].

Vitamin D receptors to $1,25(OH)_2D_3$ have been identified in more than 38 tissues where vitamin D clearly controls vital genes related to bone metabolism, oxidative damage, chronic disease and inflammation.

The war in Ukraine has disrupted the healthcare system in the country, making it challenging for people to receive proper medical attention, including eye care. This may lead to delayed diagnosis and treatment of AMD, potentially exacerbating the condition and increasing the risk of vision loss. Continued efforts to improve access to eye care and promote healthy lifestyle habits can help mitigate the risk of AMD.

CONCLUSIONS

Patients with age-related macular degeneration, dry form, have low levels of vitamin D. We have identified varying degrees – vitamin D insufficiency (51-75 nmol/l) and vitamin D deficiency (up to 50 nmol/l), with a predominance of its deficiency.

Patients with vitamin D deficiency have lower numbers of LogMAR visual acuity (ETDRS) and logarithmic contrast sensitivity indexes compared to patients with vitamin D insufficiency.

It is determined that due to age-related macular degeneration, functional losses are observed when perceiving objects of low contrast. At high visual acuity levels, this method can be used as a screening method to detect functional changes in AMD in the early stages.

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ORIGINAL ARTICLE

ENDOVASCULAR DIAGNOSTICS AND TREATMENT OF HEMORRHAGES IN MILITARY AND CIVILIAN PATIENTS FOLLOWING ABDOMINAL SURGERY

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ABSTRACT

The aim: The retrospective analysis of the angiographic picture and clinical results of endovascular treatment of patients with postoperative abdominal and gastrointestinal bleeding was carried out.

Materials and methods: The results of 447 endovascular diagnostic and therapeutic interventions in 391 patients (46 military and 345 civilians) with postoperative bleeding performed from 2012 to 2022 were studied. According to computer tomography with contrast enhancement, the source of bleeding was identified in 216 (67.7%) cases.

Results: In 345 (88.2%) patients, it was possible to reliably identify the source of bleeding on angiography. In 46 (11.8%) patients with an unexplained source of bleeding, the target arterial pool was determined on the basis of localization, volume, and features of surgical intervention and considered as preventive interventions. A total of 447 endovascular hemostatic interventions were performed on 391 patients. A stent graft was installed in 27 patients, 420 embolization were performed in 364 patients. Thus, in 43 (11.0%) patients, embolization was performed repeatedly, in 12 cases - three times, in 1 case - four times. In 16 cases (15 cases of prophylactic embolization), endovascular hemostasis was ineffective and required subsequent surgical intervention

Conclusions: Endovascular interventions are an effective method of diagnosis and treatment of postoperative abdominal bleeding. Prophylactic embolization allows you to prevent the recurrence of postoperative bleeding with an instrumentally undiagnosed source, however, you need to be prepared for the multi-stage treatment aimed at sequentially shutting down the collateral blood supply to the damaged area.

KEY WORDS: abdominal bleeding, embolization, stent-graft

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INTRODUCTION

Abdominal bleeding remains one of the most dangerous surgical complications due to chronic diseases and military injuries. The frequency of such complications, depending on the intervention, ranges from 0.9 to 15%, and causes 54% of postoperative mortality [1, 2]. Most often, postoperative bleeding occurs after interventions on the pancreas, kidneys, liver, and pelvic organs, however, there are cases of arrosive bleeding during extra-abdominal surgical interventions [3]. Traditionally, open surgery is the main method of stopping postoperative bleeding, but in many cases, it does not make it possible to identify the source of bleeding and eliminate it. Besides, such repeated interventions are associated with increased mortality [4]. That is why endovascular methods for diagnosing and stopping bleeding come to the first line. The advantage of endovascular techniques is minimal invasiveness, repeatability, and a combination of diagnostic and therapeutic stages [5].

THE AIM

The aim of this study is the retrospective analysis of the angiographic imaging and clinical results of endovascular treatment of patients with postoperative abdominal and gastrointestinal bleeding.

MATERIALS AND METHODS

This study includes the results of 447 endovascular diagnostic and therapeutic interventions in 391 patients with

Table I. The frequency (n) of surgical interventions and the type of hemorrhagic complications

Bleeding site / Intervention area	Stomach	Upper intestine	Lower intestine	Abdomen	TOTAL
Pancreatic	4	133	0	90	227
Hepatobiliary	0	46	0	38	84
Splenic	0	21	0	26	47
Gastric	22	0	0	0	22
Intestinal	0	4	7	0	11
TOTAL	26	204	7	154	391

Table II. The frequency (n) of the performed endovascular interventions

Bleeding site / Intervention	Stomach	Upper intestine	Lower intestine	Abdomen	TOTAL
Stent grafting	0	16	0	11	27
Gastroduodenal artery embolization	0	101	0	83	184
Left gastric artery embolization	29	5	0	19	53
Hepatic arteries embolization	2	25	0	15	42
Splenic artery embolization	0	73	0	33	106
Superior mesenteric branches embolization	0	13	0	11	24
Inferior mesenteric branches embolization	0	0	7	4	11
TOTAL	31	233	7	176	447

postoperative bleeding performed from 2012 to 2022. The mean age of the patients was 46 years (from 22 to 74), there were 245 (62.7%) men and 146 (37.3%) women, 345 were civilian and 36 were military patients with chronic diseases and military injuries. Early postoperative bleeding included bleeding that occurred in the first 3 days after surgery was in 196 patients (50.1%), late - in the first month after surgery – 133 (34.0%), remote - more than 1 month after surgery in 62 (15.9%). The data on surgical interventions that caused bleeding, and bleeding types are presented in Table I and Figures 1-2.

According to the data in Table I and Figures 1-2, most often bleeding occurred during interventions on the pancreas, with a predominance of bleeding from the upper intestine (virsungorrhagia).

The decision on endovascular intervention was made at a multidisciplinary consultation based on an analysis of the features of performed surgical intervention and the determination of the probable source of bleeding. According to contrast-enhanced computed tomography, the source of bleeding was identified in 216 (67.7%) cases. Depending on the anatomical situation, femoral (247, 63.2%), brachial (95, 24.3%) or radial (49, 12.5%) catheter access was used. In 36 cases, to perform stable super-selective catheterization, intraoperative conversion of the femoral access to brachial or radial, or vice versa, was performed. In case of gastrointestinal bleeding, the intervention was started with angiography of the celiac trunk and superior mesenteric artery; in case of bleeding from the lower intestine, the inferior mesenteric artery and internal iliac arteries were additionally examined. If the source of bleeding was a distal arterial branch, arterial embolization was preferred. In this case, a catheter was advanced into the damaged arterial branch, the shape of which was selected individually. If super-selective catheterization of the damaged arterial branch was not possible, a microcatheter was used. Embolizing particles (distal embolization), embolization coils (proximal embolization), or their combination (combined embolization) were used.

In the case of branches of the celiac trunk and superior mesenteric artery, embolization was performed both distal and proximal to the site of injury to avoid the development of distal collateral overflow. If the main arterial trunk of the hepatic or mesenteric artery was the source of bleeding, preference was given to endovascular grafting. In this case, the diagnostic catheter was replaced with a guide catheter, and a stent graft was inserted through it into the injury site and deployed. The follow-up period for patients was at least 3 months.

The study was provided with compliance of the Council of Europe Convention on Human Rights and Biomedicine principles, World Medical Association Declaration of Helsinki on the ethical principles for medical research

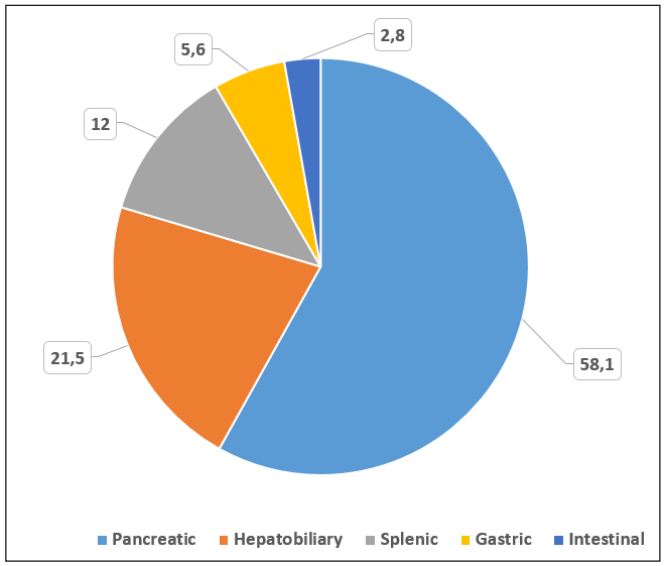

Fig. 1. The frequency (%) of surgical interventions, that caused bleeding (N=391).

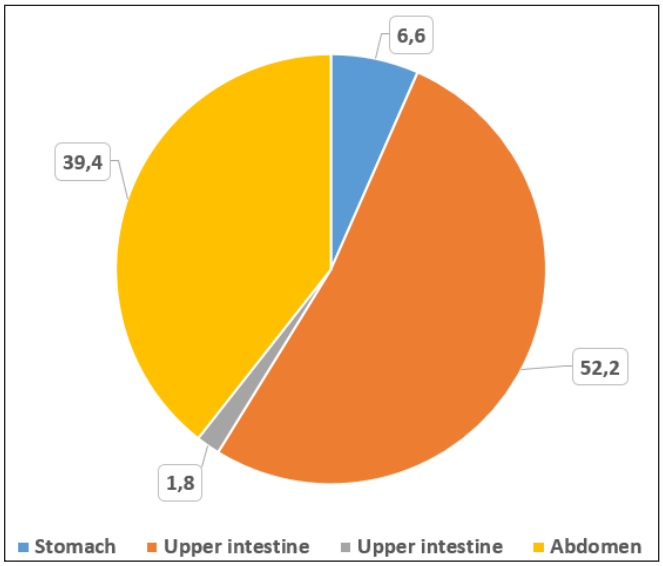

Fig. 2. The frequency (%) of different types of bleeding complications (N=391).

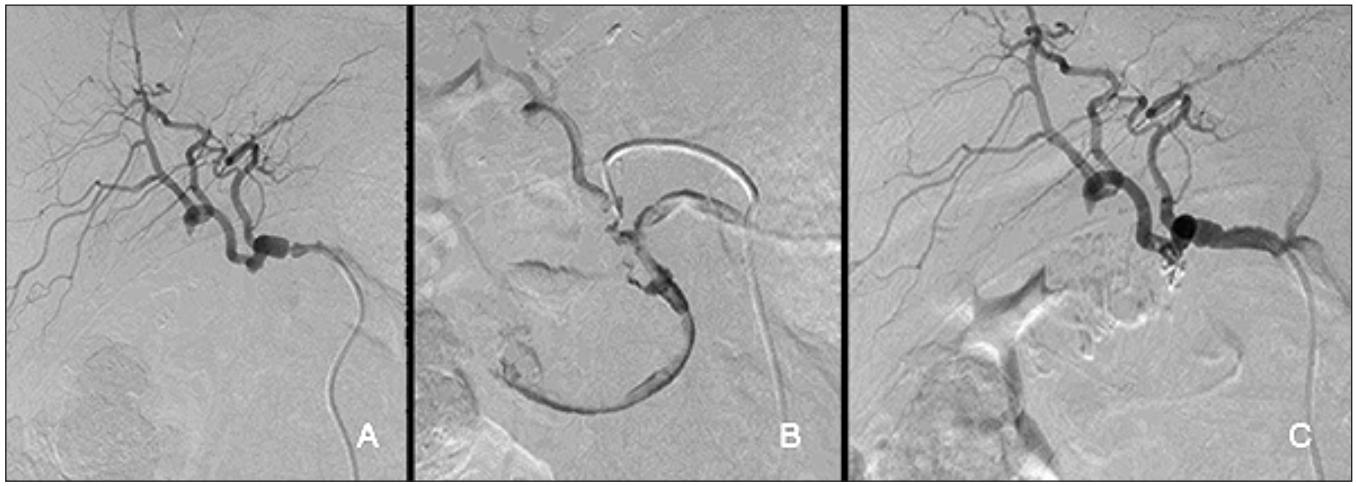

Fig. 3. Selective celiac trunk angiography: A) gastroduodenal artery occlusion; B) superselective angiography: source of bleeding is revealed; C) after coil embolization.

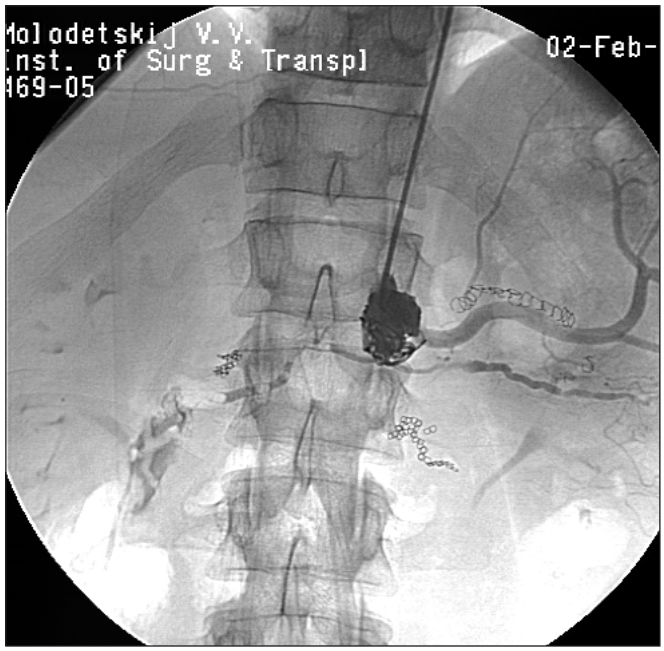

Fig. 4. Contrasting of the Wirsung duct 1 month after coil embolization of pseudoaneurism.

involving human subjects, and current regulations of the Ministry of Health of Ukraine. All patients signed an informed consent to participate in the study. The study protocol was approved by the local ethics committee.

RESULTS

In 345 (88.2%) patients, angiography was able to identify the source of bleeding. To reliable angiographic signs of the source of bleeding, we attributed the contrasting of pseudoaneurysm, a local area of extravasation, contrasting of the Wirsung duct or intestinal lumen. To the supposed signs of the source of bleeding, we attributed a local area of hypervascularization, a break in the contrast of the arterial branch, and an uneven contour of the artery trunk. In 46 (11.8%) patients with an angiographically unclear source of bleeding, the target arterial site was determined based on the location and characteristics of the surgical intervention. Embolization in the case of an unidentified source of bleeding,

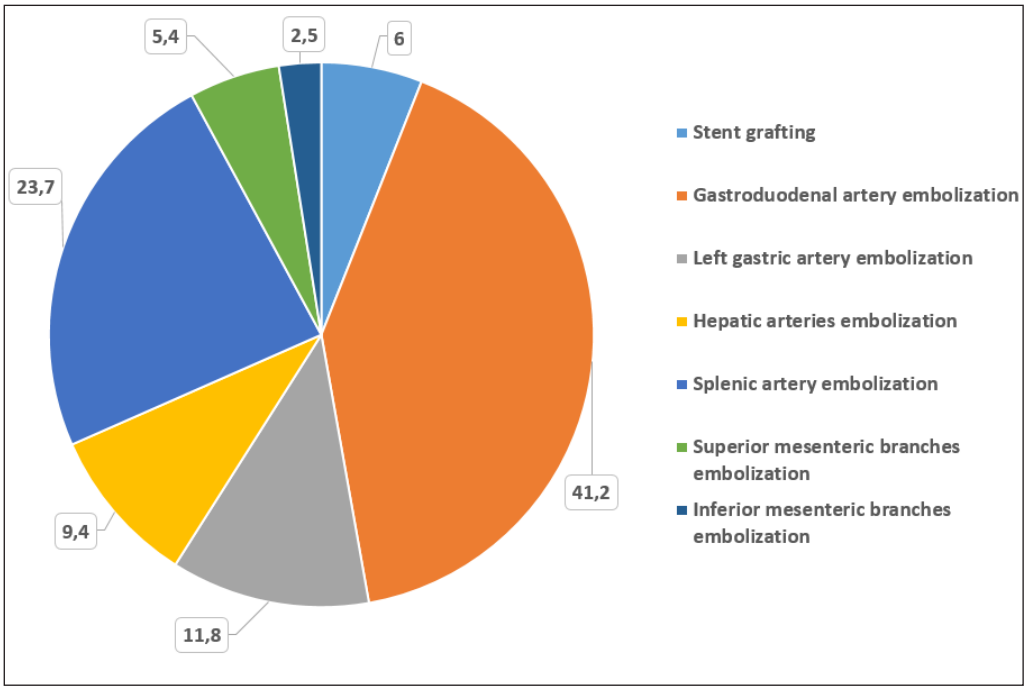

Fig. 5. The frequency (%) of different endovascular intervention types (N=447).

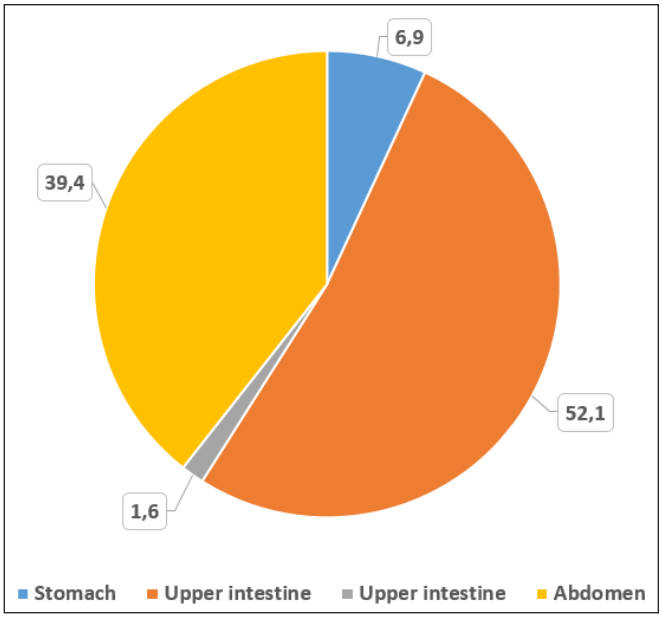

Fig. 6. The frequency (%) of the endovascular interventions according to the bleeding site (N=447).

we defined as prophylactic, since there wasn't active bleeding at the time of intervention. Plain angiography revealed occlusion of the gastroduodenal artery in 3 cases, and super-selective placement of a catheter into it revealed reliable signs of a bleeding source (Figure 3).

A total of 447 endovascular hemostatic interventions were performed in 391 patients. A stent graft was installed in 27 patients, 420 embolization were performed in 364 patients Thus, 43 (11.0%) patients were embolized repeatedly, in 12 cases - three times, in 1 case - 4 times. Among repeated cases, additional embolization of the previously embolized arterial branch was performed in 12 cases, and embolization of other arterial branches, presumably being additional sources of bleeding, was performed in 44 cases. Embolization was performed 4 times in a patient with virsungorrhagia as a result of a stab wound to the abdominal cavity and numerous operations on the intestines. In this case, a pseudoaneurysm of the splenic artery was found in the splenic artery near the bifurcation zone of the celiac trunk; therefore, the installation of a stent graft was impossible, and embolization of the pseudoaneurysm cavity with coils gave a short-term effect due to the lysis of the thrombus by the active contents of the Wirsung duct (Figure 4). Nevertheless, such a multi-stage intervention allowed us to gain time to stabilize the patient's condition and achieve healing of a purulent wound on the anterior abdominal wall and subsequently, 4 months after the first embolization, to perform a successful open operation.

The data on the performed interventions are presented in Table II and Figures 5-6.

The embolized branches of the superior mesenteric artery included the arcade branches of the small intestine, as well as the inferior pancreaticoduodenal artery, the embolization of which we supplemented the embolization of the gastroduodenal artery in case of impossibility of placing a coil distal to the injury site.

In 166 (37.1%) patients after embolization, there was several pain lasting up to 12 hours, which required the administration of narcotic analgesics. In the case of proximal embolization of the splenic artery trunk, in 28 cases, zones of splenic infarction were noted that did not require surgical intervention. Necrosis of other tissues and parts of the intestine was not detected.

In 16 cases (15 cases of prophylactic embolization), endovascular hemostasis was ineffective and required subsequent surgical intervention. Immediate mortality within 3 days after embolization was 2.7% (12 cases), in all cases due to progressive renal and hepatic failure.

DISCUSSION

Angiography reliably detects the source of gastrointestinal bleeding in 60-73% of cases, reaching 100% in the case of active bleeding [6], computed tomography in a similar situation, according to the literature, provides 79-96% of the bleeding source detection [7, 8]. In our study, computed tomography revealed the source of 67.7% of bleeding, by selective and super-selective angiography - 88.2%. Obviously, this is due to the high resolution of modern angiographic devices in combination with subtraction, the ability to track blood flow in dynamics, to provide enhanced flow in the area under study, which is a kind of provocative test.

An important technical factor is the type of embolization, however, the problem of choosing the optimal embolizing material remains debatable [9]. In addition, in the choice of materials, their availability matters. So we did not use adhesive mixtures due to the absence on the territory of our state.

Spleen infarction is considered a post-embolization complication only if it takes more than 25% of the spleen volume or an abscess occurs [10]. In our study, splenic infarcts after splenic artery embolization occurred in 28 (26.4% of 106 splenic artery embolizations) cases, none of them didn't exceed 15% of the spleen volume, and there were no purulent complications either. Ischemia and necrosis of the intestine are a rare complications of embolization, but the probability of its occurrence increases significantly after the use of distal embolization with liquid embolizates or small particles, as well as after previous surgical interventions that have damaged the collateral circulation in this zone [11, 12]. For embolization of intestinal branches, we used exclusively coils, never having significant ischemic complications.

Prophylactic embolization is an effective technique for preventing bleeding in situations of increased risk of their occurrence - ulcers, arrosions, and injuries, including iatrogenic ones [13], however, the probability of rebleeding in the case of prophylactic embolization is higher than in the case of a detected source of bleeding [14]. Our study confirms these data - the probability of rebleeding in the case of prophylactic embolization was 37% (19 rebleeds out of 46), and in the case of therapeutic embolization - 10.2% (37 rebleeds out of 364). All cases of conversion of endovascular to surgical hemostasis were associated precisely with prophylactic embolization (except for one case of splenic artery pseudoaneurysm described above).

If the trunk of the main arterial branch is the source of bleeding, the most effective endovascular option is a stent graft placement. This makes it possible to eliminate the source of bleeding along with maintaining the patency of the artery. However, this technique has certain limitations: the section of the artery must be relatively straight and not have significant side branches, in addition, the patient should not have antiplatelet therapy contraindications. This makes it possible to install a stent graft in 30% of the required cases. In our study, the stent graft placement was performed only in case of damage to the trunk of the superior mesenteric artery and the main hepatic arterial branches; in all other cases, embolization was preferred as a less costly and complex technique.

CONCLUSIONS

Endovascular interventions are an effective method for diagnosing and treating postoperative abdominal and gastrointestinal bleeding in patients with chronic diseases and due to military injuries due to their minimal invasiveness, repeatability, high diagnostic capabilities, and compatibility with any other treatment methods. Prophylactic embolization helps to prevent the recurrence of postoperative bleeding with an instrumentally undiagnosable source, however, one must be prepared for the multi-staging of such treatment aimed at successively turning off the collateral blood supply to the damaged area.

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ORIGINAL ARTICLE

MANIFESTATIONS AND TREATMENT OF LOWER BACK PAIN SYNDROME IN WARTIME

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ABSTRACT

The aim: To improve treatment of patients with lower back pain through identification of pathogenetic factors in its formation.

Materials and methods: The early results of treatment of 84 patients with lower back pain (main group) were analysed. Patients of the main group were divided into two subgroups: one group involved patients with mental disorders, the other – patients not suffering from such disorders (the Spielberger-Hanin Anxiety Test used). The patients of the main group with mental disorders (49 patients) were administered with epidural steroid injections and antidepressants. The patients with no mental disorders (35 patients) were administered with epidural steroid injections only. The control group involved 36 patients with lower back pain who did not undergo any psychological testing and were administered with epidural steroid injections only. The Visual Analog Scale (VAS) and the Oswestry Disability Index questionnaire were used to assess pain syndrome. The assessment was carried out twice: in the pre-operative period and in three months after the treatment.

Results: A significant difference in the early treatment results between the main and control groups was established according to both the Visual Analog Scale and the Oswestry Disability Index in favour of the main group patients, who were differentiated by pathogenetic factors of the pain syndrome formation.

Conclusions: Lower back pain syndrome necessitates clarification of its components in order to develop pathogenically based treatment.

KEY WORDS: lower back pain, degenerative-dystrophic spinal cord damage, epidural steroid injections, antidepressants

Wiad Lek. 2023;76(5 p.2):1185-1190

INTRODUCTION

A high frequency of lower back pain syndrome and unsatisfactory results of its treatment makes research on the treatment of this pain syndrome an urgent matter, especially for various factors in the genesis. There are several factors for development of this complex syndrome. Most often it is a degenerative-dystrophic spine damage and mental disorders, such as depression; moreover, in the most diverse their combinations. Degenerative-dystrophic diseases of the spine are among the most widespread disorders in present society. Lower back pain is the main cause of disability in the world [1]. Mechanisms and sources of pain in spinal osteochondrosis are irritation of pain receptors, compression of nerve roots and nerve endings, swelling of nerve endings and disc, chemical inflammatory factor. The main mechanisms forming this pathological process are autoimmune diseases, inflammation, connective tissue disorders, compression and ischemia. They are correlated and constitute a vicious circle in the persistence of pain syndrome in cases of spinal osteochondrosis with swelling of the nerve ending or root as a chief pathogenetic factor [2].

Pain is a kind of psychophysiological state that is accompanied not only by organic and functional disorders in the body, but also leads to psycho-emotional changes. The psychological and emotional effects of pain often influence patient's subjective reaction, exaggerating or downplaying the significance of pain. The doctor often has to deal with psycho-emotional manifestations of the pain syndrome, which form the so-called pain behaviour. Psychological state can also significantly affect the perception of pain. Depression and anxiety are associated with increased pain in pain syndrome and can cause more intense pain. Anxiety associated with the expectation of pain has a negative impact on the functional state of patients and increases pain sensations [3]. Mental disorders manifested by depression and anxiety is typical for some patients with chronic back pain. They affect the severity, emotional colouring of the pain syndrome and confirm the importance of psychogenic factors in the pathogenesis of pain.

Taking into account the psycho-emotional characteristics of pain perception would contribute to optimization of treatment and rehabilitation of patients with

chronic back pain. Thus, studying the psycho-emotional aspects of back pain syndrome is an urgent matter. After all, these days, investigation of the peculiar features of personality in the conditions of various somatic changes has become more crucial due to hostilities on the territory of our country taking into account psychological and social aspects of health, ways of its preservation and improvement. Biological factors can initiate, maintain, and modulate physical disorders, while psychological changes affect evaluation and perception of internal physiological signals. Sequentially, psychological factors affect biological ones changing production of hormones, neurotransmitters, state of the autonomic nervous system, and biochemical processes in the brain [4]. The prevalence and association of depressive symptoms in patients with chronic lower back pain have been studied in various countries, particularly in China. It involved 1172 patients with chronic lower back pain. The prevalence of depressive symptoms was 25.00% with more severe pain and its longer duration being associated with a higher risk of depressive symptoms [5].

Despite the variety of neurological manifestations of degenerative spine damage, pain syndrome is a chief clinical manifestation. Lower back pain with consistent clinical manifestations is characterized by polymorphism of pathogenetic situations, chronic recurrent course, resistance to treatment. Since often only one of the factors of this pain syndrome is taken into account or the importance of one or the other is exaggerated, it is really important to differentiate the pathogenetic factors in the genesis of lower back pain syndrome. the treatment of degenerative spine damage can have optimal results only with adequate choice of treatment methods for each patient specifically taking into account the stage and clinical manifestations of the disease, anatomical features, their neurological and psycho-emotional state. However, to date, various specialists do not have a single approach to the treatment of lower back pain syndrome. The studies showed variable results regarding the effectiveness of epidural steroid injections for treatment of pain syndrome caused by degenerative-dystrophic spine damage [6-11]. Ambiguous results were presented regarding the use of antidepressants as well [12, 13].

After some time since the beginning of hostilities, the unusual complaints of patients, who referred to the institution with lower back pain, draw our attention that was the direct impetus for the research. This study covers a multifactorial approach to treatment and rehabilitation of patients with lower back pain syndrome caused by degenerative diseases of the spine accompanied by mental disorders, such as anxiety and depression. In order to develop adequate approaches to treatment of this syndrome, clear pathogenetic factors in the formation of lower back pain should be defined.

THE AIM

The aim of the study is to improve the effectiveness of treatment of lower back pain syndrome by identifying the factors of pain syndrome and the mechanisms of its formation and, subsequently, by pathogenetically justified treatment.

MATERIALS AND METHODS

The early results of treatment of 84 patients aged 36 to 83 years (main group) with lower back pain caused by degenerative-dystrophic spine damage were analysed (all the patients underwent MRI of the lumbar spine that confirmed structural and morphological changes). The patients were included in the study during the period from May to September 2022. Taking into account that at present people in Ukraine live in wartime that is with chronic stress, all patients of the main group underwent psychological testing (the Spielberger-Hanin Anxiety Test) before treatment. According to the test results, the patients of the main group were divided into two subgroups: one group involved patients with mental disorders (subgroup A), the other – patients not suffering from such disorders (subgroup B). The patients of the main group with mental disorders, subgroup A (49 patients), were administered with epidural steroid injections (1-2 times with a 2-week interval) and antidepressants (for 2-3 months). The patients of the main group not suffering from such disorders, subgroup B (35 patients), were administered with epidural steroid injections only (1-2 times with a 2-week interval). The control group involved 36 patients aged 40 to 79 years with lower back pain (all the patients of this group also underwent MRI for lumbar spine that confirmed structural and morphological changes), who did not undergo psychological testing and epidural steroid injections only (1-2 times with a 2-week interval) were used for treatment. The groups were comparable in terms of age, sex, structural and morphological changes in the lumbar spine. The Visual Analog Scale (VAS) and the Oswestry Disability Index questionnaire were used to assess the pain syndrome. The assessment was carried out twice: in the pre-operative period and in three months after treatment. The philosophy of our study was to study the impact of psycho-emotional factors on lower back pain syndrome caused by degenerative-dystrophic spine damage that is an urgent issue especially in wartime nowadays.

Table I. Evaluation of the average indicators (according to the VAS) of pain syndrome in the patients of the main and control groups

Groups of patients	Before treatment	In 3 months
Main subgroup A	7.12±0.14 (n=49)	3.32±0.12* (n=42)
Main subgroup B	8.11±0.13 (n=35)	3.52±0.11* (n=31)
Control	7.61±0.21 (n=36)	5.11±0.18 (n=30)

Note: *p<0.05, significant difference in early treatment outcomes between the main (subgroup A and subgroup B) and control groups according to the Visual Analog Scale.

Table II. Evaluation of functional state of patients (according to the Oswestry Disability Index) in the main and control groups (in points)

Groups of patients	Before treatment	In 3 months
Main subgroup A	48±0.6 (n=49)	29±0.4* (n=42)
Main subgroup B	51±0.5 (n=35)	31±0.4* (n=31)
Control	47±0.4 (n=36)	40±0.3 (n=30)

Note: *p<0.05, significant difference in early treatment outcomes between the main (subgroup A and subgroup B) and control groups according to the Oswestry Disability Index.

The study was conducted in accordance with the principles of the Council of Europe Convention on Human Rights and Biomedicine, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current regulations of the Ministry of Health of Ukraine. The study protocol was approved by the local ethics committee. All patients signed an informed consent to participate in the study.

The Student's t-test was used to assess the statistical difference between the comparison groups. The results were presented in the form of arithmetic mean (M) and standard deviation (SD). A difference of $p<0.05$ was statistically significant. Statistical analysis was performed on a personal computer by means of Microsoft Excel 2000 programs, Windows 98 operating system.

RESULTS

The patients of the main group having high indicators of personal and reactive anxiety were involved into subgroup A. In this subgroup, reactive anxiety rate was 49.12±1.34 points, personal – 45.24±1.57 points, which significantly ($p<0.05$) differed from the indicators in practically healthy individuals. Reactive anxiety rate of the patients of subgroup B was 34.64±1.32 points and personal anxiety – 39.27±1.8, which corresponded to the indicators of practically healthy individuals. The indicators of reactive anxiety in the patients in subgroups A and B differed significantly ($p<0.05$). The indicators of personal anxiety showed a significant ($p<0.05$) difference between subgroups A and B.

Thus, two subgroups of patients with chronic lower back pain syndrome were distinguished according to the rates of personal and reactive anxiety, which allowed applying a differentiated approach to the treatment of such patients. In one case, epidural steroid injections only were used (subgroup B), and in the other, such injections were combined with antidepressants (subgroup A). In the control group, this psycho-emotional factor was not taken into account (testing on this issue was not conducted), therefore only epidural steroid injections were used for treatment (similar to the subgroup B with no mental disorders revealed).

The assessment of the average indicators of pain syndrome and functional state of patients in the main and control groups are presented in Tables I and II, respectively.

As seen from Tables I and II, there was a clear significant difference in early treatment outcomes between the main and control groups according to both the Oswestry Disability Index and the Visual Analog Scale in favour of differentiated treatment. Analysis of the results showed significantly higher treatment results in the groups of patients with psycho-emotional factors revealed, while in the control group (no such factors revealed) significantly lower results were attained. So, in the early period, a significant result of treatment of chronic lower lumbar pain syndrome was obtained only in the main group (with differentiation of pathogenetic factors of pain syndrome carried out), while in the control group (where component pain syndromes were not identified) there was no significant improvement. The results of the study prove high efficacy of the therapy with epidural steroid injection and antidepressants in the patients with lower back pain syndrome caused by degenerative spine damage combined with mental disorders. In the case of degenerative-dystrophic spine damage and no mental disorders, high efficacy is obtained by the monotherapy for lumbar pain with epidural steroid injections. Epidural steroid injections are indicated for all structural and morphological causes of chronic pain syndrome.

DISCUSSION

The association between depression and lower back pain has been studied a lot; various psycho-social aspects and even different scales and techniques for self-assessment according to depression scales have been also discussed [14]. These studies have noted that a significant share of adults with lower back pain suffer from depressive symptoms [15]. Screening, early revealing and treatment of depression are important to reduce pain and disability associated with lower back pain [16]. Rehabilitation programs, which take into account the symptoms of depression, can improve treatment outcomes for patients with lower back pain without specifying the rehabilitation type or reducing it to rehabilitation only. [17]. A number of authors note the significance of patients' acceptance of pain; such acceptance means participation in the activity, which causes pain and doing it without resisting the pain or trying to reduce it. Accepting the pain really helps because it allows people doing what they want rather than fighting the pain. Treatment focused on increasing acceptance is very effective for chronic pain [18,19].

The association of chronic lower back pain caused specifically by lumbar disc degeneration or herniation with depression and anxiety has been poorly studied. Thus, inflammatory biomarkers were studied, which were usually evidenced in cases of herniated disc. Early revealing and combined treatment of depressive symptoms would benefit patients with high inflammatory biomarkers due to intervertebral disc degeneration [20].

Conflicting data is provided regarding antidepressants for lower back pain. Giovanni E Ferreira et al. investigated efficacy and safety of antidepressants for treatment of back pain compared with placebo. A systematic review and meta-analysis of 33 studies was conducted. The evidence of moderate-certainty showed that serotonin-norepinephrine reuptake inhibitors reduced back pain [12]. The authors of another systematic review of ten randomized placebo-controlled trials showed that there was no clear evidence to support the use of antidepressants for treatment of lower back pain. The authors emphasize the need for further studies to confirm the effect of antidepressants on chronic lower back pain. [13]. Hence, the effect of antidepressants on lower back pain was studied in comparison with placebo without taking into account the factor of structural and morphological damage to the spine. Without taking into consideration this important factor it is not correct to talk about the efficacy of antidepressants for lower back pain.

Thus, the significance of depression and anxiety in the influence of their interdependence on the development and management of lower back pain has been established. However, the is no literature on the association between two factors in lower back pain: degenerative-dystrophic spine damage and mental disorders, especially in cases of chronic stress. This research was focused on the impact of both pathogenetic factors: pathomorphological and psycho-emotional, in the patients with lower back pain and suggested a differentiated approach to treatment according to these factors.

CONCLUSIONS

The study results may improve the knowledge of the complexity of lower back pain perception and its treatment. The study showed the high effectiveness of a differentiated approach to the treatment of lower back pain, which takes into account the factor of structural and morphological damage of the spine as well as mental disorders combined or autonomously manifested. In case of structural and morphological changes, epidural steroid injections only as monotherapy was used. In cases of combination of structural and morphological changes and mental disorders, combined treatment with epidural steroid injections and antidepressants was used.

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ORIGINAL ARTICLE

PROSPECTS OF THE HIGH-SPEED MULTIMEDIA DATA TRANSMISSION TECHNOLOGIES USE IN THE STRUCTURE OF THE SYSTEM FOR PROVIDING AID TO INJURED PERSONS HAVING A GUNSHOT DEFECT OF SOFT TISSUES

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ABSTRACT

The aim: To improve the results of providing medical care in the conditions of a full-scale war in Ukraine due to the use of medical technologies

Materials and methods: From the first days, the Military Medical Clinical Center of the Southern Region provided medical assistance to the persons wounded as a result of the Russian Federation's armed aggression. The presented multidisciplinary observation includes data received from 24.02.22 to 26.05.22. During this term, the multidisciplinary team assisted by the Teladoc Health system (the connection between the Charite Clinic, Berlin, and the MMCC of the Southern Region, Ukraine) performed 39 reconstructive and remedial operations in the MMCC of the Southern Region (Department of Surgical Infection).

Results: It has been found that the implementation of differentiated surgical tactics (developed in cooperation between Charite clinics, Berlin, and MMCC of the Southern Region, Ukraine, using the Teladoc health system) in wounded patients with gunshot defects of soft tissues at the III and IV levels of medical care improves functional results, increases indicators of satisfactory from 46.9 % to 53.7 %, reducing the relative number of unsatisfactory from 18.8 % to 11.6 %.

Conclusions: The information exchange in the Teladoc Health system is performed in telephone mode through protected communication channels. It enabled real-time treatment strategy recommendations and improved functional outcomes, increasing the satisfactory rate from 46.9 % to 53.7 %, and reducing the relative unsatisfactory rate from 18.8 % to 11.6 %.

KEY WORDS: telemedicine, teladoc health system, multimodal algorithm, gunshot wound, multidisciplinary observation

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INTRODUCTION

Nowadays, electronic communications are part of the daily life of the majority of people around the world. They include text messages between loved ones, communication in social networks, photo, and video materials transfer, and numerous multimedia channels allowing to receive and transfer information at lightning speed. The electronic communication technologies expansion in the field of medicine has transformed into what is now known as telemedicine [1, 2].

Long-distance communication between people originated as signaling by burning bonfires, waving colorful flags, etc. The continuous technology improvement process ensured the creation of devices that allowed information transmission over much greater distances. The telegraph was invented in the early 1800 by Samuel Morse, who developed the famous code that is called by his name. It was the first time when international and transatlantic communication became available almost instantly. Telegraphs were used to transmit casualty lists and requests for medical supplies during the war. This can be considered the beginning of telemedicine, as the telegraph may have been used for medical consultations.

In 1876, Alexander Graham Bell patented the first telephone. As telephone technology improved, people's ability to communicate with each other increased dramatically [1].

Table I. The injuries according to anatomical areas

Anatomical structure	Number of injured (with defined anatomical structure)	The injury of anatomical structures and systems	Combined injuries
Head	2	Penetrating - 2	Eyes injuries – none
		Non-penetrating - none	Jaws injury - none
Neck	1	With vascular damage - 1	Spine - none
		With trachea damage - none	Esophagus - none
Chest	4	With rib cage injury - 3	With lung, heart injury - none
		Hemopneumothorax - 3	With diaphragm injury - none
Abdomen	2	Liver -1 , Spleen - none	Colon - 7
		Small intestine - 1, stomach - 1	Kidneys - 1, ureters - 3
		Gallbladder - none, rectum - 2	Bladder - 2
Limbs	Upper – 10 Lower – 20	Soft tissues - 30	Fiery hip fracture - none
		With vascular damage - 4	Fiery tibia fracture - 3
		With nerves damage - 5	Fiery joint disorder - 4
		Fiery forearm fracture - 8	Fiery shoulder fracture - 7
		Fiery hand fracture - 8	Fiery foot fracture - 7

The invention of television can be considered a turning point in the field of telemedicine. Television, which was invented in 1927 by Philo Taylor Farnsworth, provided a visual image with real-time sound.

The sources dating back to 1905 are indicating the transmission of electrocardiograms over long distances by a Dutch doctor named Willem Einthoven. In France from 1920–1940, radio consultations were carried out to patients on ships at sea. Thus, the doctors in the United States carried out the X-ray images' transmission [2].

Telemedicine development has accelerated during the last decade due to rapid technological progress. The possibilities of telemedicine are growing rapidly, which makes the challenge of its technologies' integration into the health care system and new telemedicine programs development.

THE AIM

The aim was to increase the efficiency of diagnostics and treatment of wounded with gunshot defects of covering tissues by implementing the Teladoc health telecommunication system at various stages of providing medical care in conditions of military conflict.

MATERIALS AND METHODS

A clinical examination was carried out with the help of a multidisciplinary team through the Teladoc health system (Figure 1) and a surgical (reconstructive-restorative) one after the agreement of both parties. In the course of diagnostics, multimodal screening was used, which specialists of the Charité Berlin clinic and the military-medical clinical center of the Southern region used to objectify the gunshot transformation of damaged anatomical structures.

With the help of multimodal dynamic screening, 39 wounded people aged 23 to 58 were treated at the second, third and fourth levels of medical care. All the injured were male with gunshot defects of covering fabrics.

An additional component of the examination, in addition to preoperative, intraoperative and postoperative control, was a multimodal monitoring system, which consisted of the use of dynamic digital thermography and audio doppler (at the second level of medical care) and sonographic monitoring by an expert class system at the third and fourth levels of medical care. The multidisciplinary team consisted of the following specialists: reconstructive - plastic surgeon, traumatologist, vascular surgeon in case of damage to main vessels, abdominal surgeon in case of damage to the abdominal cavity, thoracic surgeon in case of damage to the chest and neurosurgeon in case of damage to the head and spinal cord. In the pre-operative period, after admission to the structural unit, a conference was held with the Charite clinic (Berlin), where additional examination options were established, if necessary, and a plan for reconstructive and plastic restoration of the damaged anatomical area. The second stage of using the Teladoc health system was postoperative monitoring in the dressing room every 3 days. Factors of objectification were indicators of digital thermography of the affected anatomical structure (comparative analysis with a symmetrical undamaged structure) and

Fig. 1. Teladoc health system.

sonographic monitoring of perforating vessels at the base of the flaps that "closed" gunshot defects.

Special attention was paid to the preparation of the wound defect, which consisted of: debridement, pulse lavage, ultrasonic cavitation of the wound surface and the use of controlled negative pressure systems. Indicators of readiness of the wound for closure were the main factors: stabilization of the general condition of the wounded and vital functions, restoration of general blood analysis norms, absence of inflammatory phenomena (stable leukocyte formula and stable indicators of biochemical blood analysis), the norm in the proteinogram and the indicator of total protein. Additional factors were: 4 K (according to NATO standards), a temperature indicator from the wound surface of 31.5 °C, an increase in the speed and volume of blood flow in the affected area by 20% compared to the indicators upon admission to the hospital (Figure 2).

Statistical processing of research results was performed on a PC using Microsoft Excel software package.

RESULTS

From the first days, the MMCC of the Southern Region provided medical assistance to the persons wounded as a result of the Russian Federation's armed aggression. Taking into account the human dignity of this terrible problem in Ukraine, the international Charite clinic (Berlin, Germany) after preliminary agreements created a Telemedicine project for cooperation in providing medical care to persons injured with soft tissue defects. The presented multidisciplinary observation includes data received from 24.02.22 to 26.05.22. (Table I)

The total number of wounded – 227. During this term, the multidisciplinary team assisted by the Teladoc Health system (the connection between the Charite Clinic, Berlin, and the MMCC of the Southern Region, Ukraine) performed 39 reconstructive and remedial operations in the Military Medical Clinical Center of the Southern Region (Department of Surgical Infection). Of which gunshot defects of the soft tissues of the limbs were observed in 30 patients (76.9 %), the head and spine — 2 (5.1 %), the chest — 4 (10.35 %), the abdomen — 2 (5.1 %) and the pelvis — 1 (2.55 %) (Figure 3).

Those wounded persons who received damage to various anatomical structures of the human body in the form of soft tissue defects: chest, abdomen, pelvis, and limbs were selected for observation. The average age was 33.7 ± 4.1 years. The vast majority of the treated wounded persons received shrapnel wounds — 31 (79.5 %), bullet wounds — 5 (12.8 %), and explosive wounds — 3 (7.7 %) (Figure 4).

Fig. 2. Thermographic monitoring of the wound surface of the forearm (working distance 50 cm) (A); thermographic monitoring indicator (thermographic camera) (B); Doppler audio monitoring of the perforating vessel after flap rotation by 180 degrees (C).

The isolated combat surgical injury was observed in (55.5 %), multiple in (23.2 %), and a combined 30 (21.3 %) (Figure 5)

The torso – 34 (25.0 %), hips – 30 (22.4 %), lower legs – 24 (17.9 %), shoulder – 17 (13.0 %), forearm – 12 (8.5 %), hands – 10 (6.7 %) and feet – 9 (6.5 %) were the dominant injuries (Figure 6).

According to the characteristics, 93 (67.8 %) cases of wounds were blind, through-and-through were observed in 34 (25.3 %) and 9 (6.9 %) were tangential (Figure 7).

In order to determine the main metric characteristics of the wounds, the length (the greatest distance between the ends of the wound), the width (the greatest perpendicular to l segment h), and the depth (the greatest perpendicular from the plane to the bottom of the wound d) were measured. The wound's area (S) in square centimeters was determined by the formula: $S = l \times h / 2$, where l is the length of the wound, and h is the width of the wound. When conducting planimetric studies of the wound defect, in addition to the total area of the wound, the volume of the wound defect was determined in cubic centimeters using the formula: $V = l \times h / 2 \times d / 4$, where h is the width of the wound, d is the depth of the wound. The definition of differentiated surgical tactics for closing soft tissue defects was carried out on the basis of the gunshot wounds metric classification developed at the Ukrainian Military Medical Academy [5,9]. The needs for fast and dynamic screening were based on a multimodal algorithm: a

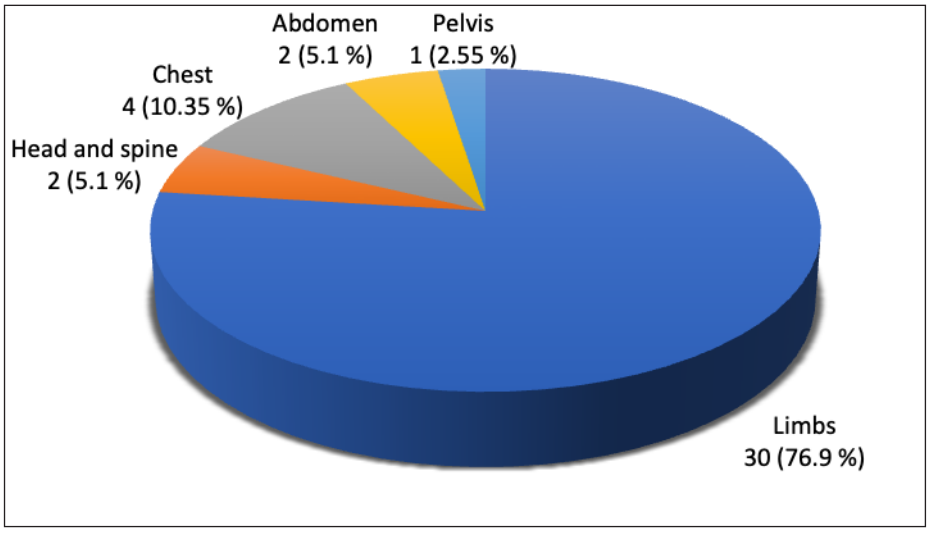

Fig. 3. Injuries distribution according to anatomical localization

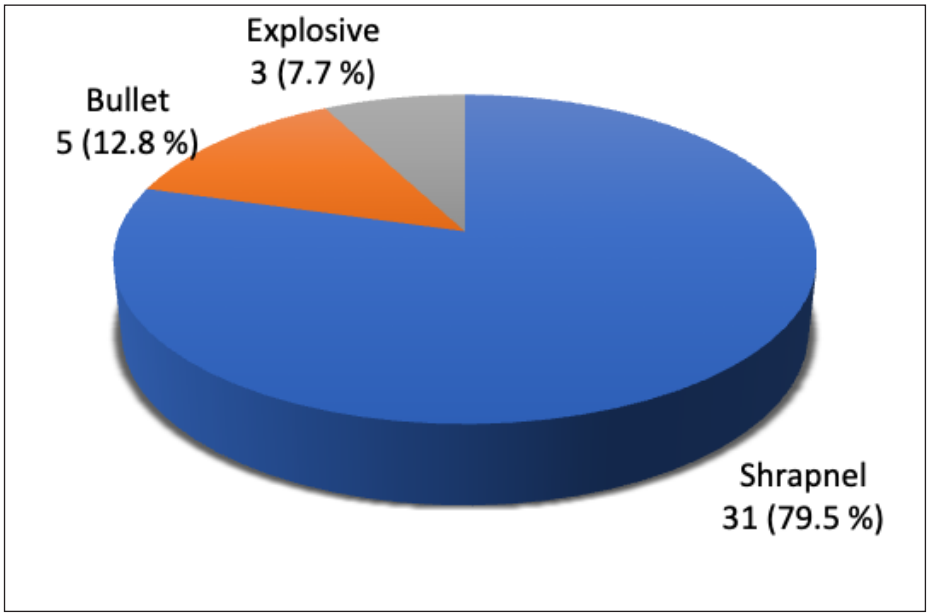

Fig. 4. Injuries distribution according to the damaging factor nature

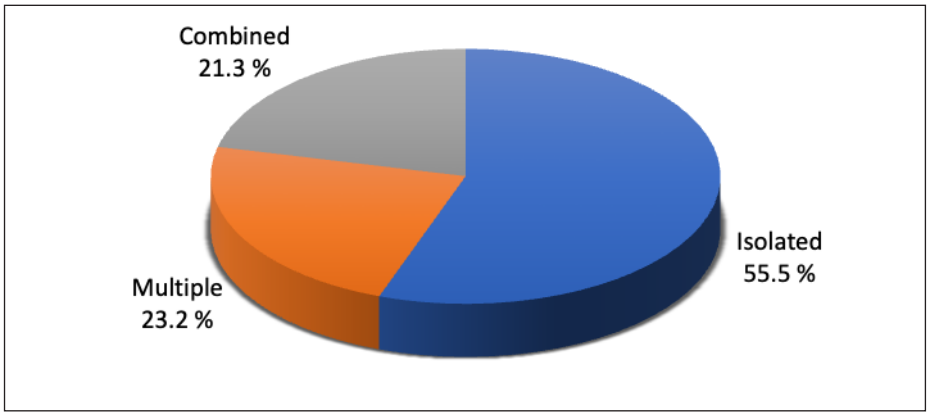

Fig. 5. Injuries distribution according to the number of injuring shells and damaged anatomical areas

combination of dynamic digital thermography and audio doppler.

The data analysis received from the dynamic thermography and audio doppler made it possible to change the tactics of primary or secondary surgical treatment in the MMCC of the Southern Region conditions: the volume of necrotic tissue excision was decreased, and the time for surgical intervention was shortened.

In the absence of signs of inflammation, primary or delayed sutures were applied to the wounded patients referred from the II and III levels. However, primary sutures were not applied and no plastic surgery was performed for wounded patients with clinical signs of wound infection after primary surgical treatment. For

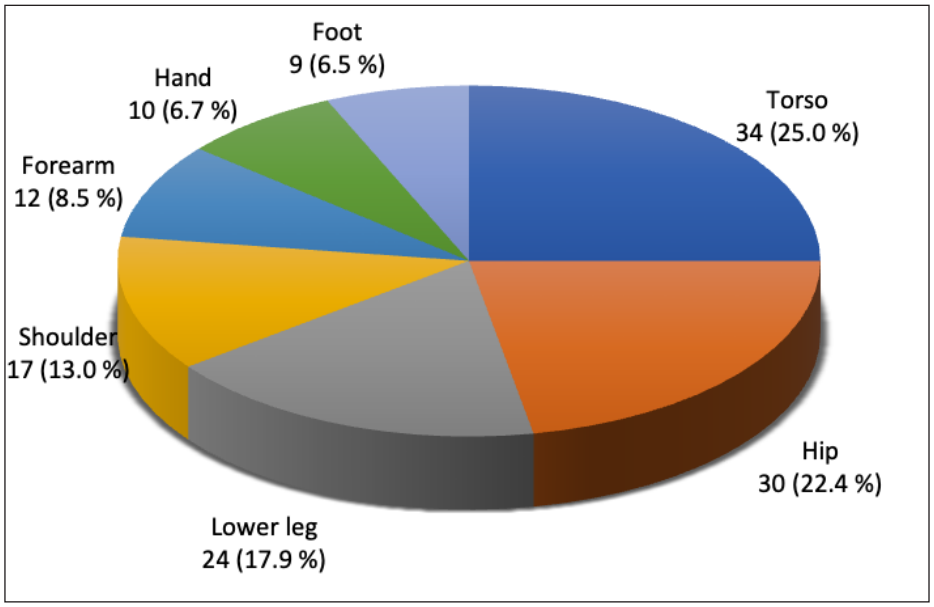

Fig. 6. Isolated injuries distribution according to anatomical localization

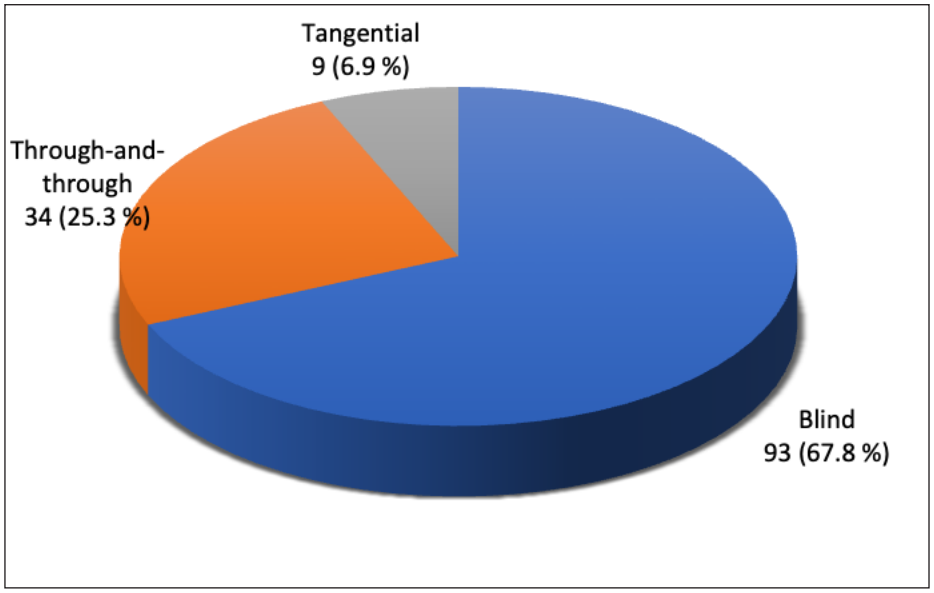

Fig. 7. Injuries distribution according to the wound channel nature

tissue defects, secondary tension was applied under the bandage before applying secondary sutures at the III and IV levels.

The autodermoplasty with a split-skin graft was the optimal method for closing medium-sized surface defects having a shortage of donor resources. The advantages of the method: instantaneous closure, low level of trauma, and technical simplicity.

Plastic surgery by local tissues was used for wounded patients with deep defects of small areas, and the edge mobility was ensured by sufficient mobilization and the use of hypodermis and muscles. The duration of treatment was significantly reduced when using NPWT systems and ultrasonic cavitation. The wounded patients with large soft tissue defects were evacuated to the III and IV levels. Plastic surgery with full-layer local flaps was used to close wounds, which provided better functional results, but had a higher risk of complications, in particular. Excessive soft tissue defects require highly specialized treatment at the IV level [9].

DISCUSSION

Telemedicine provides a unique opportunity to solve many problems faced by doctors, medical administrators, and patients. It has been found that about 74% of patients would prefer online consultations to a personal visit to a doctor [1,4]. In addition, reducing the number of visits to the doctor provides significant financial benefits and time savings. [2,3].

The provision of specialized assistance to patients in remote rural communities remains one of the most important areas of telemedicine use. Such patients often have to travel long distances and may face long waiting times for appointments. Telemedicine increases access to healthcare, resulting in fewer missed appointments and better patient observation.

Telemedicine, as a new direction in the patient's treatment, has its problems and difficulties. The creation of the infrastructure necessary for telemedicine programs involves personnel training in Internet technologies, uninterrupted access to the Internet, and the medical service providers' wide integration into a single telecommunications system [5,6].

Given the rapid and unpredictable nature of hostilities during the armed conflict with the Russian Federation, surgeons often encounter severe soft tissue defects of gunshot origin that require a multidisciplinary approach (with the involvement of several specialists: abdominal surgeon, thoracic surgeon, traumatologist, vascular surgeon). Therefore, the question of considering timely specialized medical care and staffing the initial levels of medical care by specialists with a narrow specialization, or the implementation of other options, becomes relevant [7].

In our opinion, Telemedicine use during the medical assistance provision to a person wounded with gunshot defects of soft tissues can be an alternative option for a multidisciplinary team at all levels of medical assistance provision in the military and medical forces of the Armed Forces of Ukraine.

In cases where agreements have been made with leading institutions in other countries, telemedicine not only enables the provision of world-class medical assistance to those injured with GDST, but also allows for complex situations to be handled under the guidance of the most experienced doctors [7-9].

During the work with the wounded persons assisted by the Teladoc Health system, a conference was held between the Charite clinic, Berlin, and the MMCC of the Southern region. The implementation of the multimodal screening scheme and the analysis of its indicators were coordinated, thorough preoperative preparation was carried out, and optimal ways of reconstruction and monitoring in the postoperative period were discussed. During the analysis of the condition of the wounded person and the wound of the damaged anatomical area, the following specialists were additionally involved: the department of plastic surgery, the department of traumatology, the department of anesthesiology and resuscitation, which reflected the multidisciplinary approach of the created project.

According to the developed metric classification of soft tissue defects, small gunshot wounds were observed in 7 (18 %), medium in 21 (54 %), large in 9 (23.9 %), and extra-large in 2 (4.1 %) cases. The structure of explosive injuries was significantly different from shrapnel and bullet injuries due to an increase in the area and volume of limb damage, the predominance of large and very large soft tissue defects (χ 2 $p < 0.001$, respectively) was observed. There was no significant difference between the structure of shrapnel and bullet wounds (χ 2 = 4.13; $p = 0.248$). The mentioned above results made it possible to distinguish surgical, triage, and evacuation principles at the medical care levels depending on the place of injury, taking into account metric characteristics. The combination of wound defects' metric characteristics by area and volume with the wounds' localization in one classification made it possible to propose a comprehensive approach to sorting the wounded according to the medical care level and determining further surgical tactics for closing soft tissue defects [9].

It has been found that the implementation of differentiated surgical tactics (developed in cooperation between Charite clinics, Berlin, and MMCC of the Southern Region, Ukraine, using the Teladoc health system) in wounded patients with gunshot defects of soft tissues at the III and IV levels of medical care improves functional results, increases indicators of satisfactory from 46.9 % to 53.7 %, and reduces the relative number of unsatisfactory outcomes from 18.8% to 11.6%.

CONCLUSIONS

The cooperation project of the Charite Clinic, Berlin, and the MMCC of the So`uthern Region, Ukraine, using the Teladoc Health system, gives the possibility of communication in electronic correspondence mode using a secure information exchange system, provides the prompt exchange of current information on health status, the severity of gunshot damage and feedback with recommendations on the current volume and type of assistance at the III and IV levels of medical assistance. It adds visual information in the form of photos and videos for the local status qualitative assessment, etc.

The information exchange in the Teladoc Health system is performed in telephone mode through protected communication channels. It enabled real-time treatment strategy recommendations and improved functional outcomes, increasing the satisfactory rate from 46.9 % to 53.7 %, and reducing the relative unsatisfactory rate from 18.8 % to 11.6 %.

The two-way transmission of information with the simultaneous use of video and audio formats in the online conference has shown that the created project of using Teladoc Health can practically be an alternative to live communication. In the conditions of hostilities, it acquires new expediency and opens alternative ways of introducing high-speed data transmission technologies into the medical support system of the Armed Forces of Ukraine.

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ORIGINAL ARTICLE

GUNSHOT SHRAPNEL WOUND OF THE THIGH WITH DAMAGE TO THE SUPERFICIAL FEMORAL ARTERY (FEATURES OF CLINICAL MANIFESTATIONS, DEVELOPMENT OF COMPLICATIONS WITH LATE MEDICAL CARE AND PRESERVATION OF THE LIMB)

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ABSTRACT

The aim: To demonstrate the features of clinical manifestations and complications that occur with delayed medical treatment in cases of gunshot shrapnel through a wound of the thigh with damage to the superficial femoral artery.

Materials and methods: The wounded individual, S., was 52 years old and had sustained a gunshot wound through a shrapnel wound of the left thigh with damage to the superficial femoral artery and soft tissue defect. Medical assistance was provided during the stages of medical evacuation.

Results: The soldier sustained a gunshot wound through the upper third of the left thigh, resulting in damage to the vascular-nerve bundle and a soft tissue defect. First aid was provided at the scene, and surgical procedures were performed during the stages of medical evacuation, including primary surgical treatment of wounds in the upper third of the left thigh.

On the second day following the injury, the wounded man was transferred to the Vinnytsia Military Medical Clinical Center and admitted to the vascular surgery department. After an ultrasound examination and repeated surgical treatment of the wound on the left thigh, damage to the superficial femoral artery was identified.

Conclusions: The presence of features of blood circulation in gunshot wounds of the main vessels of the lower limbs can favorably affect the possibility of saving the limb, as evidenced by the case presented.

KEY WORDS: gunshot wound, superficial femoral artery, thrombosis, limb preservation

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INTRODUCTION

The frequency of wounds and injuries of blood vessels in modern military conflicts has increased significantly (7.5–12.0%). At the same time, despite the increase in the number of injuries to the large vessels of the chest and abdomen, the main vessels of the neck - 90% of combat vascular injuries are injuries to the arteries and veins of the extremities [1-3].

In more than 90% of cases of vessel damage, they are severe, and 8% are extremely severe. The most frequent injuries and injuries of the vessels of the femoral-popliteal segment (up to 40–50%), and vessels of the lower leg and shoulder (20–30% each) [1, 4].

In the case of gunshot wounds of arteries, there is often simultaneous damage to veins (40–50% of cases), nerve trunks (30–70%), and bone fractures (40–60%) [3, 5].

Vascular injury is associated with a high risk of critical ischemia, limb amputation, and high mortality [6-8]. The ongoing war is associated with the frequent use of rocket launchers and other high-energy weapons, causing significant damage to soft tissues and internal

Fig. 1. Wounded S, 52 years old. The second day after a gunshot wound to the left hip with damage to the superficial femoral artery. The appearance of the postoperative wound with the existing label before the repeated surgical treatment of the wound.

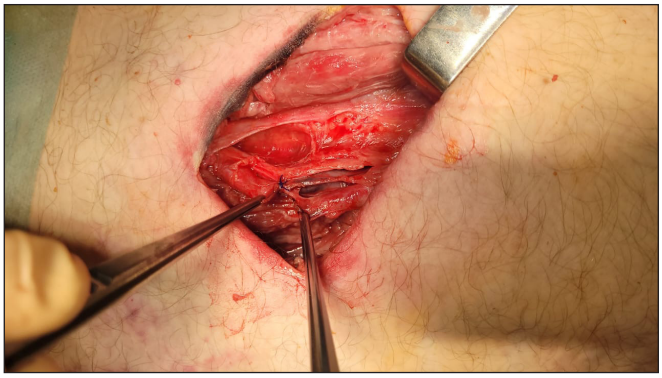

Fig. 2. Wounded S, 52 years old. The second day after a gunshot wound to the left hip with damage to the superficial femoral artery. Damage to the superficial femoral artery was detected during repeated surgical treatment of the wound.

Fig. 3. Wounded S, 52 years old. The second day after a gunshot wound to the left thigh with damage to the superficial femoral artery. Removed blood clots.

organs, limb amputations, longer treatment and rehabilitation times, or fatal outcomes [9, 10].

A frequent violation of the international law for humanitarian treatment during the war by the Russian army is associated with problems of the safe evacuation of injured people to appropriate Levels of medical care and interrupted supply of medical equipment, due to frequent artillery strikes on medical facilities. There is a clinical challenge for the management of gunshot wounds under the above-mentioned conditions as well as the application of damage control surgery in case of severe vascular injury [6].

THE AIM

The aim was to demonstrate the clinical features and complications that arise when medical assistance is provided late in the case of a gunshot wound with shrapnel through the thigh, resulting in damage to the superficial femoral artery.

MATERIALS AND METHODS

Wounded S., 52 years old, sustained a gunshot through a shrapnel wound of the left thigh with damage to the superficial femoral artery and soft tissue defect. Medical assistance was provided during the stages of medical evacuation.

Damage to the left superficial artery was detected on the 2nd day after the injury when the injured person arrived at the III level of medical care at the Military Medical Clinical Center of the Central Region.

The wounded man was examined. General tests of blood, urine, biochemical blood analysis, blood coagulogram, and ultrasound examination of the vessels of the lower extremities were performed using an ultrasonic diagnostic HM70 EVO Samsung Medison scanner (Korea, 2021).

RESULTS

According to the patient S.'s account and accompanying medical documentation, the wound was a gunshot wound that occurred during the performance of official duties on February 5, 2023, around 02:00 near one of the settlements in the Donetsk region. The wound was located in the upper third of the left thigh and resulted in damage to the vascular-nerve bundle and a soft tissue defect. First aid was provided on site, and initial surgical treatment of the wound in the upper third of the left thigh was performed during medical evacuation on February 5, 2023. The patient was then transferred to the Vinnytsia Military Medical Clinical Center for further treatment on February 7, 2023, where he was admitted to the vascular surgery department. Ultrasound examination of the arteries of the left lower limb revealed collateral blood flow in the popliteal fossa and periphery. Examination of the wound revealed a mark indicating that the bleeding was stopped by stitching it with blue polypropylene, as seen in Fig.1.

Fig. 4. Wounded S, 52 years old. The second day after a gunshot wound to the left thigh with damage to the superficial femoral artery. A – Superficial femoral artery with end-to-end anastomosis. B – installed VAC system.

Fig. 5. Wounded S, 52 years old, after a gunshot wound to the left hip with damage to the superficial femoral artery. A – alloprosthesis of the superficial femoral artery. B – the appearance of the limb after alloprosthesis of the superficial femoral artery.

On the day of receipt, 07.02.23 performed: Repeated surgical treatment of the wounds of the left thigh, necrectomy, revision of the vascular-nerve bundle, and damage to the superficial femoral artery was detected (Fig. 2).

Thrombectomy was performed from the proximal and distal ends of the superficial femoral artery with a Fogarti catheter No. 5, 6 (Fig. 3)

The left superficial femoral artery was restored with end-to-end anastomosis, and installation of the VAC system (Fig. 4).

Fig. 6. Wounded S, 52 years old. The 40th day after a gunshot wound to the left hip with damage to the superficial femoral artery and surgical treatment. Echogram of the vessels of the lower extremities, there are no circulatory disorders.

During the initial stages of evacuation, the patient did not notice any progression of ischemia of the left lower extremity. Upon examination upon admission, 2 days after the injury in Vinnytsia, the left lower limb was somewhat cooler compared to the right, sensitivity and movements in the toes and ankle joint were preserved, and pulsations on a. poplitea et a. dorsalis pedis were not felt. During ultrasound diagnosis of the arteries of the left lower limb, collateral blood flow was diagnosed distal to the injury site and an anastomosis between the deep femoral artery and the superficial femoral artery on the left in the lower third of the thigh was revealed.

02/13/23, 02/20/23: Repeated surgical treatment of the wound of the left thigh, and repair of the VAC system.

21.02.23 Erosive bleeding occurred and the following procedures were performed: revision of the postoperative wound of the left thigh, thrombectomy from the left superficial femoral artery, taking a vein from the right leg in the lower third, autovenous grafting of the superficial femoral artery.

27.02.23 noted a deterioration in the patient's general state of health, including an increase in body temperature to 39°C. The patient was examined by an infectious disease doctor and an express test for Covid-19 Ag was performed, which came back positive. The patient was then transferred to a specialized hospital.

03.03.23 Erosive bleeding occurred and the following procedures were performed: revision of the postoperative wound of the left thigh, thrombectomy of the left superficial femoral artery, and alloprosthesis of the superficial femoral artery (Fig. 5).

During the ultrasound examination of the main vessels of the lower extremities in the postoperative period without blood circulation disorders (Fig. 6)

In the postoperative period, he received 1000 units of heparin/hour/day for 5 days, after which 0.4 enoxaparin 2 times a day for 2 weeks, then rivaroxaban 10 mg, 1 tablet a day.

Recovery occurred on the 45th day.

DISCUSSION

The main cause of death of victims of gunshot wounds is acute blood loss, which is about 85% when the main vessels are injured. The second most important problem in the conditions of modern military field surgery is the detection, treatment, and prevention of acute limb ischemia, which occurs in patients with severe hemorrhagic and traumatic shock.

Timely diagnosis and rationality of actions at the stages of medical evacuation are important to ensure optimal care in case of injury to main vessels [10].

Specialized assistance in multidisciplinary hospitals and vascular centers for injuries of blood vessels consists of the fastest possible diagnosis of vascular pathology and its complications and the full range of reconstructive interventions [8].

In this clinical case, despite the untimely diagnosis and late detection of damage to the superficial femoral artery, the peculiarities of the existing blood circulation due to the presence of collateral blood flow played an important role in preserving the limb.

Features of blood circulation also caused difficulties in the diagnosis of this injury. At the initial stages of evacuation, the clinical picture of acute limb ischemia was not clear. On the 2nd day after the injury, when the injured person was admitted to Vinnytsia, the left lower extremity was somewhat cool compared to the right, sensitivity and movements in the toes and ankle joint were preserved, pulsations on a. popliteal et a. dorsalis pedis was not felt.

Arteriography is the gold standard for confirming the violation of the integrity of the arterial bed, but this method was not used in this case due to technical difficulties, as the angiograph was temporarily not working.

As a screening method, ultrasound dopplerography continues to play an important role in the diagnosis of

vascular injuries. The advantages of ultrasound in comparison with other imaging methods are: non-invasive technique, ease of execution and interpretation of data; the absence of ionizing radiation, the possibility of conducting multiple studies in the conditions of plaster immobilization, splinting, osteometallosynthesis, foreign metal bodies, the presence and prevalence in medical institutions [5].

In the above case, ultrasound was also of great importance in making the diagnosis. Ultrasound diagnosis of the arteries of the left lower limb revealed collateral blood flow distal to the injury site and revealed an anastomosis between the deep femoral artery and the superficial femoral artery on the left in the lower third of the thigh.

Limited medical resources were and remained a common problem for medical care in Ukraine due to various causes, including insufficient planning [6]. However, military and civilian surgeons are able to diagnose and manage such severe vascular injuries even in unstable combat conditions while considering the available resources.

CONCLUSIONS

The presence of features of blood circulation in gunshot wounds of the main vessels of the lower limbs can favorably affect the possibility of saving the limb, as evidenced by the case presented.

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The Authors declare no conflict of interest.

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ORIGINAL ARTICLE

INTRACARDIAC HEMODYNAMICS, CEREBRAL BLOOD FLOW AND MICROEMBOLIC SIGNAL BURDEN IN STABLE CORONARY ARTERY DISEASE PATIENTS WITH CONCOMITANT COVID-19

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ABSTRACT

The aim: To estimate the changes in intracardiac hemodynamics, cerebral blood flow (CBF), and microembolic signals` (MES) burden in stable coronary artery disease (SCAD) patients with concomitant COVID-19.

Materials and methods: The cross-sectional study analyzed the data from 80 patients, being subdivided as follows: group 1 (G_1) – SCAD without COVID-19 (n=30); group 2 (G_2) – SCAD with concomitant COVID-19 (n=25); group 3 (G_3) – COVID-19 without SCAD (n=25). The control group (CG) included 30 relatively healthy volunteers. CBF and total MES count were assessed by transcranial Doppler ultrasound.

Results: Transthoracic echocardiography data from G_2 revealed the most pronounced left ventricular (LV) dilation and its contractility decline (the rise of end-systolic volume (ESV) and ejection fraction decrease), as compared to G_1 and G_3. G_1-G_3 patients (vs. CG) presented with lower peak systolic velocities in all the studied intracranial arteries (middle and posterior cerebral arteries bilaterally, and basilar artery), along with the higher MES count. Such a drop in CBF was the most pronounced in G_2. Both G_2 and G_3 demonstrated the highest amount of MES, with slightly higher count in G_2. We built a linear neural network, discriminating the pattern of both higher LV ESV and MES count, being inherent to G_2.

Conclusions: G_2 patients demonstrated the LV dilation and its systolic function impairment, and presented with CBF drop and MES burden increase, being more advanced in contrast to G_1 and G_3. LV contractility decrease was associated with the higher MES load in the case of SCAD and COVID-19 constellation.

KEY WORDS: SARS-CoV-2 infection, COVID-19, myocardium, myocardial ischemia, cerebrovascular circulation

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INTRODUCTION

As the coronavirus disease 2019 (COVID-19) pandemic unfolds throughout the world, the global scientific community has endeavoured to study not only respiratory, but also extrapulmonary manifestations of this infection [1]. General infectious and respiratory symptoms are traditionally considered to occur in the majority of COVID-19 patients. Nevertheless, many studies suggest the neuroinvasive potential of SARS-CoV-2 (severe acute respiratory syndrome coronavirus type 2), implemented by the use of a series of strategies and mechanisms, leading to central and peripheral nervous systems injury [1-5].

Current evidence indicates that patients with risk factors and comorbidities are more prone to a severe course of COVID-19, with involvement and dysfunction of multiple organs and systems [1, 2, 6, 7]. Moreover, the simultaneous damage to the cardiovascular and central nervous systems is recognized as one of the determinants of multi-organ involvement in COVID-19, being associated with worse outcomes [8, 9]. Such an issue, therefore, raises the question of cardio-cerebral interactions in COVID-19, particularly in patients with cardiovascular comorbidities, including those with stable coronary artery disease (SCAD) [7-10].

Cardio-cerebral interactions are implemented, in particular, through the myocardium and vascular bed interplay, including extra- and intracerebral vessels, which all are jeopardized in COVID-19 [9, 11]. In particular, SARS-CoV-2 can provoke various cerebral blood flow (CBF) disorders due to a number of mechanisms, including systemic endothelial damage, hypercoagulation, microvascular thrombosis, myocardial

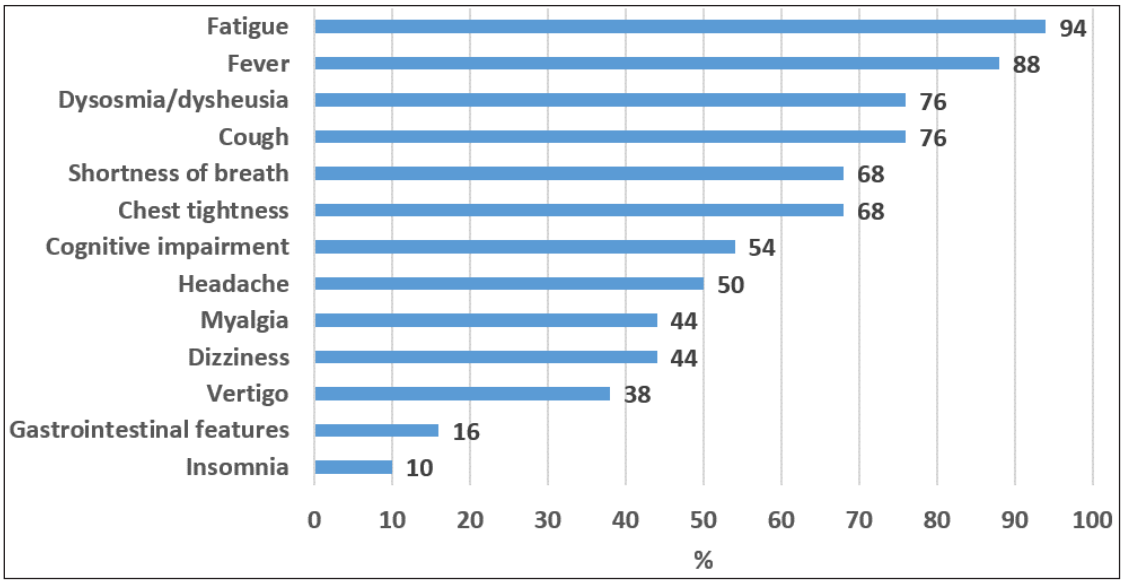

Fig. 1. COVID-19-associated symptoms in G_2 and G_3 patients (in total, n=50).

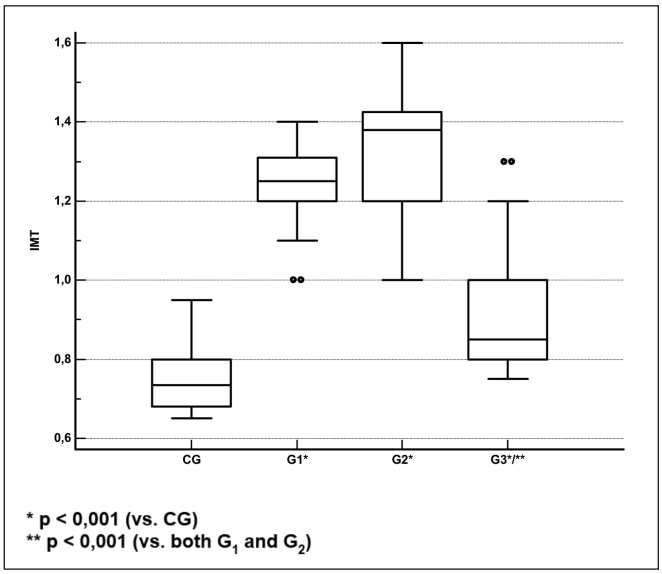

Fig. 2. IMT (mm) in G_1-G_3 patients and controls (box-and-whiskey plot).

damage, destabilization of existing atherosclerotic plaques, vessel embolization of various genesis, etc. [12, 13]. In this respect, one could benefit from the comprehensive study of intracardiac and cerebral hemodynamics in COVID-19 patients with comorbidities, along with the monitoring of micro-embolic signals (MES), corresponding to micro-embolic particles, circulating in the cerebral arteries [12-14]. At the same time, the pathogenetic factors related to myocardial dysfunction, particularly in SCAD patients, directly or indirectly affecting CBF homeostasis, require further deep research [10].

THE AIM

The aim of the study was to estimate the changes in intracardiac hemodynamics, CBF and MES burden, and to assess the relationship between them, in SCAD patients with concomitant COVID-19.

MATERIALS AND METHODS

The cross-sectional study consecutively enrolled 55 patients with SCAD (including those with concomitant COVID-19), and 25 patients with SARS-CoV-2 infection without SCAD, during the period December 10, 2019 – December 31, 2022.

COVID-19 was verified by the detection of SARS-CoV-2 RNA in upper respiratory specimens by the use of polymerase chain reaction (PCR). The presence and severity of COVID-19-associated lung injury were assessed by means of multi-slice computed tomography (MSCT) [15]. SCAD was verified according to current guidelines [16].

The exclusion criteria were as follows: acute coronary syndrome; previous documented acute cerebrovascular events; certain arrhythmias at baseline (atrial fibrillation/flutter, frequent supraventricular premature beats, ventricular premature beats grade 2 and higher [17]); severe and/or decompensated baseline comorbidities, including malignancies; previous neurosurgery; carotid diameter stenosis ≥30 % [18]; occlusive lesions of intracranial arteries; inappropriate transcranial acoustic window; previous heart valve replacement; previous vaccination against COVID-19; and the lack of informed consent.

The enrolled sample of 80 patients was subdivided into 3 groups: group 1 (G_1) – SCAD patients without COVID-19 (n=30; mean age (hereinafter – median (Me) and interquartile range (IQR) 60 (52-71) years; 18 (60 %) males); group 2 (G_2) – SCAD patients with concomitant COVID-19 (n=25; mean age 61 (55-67) years; 21 (84 %) males); and group 3 (G_3) – COVID-19

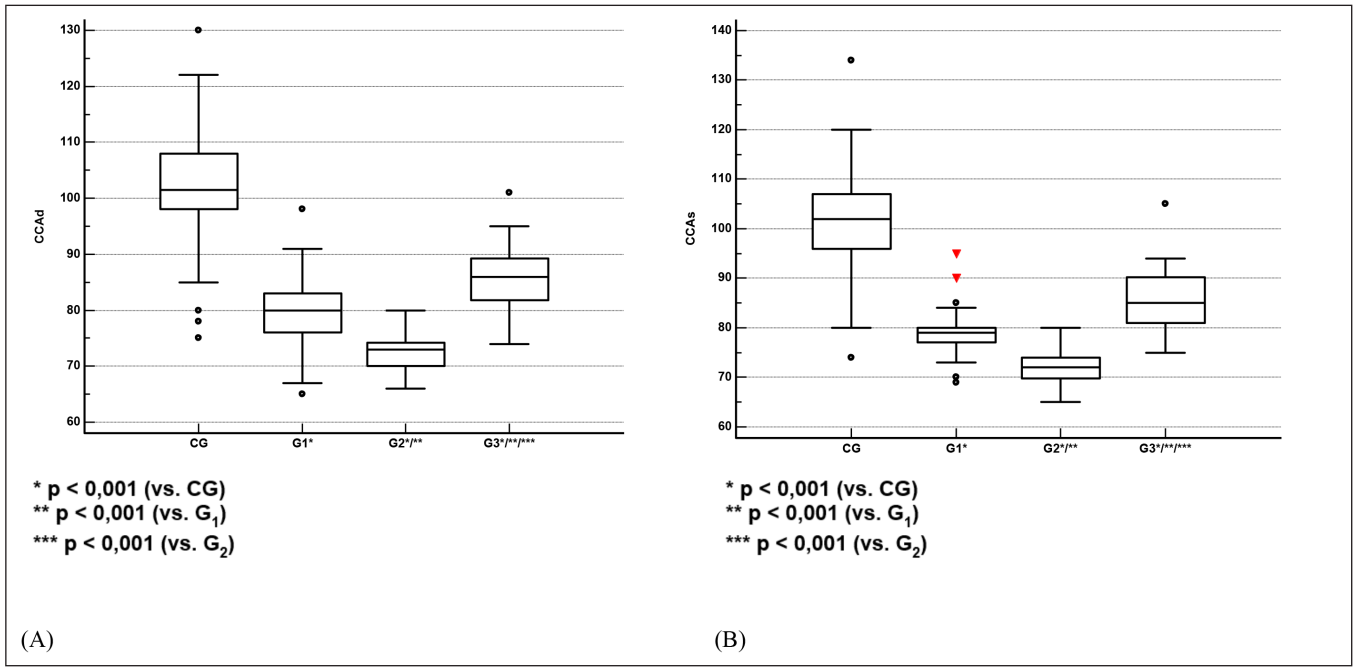

Fig. 3. V_{ps} (cm/s) in CCA (A – right (d); B – left [s]) in G_1-G_3 patients and controls (box-and-whiskey plots).

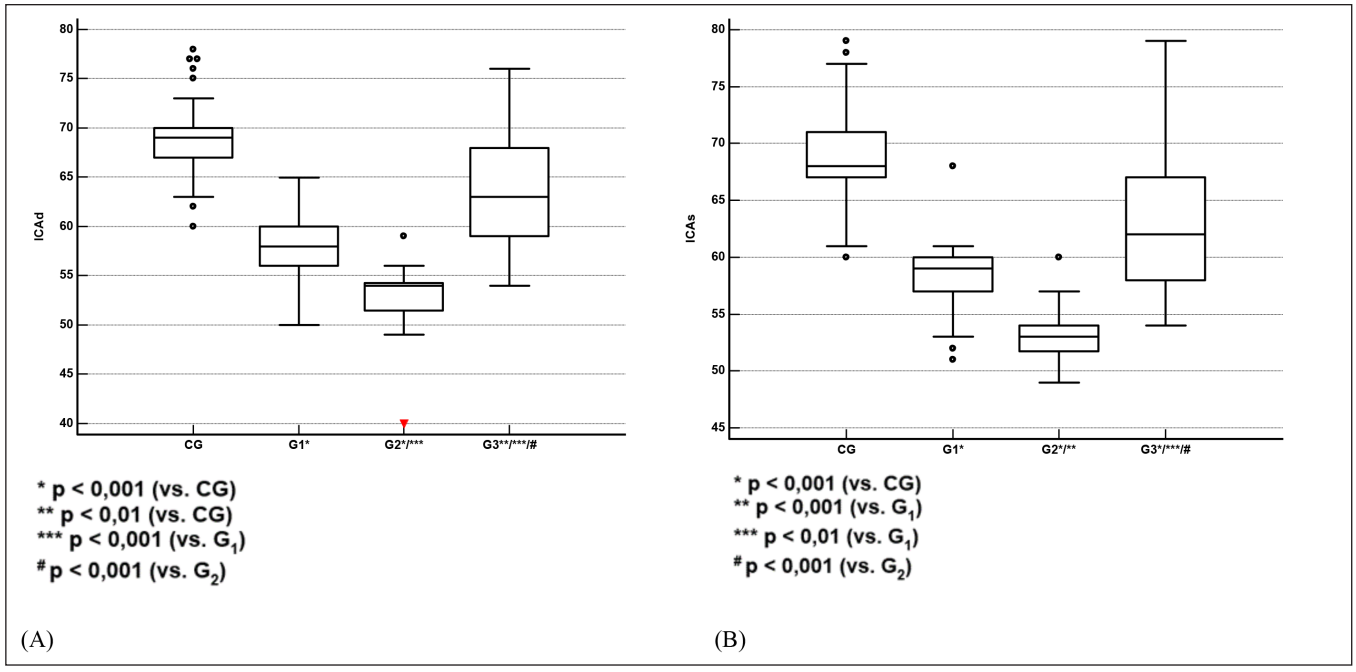

Fig. 4. V_{ps} (cm/s) in ICA (A – right (d); B – left [s]) in G_1-G_3 patients and controls (box-and-whiskey plots).

patients without SCAD (n=25; mean age 54 (37-67) years; 20 (80 %) males).

The COVID-19-associated symptoms, including the neurological ones, in patients with verified SARS-CoV-2 infection (G_2 and G_3; n=50) are demonstrated in Fig. 1.

The control group (CG) included 30 relatively healthy volunteers (mean age 48 (37-59) years; 23 (77 %) males), were free from previous SARS-CoV-2 infection, and had not been vaccinated against COVID-19 earlier.

Transthoracic echocardiography (TTE) was performed in all the patients by the use of harmonic imaging ultrasound system (HD11XE, Philips, USA; S4-2 phased array probe [2-4 MHz]). We assessed the parameters of cardiac remodeling, left ventricular (LV) systolic, and diastolic function according to ASE guidelines [19].

Duplex scanning of extracranial carotid arteries was performed by the use of L17-5 linear array probe (5-17 MHz) in line with the standard practice. We assessed the

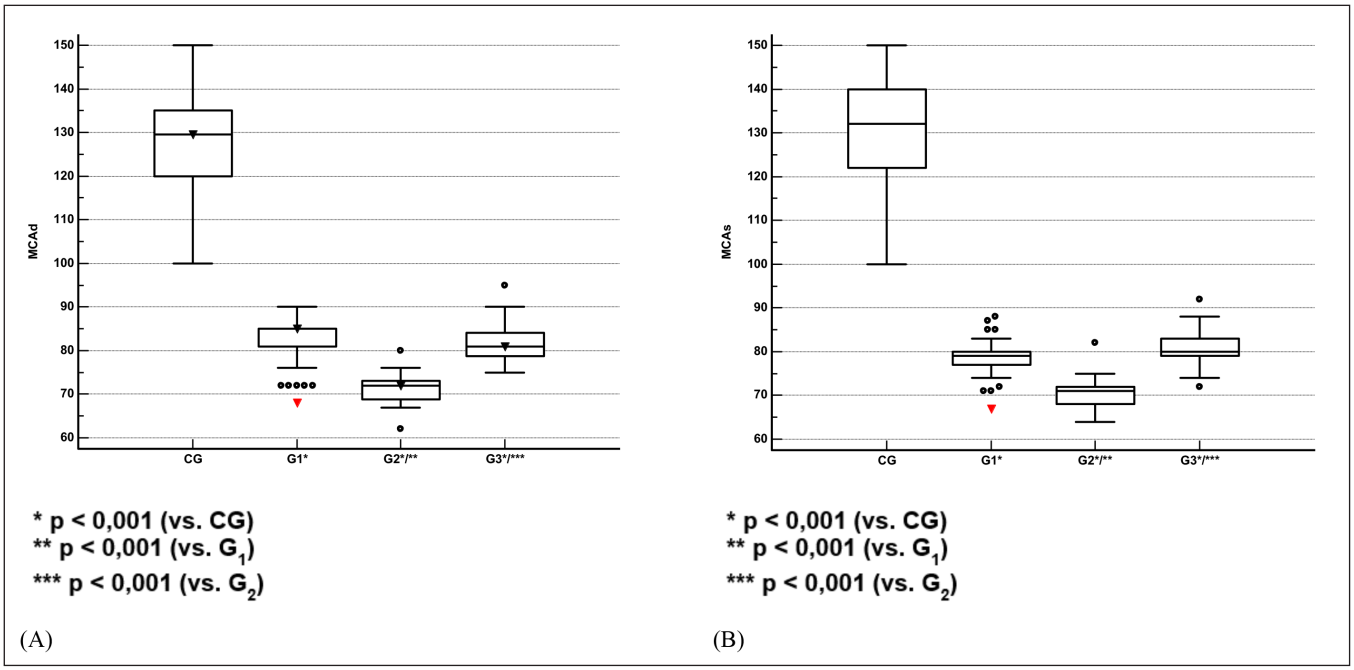

Fig. 5. V_{ps} (cm/s) in MCA (A – right (d), black triangle markers as median; B – left [s]) in G_1-G_3 patients and controls (box-and-whiskey plots).

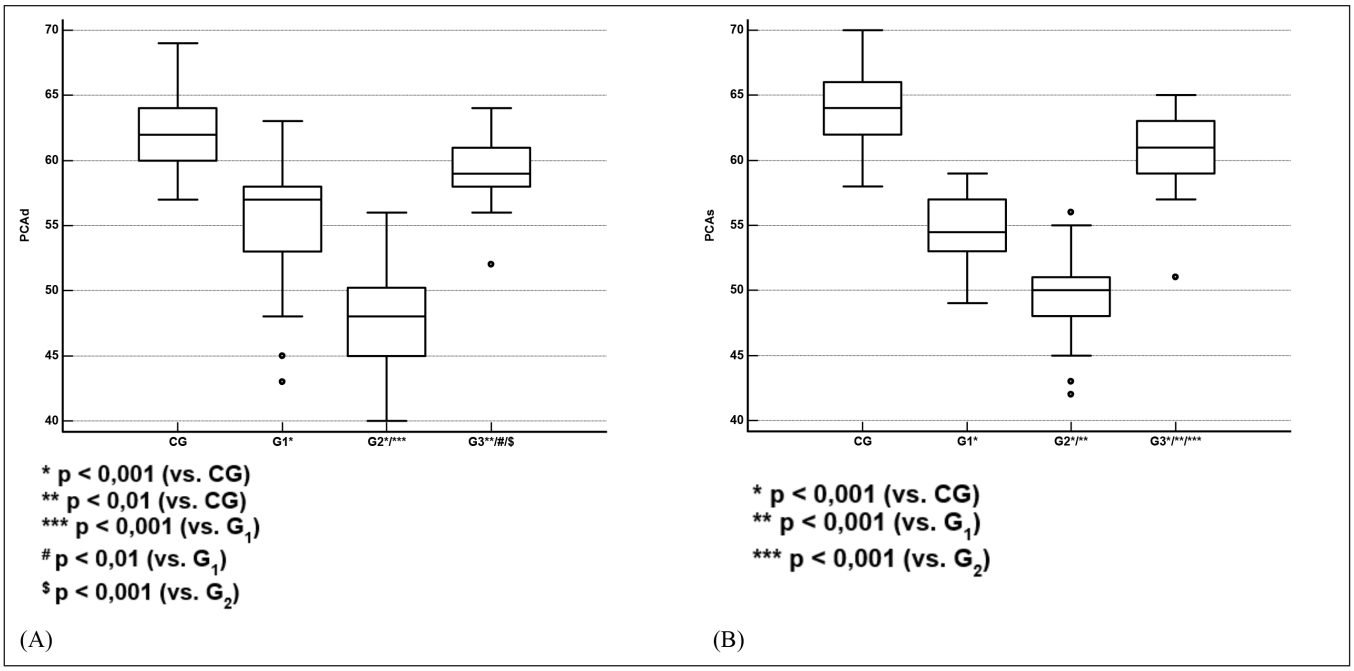

Fig. 6. V_{ps} (cm/s) in PCA (A – right (d); B – left [s]) in G_1-G_3 patients and controls (box-and-whiskey plots).

following parameters: intima-media thickness (IMT) of the common carotid artery (CCA) bilaterally; peak systolic velocity (V_{ps}) in CCA and internal carotid artery (ICA) (bilaterally). Among the bilateral IMT values per patient, the maximum one was considered for further analysis.

Transcranial Doppler ultrasound (TCD) was performed by the use of S4-2 phased array probe (2-4 MHz) according to standard procedures. We assessed the following parameters: V_{ps} in the middle cerebral artery (MCA) (M1 segment; bilaterally); V_{ps} in a posterior cerebral artery (PCA) (P2 segment; bilaterally); V_{ps} in a basilar artery (BA); maximal blood flow velocity (V_{max}) in the vein of Rosenthal (VR) (bilaterally).

All the patients underwent 1-hour bilateral TCD monitoring to detect MES using a portable Doppler device with a 7 dB threshold. MCA (M1 segment) was insonated bilaterally by the use of a low-frequency probe (2-4 MHz) in accordance with standard protocol [20]. The sum of MES, obtained bilaterally per patient, was considered as the total MES count.

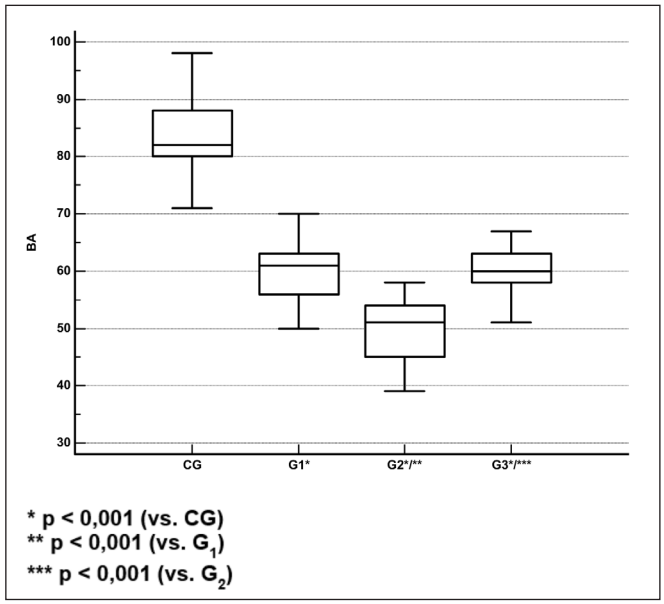

Fig. 7. V_{ps} (cm/s) in BA in G_1-G_3 patients and controls (box-and-whiskey plot).

We performed the data analysis by the use of certain software (Statistica v. 7.0 and v. 14.0 (TIBCO Software Inc., USA); IBM SPSS Statistics v. 27.0 (Armonk, NY: IBM Corp., USA); MedCalc v. 20.218 (MedCalc Software Ltd., Belgium); and EZR v. 1.61). Quantitative variables were presented as Me with IQR or 95 % confidence interval (CI), and qualitative ones – as absolute and relative (%) frequency. To compare the studied groups, we used Kruskal-Wallis H test (for continuous variables) and χ^2 test (for categorical variables), with the following Mann-Whitney U-test and Fisher`s exact test, respectively, for *post hoc* comparisons (the Bonferroni correction was applied). The relationship between the quantitative variables was determined by the use of *Spearman`s rank coefficient* of correlation (ρ). The discrimination of the studied groups in the space of associated variables was performed by the neural networks analysis. The genetic algorithm was used for the input feature selection. A 2-tailed p<0,05 was considered statistically significant (considering the Bonferroni correction).

RESULTS

Patients from G_1-G_3 were comparable in terms of age, sex, BMI, and current smoking frequency (Table I). G_1 and G_2 were comparable by the frequency of previous MI and coronary angiography/PCI cases. Moreover, G_2 and G_3 matched each other by the degree of COVID-19-associated lung injury [15] (Table I). Baseline diabetes mellitus type 2 was more frequent among SCAD patients (17 of 55 [31 %]), as opposed to G_3 (2 of 25 (8 %); p=0,035).

As opposed to controls, the enrolled patients, in general, demonstrated the signs of left heart chambers and right ventricular (RV) remodeling, along with the worse LV systolic and diastolic function, and the higher systolic pulmonary artery pressure (SPAP) value. Particularly, LV diastolic abnormalities (by lower E/A and increased DT and IVRT) were more evident in SCAD patients, in contrast to G_3 (Table II). At the same time, G_1 and G_3 patients presented with the preserved average LV ejection fraction (EF). On the contrary, TTE data from G_2 patients were indicative of the most pronounced LV dilation and its contractility decline (reflected by the rise of ESV and EF decrease), as compared to the rest of the studied groups, including the patients with SCAD alone. Moreover, G_2 was additionally characterized

Table I. The certain demographic, anthropometric and clinical characteristics of G_1-G_3 patients and controls

Parameters		CG N=30	Groups of patients			p_{1-2}	p_{1-3}	p_{2-3}
			G_1 N=30	G_2 N=25	G_3 N=25			
Age, years		48 (37-59)	60 (52-71)*	61 (55-67)*	54 (37-67)	NS	NS	NS
Males, n (%)		23 (77)	18 (60)	21 (84)	20 (80)	NS	NS	NS
BMI, kg/m^2		27,0 (25,8-28,7)	28,6 (27,2-30,5)	28,9 (28,1-31,0)**	28,7 (26,4-29,1)	NS	NS	NS
Current smoking, n (%)		4 (13)	7 (23)	4 (16)	5 (20)	NS	NS	NS
HTN, n (%)		-	30 (100)	25 (100)	10 (40)	NS	<0,001	<0,001
MI, n (%)		-	15 (50)	8 (32)	-	NS	-	-
CAG/PCI, n (%)		-	16 (53)	19 (76)	-	NS	-	-
COVID-19-associated lung injury, n (%)	Stage 2	-	-	10 (40)	9 (36)	-	-	NS
	Stage 3	-	-	10 (40)	12 (48)	-	-	
	Stage 4	-	-	5 (20)	4 (16)	-	-	

Notes: p_{1-2} – the significance of difference between G_1 and G_2; p_{1-3} – the significance of difference between G_1 and G_3; p_{2-3} – the significance of difference between G_2 and G_3; * – p<0,01 vs. CG; ** – p<0,05 vs. CG; NS – non-significant difference; BMI – body mass index; HTN – hypertension; MI – myocardial infarction; CAG – coronary angiography; PCI – percutaneous coronary intervention

Table II. The structural and functional state of myocardium by TTE in G_1-G_3 patients and controls

Parameters	CG N=30	Groups of patients			p_{1-2}	p_{1-3}	p_{2-3}
		G_1 N=30	G_2 N=25	G_3 N=25			
LA, cm	3,6 (3,5-3,7)	4,4 (4,2-4,5)*	4,4 (4,2-4,8)*	3,7 (3,7-4,0)**	NS	<0,001	<0,001
LV MMi, g/m^2	81,0 (77,7-88,7)	122,1 (109,9-129,3)*	135,4 (127,4-142,0)*	90,8 (84,5-96,1)	<0,01	<0,001	<0,001
EDV, ml	121 (115-125)	176 (165-180)*	205 (195-220)*	130 (125-140)**	<0,001	<0,001	<0,001
ESV, ml	37 (35-40)	85 (80-90)*	113 (100-123)*	55 (52-59)*	<0,001	<0,001	<0,001
EF, %	69 (68-72)	51 (50-53)*	44 (40-50)*	58 (55-60)*	<0,001	<0,001	<0,001
E/A, c.u.	1,39 (1,20-1,50)	0,75 (0,70-1,00)*	0,90 (0,90-1,10)*	1,10 (1,00-1,30)**	<0,05	<0,001	NS
IVRT, ms	83 (80-88)	94 (88-96)*	90 (88-94)*	81 (74-88)	NS	<0,001	<0,001
DT, ms	179 (170-192)	203 (196-216)	203 (188-216)	180 (169-196)	NS	<0,001	<0,01
RVD, cm	2,3 (2,2-2,5)	2,9 (2,8-3,0)*	3,3 (3,2-3,5)*	3,1 (2,8-3,3)*	<0,001	NS#	NS
RVTd, cm	0,33 (0,30-0,33)	0,37 (0,31-0,40)***	0,50 (0,45-0,55)*	0,45 (0,40-0,50)**	<0,001	<0,05	NS
SPAP, mm Hg	24 (21-25)	29 (28-30)*	37 (31-40)*	35 (34-38)*	<0,001	<0,001	NS

Notes: p_{1-2} – the significance of difference between G_1 and G_2; p_{1-3} – the significance of difference between G_1 and G_3; p_{2-3} – the significance of difference between G_2 and G_3; NS – non-significant difference; * – p<0,001 vs. CG; ** – p<0,05 vs. CG; *** – p<0,01 vs. CG; # – p=0,074; LA – left atrial anteroposterior diameter; LV MMi – left ventricular (LV) myocardial mass (ASE cube method [19]), indexed by body surface area; EDV – LV end-diastolic volume; ESV – LV end-systolic volume; EF – LV ejection fraction; E/A – the ratio of peak velocity blood flow from LV relaxation in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave); IVRT – isovolumic relaxation time; DT – deceleration time; RVD –right ventricular (RV) basal diameter at end-diastole; RVTd – RV wall thickness at end-diastole; SPAP – systolic pulmonary artery pressur

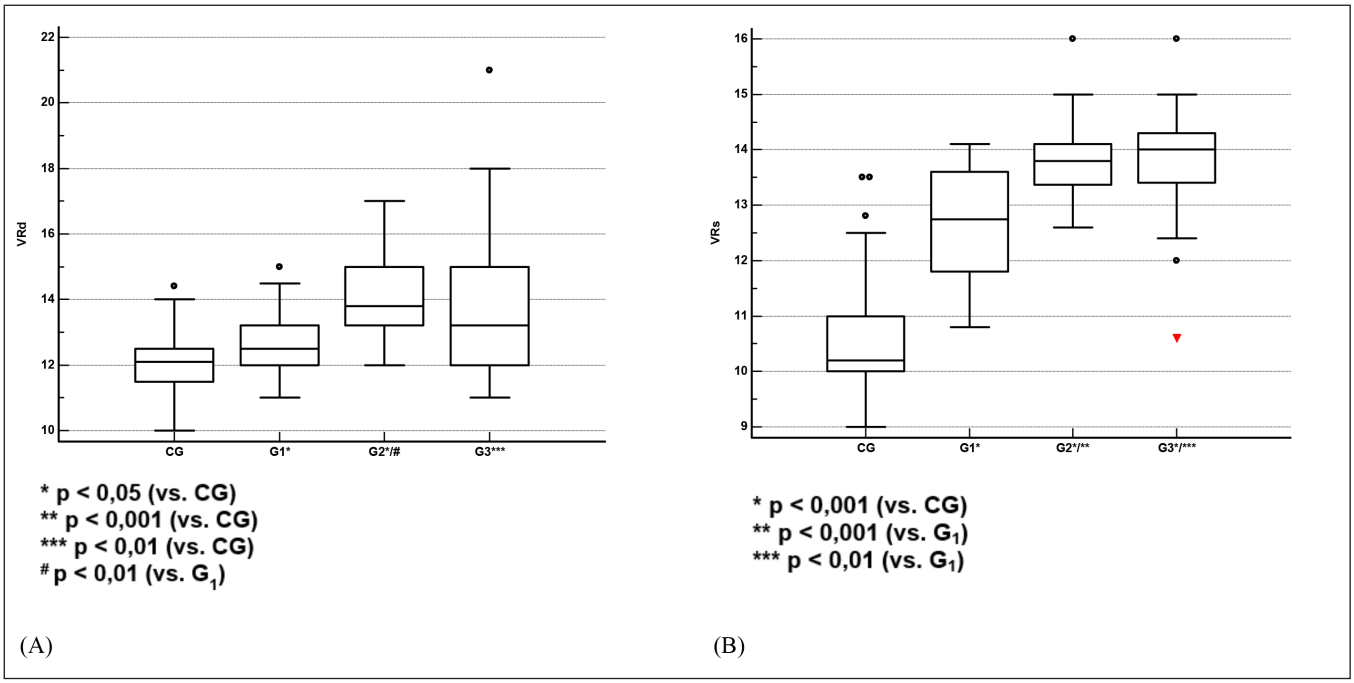

Fig. 8. V_{max} (cm/s) in the veins of Rosenthal (A – right (d); B – left [s]) in G_1-G_3 patients and controls (box-and-whiskey plots).

by more advanced RV dilation and SPAP elevation, in contrast to G_1, but without significant differences as opposed to G_3 (Table II).

SCAD patients (G_1 and G_2) demonstrated the higher values of IMT, in comparison to CG and G_3 (Fig. 2). In contrast to controls, all the enrolled patients presented with lower V_{ps} values in extra- and intracranial arteries (Fig. 3-7), and with the increase of V_{max} in both VRs (Fig. 8). The latter finding, suggesting the impairment of cerebral venous circulation, was more evident in COVID-19 patients (G_2 and G_3), in contrast to CG and G_1. Such a drop in CBF and blood flow in extracranial carotid arteries was the most pronounced among G_2 patients. Along with the absence of single signals in controls, we detected a substantially higher amount of MES in all the enrolled patients. Additionally, COVID-19

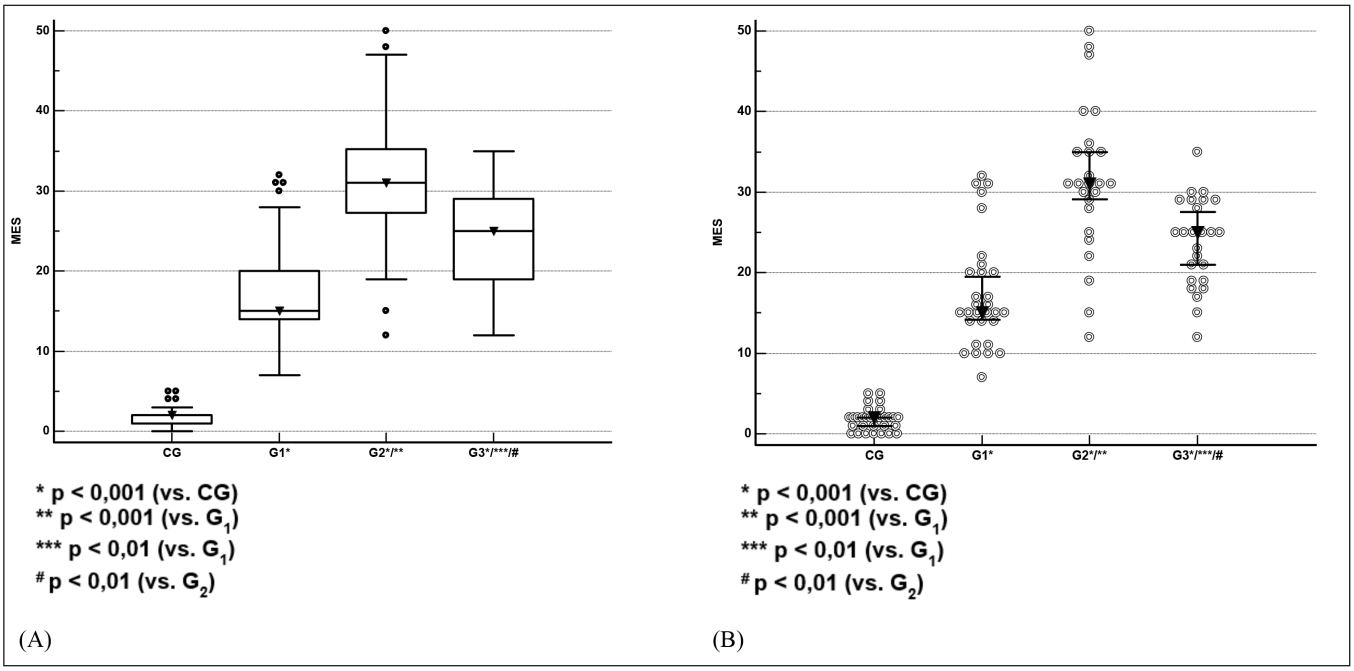

Fig. 9. Total MES count in G_1-G_3 patients and controls (A – box-and-whisker plot, triangle markers as median; B – dot plot (all the data), median and 95 % CI). MES were not detected in 7 controls.

Parameters	MES	IMT	CCAd	CCAs	ICAd	ICAs	MCAd	MCAs	PCAd	PCAs	BA	VRd	VRs
LA	0,540	0,763	-0,718	-0,720	-0,729	-0,705	-0,605	-0,672	-0,616	-0,761	-0,638	0,343	0,409
EDV	0,652	0,770	-0,835	-0,834	-0,842	-0,797	-0,726	-0,770	-0,767	-0,853	-0,768	0,387	0,495
ESV	0,708	0,814	-0,851	-0,863	-0,875	-0,831	-0,803	-0,843	-0,797	-0,867	-0,816	0,402	0,556
LV MMi	0,595	0,750	-0,785	-0,791	-0,808	-0,774	-0,672	-0,726	-0,717	-0,812	-0,728	0,359	0,523
E/A	-0,364	-0,494	0,578	0,595	0,543	0,557	0,424	0,477	0,372	0,489	0,389	**-0,283**	-0,353
IVRT	0,322	0,521	-0,545	-0,537	-0,543	-0,516	-0,357	-0,442	-0,441	-0,540	-0,373	**0,232**	**0,249**
DT	0,353	0,498	-0,527	-0,497	-0,521	-0,493	-0,348	-0,438	-0,452	-0,541	-0,406	0,244	0,208
RVTd	0,640	0,427	-0,493	-0,508	-0,532	-0,557	-0,570	-0,526	-0,449	-0,484	-0,620	0,540	0,627
RVD	0,712	0,566	-0,618	-0,639	-0,630	-0,652	-0,721	-0,682	-0,592	-0,613	-0,719	0,581	0,672
SPAP	0,716	0,433	-0,527	-0,555	-0,525	-0,535	-0,725	-0,654	-0,457	-0,489	-0,664	0,534	0,682
MES	1,000	0,644	-0,674	-0,689	-0,693	-0,678	-0,851	-0,805	-0,633	-0,649	-0,820	0,495	0,692
IMT	0,644	1,000	-0,720	-0,755	-0,803	-0,774	-0,715	-0,785	-0,734	-0,828	-0,772	0,414	0,508

Fig. 10. The correlations of the parameters of myocardial structure and function with MES, IMT and blood flow velocities in extracranial carotid arteries and intracranial vessels. All the correlations are significant at p<0,001, except bold (significant at p<0,01) and underlined (significant at p<0,05). D – right; s – left.

patients (G_2 and G_3) demonstrated the highest amount of MES, with a slightly higher number of signals among those with SCAD comorbidity (Fig. 9).

The more advanced LV and RV remodeling, along with LV systolic and diastolic function impairment, correlated significantly with the increase of IMT and MES, as well as the decrease in CBF (Fig. 10).

Aiming at appropriate discrimination of the studied groups based on the minimal set of associated variables, we performed an input feature selection via the genetic algorithm, with the following selection of two parameters, namely LV ESV and total MES count. Based on the selected input parameters, and the originally studied groups, we built a linear neural network (LNN) of two input and four output «neurons» (Fig. 11). The response surface of LNN, with the corresponding ESV and MES scatter plot is presented in Fig. 12.

The obtained response surface is indicative for the built LNN to discriminate the presented 2D-space of input variables into several relatively distinct areas (Fig. 12). In particular, one could distinct an area of a combination of both lower LV ESV and MES values (LNN`s b-coefficients: [–0,413] and [–0,953], respectively), corresponding to CG; higher LV ESV and lower MES values ([0,952] and [–0,797], respectively) – G_1; and lower LV ESV with higher MES values ([–1,507] and [1,452], respectively) – G_3. At the same time, the built LNN allowed us also to distinguish the upper right pattern of both higher LV ESV and MES values combination (b-coefficients: [0,968] and [0,298], respectively), being inherent to SCAD patients with concomitant COVID-19 (G_2) (Fig. 12).

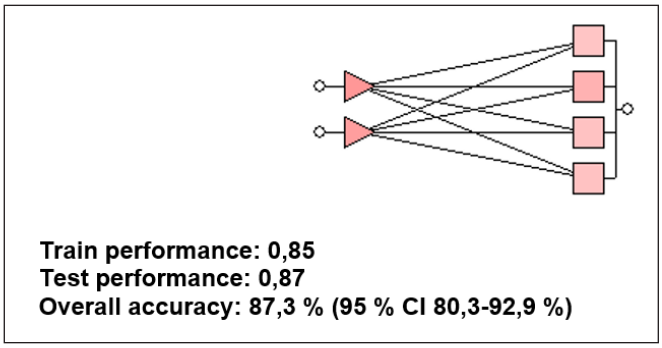

Fig. 11. The architecture and certain features of the built LNN.

DISCUSSION

Our interest in the presented problem was stimulated by recent findings on the impact of COVID-19 on cerebral hemodynamics [2, 12, 21,22], and regarding the way that SARS-CoV-2 interfere in cardio-cerebral cross-talk in such patients [3, 9]. The latter issue, being a subject of growing interest, raises specific questions related to the differentiated assessment of the leading underlying pathomechanisms, and the degree of cardio-cerebral interplay disruptions in various categories of COVID-19 patients, including those with SCAD.

The present study demonstrated the CBF decline in all three groups of enrolled patients, as compared to controls. Considering the preserved average LV EF, such a finding in SCAD patients could be primarily attributed to the pathomechanisms, being independent of LV systolic dysfunction. In particular, LV diastolic abnormalities could reflect the increased myocardial and arterial stiffness. The latter factor, while associated with LV remodeling and dysfunction, is considered to be a possible contributor to cerebral hypoperfusion [10].

In its turn, the numerous triggers of CBF dys-autoregulation and impairment in COVID-19 patients include direct viral neurotropism towards the neural cardiovascular control centers, endothelial cells infection with the consequent endothelial dysfunction and damage, enhanced microparticles release (including those derived from endothelium), the downregulation of membrane-bound angiotensin converting enzyme 2 receptor and renin-angiotensin system disruption, cytokines release syndrome, hypoxia, increased reactive oxygen species generation, blood hyperviscosity, hypercoagulability, micro- and macro thrombosis [1, 2, 4, 6, 12, 13, 23, 24]. It is noteworthy that LV contractility decline, observed in SCAD patients with concomitant SARS-CoV-2 infection, could be an additional contributor to the CBF drop, being the most pronounced in such cases [10].

From the clinical perspective, MES burden could be used not only for the risk stratification of acute cerebrovascular events in large arteries, justifying the search for embolic sources, but also can be interpreted as an additional pathomechanism of cerebral small vessel (microthrombotic) disease [14, 24, 25]. In the settings of SARS-CoV-2 infection, enhanced MES formation is related to systemic endothelial dysfunction and damage, particularly the endothelial shedding from the erosive carotid atherosclerotic plaques (not necessarily obstructive) and the increased IMT loci, along with COVID-19-associated cytokines release syndrome and hemostatic disorders [12-14, 24-26]. These points could be, at least partially, applicable to SCAD itself [27]. However, while interpreting the higher MES count in G_2 and G_3 (vs. G_1), we faced the scarcity of available evidence regarding the differences between SCAD and COVID-19 with respect to

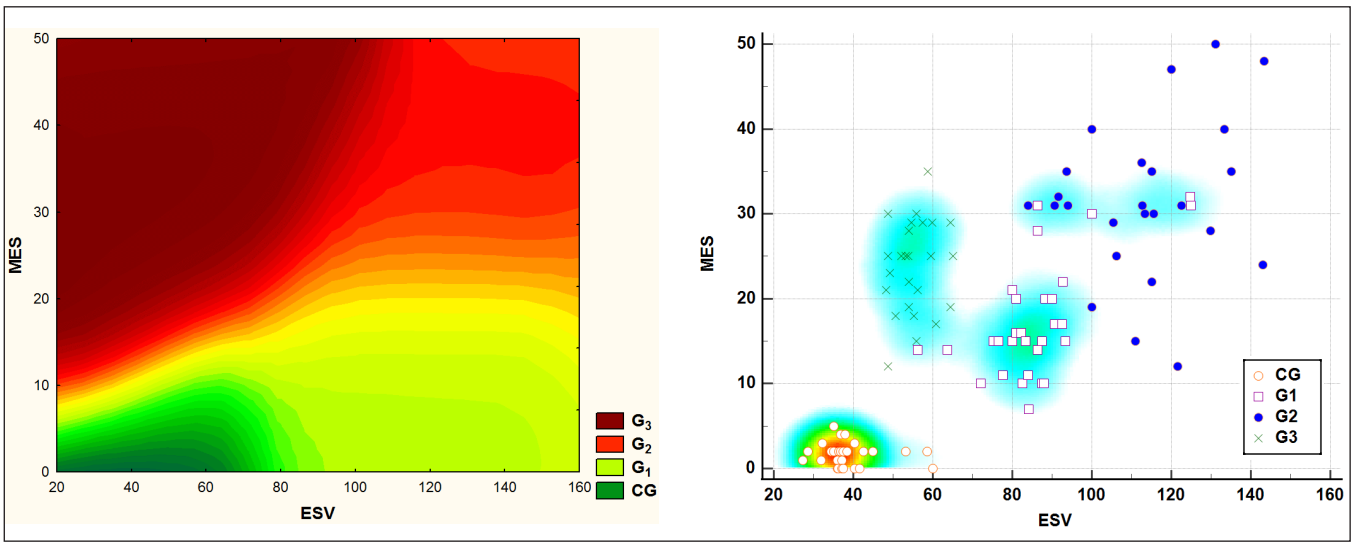

Fig. 12. The response 2D-surface of the built LNN (A) and the scatter plot of LV ESV (ml) and MES (units) with the heat map applied (B).

the impact of the degree of endothelial dysfunction/damage and systemic inflammation, along with other factors, on the intensity of MES generation in both conditions. Nevertheless, the present study revealed an association of elevated LV ESV with higher MES count in G_2, assuming the virus-related cardiac injury to be an additional pathomechanism of microembolization in SCAD patients with concomitant SARS-CoV-2 infection, as compared to SCAD alone [28].

In the light of the present study results, and taking into account the existing data [1, 2, 4-6, 12, 13, 23, 28], the «portrait» of a SCAD patient, infected by SARS-CoV-2, could be characterized by the higher risk of severe COVID-19 with multiple organ involvement, including the affection of central nervous system and myocardial dysfunction, and, importantly, the predisposition to thrombotic complications. Moreover, a SCAD patient, suffering from COVID-19, could demonstrate more apparent heart-brain axis dysfunction [3, 9], with increased susceptibility for a post-COVID-19 condition [29], being additionally characterized by a persistence of CBF decrease and brain microstructural changes at long-term follow-up [21, 22, 30].

Thus, considering the SCAD patients, suffering from COVID-19, as having a «brain at risk», the widespread implementation of multidisciplinary individualized management, although not easily applicable in real-world clinical practice, is highly justified to positively affect on patients` recovery after an acute phase of SARS-CoV-2 infection, and to improve their quality of life and outcomes in the long-term perspective [4].

The limitations of the present study are mainly related to its cross-sectional design, modest sample size, and the enrollment of unvaccinated patients and controls. Obviously, the cardio-cerebral interactions need to be analyzed in the short- and long-term follow-up after the acute phase of COVID-19, considering a broader spectrum of studied parameters, including cerebrovascular reactivity, CBF autoregulation, arterial stiffness assessment, brain imaging, more precise evaluation of myocardial function, and data on applied pharmacotherapy.

CONCLUSIONS

SCAD patients with concomitant COVID-19 demonstrated particular changes in myocardial remodeling and intracardiac hemodynamics, namely the dilation of LV and its systolic function impairment, and additionally presented with the drop of CBF and MES burden increase, being altogether more pronounced in contrast to patients with both conditions alone. Given the association of LV contractility decrease with the higher micro embolic load, along with the cerebral hemodynamics being more compromised in the case of SCAD and COVID-19 constellation, one should consider the assessment of myocardial structure and function, as well as TDI parameters, to be tightly incorporated into the management of SCAD patients, suffering from COVID-19.

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The study was conducted in accordance with the basic principles of the Council of Europe Convention on Human Rights and Biomedicine, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current national regulations. The study protocol was approved by the local ethics committee. All the patients provided written informed consent to participate in the study.

The study was conducted as a fragment of the complex scientific projects of the Department of Propaedeutics of Internal Medicine № 1 (Bogomolets National Medical University) «Features of changes in the system of hemocoagulation in the comorbid state of coronary heart disease and hypertension, laboratory and genetic predictors of thrombotic complications» (state registration number 0118U001391; term: 2018-2020) and «Correction of changes in platelet and plasma hemostasis in patients with coronary syndromes and hypertension, taking into account the presence of comorbid pathology» (state registration number 0121U110275; term: 2021-2023), in collaboration with State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department (the complex scientific project of the Scientific Department of Internal Medicine «Improvement of patient-oriented approaches to the management of patients with cardiovascular and cerebrovascular diseases with comorbid conditions, in particular in those suffered from COVID-19» [state registration number 0122U000234; term: 2022-2024]).

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ORIGINAL ARTICLE

DRUG-ELUTING STENTS IN THE TREATMENT OF PATIENTS WITH OCCLUSIVE-STENOTIC LESIONS OF THE SUPERFICIAL FEMORAL ARTERY

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ABSTRACT

The aim: To analyze the results of endovascular revascularization of the femoropopliteal segment using drug-eluting stents.

Materials and methods: Endovascular intervention was performed in 23 patients with occlusive-stenotic lesions of the superficial femoral artery (SFA). Paclitaxel-eluting stents were used. There were 16 (69.6%) patients with diabetes mellitus type 2 and diabetic angiopathy, and 7 (30.4%) patients had obliterating atherosclerosis of the arteries of the lower limbs. Critical ischemia of the lower extremities was diagnosed in 18 (78.3%) cases, and intermittent claudication - in 5 (21.7%).

Results: Twenty (86.6 %) scheduled procedures for stenting of the SFA were technically successful. During follow-up period (3 months), there were no cases of reocclusion or clinically significant restenosis at the stented level. There were no "major" amputations during follow -up period. "Small" ankle amputations were performed in 7 (35%) patients with diabetic gangrene.

Conclusions: Implantation of drug-eluting stents is an effective method of endovascular revascularization in patients with SFA lesions. To compare the results of implantation of drug-eluting stents with other methods of revascularization of the lesions of the femoro-popliteal segment, it is necessary to accumulate more data and increase the duration of the follow-up period.

KEY WORDS: stenting, restenosis, angioplasty

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INTRODUCTION

With the advancement of minimally invasive techniques in the treatment of occlusive-stenotic lesions of peripheral arteries, endovascular revascularization is becoming increasingly important. The use of drug-eluting stents (DES), according to some studies [1], has an advantage over both balloon angioplasty and the use of bare stents in the femoropopliteal segment, as well as over femoropopliteal bypass grafting [2]. Another modern approach in the treatment of peripheral artery disease is the performance of endovascular angioplasty using drug-eluting balloons (DEB) [3, 4]. However, in many cases, patients with superficial femoral artery (SFA) lesions require stenting, making the implantation of DES a relevant treatment method for this category of patients.

When determining the localization of implanted stents in the femoropopliteal segment, we adhered to the opinion that placing stents in the popliteal and common femoral arteries is not desirable and can only be performed in extreme cases. The reasons for this are the risk of stent fracture in limb flexion zones at the knee and hip joints and the fact that stent implantation in the area of a possible vascular anastomosis "blocks the way" for open vascular surgery. Therefore, the DES implantation area was limited to the SFA.

THE AIM

To analyze the results of endovascular revascularization of the femoropopliteal segment using drug-eluting stents.

Table I. Distribution of patients with femoropopliteal segment lesions according to the GLASS classification

Grades of GLASS classification	Number of patients	Percentage of the total (%)
1	4	17.4
2	10	43.5
3	6	26.1
4	3	13.0
Total	23	100

Table II. Distribution of patients according to the localization of lesions in the arterial segments of the lower limbs

Lesions of the arterial segments of the lower limbs	Number of patients	Percentage of the total (%)
Isolated femoropopliteal segment	3	13.0
Iliac and femoropopliteal segment	4	17.4
Femoropopliteal and tibial segment	16	69.6
Total	23	100

Table III. Clinical outcomes of SFA stenting 3 months after surgery

Clinical outcome cases	Number of patients	Percentage of the total (%)
Clinically significant restenosis	1	5
«Major» amputations	0	0
«Minor» foot amputations	7	35
Total	20	100

MATERIALS AND METHODS

Endovascular interventions were performed in 2021-2022 for 23 patients with occlusive-stenotic lesions of the superficial femoral artery (SFA). There were 10 men (43.5%) and 13 women (56.5%). The average age of the patients was (66.0 ± 3.5) years. There were 16 patients (69.6%) with type 2 diabetes and diabetic angiopathy, and 7 patients (23.4%) with lower limb arterial obliterative atherosclerosis. Critical limb ischemia was diagnosed in 18 cases (78.3%), and intermittent claudication in 5 cases (21.7%). All patients underwent general clinical analyses, electrocardiography, echocardiography, lower limb arterial Doppler ultrasonography, and computed tomography (CT) angiography of the lower extremities. Patients received dual antiplatelet therapy, statins, and proton pump inhibitors. In patients with wet diabetic gangrene (3 (13.04%)), necrectomy was performed on the foot before the endovascular stage to reduce the risk of reperfusion syndrome complications, and in patients with dry gangrene (4 (17.4%)), necrectomy was performed within the viable tissue after endovascular revascularization to promote wound healing. Indications for endovascular revascularization of the SFA were established according to the European Society for Vascular Medicine (ESVM) recommendations for peripheral artery diseases [5].

The grade of femoropopliteal segment involvement was determined according to the Global Limb Anatomic Staging System (GLASS) classification [5, 6].

The distribution of patients by rank is presented in Table I.

In most patients, the occlusive-stenotic lesion of the SFA was not the only lesion of the lower limb arterial bed.

The distribution of patients by localization of lower limb artery segment lesions is presented in Table II.

In patients with combined arterial bed involvement, in addition to SFA stenting, endovascular revascularization of other affected segments was performed. In cases of extensive SFA occlusions involving the popliteal artery (PA), the most "problematic" area was stented after angioplasty if residual stenosis, intimal dissections that limited blood flow in the operated segment, were observed on control arteriograms.

This study was conducted in compliance with the principles of bioethics according to the Helsinki Declaration (1964) and the Universal Declaration on Bioethics and Human Rights (Paris, 2005). All patients signed informed consent to participate in the study.

RESULTS

Technically successful were 20 (87.0%) SFA stenting operations. The first step involved intraluminal or subintimal angioplasty in the affected segment, followed by the placement of drug-eluting stents (DES) in the restored lumen of the vessel. The study included 3 (13.0%) patients who were planned for SFA stenting, but due to severe calcification, it was not possible to

perform re-entry during subintimal angioplasty and restore the lumen in the occlusion zone. In these patients with multifocal lower limb arterial bed involvement, endovascular correction of lesions proximal to the SFA occlusion zone was performed. These patients were referred to vascular surgeons for femoropopliteal bypass surgery. In the postoperative period, the patency control of the operated segment was performed using ultrasound Doppler imaging. During the study period (3 months), there were no cases of reocclusion or clinically significant restenosis at the stent level. In one case, a patient experienced the recurrence of clinical signs of intermittent claudication 2 months after surgery. CT angiography revealed hemodynamically significant stenosis of the SFA outside the implanted stent. Angioplasty of the SFA stenosis was successfully performed for the patient.

Clinical outcomes of SFA stenting 3 months after surgery are presented in Table III. Limb support function was preserved in all patients throughout the observation period. "Minor" foot amputations were performed in 7 patients (35%) with diabetic gangrene, for whom endovascular revascularization of the femoropopliteal and tibial segments was part of the surgical treatment.

DISCUSSION

Endovascular methods of limb artery revascularization have several advantages over open vascular interventions: minimally invasive, no postoperative wound, the ability to control and correct inflow and outflow arteries during surgery, and the possibility of repeated operations.

In the context of war, with the possibility of missile or air strikes, instability in infrastructure operation, and power supply, the advantages of minimally invasive surgical interventions are of particular importance. After endovascular revascularization of the lower limbs using Angioseal to close the puncture hole, the patient can move on the day of surgery and therefore can be evacuated, can independently go down to a bomb shelter, and can seek outpatient treatment at their place of residence without a high risk of complications.

Potentially, endovascular revascularization of limb arteries can significantly replace "open" vascular surgeries. To achieve this, the technical success and long-term outcomes of minimally invasive procedures should match those of "open" bypass surgeries.

A pressing issue in performing endovascular interventions in the femoropopliteal segment is restenosis in the long term. Although studies do not demonstrate a statistically significant advantage of any revascularization method for the femoropopliteal segment regarding survival or limb preservation [7], restenosis is a significant clinical problem affecting the patient's quality of life. Bare-metal stenting (BMS), drug-eluting stents (DES), and drug-eluting balloon (DEB) angioplasty have a statistically significant advantage over angioplasty in the medium and long term [1, 2, 4, 8]. However, data on the effectiveness of BMS, DES, and DEB are limited and conflicting, requiring further research. Another possible option for optimizing the long-term results of endovascular revascularization of the lower limb arteries is the combination of stenting with bare metal stents (BMS) and the use of a drug-eluting balloon catheter (DEB). Comparing the effectiveness of these methods with each other and with "open" bypass surgeries will help to choose the optimal strategy. In this case, not only clinical efficacy but also financial costs, which are necessary to achieve a similar result, are important.

The positive experience of using DES for femoropopliteal segment lesions makes this method a promising minimally invasive alternative to femoropopliteal bypass surgery. If the long-term results of conventional angioplasty of the femoropopliteal segment, according to the literature, can be compared with the results of allografting, the use of DES and DEB can be compared with autogenous venous bypass [1, 2, 9] with significantly lower postoperative complication rates [9]. The development of endovascular intervention technologies and the accumulation of experience will enable determining the optimal tactics for using each of the mentioned methods.

CONCLUSIONS

1. Implantation of drug-eluting stents is an effective method of endovascular revascularization for femoropopliteal segment lesions.
2. To compare the results of drug-eluting stent implantation with other revascularization methods for femoropopliteal segment lesions, it is necessary to accumulate more data and increase the duration of observation.

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ORIGINAL ARTICLE

ANALYSIS OF DEFECTS IN THE DIAGNOSIS OF TRAUMATIC BRAIN INJURY FOR THE DECEASED WITHIN 24 HOURS FOLLOWING ADMISSION

DOI: 10.36740/WLek202305213

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ABSTRACT

The aim: To conduct the analysis of medical records with the diagnosis of traumatic brain injury for the deceased within 24 hours following admission to Clinical Emergency Hospital.

Materials and methods: The study was aimed at a retrospective analysis of 102 cases of the lethality of the deceased within 24 hours following admission to Clinical Emergency Hospital for 2012-2019 in cases of traumatic brain injury. Medical histories of the deceased and data from the forensic autopsy had been analyzed.

Results: There were 62 cases (60.8%) of isolated traumatic brain injury, and 40 cases (39.2%) of combined traumatic brain injury. The following defects were identified in the diagnosis: absence of a complete description of the local status with external injuries on the head, absence of a complete and qualitative assessment and objectification of hemodynamics and the function of external breathing using laboratory indicators and electrocardiography, absence of neuroimaging.

Conclusions: The percentage of diagnostic defects prevailed among traumatic brain injury patients who died from acute blood loss. The maximum number of diagnostic defects for the patients with traumatic brain injury was observed in the polytrauma department, and the minimum - in the neurological department. The maximum number of defects of a diagnostic nature as a whole fall on those patients who were admitted to the hospital in the interval I - 6:00 a.m. – 9:59 a.m. and in the interval IV - 6:00 p.m. – 9:59 p.m.

KEY WORDS: traumatic brain injury, diagnosis defects, examination

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INTRODUCTION

Traumatic brain injury (TBI) is a significant public health problem that can lead to high morbidity and mortality rates. One of the significant problems in the diagnosis of TBI is associated with acute blood loss. Dali, Zhou, and Chen [1] identified significant genes and pathways associated with acute blood loss after TBI. However, identifying and treating blood loss in TBI patients is a complex process that requires careful evaluation and monitoring.

Another critical issue in TBI diagnosis is daily mortality rates. Costa et al. [2] found that early mortality rates were high in severe TBI patients, and they identified predictors of mortality, such as age, admission Glasgow Coma Scale score, and injury mechanism.

Diagnostic defects are another problem in TBI diagnosis. Several studies have examined the clinical characteristics and prognosis of TBI patients [3-6], but there is still a need for improved diagnostic tools and protocols. Chen et al. [3] studied patients with TBI combined with hemorrhagic shock and found that these patients had worse clinical outcomes than those without hemorrhagic shock. Edin and Kudrna [7] emphasized the importance of a systematic approach to TBI diagnosis and management to reduce the risk of diagnostic errors.

When conducting forensic medical examinations, experts often focus on medical documentation, especially when examining living persons.

THE AIM

In our study we conducted the analysis of medical records with the diagnosis of TBI for the deceased within 24 hours following admission to Kyiv City Clinical Emergency Hospital (hereinafter – the KCCEH).

MATERIALS AND METHODS

The study was aimed at a retrospective analysis of 102 cases of lethality for the deceased within 24 hours following admission to KCCEH for 2012-2019 in cases of TBI. In the study, we have analyzed the medical histories

(inpatient cards) of the deceased, which were stored in the archive, and the accompanying counterfoils of the Ambulance crew, as well as the results of medical reports with the data of the forensic autopsy (which were in the inpatient cards). The obtained data were subject to statistical processing using the STATISTICA 6.0. The following statistical indicators were determined: arithmetic mean (M), standard deviation (SD), number of cases (N, n), frequency (P) of occurrence and 95% confidence interval (95% CI). The statistical significance of the differences between the two compared values was assessed by the Student's test (t). The level of statistical significance for the study is $p \leq 0.05$.

RESULTS

Among the deceased were 68 (66,7 ± 9,1%) male and 34 (33,3 ± 9,1%) were female.

There were 62 cases (60,8 ± 9,5%) of isolated TBI, and 40 cases (39,2 ± 9,5%) of combined TBI. So, a total of 64 (62,7 ± 9,4) cases resulted in death from the direct consequences of TBI (brain swelling with dislocation, hemorrhages in the brain stem, head destruction, etc.), of which 62 cases were due to isolated TBI and 2 cases were due to combined TBI. 38 (37,3 ± 9,4%) cases have resulted in death from acute blood loss (including shock), which accounted for 95,0 ± 6,8% of all deaths with combined TBI.

The average age of the deceased patients who died directly from TBI was 41,5 ± 11,7 years. Among the deceased, 43 (67,2 ± 11,5%) were male and 21 (32,8 ± 11,5%) were female. The average age of the deceased: for men – 38,2 ± 10,8 years, for women – 43,61 ± 11,3 years.

The average age of those who died from acute blood loss was 35,25±10,3 years. Among the deceased, 27 (71,1 ± 14,4%) were male and 11 (28,9 ± 14,4%) were female. The average age of the deceased: for men – 32,2 ± 8,5 years, for women – 37,5±10,4 years.

Alcohol intoxication was ascertained in 74 cases, which amounted to 72,5 ± 8,7%, and its absence - in 28 cases, which amounted to 27,5 ± 8,7%. For the patients who died from TBI, the number of cases of alcohol intoxication was 52 cases (81,3 ± 9,6%). Among patients with TBI who died from acute blood loss – 22 cases (57,9 ± 15,7%).

Hospitalization of all patients by referral: emergency medical care was assigned in 96 cases (94,1 ± 4,6%), to a polyclinic - in 6 cases (5,9 ± 4,6%). When distinguishing patients depending on the causes of death, the following was found: 3 (4,7 ± 5,2%) cases of patients who died from TBI, and were sent to the hospital by referral from outpatient polyclinic institutions, and by referral from the staff of the same emergency hospital – 61 (95,3 ± 5,2%) observations. There were 3 (7,9 ± 8,6%) cases of patients with TBI who died from acute blood loss, and were referred to the hospital by outpatient polyclinic institutions, and by referral from the staff of the same emergency hospital – 35 (7,9 ± 8,6%) observations.

The discrepancy between the diagnosis established by the medical staff at the pre-hospital stage and the forensic diagnosis was observed in a total of 22 cases (21,6 ± 8,0%), and coincidence - in 80 cases (78,4 ± 8,0%).

When evaluating the description of the patient's local status, namely the external bodily injuries on the head, the next volume and quality were taken into account: the description of the morphological features of the injuries: color, edges, ends of the wounds, deposition, size, the presence of a crust, etc. Therefore, an incomplete description or its absence was observed in the vast majority of cases - 92 (90,2 ± 5,8%). The description of external injuries plays an essential role in the forensic assessment of TBI, because it provides information about the mechanism of injury, etc. Moreover, in case of death from TBI, the lack of description of external injuries on the head amounted to 56 cases (which amounted to 87,5 ± 8,1% of all cases - 64). The number of patients with TBI who died from acute blood loss has reached to 94,7 ± 7,1% (36 cases).

The absence of a complete examination by a neurologist/neurosurgeon with a clinical and neurological assessment according to standards and international scales (Glasgow Scale, etc.) was noted in 78 cases, which amounted to (76,5 ± 8,2%), and moreover, for the patients who died directly from TBI, the absence of such examination amounted to (46 cases (71,9 ± 11,0%); and 32 cases were related to the patients with TBI who died from acute blood loss, accounting for 84,2 ± 11,6%.

The assessment and objectification of hemodynamics and the function of external breathing using laboratory indicators and ECG was not carried out in 64 cases (62,7 ± 9,4%). For the patients who died from TBI, the specified assessment and objectification were not performed in 40 cases, which were 62,5 ± 11,9% of the total number of cases (64); for the patients with TBI who died from acute blood loss, none of this was performed in 24 cases, which accounted for 63,2 ± 15,3% of the total number of cases with isolated TBI (38).

The neuroimaging (CT/MRI, skull X-ray, etc.) wasn't performed in 70 cases, which was 68,6 ± 9,0% of all cases. For the patients who died directly from TBI, the lack of neuroimaging methods was noted in 36 cases (56,3 ± 12,2%). For the patients with TBI who died from acute blood loss, the absence of neuroimaging tests was noted in 43 cases, accounting for 89.5 ± 9.8% (Figure 1).

The lethal cases were ascertained in patients treated

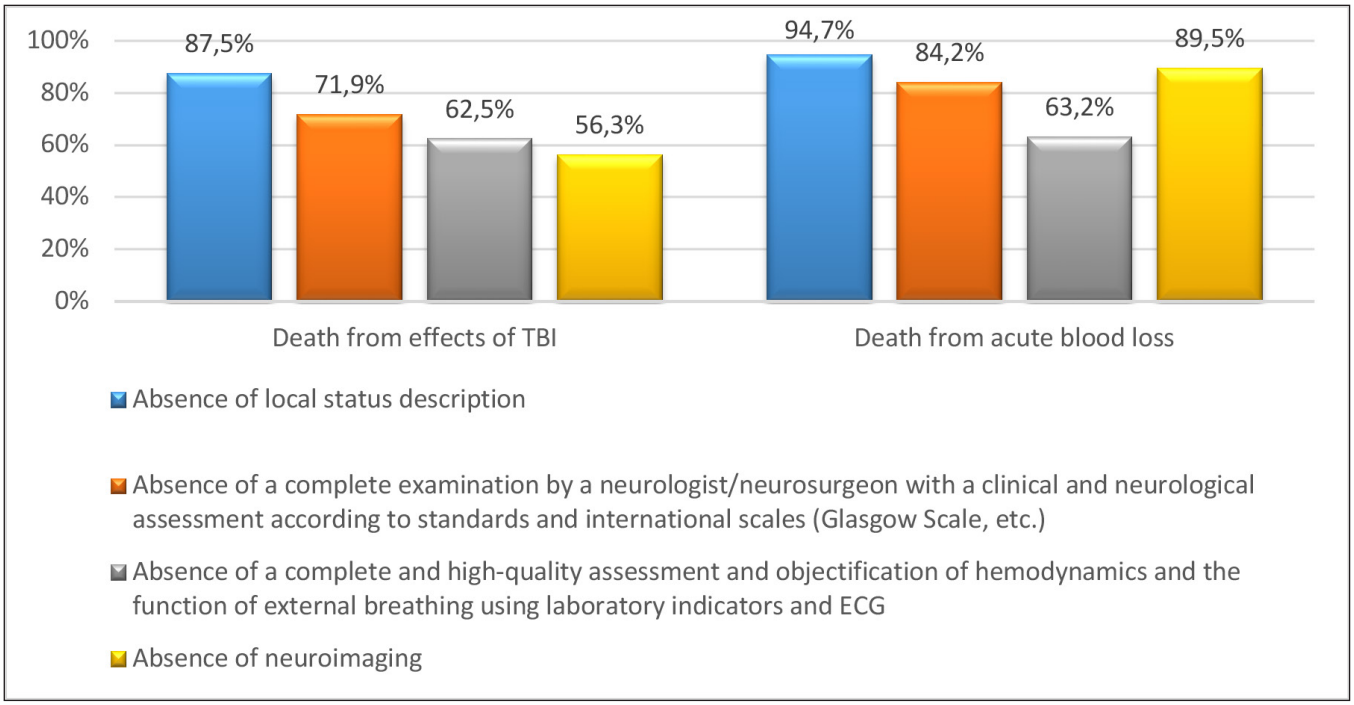

Fig. 1. Distribution of defects in diagnostic measures for deceased within 24 hours following admission from the effects of TBI and from acute blood loss, %

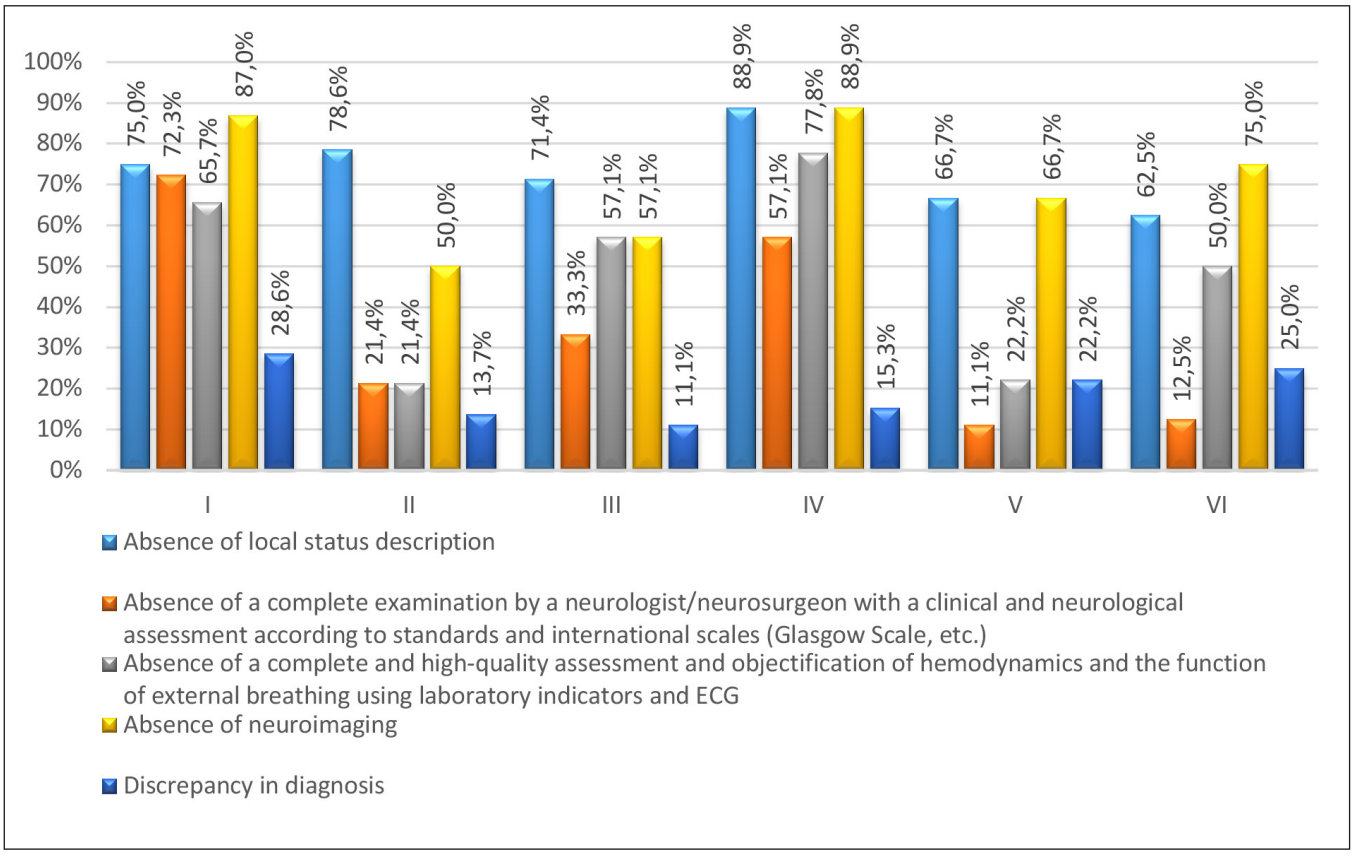

Fig. 2. Distribution of diagnostic defects for deceased within 24 hours following admission from TBI, depending on the time of admission to the hospital, %

in the following departments: polytrauma, neurosurgical department – 58 (56.9 ± 9.6%) cases, which is statistically significantly more than in the polytrauma department ($t = 3.79$, $p < 0.001$) - 32 (31.4 ± 9.0%) observations and the neurological department ($t = 7.71$, $p < 0.001$) – 12 (11.8 ± 6.3%) observations. (See Table I)

Therefore, the difference in diagnoses in the polytrauma department prevailed over other departments by almost 2 times. The least number of discrepancies in the diagnosis was observed in the neurological

Table I. The frequency of diagnostic defects in the departments of patients with TBI

Department	Neurosurgical N = 58		Polytrauma N = 32		Neurological N = 12	
Defect	n	P±CI,%	n	P±CI,%	n	P±CI,%
Discrepancy in diagnosis	10	17.2±9.7	10	31.3±16.0	2	16.7±21.1
Absence of local status description	52	89.7±7.8	30	93.8±8.4	10	83.3±21.1
Absence of a complete examination by a neurologist/ neurosurgeon with a clinical and neurological assessment according to standards and international scales	43	74.1±11.3	30	93.8±8.4	5	41.7±27.9
Absence of an assessment and objectification of hemodynamics and the function of external breathing using laboratory indicators and ECG	33	56.9±12.7	25	78.1±14.3	6	50.0±28.3
Absence of neuroimaging	37	63.8±12.4	25	78.1±14.3	8	66.7±26.7

Table II. The share of patients with TBI admitted to the hospital at different times of the day with alcohol intoxication and the method of delivery.

Interval	N, abs.	Alcohol intoxication		Emergency Medical Care	
		N, abs.	P, %	N, abs.	P, %
I	28	16	57.1	28	100.0
II	8	6	75.0	6	75.0
III	18	14	77.8	16	88.9
IV	18	12	66.7	16	88.9
V	14	10	71.4	14	100.0
VI	16	16	100.0	16	100.0
In total	102	74	72.5	96	94.1

Table III. Frequency of hospitalization to departments by periods of the day

Interval	N, abs.	Neurosurgical		Polytrauma		Neurological	
		N, abs.	P, %	N, abs.	P, %	N, abs.	P, %
I	28	18	64.3	8	28.6	2	7.1
II	8	6	75.0	2	25.0	0	0.0
III	18	10	55.6	2	11.1	6	33.3
IV	18	10	55.6	6	33.3	2	11.1
V	14	7	50.0	6	42.9	1	7.1
VI	16	7	43.8	8	50.0	1	6.3
In total	102	58	100	32	100	12	100

department. All types of defects prevailed in the polytrauma department. The lack of description of the local status prevailed in the neurological and neurosurgical departments.

The largest number ($p < 0.001$) of patients who died on the first day arrived at the hospital in the 1st – 6:00 a.m. – 9:59 a.m. - (28 (27.5 ± 8.7%) patients), the smallest number ($p < 0.001$) in II – 10:00 a.m. – 1: 59 p.m. (8 (7.84 ± 5.2%) patients). Starting from 14 hours, the level of daily mortality did not change statistically significantly and was: III – 14: 00 p.m. – 5:59 p.m. (18 (17.6 ± 7.4%) patients); IV – 6:00 p.m. – 9:59 p.m. (18 (17.6 ± 7.4%) patients); V – 10:00 p.m.- 1:59 a.m. (14 (13.7 ± 6.7%) patients); VI – 2:00 a.m. – 5:59 a.m. (16 (15.7 ± 7.1%) patients).

The average age of patients admitted to the hospital in the I interval was 39.5±11.7 years, in the II interval - 38.4±10.3 years, in the III interval - 42.1±12.0 years, in the IV interval – 39.3±11.4 years, in the V interval – 45.2±14.5 years, in the VI interval – 40.2±12.9 years. The difference in age has not reached the level of statistical significance ($p > 0.05$).

The coincidence of the diagnosis did not differ statistically significantly from the time of day and occurred: in 20 (71.4 ± 16.7%) admitted patients in the I interval, 6 (75.0 ± 30.0%) patients admitted in the II interval, 16 (88.9 ± 14.5%) patients who were admitted in the III interval, 15 (85.7 ± 16.2%) patients who were admitted in the IV interval, 11 (77.8 ± 21.8%) of patients admitted

in the V interval, 12 (75.0 ± 21.2%) patients admitted in the VI interval.

When evaluating the description of the patient's local status, namely external bodily injuries on the head, the volume and quality were taken into account. Therefore, incomplete description or its absence was observed in the vast majority of cases - 92 (90.2 ± 5.8%). The description of external injuries plays a significant role in the forensic assessment of TBI, because it provides information about the mechanism of injury, etc. Moreover, in the case of death from TBI, the lack of description of external injuries on the head amounted to 56 cases (which was 87.5 ± 8.1% of all cases - 64). In patients with TBI who died from acute blood loss, the number reached 94.7 ± 7.1% (36 cases).

The lack of a complete examination by a neurologist/neurosurgeon with a clinical and neurological assessment according to standards and international scales was noted in 78 cases, which amounted to (76.5 ± 8.2%), and in patients who died directly from TBI lack of such examinations accounted for 46 cases (71.9 ± 11.0%); 32 cases concerned patients with TBI who died from acute blood loss, accounting for 84.2 ± 11.6%.

In total, among all 102 cases, assessment and objectification of hemodynamics and the function of external breathing using laboratory parameters and ECG were not performed in 64 cases (62.7 ± 9.4%). In patients who died from TBI, the specified assessment and objectification were not performed in 40 cases, which was 62.5 ± 11.9%, in patients with TBI who died from acute blood loss, they were not performed in 24, which was 63.2 ± 15.3%.

Neuroimaging wasn't performed in 70 cases, which was 68.6 ± 9.0% of all cases. In patients who died directly from TBI, the lack of neuroimaging methods was noted in 36 cases (56.3 ± 12.2%). In patients with TBI who died from acute blood loss, the absence of neuroimaging studies was noted in 34 cases, accounting for 89.5 ± 9.8%. (See Figure 2)

As can be seen from Figure 2, there are differences in conducting diagnostic measures for patients at different times of the day. The maximum number of defects of a diagnostic nature in their totality (namely: absence of a complete description of the local status with external injuries on the head, absence of a complete and qualitative assessment and objectification of hemodynamics and the function of external breathing using laboratory indicators and ECG, absence of neuroimaging), can be referred to those patients who were admitted to the hospital in the interval I and in the interval IV.

The difference in such indicators as the presence of alcohol intoxication, the department where the patients were treated, and the implementation of hospitalization by referral (Emergency Medical Care or outpatient polyclinic institutions) among those admitted in the intervals I, II, III, IV, V and VI of the day can be seen from Tables II and III.

All patients with TBI who were admitted in the VI time period were in a state of alcohol intoxication. All patients who were admitted in the I, V, VI intervals were delivered by Emergency Medical Care teams. The maximum number of patients with alcohol intoxication was observed in interval VI, i.e. at night. The maximum number of patients was admitted to the neurosurgery department in intervals II and I, to the polytrauma department in intervals V and VI, and to the neurology department in intervals III and IV. All the patients who were brought to the hospital by the Ambulance crew brigade were admitted in intervals I, V, and VI.

The largest number of patients who died per day wa delivered to the neurosurgery department in the first period of the day, to the polytrauma department in the first and sixth periods, and to the neurological department in the third period.

DISCUSSION

According to a study by Li et al., the most common diagnostic defects in TBI are the absence of a CT scan and the absence of an examination by a neurosurgeon or neurologist [8]. Another study by Lee et al. found that the most common diagnostic defect in TBI was a lack of documentation of the neurological exam [9]. In a study by Feng et al., it was found that diagnostic defects were more common in patients with severe TBI [10]. A study by Alharthi et al. found that the most common diagnostic defects in TBI were a lack of documentation of vital signs and Glasgow Coma Scale (GCS) scores [11]. Finally, a study by Mu et al. found that the most common diagnostic defect in TBI was a lack of documentation of the mechanism of injury [12]. Comparing these findings to our study, it appears that there is some overlap in the most common diagnostic defects observed. Like Li et al., we found that the absence of a CT scan and examination by a neurosurgeon or neurologist were among the most common defects. However, our study also identified the absence of an assessment of hemodynamics and breathing function, which wasn't mentioned in the other studies reviewed.

Our study also found that cases with the presence of alcohol intoxication prevailed among all patients. This finding is consistent with the study by Dali et al. [1], which reported that alcohol use was associated with an increased risk of acute blood loss after TBI. Moreover, our study found that the maximum number of diagnostic defects in patients with TBI was observed in the

polytrauma department. This finding is consistent with the study by Alharthi et al. [11], which reported a high incidence of diagnostic errors in TBI patients. However, our study further elucidated that the minimum number of diagnostic defects was observed in the neurological department, which highlights the importance of considering the expertise of the medical staff in the diagnostic process.

Our study also found that the maximum number of defects of a diagnostic nature as a whole falls on those patients who were admitted to the hospital for the times of medical staff shift changes. This finding is consistent with the study by Lee et al. [9], which reported a lack of documentation of the neurological exam in TBI patients during shift changes.

Finally, our study found that the largest number of patients who died during the 24-hour period were brought to the neurosurgery department in the 6th hour of the 1st day. 00 min. - 9 hours 59 minutes, to the polytrauma department - in the I and VI intervals - 2 hours. 00 min. - 9 hours 59 min., and in the neurological department - in the III interval - 2 p.m. 00 min. - 5 p.m. 59 min. This finding is consistent with the study by Mireles-Cabodevila and Murugan [5], which reported that mortality prediction in TBI patients could be improved by considering the timing of injury and admission.

CONCLUSIONS

1. In the structure of the lethality for the deceased within 24 hours following admission for the patients with TBI, there are 2 times more men than women, and the average age of the deceased was able to work. Cases with the presence of alcohol intoxication prevailed among all patients.
2. The maximum number of diagnostic defects for the patients with TBI was observed in the polytrauma department, and the minimum - in the neurological department. This confirms the difficulty of diagnosing exactly for the combined TBI, and is also important when conducting forensic examinations, because the existing defects at a later time prevent the establishment of the mechanism, age of the injury, etc.
3. The maximum number of defects of a diagnostic nature as a whole fall on those patients who were admitted to the hospital in the interval I - 6:00 a.m. – 9:59 a.m. and in the interval IV - 6:00 p.m. – 9:59 p.m. (the hours of the shift change of the medical staff).
4. The largest number of patients who died per day was delivered to the neurosurgical department in the first period of the day, 6:00 a.m. – 9:59 a.m. (in the morning), to the polytrauma department - in the I and VI intervals - 2:00 a.m. - 9:59 p.m. (at night and in the morning), and in the neurological department - in the III interval - 2:00 p.m. – 5:59 p.m. (during the day).

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Given that the study was conducted on archival material of deceased patients, informed consent wasn't taken. The study was approved by the local Commission for Bioethical Expertise and Research Ethics of Bogomolets National Medical University. This scientific work is an individual research work "Expert-diagnostic system of objectification of forensic medical examination of traumatic brain injury" (state registration number: 0123U101528, term: 2023–2026) and was carried out on the basis of the Department of Forensic Medicine and Medical Law of Bogomolets National Medical University.

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ORIGINAL ARTICLE

THE MANAGEMENT OF THE VICTIMS WITH GUNSHOT WOUNDS OF THE EXTREMITIES WITH EXTENSIVE DEFECTS OF THE SOFT TISSUES AT THE LEVEL OF QUALIFIED MEDICAL CARE. CASE-SERIES

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ABSTRACT

The aim: To highlight the original experience of diagnosis and treatment of patients with gunshot wounds of the extremities with extensive defects of the soft tissues.

Materials and methods: The total number of treated patients with massive gunshot wounds from February 2022 to March 2023 was 60 males. Basic laboratory tests, X-rays of the affected limbs were performed to all patients. USS of the vessels with color Doppler was performed to those casualties who had no peripheral pulses on the wounded extremity. All injured persons underwent wound debridement and fasciotomy on the day of admission, 8 more casualties underwent surgical interventions on the major vessels and nerves.

Results: Good treatment outcomes for patients with extensive soft tissue injury were achieved by early surgical intervention to remove non-viable tissue. Limb preservation was achieved in 98.3% of cases.

Conclusions: The study's conclusion emphasizes the importance of a multidisciplinary approach to treating patients with gunshot wounds to the limbs with extensive soft tissue injury. Early surgical interventions with the removal of non-viable tissues are necessary for good outcomes. Revascularization of the affected limb is essential in case of major vessel injury if there is no thread to the life.

KEY WORDS: gunshot wounds of the extremities, extensive soft tissue defects, injury to the neurovascular bundle, limb salvage surgery, vacuum-assisted wound therapy

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INTRODUCTION

Gunshot wounds to the lower extremities are the most common among all gunshot wounds in the war time and account for 70-75% according to various authors [1-3]. The frequency of lower limb injuries is twice as common as upper limb injuries. As extremity injuries are evaluated, each of the four functional components (nerves, vessels, bones, and soft tissues) must be considered individually and together [4]. To achieve the best treatment outcomes, a multidisciplinary approach involving vascular surgeons, orthopedics, plastic surgeons, and rehabilitation specialists is necessary. In modern medicine, limb salvage is preferred in cases of severe gunshot injuries [3]. While maximum efforts are directed towards avoiding amputation in cases of extensive upper limb injuries, severe lower limb injuries can pose a threat to life and dictate the necessity of amputation under such circumstances [1,2]. Measures for early return of limb function after reconstruction are necessary but may not always be implemented.

THE AIM

To improve the diagnostics and treatment of the casualties with gunshots of the extremities with extensive soft tissue injury.

MATERIALS AND METHODS

From February the 24th, 2022 to March the 23d, 2023, the case-series 60 wounded male patients with gunshots of the lower extremities and extensive defects of the soft tissues were treated in the surgical department of the Zaporizhzhia Military Hospital. All sixty patients were men aged 21 to 63 years, with a mean age (mean (M) ± standard deviation [SD]) of 36,2±9,7 years.

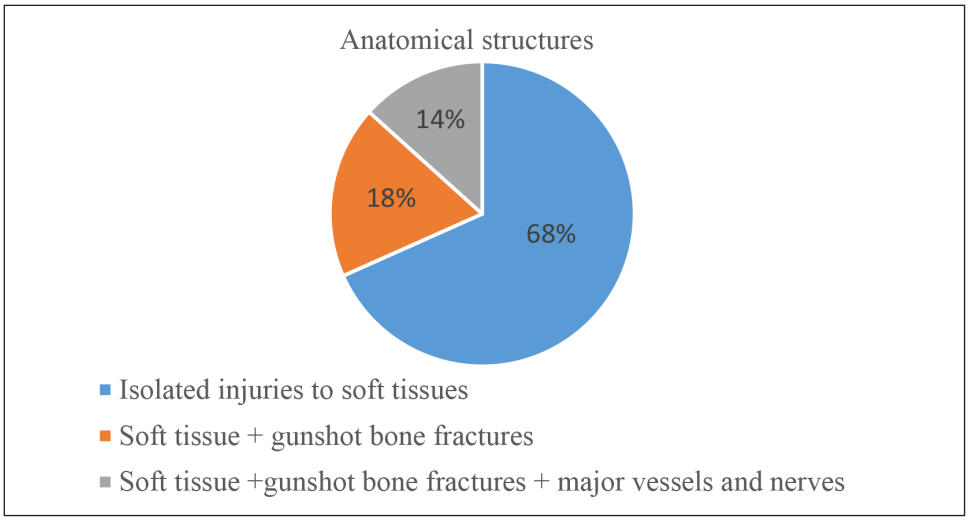

Fig. 1. Distribution of the wounded by injuries of different anatomical structures of the limb.

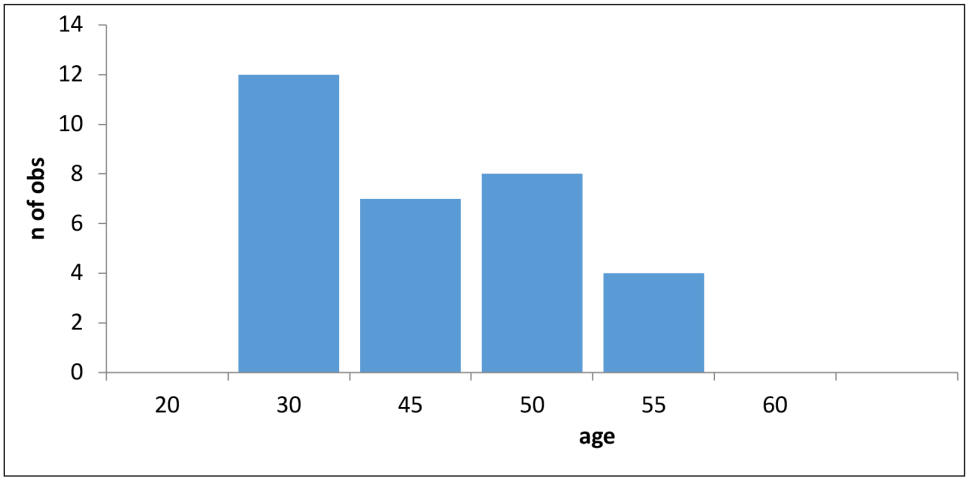

Fig. 2. Histogram of the distribution of patients by age.

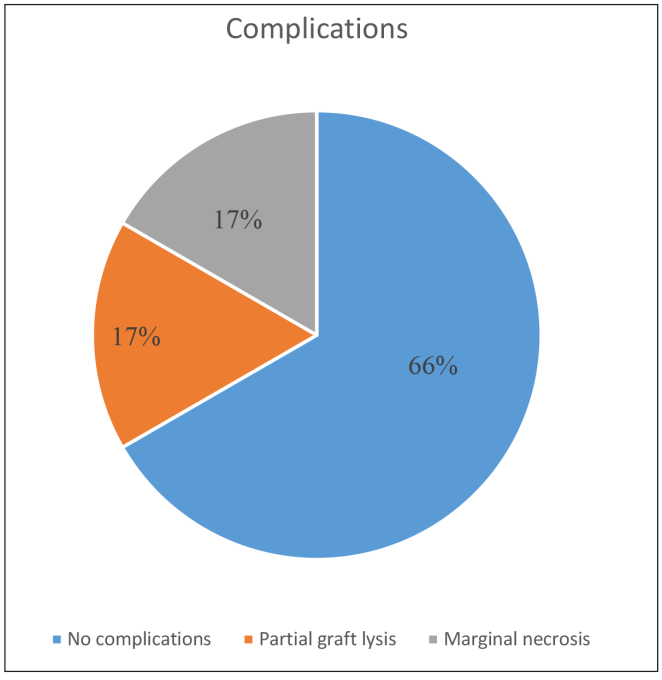

Fig. 3. The outcomes of the soft tissue defects closure.

The general condition was considered severe in 19 wounded patients, while the rest of the 41 were of moderate to severe condition. All the patients received initial medical aid on the battlefield, then at stabilization points, and later medical assistance in advanced surgical groups (medical-surgical teams, advanced surgical groups). Combined and associated injuries were accounted in 19 (32%) of the wounded militaries, while isolated limb injuries occurred in the rest of the 41. All patients gave consent for the processing of personal data. The types of associated injuries are presented in Table I.

Isolated defects of the soft tissues were present in 41 (68%) of cases, 11 (18%) were diagnosed with gunshot bones fractures, and in 8 (14%), there were gunshot fractures of large tubular bones with damage to major vessels and nerves (Figure 1).

Seventeen (28,3%) patients had comorbidities (Table II).

Upon arrival of the casualties and the triage, an assessment of their general condition and injuries was carried out. Urgent measures were taken according to the MARCH protocol. After physical examination and blood tests, the casualties underwent an X-ray examination of the affected limbs. Other additional diagnostic methods (FAST protocol, CT of the head, neck, chest,

Table I. Associated injuries in patients with gunshot wounds of the extremities with extensive soft tissue injuries

Associated injuries	Number of patients
Head injury	5
Acustic trauma	6
Hemopneumothorax	2
Eardrum rupture	2
Injury to the ligaments of the limbs	2
Total	15

Table II. Comorbidities in the patients with extensive soft tissue injury

Comorbidities	Number of patients
High blood pressure	6
Coronary artery disease	4
Chronic obstructive pulmonary disease	3
Blood diseases	1
Peptic ulcer	1
Benign prostatic hyperplasia	1
Others	1
Total	17

Table III. Surgical procedures performed on the patients

Type of surgery	Number of patients
Wound debridement	42
Wound debridement + NPWP	5
Wound debridement + External fixation of the fractures	6
Wound debridement + intervention to major vessels + External fixation of the fractures	6
Amputation	1
Total	60

abdomen, pelvis, and ultrasound examination with color doppler) were performed as indicated. Special attention was paid to ultrasound examination with color doppler using the VSCAN AIR device, which was performed on 48 patients. Arterial and venous blood flow in the distal parts of the limbs upon admission of the casualties were assessed. Before the closure of soft tissue defects with skin-muscle flaps, a thorough US examination of the vascular pedicles with marking was performed.

Patients with severe general conditions were stabilized in the intensive care room. All casualties underwent surgical interventions on the day of admission after performing basic diagnostic tests and stabilizing severe conditions. The types of surgical interventions are presented in Table III.

The decision regarding salvage VS amputation of the injured limb with major vessels injury was made using Mangled Extremity Severity Score (MESS). Primary revascularization using autologous venous graft was performed in all eight cases of injuries to major vessels, with no use of temporary shunts. An external fixation device was applied to 12 (20%) of patients with gunshot fractures of long bones. Early closure of soft tissue defects was performed in 6 (10%) of patients, using split-thickness skin grafting in 4 cases, keystone flap reconstruction in 1 case, and a rotated flap on a vascular pedicle in 1 case.

Negative pressure wound therapy (NPWT) was performed in 5 (8.3%) of the patients at this level. After the completion of the surgeries, 31 (52%) of the injured militaries were sent to the next level of care within 24-72 hours. The average length of stay for the remaining 29 patients was 8 days. Further observation was carried out through telephone interviews with the patients and retrospective analysis of medical records.

Statistical data analysis was conducted in the program Statistica 13. The data were checked for normality of distribution according to the Shapiro-Wilk criterion. Quantitative variables were presented as M±SD, qualitative ones – as percentages. The statistical significance of the differences between the groups was established by the Student's criterion. The level of statistical significance was $p < 0.05$.

RESULTS

All sixty patients were men aged 21 to 63 years, with a mean age (mean (M) ± standard deviation [SD]) of 36,2±9,7 years (Figure 2).

The figure 2 shows that the distribution has a positive asymmetry, that is, a shift towards older age, but the deviation from the normal distribution law has not acquired statistical significance ($p>0.05$ according to the Shapiro-Wilk criterion).

It should be noted that patients with comorbidities were statistically significantly older in age, their average age was 46,5±6.3 years ($p = 0.0001$ compared with the entire group of patients (36,2±9,7)). The average age of those who did not have comorbidities was 32.1±7.6.

After initial evaluation 34 patients had absent pulse on the dorsalis pedis and posterior tibial arteries, therefore injury to the major vessels was suspected. US doppler revealed the absence of the central blood flow (only collateral flow was present) in 8 patients. Injury to major vessels was confirmed intraoperatively in 7 of those, therefore the sensitivity of the USS was 87,5%. One patient whose USS of the vessels was normal was diagnosed intraoperatively with the side injury of the superficial femoral artery; thus, false negative result of the method was 12,5%.

Surgical debridement, fasciotomy, and external fixation of the fractured bones were uneventful in all patients. 4 (66%) patients who underwent primary wound closure had no graft complications. The grafts were viable and the wounds healed by primary tension. One patient with split-thickness skin graft developed partial lysis of the graft. One patient developed marginal necrosis of the flap on the vascular pedicle. Both underwent secondary grafting with good outcomes. Outcomes of soft tissue defects closure in Figure 3.

Surgical revascularization was successful in 7(87,5%) cases. One patient developed thrombosis of the popliteal artery distal to the anastomosis developed, which required reoperation, vascular exploration and thrombectomy. Below knee amputation was performed in one case due to massive soft tissue loss. All 5 patients who received NPWD tolerated the procedure well and continued at the next level. There were no mortality cases during the treatment period in our facility.

DISCUSSION

Fast diagnostics of the injuries in wounded militaries with gunshots to the extremities is essential in achieving the best outcomes, limb selvage and good functionality. A plain X-ray of the injured limb and basic laboratory tests is enough for diagnosis unless an injury to the neuro-muscular bundle or associated injury is suspected. In our study ultrasound scan with colored doppler was performed in case of absent pulses on the dorsalis pedis/posterior tibial artery in 34 patients. The sensitivity of the method was high (87,5%). The false negative result was in one case, therefore USS with color doppler is highly useful in case of a gunshot wound of the extremities with extensive soft tissue injury if an injury to the major vessels is suspected. Speed, noninvasiveness, and accessibility of the USS make the diagnosis quick and lead to improvement of the limb selvage.

The urgent surgical removal of non-viable tissue is a necessary condition for achieving best treatment outcomes in patients with extensive soft tissue injury [13]. In our study, all patients underwent surgery on the day of hospitalization, including critically ill patients after stabilization of their general condition. Application of external fixation device (EFD) in case of associated fracture of the long bones is necessary not only for restoring bone integrity but also for preventing soft tissue injury to the affected limb [4,5], creating more favorable conditions for faster wound healing, regardless of whether plastic closure of defects was performed or not. We performed wound debridement and fasciotomy to all patients on the day of admission including those in severe condition after the stabilization in intensive care room. In our study, external fixation device was applied to all twelve patients with gunshot fractures, allowing us to focus on treating soft tissue defects during the postoperative period. Revascularization of the limb in case of damage to major arteries is a priority if limb selvage surgery is feasible (less than 7 points according to the MESS scale) [7]. In our study, temporary vascular shunts were not used as the patient's stable general condition, absence of mass casualty situation, available equipment, and qualifications of vascular surgeons allowed for primary revascularization, which is a necessary condition according to most authors [8,9]. Amputation of the lower limb was performed in one case. The indication was extensive soft tissue loss and a negative prognosis for the functional state of the limb. We agree with the majority of authors' opinion [10, 14, 15] that prosthetic replacement of the lower limb provides better functional outcomes than limb salvage surgery when there is extensive muscle loss and significant nerve injury. Early closure of the soft tissue defects has reduced the time for wound healing and expedited the return to military duty despite of minor complications (33% of cases) like split-thickness graft lysis and partial necrosis of the rotated flap on the vascular pedicle. NPWT is a highly effective method of treating extensive soft tissue defects in the absence of contraindications [11,12]. In our study, NPWT was performed in five patients, and the vacuum dressing was applied on the second day after surgery - we believe that the immediate use of a vacuum dressing after surgery is not safe due to the increased risk of bleeding from the "fresh" wound. In cases of extensive extremities soft tissue injury due to gunshots the efforts are made to avoid amputation. Good outcomes were achieved in 93% of cases as a result of chosen diagnostic plan and surgical strategy in gunshot wounds of the extremities with extensive soft tissue injury. Most of the patients were evacuated in stable condition, and vacuum dressings were used on further levels of care.

CONCLUSIONS

1. Management of patients with gunshot wounds to extremities and extensive defects of soft tissues is a challenging problem that requires a multidisciplinary approach. Basic diagnostic methods are sufficient for making a treatment plan. USS with colored doppler is sensitive (87,5%) in diagnostics of injury to major vessels; false negative results are rare (12,5%).
2. Extensive soft tissue injury and gunshot bone fractures made the use of external fixation devices, NWPT, and early wound closure with a flap necessary to speed up the recovery time and the time to return to military duty.
3. Good outcomes were achieved in 93% of cases as a result of chosen diagnostic plan and surgical strategy in gunshot wounds of the extremities with extensive soft tissue injury at the level of qualified medical care.

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The ethical approval was obtained from Bioethics Committee of the Zaporizhzhia State Medical and Pharmaceutical University. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008, as well as the national law. Informed consent was obtained from all the patients included in the study.

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ORIGINAL ARTICLE

MANAGEMENT OF MINIINVASIVE TREATMENT OF PRIMARY VARICOSE SUPERFICIAL VEINS

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ABSTRACT

The aim: Determination of the optimal method for surgical correction of stages C2-C6s varicose superficial veins.

Materials and methods: The treatment results of 228 patients with stages C2-C6 of primary varicose according to the CEAP classification using thermal and non-thermal treatment methods were analyzed.

Results: All patients underwent operations under the control of ultrasound scanning. In patients after EVLA, total trunk obliteration was detected in 148 patients (98.7%) after 1 week, and in 100% after a year. In 2 patients, reflux was diagnosed in the PDSV and in the ZDSV after 1 week. In patients after RFA, inflow reflux on the leg was in 1 patient (5.2%), in others - complete obliteration (18 patients - 94.7%). In patients after MOCA, recanalization was performed in 5 patients (19.2%) with a control ultrasound investigation after 1 month. In patients after cyanoacrylate obliteration, inflow reflux on the leg after 1 month was in 2 patients (14.2%). In patients who underwent UGS of the GSV trunk, 5 patients (33.3%) had persistence of pathological reflux after 1 month with control ultrasound. All corrections were performed using Foam form sclerotherapy.

Conclusions: EVLA is the most effective method of treating varicose veins and gives the best long-term results. The advantage of non-thermal methods is the lack of influence on paravenous structures and no need for tumescent anesthesia, which is important in case of an allergic history. After applying cyanoacrylate, there is no need for mandatory compression. The advantage of foam scleroobliteration is its lowest cost among all methods. Foam sclerotherapy was the method of choice for correction of postoperative treatment.

KEY WORDS: primary varicose veins, endovenous laser ablation, mechanochemical ablation, radiofrequency ablation, foam sclerotherapy, injection of bioglue

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INTRODUCTION

Chronic venous disease is a significant spectrum of morphological and functional disorders of the venous system that last for a considerable duration and are characterized by symptoms or signs that require examination or treatment.

According to various worldwide data, the prevalence of varicose transformation of the lower extremities' superficial veins in certain age groups ranges from 21.8% to 72% of the population in developed countries.

With progression, the disease can significantly worsen the quality of patient's life by causing trophic changes in the skin in the form of pigmentation, lipodermosclerosis, skin atrophy, the formation of ulcers that, in the absence of treatment, recur (stages C4-C6), and complicated forms of varicose transformation (phlebitis and thrombophlebitis, bleeding from varicose varices) [1].

Varicose veins are an economically significant problem, due to the increase in morbidity among able-bodied people, which can cause temporary loss of working capacity or stimulate signs of disability in patients.

The "gold standard" for the diagnosis of varicose disease of the superficial veins today throughout the world is the ultrasound duplex scanning of the venous system, during the last decades [2], thanks to the spread of various techniques of minimally invasive methods, the treatment of primary varicose has gained a high level of development in all developed countries. These methods include two groups: with the use of thermal energy and non-thermal puncture. Thermal methods include endovenous laser ablation (EVLA), endovenous radiofrequency ablation (RFA), and endovenous electrowelding. Non-thermal methods include foam scleroobliteration (UGS), endovenous mechanochemical obliteration (MOCA) and adhesive methods of vein closure [3].

All of the above minimally invasive techniques are puncture-based, which allows for minimizing the need for anesthesia (making it possible to perform under

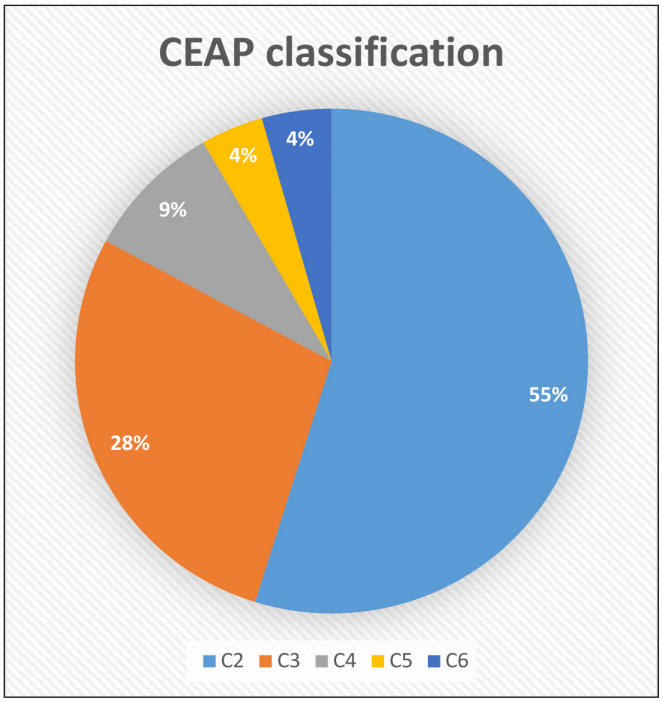

Fig. 1. The distribution of cohorts as to the stage of severity (CEAP classification).

local anesthesia, or without it at all) and for widely implementing them in outpatient settings, taking into account the shorter duration of the surgical intervention itself and the quick recovery period of the patient.

It should be noted that today there are no clear algorithms for choosing a specific minimally invasive technique for this or that case and stage of varicose. Active research is ongoing all over the world to minimize the trauma of treatment, maximize the patient's quality of life, and to optimize the cost of treatment.

THE AIM

The purpose of the work is to determine the optimal method of stages C2-C6s lower extremities varicose veins surgical correction.

MATERIALS AND METHODS

The results of the treatment of 228 patients with primary superficial varicose C2-C6s according to the CEAP classification, operated on using various minimally invasive puncture techniques in the period from 2020 to 2022 on the basis of the surgical department of the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department were analyzed.

The general sample was formed retrospectively, based on the analysis of using one or another minimally invasive method in patients. The authors adhered to the principles contained in the 1964 Declaration of Helsinki and their latest amendments. The permission to conduct the study and the study protocol were approved of by the bioethics committee of the Institution.

Inclusion criteria: patients with symptoms and clinical signs of the lower extremities' varicose, confirmed by ultrasound scanning; patients with stage C2 - C6s. Exclusion criteria: patients with deep vein thrombosis or thrombophlebitis; patients with signs of malformations. By gender, there were 146 (64%) women and 82 (36%) men. The age range was from 20 to 86 years.

The majority of patients complained of optically visible varicose veins and venous networks of the lower extremities, some patients complained of increased leg fatigue, swelling and heaviness that progressed after physical exertion or in the evening, some had changes in the skin of the legs in the form of trophic ulcers . The distribution of cohorts as to the stage of severity (CEAP classification) was as follows: stage C2 - 125 patients (54.8%), C3s - 64 patients (28%), C4s - 20 patients (8.8%), C5s - 9 patients (4%), C6s – 10 patients (4.4%). (Fig. 1).

It can be seen from the Fig. 1, that the largest number of patients belonged to the C2 of the CEAP classification, that is, without the presence of chronic venous insufficiency.

During the initial examination, the patients had to undergo an ultrasound duplex scan of the lower ex-

Table I. Groups of patients were formed depending on the selected and performed minimally invasive method and comparative results are shown.

Method of treatment	Number of patients	Anaesthesia tumescent	Compressive therapy after operation	Recanalization on USDS 1st week after	Other complications
EVLA	150 (65,8%)	Modified cold Klein's solution	Yes, 1 month	2 patients – in the AASV or PASV (1,3%)	No
RFA	19 (8,3%)	Modified cold Klein's solution	Yes, 1 month	1 patient (5,2%)	No
MOCA	26 (11,4%)	None	Yes, 1-1,5 month	5 patients (19,2%)	No
Electrowelding	4 (1,8%)	Modified cold Klein's solution	Yes, 1-1,5 month	Only for patients with the diameter of the proximal area more 20 mm	
Echo-controlled UGS	15 (6,6%)	None	Yes, 1-1,5 month	5 patients (33,3%)	No
Echo-controlled injection of bioglue	14 (6,1%)	None	No	2 patients (14,2%)	Temperature 37,5 degree 3 days after

tremities' venous system, which verified the presence of reflux in different segments of the GSV (188 cases - 82.5%), SSV (25 cases -11%), or in both systems (15 patients – 6.5%). The length of the pathological reflux path was: along the entire length of the GSV in 16 patients (8.5%), up to the level of m/3 leg – in 40 patients (21.3%), up to the level of u/3 leg – in 75 patients (39, 9%), to the l/3 femur – in 36 patients (19.1%), to the m/3 femur – in 21 patients (11.2%).

Pathological reflux path throughout the MPV was detected in 3 patients (12%), up to m/3 tibia - in 19 patients (76%), and up to u/3 tibia - in 3 patients (12%).

The location of the SSV (small saphenous vein) in relation to the superficial fascia of the thigh: i-type in 155 cases (82.5%), h-type in 7 (3.7%), s-type in 26 cases (13.8%). The diameter of the SSV in the area of the saphenofemoral junction was from 4 to 30 mm, and the SSV in the area of the saphenopopliteal junction was from 3.9 to 16 mm. The sizes of ulcer defects in the C6s ranged from 1.7*2.5 cm to 8.0*6.3 cm.

Among the accompanying pathologies, obesity or excess weight (BMI>25) was observed in 23 patients, severe allergic history in 14 patients, coronary heart disease in 23 patients, and endocrinological diseases in 25 patients. When choosing a specific method of operative treatment, we took into account the individual wishes of patients, after discussing with them the advantages, disadvantages, and possible complications of each method according to world data and protocols, as well as the socio-economic component.

Groups of patients were formed depending on the selected and performed minimally invasive method of pathological reflux elimination: 150 patients (65.8%) - EVLA, 19 (8.3%) - RFA, 26 patients (11.4%) - endovenous mechanochemical ablation (MOCA), 14 patients (6.1%) - using the method of echo-controlled injection of bioglue, 15 patients (6.6%) - foam echo-controlled scleroobliteration (UGS), 4 patients (1.8%) - endovenous electrowelding.

Before surgery, each patient underwent repeated ultrasound examination in the standing position to assess vertical and horizontal reflux, as well as to mark deformed saphenous veins and sites of failed perforators.

For EVLA, the "LIKA-KHIRURG" laser device of 1470 nm of continuous laser irradiation with a power of 12 W was used. For tumescent anesthesia, administration with a Nouvag DP-30 dispenser of modified Klein's solution was used.

After the intervention, all patients were fixed with compression bandages in the area of the operation with adhesive bandages of the Peha-haft type and compression knitwear.

For RFA, the COVIDIEN VNUS radio frequency generator and the ClosureFast intravenous catheter were used. A special bipolar electrode and coagulator "Swarmed" were used for electric welding.

For MOCA, the Flebogrif vein closure system was used, which consisted of a special catheter and a sclerosant solution (polidocanol). This technique does not require tumescent anesthesia, as there is no thermal damage to the surrounding paravasal tissues. The basis of the technique is mechanical damage to the inner wall of the vein (endothelium) with sharp microhooks, which open at the end of a special delivery catheter during reverse traction, and subsequently – chemical damage due to the effective action of the injected sclerosant. After this operation, it is mandatory to apply a compression bandage to the projection zone of the treated segment of the vein and wear compression knitwear.

For echo-controlled injection of cyanoacrylate, the VenaSeal and VenaBlock adhesive obliteration system was used, consisting of a special dispenser gun, an echogenic catheter and a device (5 ml) with inert cyanoacrylate glue. No compression was used.

RESULTS

All interventions were performed percutaneously using the puncture technique and monitored intraoperatively using an ultrasound linear sensor and an expert class ultrasound machine. Tumescent anesthesia, if necessary, was applied in the form of injection of modified cold Klein's solution around the trunk of the treated vein. In the presence of varicose vein tributaries, they were isolated and ligated. All patients in the postoperative period underwent scheduled control ultrasound investigations and examinations the day after surgery, after 1 week, after 1, 3, 6, 12 months.

In the group of patients after EVLA, total obliteration of the GSV trunk or SSV was detected in 148 patients (98.7%) after 1 week, and in 100% during the year. In 2 patients, reflux was diagnosed in the PDSV (1 patient) and in the ZDSV (1 patient) at the control after 1 week. In our opinion, this is due to insufficient exposure to laser irradiation in the estuarine section in the area of departure of large tributaries. Clinically, nothing bothered the patients. To correct the detected reflux, a single injection of foam sclerosant Foam form (3%) was used under ultrasound control, successful obliteration after 1 month.

In the group of patients after RFA, inflow reflux was detected on the lower leg in 1 patient (5.2%), in other cases complete obliteration was observed (18 patients - 94.7%). This is due to the fact that monoablation was performed without removing pathological tributaries up to 6 mm in diameter. At the follow-up examination, the reflux was eliminat-

ed by foam sclerotherapy. At the follow-up after 1 month, a significant decrease in the venous diameter and the absence of reflux were noted.

In the group of patients after MOCA, recanalization was noted in 5 patients (19.2%) with control ultrasound after 1 month. It was corrected by carrying out the procedure of foam scleroobliteration (3% polidocanol). Recanalization was again detected in two patients at the examination after a week. Scleroobliteration was performed a second time, successfully. A week after the correction, the degradation of the venous diameter without pathological reflux was visualized.

In the group of patients after cyanoacrylate obliteration, inflow reflux on the leg was detected in 2 patients (14.2%) at examination after 1 month. The correction was carried out by foam sclerotherapy, by single-use, successfully. According to our observations, three patients noted a short-term rise in temperature to 37 - 37.5 degrees during the next 3 days after the operation, which did not require correction.

In the group of patients who underwent echo-controlled UGS of the GSV trunk, 5 patients (33.3%) were diagnosed with the preservation of pathological reflux during the follow-up examination 1 month later with control ultrasound duplex scanning (USDS), and repeated sclerotherapy was performed. At the follow-up examination after 1 month, repeated reflux was detected in 2 patients (13.3%), and corrective sclerotherapy was performed a second time. At the subsequent follow-up, no reflux was detected.

In the group where electrowelding was performed, at the control after 1 month, a recurrence was found of GSV, the diameter of the proximal area being more than 20 mm.

Comparative results are presented in the Table I.

Patients at stage C6s were treated using the main method of EULA or RFA. The control of this patients' group was carried out once every 2 weeks during the first 2 months with modified plasmatherapy of wounds (4 procedures for each case).

Trophic defects healed completely after a month in 8 patients (80%), in 2 – ulcer defects decreased by 3 times in area after a month and completely healed 3 months after the intervention, which is probably related to a deeper skin lesion and the presence of concomitant pathology in the patients - type 2 diabetes mellitus.

Compression therapy after EULA, RFA, electrowelding techniques was used for a period from 14 days to 1 month, and in the presence of trophic ulcers, it was prescribed for the entire healing period; after MOCA and UGS, the compression knitwear was used for a period of 1 to 1.5 months. Compression therapy was not used in patients after the injection of biocyanoacrylate.

DISCUSSION

Over the past 20 years, minimally invasive puncture methods for treating the lower extremities' varicose veins have been increasingly used in the world, becoming an effective alternative to classic open surgery. Taking into account the world data and our experience, endovenous thermal methods have shown the highest efficacy and safety in the treatment of primary varicose veins, as well as the best late long-term results [4].

The purpose of thermal methods is to achieve stable occlusion of the vein lumen by the effect of thermal energy on the venous wall. Technically, each method has its own characteristics regarding the amount of energy absorbed by the vein. If all stages of the surgical intervention are followed, namely, with sufficient high-quality thermal insulation of paravenous structures with tumescent anesthesia and correct calculation of the energy amount, EULA remains the method of choice for the ablation of veins of various diameters.

Literature data indicate that a 1470 nm diode laser requires an energy density of 65-100 J/cm to obtain complete occlusion of the vein lumen within 1 year after ablation. Radiofrequency ablation and thermal ablation have a technically simpler technique due to the operation of the device itself, which, in our opinion, is more comfortable and easier for a novice phlebologist surgeon, since the device in sound mode shows the completed cycle of treating a certain length of vein. At that time, the techniques also require tumescent anesthesia-coupling of paravenous structures and larger puncture access due to the larger working diameter of the optical fiber light guide [5].

EVLA remains the operation of choice for truncal varicose veins in the world. But taking into account the need for tumescent anesthesia and the possibility of complications from thermal energy, non-thermal methods for treating vein pathology are being actively considered. For example, global research on mechanochemical ablation indicates that the technique combines physical (mechanical) damage to the endothelium at the expense of an endovenous device with the chemical effect of a liquid sclerosant. According to various data, the technique has less pronounced postoperative pain and discomfort in patients.

Regarding our data, with the correct protocol of thermal techniques, postoperative pain is practically not pronounced in our patients. But the MOCA technique is faster and required only one injection for access, unlike laser ablation, due to the absence of the need for a tumescent coupling. Therefore, intraoperative MOCA was slightly, but more comfortable for patients,

and was also the method of choice in patients with allergies to the components of the tumescent solution. According to the data of studies in the world, MOCA is the method of choice in patients with various stages of varicose disease in the presence of trunk reflux of at least 10 cm [6].

One of the first comparative studies of thermal techniques, MOCA and UGS showed better results in terms of reduced postoperative pain in patients who underwent non-thermal techniques. But research continues on the possible amount of sclerosant administration per procedure, taking into account the possible side effects of sodium tetradecyl sulfate (the most common are hyperpigmentation, skin necrosis, telangiectasia, mitting, or even venous thrombosis and anaphylaxis or pulmonary embolism). We did not notice these complications in our patients from the MOCA.

And the method of foam sclerotherapy (0.5-1%) was used as a correction method in case of recurrence or detected areas of venous incompetence after other methods, taking into account its availability, ease of use in conditions of manipulation or ligation, and short duration of the procedure. As a monotherapy, foam sclerotherapy had a higher percentage of relapses, so it required more frequent corrections (repeated procedures).

According to a review of 19 primary studies, described in 25 publications, on the comparison of thermal and non-thermal techniques in different variations for the treatment of varicose veins, in most cases mechanochemical ablation had slightly worse technical results in closing veins due to existing recanalizations. At the same time, clinical results, patient satisfaction, and improvement in quality of life were at the same level as in patients after thermal treatment methods. Regarding the technique of using cyanoacrylate glue, neither technically superior quality nor improvement in quality of life was noted in comparison with EVLA or RFA [7].

There was a slightly shorter recovery period after non-thermal methods compared to thermal ones. Regarding the economic significance and costs of the techniques, an analysis was carried out, which revealed the most cost-effective method to be thermal ablation in comparison with open surgical interventions and non-thermal techniques. The analysis showed that open classical vein surgery was the most expensive method.

As for another important factor – the rapid recovery of the patient after the procedure – a slightly shorter rehabilitation period was noted by patients after cyanoacrylate obliteration and mechanochemical ablation [8]. However, these methods required corrections due to a higher percentage of recanalizations.

Taking into account world studies and according to the data of our study, we can recommend minimally invasive techniques as the method of choice during martial law, given the possibility of surgical treatment under local anesthesia or without it at all. This enables outpatient intervention, as it does not require a stationary operating room and a long stay of patients in the ward under the supervision of medical personnel.

Another important factor is rapid rehabilitation due to the patient's activity immediately after the intervention and the possibility to return to the usual rhythm of life. Minimal perioperative pain and improvement in quality of life were noted by patients in all groups of minimally invasive intervention.

CONCLUSIONS

Endovenous laser ablation is the most effective method of treating primary varicose veins, as it gives the best late results in the treatment of varicose veins. The electrowelding technique is more accessible and simpler in the technical aspect than EVLA and RFA, therefore it has quite strong prospects for further wider implementation in the clinical practice of varicose vein management in outpatient settings.

The advantage of non-thermal methods is the absence of thermal influence on paravenous structures and the faster operation technique. Another advantage of non-thermal methods is the absence of the need for tumescent analgesia, since only one puncture is required for the introduction of the drug or device, which is mostly painless. The reduction of the risk of allergic reactions should also be noted, which sometimes occur to the components of the tumescent solution, and therefore the advantage of this method is the possibility of its use in patients with a heavy allergic history.

After using bioglue, according to the recommendations, there is no need for mandatory compression in the intervention area, which makes the technique convenient for the patient and can be used more often in warm seasons. The advantage of echo-guided foam scleroobliteration is its lowest cost per procedure among all minimally invasive methods, which is a significant factor when choosing an intervention for low-income population stratum.

In our study, foam sclerotherapy was the method of choice for treatment correction, if necessary. It is a technically simple method, it is performed in outpatient conditions during a control examination, it is fast in terms of time and the least expensive procedure, which is a significant economic factor.

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ORIGINAL ARTICLE

LATE RESULTS OF TREATING PATIENTS WITH OCCLUSIVE-STENOTIC LESIONS OF THE AORTA INFRARENAL SEGMENT'S MAIN ARTERIES

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ABSTRACT

The aim: To analyze the results of surgical treatment in the late postoperative period after using modern types of surgical technologies for occlusive-stenotic atherosclerotic lesions of the infrarenal aorta's main arteries.

Materials and methods: The total of 420 patients were operated on. The patient's age ranged from 45 to 87 years (in the mean, 66.7±2.3 years). Men predominated – 375 (89.29%), and women were 45 (10.71%). According to the ischemia classification by Rutherford - 324 (77%) patients fell under categories 4, 5, 6 of the classification. 98 patients were operated on by the open method, 243 by the endovascular method, and 79 by the hybrid method. We assessed such indices as: postoperative thrombosis, limb amputations, mortality, and repeated operations performed due to complications or unsuccessful results of the primary operation.

Results: It was ascertained, a decrease in the number of postoperative complications from 7.87% to 4.39% (t=2,11, p=0,035), repeated operations – from 7.87% to 4.39% (t=2,11, p=0,035), amputations – from 3.63% to 2.19% (t=1,24, p=0,214) and mortality – from 3.03% to 1.09% (t=2,03, p=0,042) in the group where in-depth examination methods were applied, a treatment algorithm based on individual anatomical and hemodynamic features was implemented, techniques for performing operations were improved.

Conclusions: The analysis of late results of surgical interventions showed that the largest number of complications was found in the group of patients with multistory occlusive-stenotic lesions of arteries.

KEY WORDS: obliterating atherosclerosis of the lower extremities' arteries, chronic threatening ischemia of the lower extremities, revascularization, late results of revascularization

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INTRODUCTION

To date, atherosclerosis of the lower extremity's vessels remains an unsolved problem of vascular surgery. Today, in Europe and North America, the incidence of atherosclerosis ranges from 3% to 10%, with an increase of 15% to 20% among individuals over 70 years of age [1, 2]. The extreme degree of occlusive-stenotic artery disease manifestation is chronic critical ischemia of the lower extremities. A significant obliterating process in the arterial bed of the limb leads to such a pathophysiological state, which in the case of critical ischemia can have both a local and a multistory nature of the lesion.

Therefore, such patients must be hospitalized due to the real risk of losing the affected limb and death of the patient due to complications [3, 4].

The annual frequency of major amputations in total varies from 120 to 500 per 1 million population. The relevance of the problem is also related to the disability of patients after amputation of a limb, which has great economic, medical and social significance [5, 6].

Today, endovascular operations occupy a leading and priority place among other operative interventions due to the undeniable advantages of this method: low trauma, good visualization of occlusive and stenotic lesions of the artery, accurate positioning of delivery devices, lower operational risk, fewer bed days of the patient in the hospital, less number of perioperative complications and mortality [7].

Among operations on main vessels, a certain percentage is occupied by open methods of reconstructive operations, which are determined by a number of indications and anatomical conditions for their performance. Thus, open methods of revascularization remain the method of choice in patients with extensive atherosclerotic occlusive-stenotic lesions of the arteries in the absence of hybrid intervention options, and the

allo-shunt is the material of choice in the absence of an autovein. In the late postoperative period, a large number of amputations and deterioration of the patient's quality of life are still noted [8].

Evaluation of the late results of surgical interventions is of great importance for determining the efficacy of the lower extremities' revascularization method in patients with occlusive-stenotic lesions of the aorta infrarenal segment arteries, in order to find out which methods of surgical treatment were used to improve the late results of treatment.

The development of complications caused by the progression of the atherosclerotic process in vascular pools that underwent reconstruction and which remained without reconstruction – a certain number of years after the operation, they progress. That is why late indices, namely: preservation of the limb, survival of patients and especially survival of patients without amputation, is an extremely important, valuable and informative index, on a par with immediate results.

The analysis of the results of treating patients with critical ischemia of the limb in the late postoperative period has not been sufficiently studied, therefore it needs to be worked out in detail.

THE AIM

The purpose of the study was to analyze the results of surgical treatment in the late postoperative period after using modern types of surgical technologies for occlusive-stenotic atherosclerotic lesions of the infrarenal aorta's main arteries.

MATERIALS AND METHODS

In the surgical center of minimally invasive surgery of the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department (Kyiv, Ukraine) from 2014 to 2021 420 patients with occlusive-stenotic lesions of the aorta infrarenal segment main arteries were treated, who were operated on by various surgical methods.

The patients' age ranged from 45 to 87 years, with in mean of 66.7±2.3 years. The majority of patients (311 people) were aged from 60 to 87 years, that is, the elderly and senile people predominated. The right lower extremity was affected more often in 260 (61.9%) patients than the left – 160 (38.1%). When distributing by gender, men prevailed – (89.29%), women – 45 (10.71%).

In our work, we used the lower extremities classification of chronic ischemia according to Rutherford 1997. Categories 4,5,6 included 324 (77%) patients, which corresponds to critical ischemia of the lower extremities' vessels.

Out of 420 patients with occlusive-stenotic lesions of the aorta infrarenal segment's main arteries, 98 (23.3%) were operated on by the open method, 243 (57.9%)– by the endovascular method, and 79 (18,8%) – by the hybrid method (Table I).

As can be seen from Table I, the largest number of patients with occlusive and stenotic lesions of the aorta infrarenal segment's arteries was observed in the femoral-popliteal and popliteal-tibial segments. And the largest number of operated patients – with the endovascular method, which corresponds to today.

98 (23.3%) patients were operated on by the open method. Open interventions on arteries included: shunting (allo- and autovenous), prosthetics (allo- and autovenous), endarterectomy, thrombintimectomy, thrombectomy.

Endovascular surgical interventions were performed in 243 (57.9%) patients. They underwent balloon angioplasty, stenting, thromboaspiration, and rotary-mechanical thromboaspiration.

Hybrid surgical interventions were performed in 79 (18.8%) patients, combining various variants of single-stage endovascular and open surgical interventions.

To determine the efficacy of various surgical treatment methods in patients with occlusive-stenotic lesions of the aorta infrarenal segment's arteries, we analyzed the late results of all types of surgical interventions (open, endovascular, hybrid) associated with revascularization of the lower extremities.

RESULTS

When analyzing the late results of surgical interventions, we compared the following indices: postoperative complications (thrombosis), repeated operations performed due to complications or an unsuccessful outcome of the primary operation, limb amputations, and mortality.

In order to evaluate the late results of patients' surgical treatment, the following time intervals were used: from 1 to 2 years, from 2 to – 3 years and 3–5 years.

The above-mentioned gradation is due to the peculiarities of the postoperative period's course in patients with atherosclerotic lesions of the lower extremities' vessels, namely: the highest frequency of the reconstructed segments' restenoses; the highest probability of developing other complications in all arterial pools during the specified period after surgery.

When analyzing late results in the period from 1 to 2 years, we compared (as in the following groups of results) such indices as: postoperative complications

Table I. Distribution of patients by segments and types of surgical interventions

Segments	Number	Types of surgical interventions		
		Open	Endovascular	Hybrid
Aorto-iliac vein	20 (4,76%)	16	4	0
Iliofemoral	45 (10,72%)	11	14	20
Femoral-popliteal	166 (39,5%)	48	92	26
popliteal-tibial	124 (29,52%)	19	84	21
talocrural	65 (15,5%)	4	49	12
Total:	420 (100%)	98 (23.3%)	243 (57,9%)	79 (18,8%)

Table II. Late results of surgical treatment in patients with occlusive-stenotic lesions of arteries in 1–2 years

Types of operations	Number of patients	Groups: Reference / main	Thromboses	Repeated operations	Amputations	Mortality
Open	71	41 30	4 (t=1,13, p=0,262) 1	4 (t=1,13, p=0,262) 1	2 (t=0,33, p=0,743) 1	2 (t=1,45, p=0,152) -
			5 (7,04%)	5 (7,04%)	3 (4,22%)	2 (2,81%)
Endo-vascular	178	118 60	11 (t=1,11, p=0,267) 3	10 (t=0,91, p=0,363) 3	6 (t=1,31, p=0,192) 1	3 (t=0,40, p=0,691) 1
			14 (7,86%)	13 (7,3%)	7 (3,93%)	4 (2,25%)
Hybrid	59	31 28	5 (t=1,68, p=0,099) 1	5 (t=1,68, p=0,099) -	2 (t=0,51, p=0,611) 1	1(t=1,02, p=0,314) -
			6 (10,17%)	5 (8,47%)	3 (5,08%)	1 (1,69%)
Total:	308 (73,33%)	308 190 118	25(6,49%) 20(10,52%) (t=0,89, p=0,375) 5 (4,23%) (t=1,60, p=0,110)	23 (7,46%) 19 (10,0%) (t=0,96, p=0,338) 4 (3,38%) (t=1,82, p=0,069)	13 (4,22%) 10 (5,26%) (t=0,53, p=0,600) 3 (2,54%) (t=0,91, p=0,364)	7 (2,27%) 6 (93,15%) (t=0,58, p=0,562) 1 (0,84%) (t=1,19, p=0,234)

(thrombosis), repeated operations, limb amputations and mortality after all types of surgical interventions related to lower limb revascularization.

With the help of repeated examinations and questionnaires, it was possible to examine and analyze 308 (73.33%) patients who were operated on by various methods: 71 were operated on by the open method, 178 – by the endovascular method, and 69 – by the hybrid method.

When analyzing the late results of surgical interventions in the period from 1 to 2 years, it was established that the number of thromboses, repeated operations, limb amputations and mortality in the group of open operations was 5 (7.04%), 5 (7.04%), 3 (4.22%) and 2 (2.81%), respectively.

In the group of patients who underwent endovascular revascularization, the number of thromboses, repeated operations, limb amputations, and mortality was 14 (7.867%), 13 (7.3%), 7 (3.93%), 4 (2.25%), respectively. In the group of patients who underwent revascularization by the hybrid method, the number of thromboses, repeated operations, limb amputations and mortality was 6 (10.17%), 5 (8.47%), 3 (5.08%), 1 (1.69%), see Table II.

As Table II implies, we note better late results in the period from 1 to 2 years with open and hybrid surgical interventions in comparison with immediate and short terms. Along with this, in the group of patients with endovascular operations, we note the deterioration of long-term indices in comparison with the immediate and short terms. However, there is no reliable statisti-

Table III. Late results of surgical treatment in patients with occlusive-stenotic lesions of arteries in 2–3 years

Types of operations	Number of patients	Groups: Reference / main	Thromboses	Repeated operations	Amputations	Mortality
Open	68	39 29	3 (t=0,78, p=0,439) 1	3 (t=0,78, p=0,439) 1	1 (t=0, p=1) 1	1 (t=1,01, p=0,315) -
			4 (5,88%)	4 (5,88%)	2 (2,94%)	1 (1,47%)
Endo-vascular	160	115 45	10 (t=0,45, p=0,656) 3	9 (t=0,26, p=0,796) 3	5 (t=0,73, p=0,466) 1	3 (t=0,15, p=0,884) 1
			13 (8,13%)	12 (7,5%)	6 (3,75%)	4 (2,5%)
Hybrid	57	37 20	4(t=0,82, p=0,414) 1	3 (t=0,47, p=0,641) 1	2 (t=0,07, p=0,947) 1	1 (t=1,01, p=0,315) -
			5 (8,77%)	4 (7,02%)	3 (5,26%)	1 (1,75%)
Total:	285 (67,9%)	285 188 97	22 (7,72%) 17 (9,04%) (t=0,50, p=0,614) 5 (5,15%) (t=0,93, p=0,351)	20 (7,01%) 15 (7,97%) t=0,39, p=0,700) 5(5,15%) t=0,69, p=0,492)	11(3,85%) 8 (4,25%) (t=0,21, p=0,832) 3 (3,09%) (t=0,37, p=0,715)	6 (2,1%) 5 (2,65%) (t=0,38, p=0,702) 1 (1,03%) (t=0,81, p=0,421)

Table IV. Late results of surgical treatment in patients with occlusive-stenotic lesions of arteries in 3–5 years

Types of operations	Number of patients	Groups: Reference / main	Thromboses	Repeated operations	Amputations	Mortality
Open	60	35 25	2(t=0,31, p=0,758) 1	2(t=0,31, p=0,758) 1	1(t=1,01, p=0,314) -	1(t=1,01, p=0,314) -
			3(5,0%)	3(5,0%)	1(1,66%)	1(1,66%)
Endovascular	144	98 46	9(t=1,15, p=0,250) 2	9(t=1,15, p=0,250) 2	4(t=0,65, p=0,517) 1	3(t=0,32, p=0,749) 1
			11(7,63%)	11(7,63%)	5(3,47%)	4(2,77%)
Hybrid	52	32 20	2(t=0,19, p=0,848) 1	2(t=0,19, p=0,848) 1	2(t=1,46, p=0,150) 0	1(t=1,02, p=0,314) -
			3(5,7%)	3(5,7%)	2(3,84%)	1(1,92%)
Total:	256 (60,95%)	256 165 91	17(6,64%) 13(7,87%) (t=0,47, p=0,636) 4(6,64%) (t=0,84, p=0,398)	17(6,64%) 13(7,87%) (t=0,47, p=0,636) 4(6,64%) (t=0,84, p=0,398)	8(3,12%) 6(3,63%) (t=0,28, p=0,779) 2(2,19%) (t=1,23, p=0,219)	6(2,34%) 5(3,03%) (t=0,42, p=0,675) 1(1,09%) (t=0,86, p=0,390)

cal difference between the indices of these groups of patients, since the indices of the latter are practically the same.

When analyzing late results in the period from 2 to 3 years, we analyzed 285 (67.9%) patients who were operated on by various methods: 68 patients were operated on by the open method, 160 by the endovascular method, and 57 patients – by the hybrid method.

When analyzing the late results of surgical interventions in the period from 2 to 3 years, it was established that the number of thromboses, repeated operations, limb amputations and mortality in the group of open operations was 4 (5.88%), 4 (5.88%), 2 (2 .94%) and 1 (1.47%), respectively.

In the group of patients who underwent endovascular revascularization, the number of thromboses, repeated

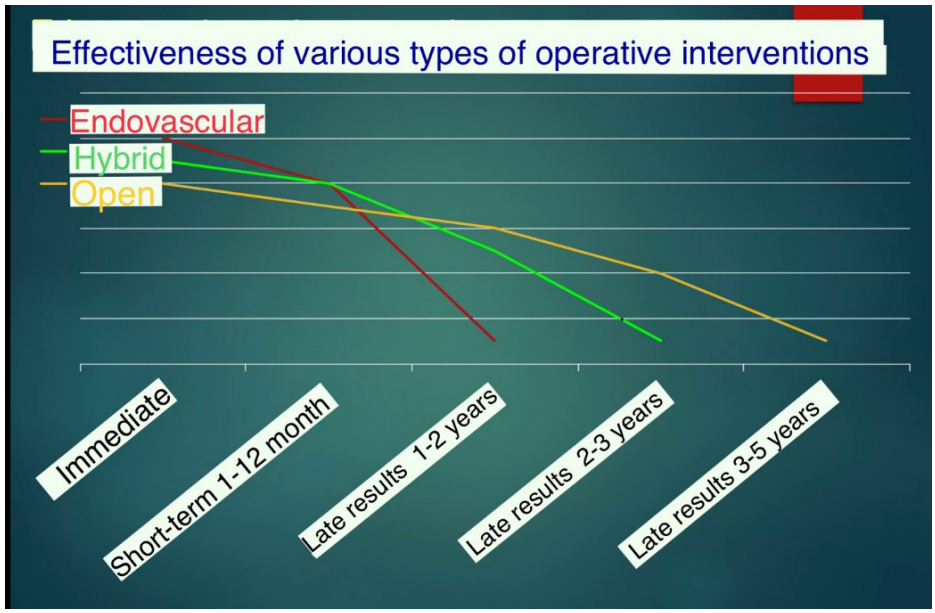

Fig. 1. Schedule of the operative interventions efficacy in different periods of observation

operations, limb amputations and mortality was 13 (8.137%), 12 (7.5%), 6 (3.75%), 4 (2.5%), respectively. In the group of patients who underwent revascularization by the hybrid method, the number of thromboses, repeated operations, limb amputations and mortality was 5 (8.77%), 4 (7.02%), 3 (5.26%), 1 (1.75%), see Table III.

As Table III implies, we note better late results in 2–3 years with open and hybrid surgical interventions, which prevail in terms of results in comparison with endovascular indices with a statistically significant difference ($p<0.05$). At the same time, in the group of patients with endovascular operations, we note a statistically significant difference ($p<0.05$) in the deterioration of late indices in comparison with short and long terms.

When analyzing long-term results within 3-5 years, we examined and analyzed 256 (60.95%) patients who were operated on by the open method – 60, endovascular – 144, and hybrid method – 52 patients.

When analyzing the long-term results of surgical interventions in the period of 3-5 years, it was established that the number of thrombosis, repeated operations, limb amputations and mortality in the group of open operations was 3 (5.0%), 3 (5.0%), 1 (1, 66%) and 1 (1.66%), respectively.

In the group of patients who underwent endovascular revascularization, the number of thromboses, repeated operations, limb amputations and mortality was 11 (7.63%), 11 (7.63%), 5 (3.47%), 4 (2.77%)) respectively. In the group of patients who were revascularized by the hybrid method, the number of thromboses, repeated operations, limb amputations and mortality was 3 (5.7%), 3 (5.7%), 2 (3.84%), 1 (1.92%), see Table IV.

From Table IV, we note statistically better ($p<0.05$) late results in the period from 3 to 5 years with open and hybrid surgical interventions in comparison with endovascular indices. At the same time, in the group of patients with endovascular operations, we note a statistically significant difference in the deterioration ($p<0.05$) of late indices in comparison with short and long terms (Fig. 1).

DISCUSSION

Although lower extremity revascularization is widely used in peripheral artery disease and can offer significant benefits, patients undergoing peripheral revascularization face long-term risk for cardiovascular and limb ischemic events. After revascularization, the risk for limb events increases quickly and plateaus after the first year, whereas cardiovascular risk increases steadily post-procedure [9].

As we also studied the immediate results (up to 1 month) of surgical interventions on the arteries of the aorta infrarenal section in patients with atherosclerosis using various methods of revascularization, which showed that the largest number of complications was found in the group of patients with multistory occlusive-stenotic lesions of the arteries. The direct efficacy of endovascular interventions is higher than that of open revascularizations and hybrid operations, and the trauma of mini-invasive endovascular techniques is significantly less compared to the methods of open reconstructive surgery.

The analysis of short-term results (within 1 to 12 months) of surgical interventions showed a clear tendency to improve the short-term results of open surgical interventions in comparison with the indices of immediate results. At the same time, in the group of patients with endovascular operations, we note a deterioration of short-term indices compared to immediate ones. However, there is no significant statistical difference

between the two groups of patients. The largest number of complications was found in the group of patients with multistory occlusive and stenotic lesions of arteries.

In the group of hybrid operations, indices of short-term results were approximately similar to immediate results.

Thus, after carrying out a comparative assessment of the analyzed results of treating patients in the retrospective and main group where in-depth examination methods were applied, a treatment algorithm based on individual anatomical and hemodynamic features was developed and implemented, technical techniques for performing operations were improved, as well as preoperative prediction of the possible risk of the operated limb's postoperative thromboses of the arterial bed, it was established that in the distant postoperative period it was possible to increase the efficacy of treating patients with occlusive-stenotic lesions of the aorta infrarenal segment's arteries, as evidenced by a decrease in the number of postoperative complications from 7.87% to 4.39% (t=2,11, p=0,035), repeated operations – from 7.87% to 4.39% (t=2,11, p=0,035), amputations – from 3.63% to 2.19% (t=1,24, p=0,214) and mortality – from 3.03% to 1.09% (t=2,03, p=0,042). The quality of life after surgery was higher for patients in the main group.

The results of treating the main group of patients in the remote postoperative period indicate that more than 82% of patients achieved good and satisfactory results.

CONCLUSIONS

1. Evaluating the results of open, endovascular, and hybrid surgical interventions in patients with occlusive-stenotic lesions of the aorta infrarenal segment's arteries, it can be established that the number of complications, repeated operations, amputations, and mortality after endovascular revascularization was higher in the long-term postoperative period than after open ones and hybrid reconstructive operations.
2. The analysis of late results of surgical interventions showed that the largest number of complications was found in the group of patients with multistory occlusive-stenotic lesions of arteries.

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ORIGINAL ARTICLE

FLUCTUATING HEARING LOSS AS A SYMPTOM OF ACQUIRED PERILYMPHATIC FISTULA (PLF) UNDER EXTERNAL INJURIES FACTOR

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ABSTRACT

The aim: To evaluate the effectiveness of treatment patients with spontaneous PLF and labyrinthine window ruptures by studying the clinical and audiological results.

Materials and methods: 52 patients after exposure to traumatic factors in the anamnesis were evaluated. The perilymphatic fistula was diagnosed in 18 patients after the complex examination. All patients with PLF underwent surgical treatment.

Results: Vestibular disorders and hearing loss were the predominant symptoms. The fistula test was positive in 11 (61%) patients. Fluctuating hearing loss was determined in 9 (50%) patients. Labyrinthine window ruptures were detected in 16 (88%) patients: oval window membrane rupture was identified in 6 patients, and in another 10 patients round window membrane rupture was found and was detected on CT scan. The surgical treatment included minimally invasive tympanotomy with combined microscopic and endoscopic visualization and sealing techniques. Results were evaluated in 6 months after surgical treatment, patients had a decrease in bone and air conduction thresholds at all evaluated frequencies and a significant decrease in the level of the air-bone interval.

Conclusions: Fluctuating hearing loss is considered one of the key symptoms, which suggests the presence of PLF. Determination of PLF and its surgical treatment, by using minimally invasive tympanotomy with sealing technique using optimal combined visualization, allows obtaining a stable functional result, with hearing improvement and vestibular symptoms reducing.

KEY WORDS: acoutrauma, blast injuries, perilymphatic fistula, treatment, tympanotomy

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INTRODUCTION

High-level noise caused by intense acoustic weapons and blasting is a common source of acute acoustic trauma, especially within the zone of military conflict [1-5].

The baroacoustic effect in mine-explosive injuries can lead to traumatic damage of the middle and inner ear in the form of cochleovestibular disorders and mixed hearing loss [6]. Auditory and non-auditory effects accompany these damages [7-9].

Hearing loss in this case can manifest with the development of sensorineural, mixed, or conductive hearing loss and even deafness. In most cases, the nature of hearing loss is represented by fluctuations in auditory function in the form of fluctuating hearing loss. [10,11].

The high-level noise caused by intense acoustic weapons and blasting is a source of acute acoustic trauma and, in the absence of in-time treatment, can lead to irreversible changes in auditory and vestibular function [3, 4, 12, 13].

Since the 1990s, the intense acoustic weapon has become a hot research field for the military sector around the world. In the past 20 years, the intense acoustic weapon has developed towards multi-functionality, intelligence (with powerful physiological and psychological control), miniaturization, long-distance, multiplatform compatibility, and good environmental adaptability, showing great potential for application [4, 14].

During modern warfare, soldiers on the front line are considered the most vulnerable contingent, due to the influence of the action of acoustic weapons and the baroacoustic effect that occurs due to the explosion of artillery shells.

In case of the absence of proper personal protective equipment, traumatic effect on human health becomes inevitable. The consequences can be varied: temporary or permanent changes in sound perception thresholds, hearing loss, sometimes, fluctuating hearing loss, sec-

ondary additional pathological sound and noise effects, deafness, tinnitus, and vertigo [2, 15].

From March 2014 to 24 of February 2022, a hybrid military conflict has been taking place in the East of Ukraine (Donetsk and Lugansk regions, anti-terrorist operation (ATO) (2014-2018); Joint Forces Operation (JFO) (2018-2021).

During military conflicts, with the use of modern weapons, in addition to the direct impact of a wounding projectile (shrapnel, bullets) on a soldier, there is damage to the auditory and vestibular analyzer of varying severity and localization because of exposure to an intense baroacoustic effect that occurs when artillery shells burst [13].

In some cases, due to an impact of a mine-explosive injury, patients have clinical symptoms of perilymphatic fistula (PLF) development within the labyrinth windows localization and fluctuating hearing loss.

In the acute period, the military personnel underwent special treatment at level II (the stage of providing qualified assistance in a mobile hospital) and level III (in the conditions of military medical clinical hospitals in Kyiv, Kharkiv, Dnipro, Vinnytsia, Odesa, Lviv). Patients with no positive results in hearing improvement after that kind of treatment in the acute period were referred to higher levels of specialized (National Military Medical Clinical Center "Main Military Clinical Hospital", Kyiv, Ukraine) and highly specialized medical care (Institute of Otolaryngology named after prof. A.S. Kolomiychenko NAMS of Ukraine).

THE AIM

The study aimed to evaluate the effectiveness of treatment of patients with PLF and labyrinthine window ruptures by examining the clinical and audiological results after using minimally invasive microsurgical methods of surgical treatment with optimal combined visualization of the lesions.

MATERIALS AND METHODS

During current research, the main principles of bioethics were observed, according to the conclusion of the bioethical commission. Voluntaries informed consent of patients to participate in the current study was obtained in each specific clinical case.

We evaluated on 52 patients after exposure to a traumatic factor in history (military personnel of the JFO zone), in 18 of which, after a comprehensive examination, PLF was determined.

All patients, in addition to assessing the somatic status and ENT examination, underwent otomicroscopy, pure tone threshold audiometry, impedancemetry, computed tomography of the temporal bones (CT scan), and magnetic resonance imaging of the brain (MRI).

An audiological study of auditory function was carried out on an ITERA audiometer (Denmark) according to the generally accepted scheme using pure tone threshold tonal and speech tests. The results were evaluated before and after treatment 6 months after surgery, using the international classification of hearing impairment according to WHO at frequencies of 500 Hz; 1; 2, and 4 kHz. [10].

CT scan was performed on a Philips Brilliance 64 CT scanner with a slice thickness of 0.67 mm, with axial and coronal projections reconstruction.

All 18 patients underwent surgical treatment - minimally invasive tympanotomy using a combined microscopic and endoscopic technique to visualize the PLF area, followed by the closure of the fistula area with filling material (connective tissue, fat graft, bone dust, temporal muscle fascia and gelaspon soaked in dexamethasone solution).

Statistical analysis of the results was carried out using the licensed package STATA 12.1 using the appropriate methods of statistical data processing. The differences were considered significant if $p<0.05$. Qualitative data are presented in the form of distribution of patients – n (%); Quantitative characteristics (bone conduction thresholds, air conduction thresholds) are presented in the form of arithmetic mean and standard deviation (M±SD). Evaluation of treatment effectiveness (comparison of results) was carried out according to the studied quantitative parameters using the Wilcoxon test. The choice of the statistical criterion was based on the assessment of the normality of the distribution of the primary data and the number of patients.

RESULTS

The dominant complaints in patients were vestibular disorders (the presence of dizziness, unsteady gait, aggravation with a change in body position), hearing loss (HL) from conductive to mixed, fluctuating HL, and tinnitus (Table I).

In 11 (61%) patients, a positive fistula test was determined. Dizziness, to a greater or lesser degree, occurred in all patients. Conductive hearing loss was observed in 2 patients, while mixed hearing loss was observed in 7 (39%) of 18 patients studied, and fluctuating hearing loss in 9 (50%) patients. The noise was determined in 6 patients.

PLF localization was determined according to CT scan data of the temporal bones (see Table II).

According to the temporal bone CT scan, ruptures in the region of the labyrinthine windows were deter-

Table I. Clinical signs in study patients.

Clinical signs	Number of patients
Dizziness	18 (100 %)
Positive fistula test	11 (61%)
Conductive hearing loss	2 (11%)
Mixed hearing loss	7 (39 %)
Fluctuating hearing loss	9 (50%)
Noise	6 (33%)

Table II. PLF localization.

CT features	Studied patients
Round window membrane rupture	10 (55%)
Air in the vestibulum	5 (28%)
Defect (fistula) in the area of the oval window	6 (33%)
Dehiscence and fistula of superior semicircular canal	2 (11%)

Table III. Mean values bone conduction (BC) thresholds in dB according to pure tone threshold audiometry in patients with PLF before and after minimally invasive surgery, (M±SD).

Investigated frequencies		n =18	p (before/after)
500 Hz	Before surgical treatment	29,2±6,8	0,166
	After surgical treatment	21,9±7,0	
1 kHz	Before surgical treatment	51,2±13,0	0,019*
	After surgical treatment	28,8±7,7	
2 kHz	Before surgical treatment	56,2±13,3	0,039*
	After surgical treatment	31,9±6,5	
4kHz	Before surgical treatment	58,8±13,2	0,022*
	After surgical treatment	31,2±7,1	
Mean (dB)	Before surgical treatment	48,8±11,3	0,024*
	After surgical treatment	28,4±6,7	

Note: * - $p<0.05$ - a statistically significant difference in the thresholds of perception before and after treatment (according to the Wilcoxon criteria)

Table IV. Mean values of air conduction (AC) sound perception thresholds in dB according to pure tone threshold audiometry in patients with PLF before and after surgical treatment threshold audiometry from different genesis PLF before and after surgical treatment, (M±SD).

Investigated frequencies		n=18	p
500 Hz	Before surgical treatment	58,8±10,2	0,007*
	After surgical treatment	36,1±6,3	
1kHz	Before surgical treatment	61,9±10,3	0,017*
	After surgical treatment	40,0±6,3	
2 kHz	Before surgical treatment	59,6±9,6	0,008*
	After surgical treatment	42,3±6,1	
4 kHz	Before surgical treatment	70,0±8,1	0,029*
	After surgical treatment	52,3±7,2	
Mean (dB)	Before surgical treatment	62,6±9,1	0,009*
	After surgical treatment	42,7±5,6	

Note: * - $p<0.05$ - a statistically significant difference in the thresholds of perception before and after treatment (Wilcoxon criteria).

mined in 16 (88%) patients: in the region of the oval window in 6 cases; in the area of the round window - in 10 patients. Air in the vestibule was determined in 5 patients. A brain MRI was performed to exclude any severe damage.

The main approach in the treatment of patients was minimally invasive tympanotomy with combined microscopic and endoscopic visualization using a 30° endoscope. PLF localization was dominant in choosing of material for closure defect. PLF closure with localization in the round window area was carried out using a free connective tissue graft by filling the damaged area with gelaspon soaked up in dexamethasone solution. PLF plasty and defect with localization in the area of the oval window closure were carried out using fat and connective tissue graft, followed by tamponade with gelaspon soaked up in dexamethasone solution. The functional results of minimally invasive surgery in PLF were evaluated according to the clinical and audiological data. Complaints were determined in terms of 1 and 6 months after the operation and thresholds for the perception of sounds according to the air conduction, bone conduction, and the value of the air-bone interval at the main studied frequencies. (see tables III-IV).

Due to the data from Table III, all patients of the study group have decreased BC thresholds at all evaluated frequencies determined within 6 months after surgical treatment. Before the surgical treatment, the perception thresholds for sounds in BC ranged from 29.2.0 dB to 58.8 dB. This indicates severe hearing loss with the development of a combined lesion. In 6 months after surgical treatment, the tendency of decreased BC was determined, most likely due to the restoration of hydrodynamic processes in the cochlea.

Due to the data from Table IV, a decrease in the perception thresholds of AC sounds for all patients is determined with a tendency to decrease at all studied frequencies.

Mean values of the air-bone interval (ABI) according to pure tone threshold audiometry in patients with PLF were evaluated before and after surgical treatment. A statistically significant difference in ABI before and after surgery (Wilcoxon test) was demonstrated with decreasing from (40,0±3,6) dB to (25,2±2,3) dB ($p<0.05$) in all patients in 6 months after surgical treatment.

DISCUSSION

PLF describes an abnormal communication of fluid between the inner ear and the air-filled middle ear cavity [16]. Perilymph is out from a defect in the otic capsule presenting with hearing loss and/or vestibular symptoms that are induced by blunt/penetrating trauma, barotrauma, chronic inflammation, cholesteatoma, or iatrogenic injury [17, 18]. In modern military conflicts and warfare, using modern military techniques blast injuries with middle and inner ear damages occurred often enough.

In the period of the active war condition pneumolabyrinth, or air displacing the fluid spaces of the otic capsule within the labyrinthine compartment, can confirm the presence of PLF [19, 16].

Physical exam findings consistent with this diagnosis include nystagmus with insufflation (positive fistula test) and dizziness induced by sound (Tullio's phenomenon). Because this hearing loss may be conductive, sensorineural, or mixed, a tuning fork examination may be of mixed utility. Fluctuated hearing loss seems to be a more serious and hidden complaint and the diagnosis of PLF can be easily missed especially in cases of military patients staying in mobile hospitals or not arriving on time at clinical hospitals or specialized diagnostic centers.

Definitive diagnosis of PLF requires surgical middle ear exploration [16]. Conservative management is appropriate in some cases, as patients may have spontaneous resolution of symptoms. However, the vestibular symptoms can often be exhausted and there is a risk of movement from fluctuated to permanent sensorineural hearing loss (SNHL) with a persistent, unrepaired fistula, so a minimally invasive approach to early surgical confirmation and repair of PLF is appealing.

In the absence of positive clinical dynamics: persistent vestibular disorders and fluctuating hearing loss, in the presence of PLF according to CT scan, the treatment tactics are as follows: minimally invasive endometrial tympanotomy in combination with microendoscopic visualization of the labyrinthine windows: round and oval with subsequent closure and sealing of the damaged areas. This treatment algorithm is carried out at level III of medical care (specialized care).

Clinical and functional results of treatment of the patients with PLF of the study groups and the applied approach to microsurgical treatment with combined microscopic and endoscopic visualization demonstrate the effectiveness and stability of the results obtained within 6 months after surgery. However, patients need further dynamic monitoring to assess clinical and functional results in the long term with evaluation in follow-up.

CONCLUSIONS

Determination of PLF in patients with sensorineural and vestibular manifestations with fluctuating HL in the presence of the influence of a traumatic injury in histo-

ry allows for etiopathogenetic treatment. Fluctuating hearing loss is considered one of the symptoms of PLF suspicion. Determination of the PLF and its closure by using minimally invasive tympanotomy with optimal combined microscopic and endoscopic visualization. The use of filling techniques allows for obtaining a stable clinical and functional result with improved hearing and a decrease in vestibular disorders. Under conditions of constant exposure to high-intensity baroacoustic effects, among military personnel and civilians injured under active military action, rapid diagnosis, and timely etiopathogenetic treatment are quite important. Such an approach allows the avoidance of any irreversible inner ear damage with inner ear complications development.

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ORIGINAL ARTICLE

MORPHOLOGICAL FEATURES OF MAXILLARY SINUS CYSTS BASED ON THE STUDY OF PARTICULAR HISTOCHEMICAL AND IMMUNOHISTOCHEMICAL FACTORS OF INFLAMMATION

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ABSTRACT

The aim: To study the morphological structure and immunohistochemical markers of inflammatory cells in the maxillary sinus cyst wall.

Materials and methods: Biopsy samples of maxillary sinus cysts of 92 operated patients aged 18 to 74 years were studied. We used standard staining with hematoxylin and eosin, PAS reaction, and immunohistochemical analysis with monoclonal antibodies to CD68 (macrophages) and CD3 (T- lymphocytes) to determine morphological features and severity of inflammation and PanCK AE1/AE2 antibodies to identify epithelium state.

Results: All patients were divided into 2 groups: 29 patients with retention cysts and 63 with lymphagiotatic cysts (pseudocysts), depending on the unilateral or bilateral epithelial lining of the cyst wall. Retention cysts had the bilateral epithelial lining with a saving its function and structure. The thinned connective tissue layer was filled with separate clusters of lymphocytes and macrophages. Lymphagiotatic cysts were characterized by the unilateral epithelium lining of the wall with signs of degeneration, desquamation, and loss of the mucus-forming function. Dense infiltration of the connective tissue layer by inflammatory cells with pronounced expression is observed.

Conclusions: Immunohistochemical analysis with monoclonal antibodies to CD3 and CD68 demonstrated that the inflammatory infiltrate of pseudocysts is represented by T-lymphocytes and different sizes of macrophages. The inflammatory infiltration of the pseudocyst wall was significantly severe compared to retention cysts.

KEY WORDS: Retention cyst, lymphangiectatic (pseudocyst) cyst, maxillary sinus, immunohistochemistry, inflammatory markers, upper respiratory tract

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INTRODUCTION

According to various authors, the prevalence of cyst formations of the paranasal sinuses in the population ranges from 1.4% to 35.6% [1,2]. One of the reasons for such variability of indicators is their frequent asymptomatic course and inability to establish a diagnosis during a routine ENT examination, therefore, they are mainly randomly detected during head imaging performed for other medical reasons [1,3], and in view of the military activities in Ukraine, the frequency of CT and MRI of the head for the diagnosis of traumatic injuries of intracranial structures is increasing.

In cases of asymptomatic course of maxillary sinus cysts, opinions of various authors regarding the management of such patients differ, therefore there are no unequivocal recommendations in the literature. Some researchers believe that all, even randomly detected cysts need surgical removal [4], others tend to think that in case of a small cyst size, their observation is possible [2,5]. An indication in favor of observation and conservative tactics is the possibility of spontaneous regression of cysts in 25-30% of cases and stabilization of their size in 60% [3,6,7].

According to pathomorphological signs and pathogenesis, there are two types of cysts: retention and lymphangiectatic (pseudocysts). Retention cysts are formed due to obstruction of the duct of the seromucous gland, their wall is lined with epithelium on both sides, and the content is the secretion of the gland [7]. In the case of pseudocysts, the cystic cavity filled with exudate is located in the thickness of the lamina propria. A morphologically false cyst is not a classic cyst due to the absence of an inner epithelial lining [2,3,8-10].

Taking into account the pathomorphological features of pseudocysts, the dynamics of their growth with possible spontaneous regression requires a deeper study of the genesis of these formations with an investigation of the inflammatory factor as one of the triggers of their formation, which can become the basis for their etiopathogenetic treatment.

THE AIM

The aim of the paper is to establish inflammatory changes in the walls of cystic formations of the maxillary sinus on the basis of an integrated pathomorphological study to improve their comprehensive etiopathogenetic treatment.

MATERIALS AND METHODS

Ninety-two patients with maxillary sinus cysts were selected for the study. All patients were made aware of the research objective and informed consent was signed. The study involved 51 women and 41 men. The age of the patients ranged from 18 to 74 years (36.75±11.80 years).

The patients underwent a general clinical and ENT examination, including nasal endoscopy and cone beam computed tomography of the paranasal sinuses.

Inclusion criteria: patients with maxillary sinus cysts.

Exclusion criteria: patients who had clinical symptoms of acute rhinosinusitis or exacerbation of the process in the sinus.

All patients underwent endoscopic maxillary sinusotomy through the middle or lower nasal passage with the removal of the cyst.

The material of the removed cysts (biopsy samples) obtained during the intervention was examined at the Department of Pathological Anatomy and Forensic Medicine of Shupyk National Healthcare University of Ukraine. It was fixed in a 10% solution of neutral buffered formalin (pH 7.4) for 24-36 hours. After fixation, standard processing was performed in the Excelsior AS (Thermo Fisher Scientific, Great Britain), followed by embedding in paraffin on the HistoStar station (Thermo Fisher Scientific, Great Britain). From the obtained paraffin blocks, serial histological sections with a thickness of 2-3 μm were made on a rotary microtome HM 325 (Thermo Shandon, Great Britain), which were then stained with hematoxylin and eosin; PAS staining method was used for secretory function detection [11,12].

Microscopic investigation and subsequent image archiving were performed using a light-optical microscope ZEISS (Germany) with the result processing system Axio Imager.A2 at 5x, 10x, 20x, 40x objective magnification, 1.5x binocular adjustment and 10x eyepiece with ERc 5s cameras.

To establish specific features of etiopathogenesis of cyst formation, in order to identify morphological signs of the inflammatory reaction, the cellular composition of inflammatory infiltrate and immunohistochemical markers of inflammation and cell phenotyping were determined: mouse monoclonal antibodies (MAB) to CD68 (macrophages, Clone KP-1, Master Diagnostica, Spain), MAB to total cytokeratin (PanCK AE1/AE3, Clone Ab-1, Master Diagnostica, Spain) and rat MAK to CD3 (T-lymphocytes, Clone SP7, Master Diagnostica, Spain).

Immunohistochemistry (IHC) was performed on Super Frost Plus adhesion slides (Menzel, Germany). The Master Polymer Plus Detection System (Peroxidase, DAB Chromogen) (Master Diagnostica, Spain) was used, and citrate buffer (pH 6.0) and EDTA buffer (pH 8.0) were used for high-temperature processing of antigen epitopes.

The expression of the applied immunohistochemical markers was assessed depending on the presence and/or absence of cell staining of varying intensity according to a visual analog scale [13]. The intensity of expression was evaluated from 0 – no reaction, + – low intensity, ++ – moderate and +++ – high (Table I).

Statistical analysis was carried out by non-parametric statistical methods with the use of the Mann-Whitney test and the Pearson's chi-square test (χ^2). The arithmetic mean (M) and the standard deviation (SD) were used to describe data with a normal distribution. Statistical processing of the data was carried out using the licensed STATISTICA v.6.1 software product.

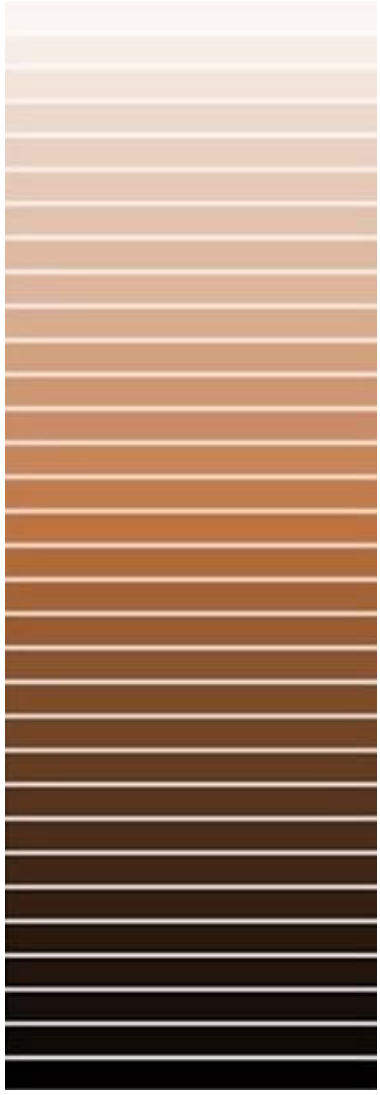
Informed consent for the research was obtained from the patients. The study was performed in compliance with bioethical principles, as well as legislative regulations and requirements: The Helsinki Declaration (2000), the Constitution of Ukraine (1996), the Civil Code of Ukraine (2006), the Fundamentals of Legislation of Ukraine on Health Care (1993), the Law of Ukraine "On Medicinal Products" (1996), the Law of Ukraine "On Protection of Personal Data" (2010), Order of the Ministry of Health of Ukraine "On Approval of the Procedure for Conducting Clinical Trials of Medicines and Examination of Clinical Trial Materials and the Model Regulations on Ethics Commissions" No. 690, dated 23.09.2009, (as amended by Order No. 523, 12.07.2012; No. 304, 06.05.2014; No. 966, 18.12.2014; No. 639, 01.10.2015), Order of the Ministry of Health of Ukraine "Procedure for Conducting Clinical Trials of Medicinal Products and Expert Evaluation of Clinical Trial Materials" (as amended by Order of the Ministry of Health of Ukraine, No. 523, 12.07.2012). Ethical approval No.12 of 29.11.2021 from the Ethics Commission of Shupyk National Healthcare University of Ukraine was obtained to carry out the research.

RESULTS

Based on the results of a pathomorphological study of biopsy samples, patients were divided into two groups (Table II).

The first group included patients with a retention cyst, the morphological criterion of which was the presence of epithelium from the outer and inner sides of its wall.

Table I. IHC scoring system *

Sign system of assessment (+/ –)	Scoring system of assessment	Colour scale of staining intensity
–	0 score	–
+	1 score	
++	2 scores	
+++	3 scores	

* according to the recommendations of D. J. Dabbs "Diagnostic immunohistochemistry" (4th Edition, 2014) in modification [13].

The second group of patients included those who had a cyst with epithelium only from the outer side, which is a pseudocyst.

The data presented in Table II indicate that the majority of patients, namely 63 (68.5%) out of 92 examined, had a pseudocyst according to histological features, and the remaining 29 (31.5%) had a retention cyst. The distribution of patients into groups by age and gender was represented.

During the histological examination, the wall of the retention cyst was represented by three layers: the middle layer of connective tissue of different degrees of maturity and thickness, surrounded on both sides by epithelium (Figure 1).

The wall of the pseudocyst was lined with epithelium only from the outer side of the connective tissue layer, which was densely infiltrated with inflammatory cells (Figure 2).

The epithelium of retention cysts in some areas was characterized by atrophic changes and partial metaplasia from cylindrical to the multi-layered non-keratinized epithelium. At the same time, the function of mucus production was preserved, which was confirmed by the PAS reaction (Figure 3).

In pseudocysts with PAS reaction in the partially desquamated cylindrical epithelium with degenerative changes, the function of mucus production was inherent in single cells (Figure 4).

The IHC of the cystic wall with a marker of general cytokeratin (PanCK AE1/AE2) was carried out, which revealed uneven positive expression in pseudocysts in the wall in one

Table II. Distribution of patients into groups by age, gender, and the results of morphological study of cysts

Study groups	Number of patients n (%)	Age*	Gender**	
		M±m	Female, n (%)	Male, n (%)
1 (retention cysts)	29 (68.5%)	36.79±10.69	16 (55.2)	13 (44.8)
2 (pseudocysts)	63 (31.5%)	36.73±12.47	35 (55.6)	28 (44.4)
Total	92 (100%)	36.75±11.80	51 (55.4)	41 (44.6)

* - p=0.736 (according to Mann-Whitney criterion); ** - p=0.973 (according to $\chi 2$ criterion)

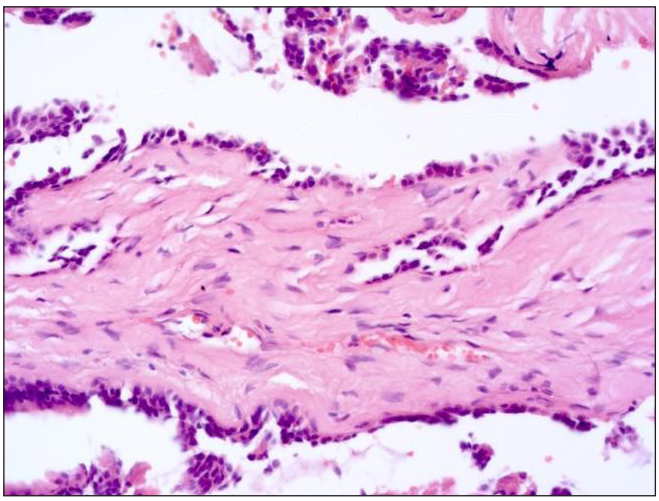


Fig. 1. Cyst wall is lined on both sides with epithelium; connective tissue of various degrees of maturity, slit-like vessels in the thickness. Hematoxylin and eosin staining. Magnification: x200.

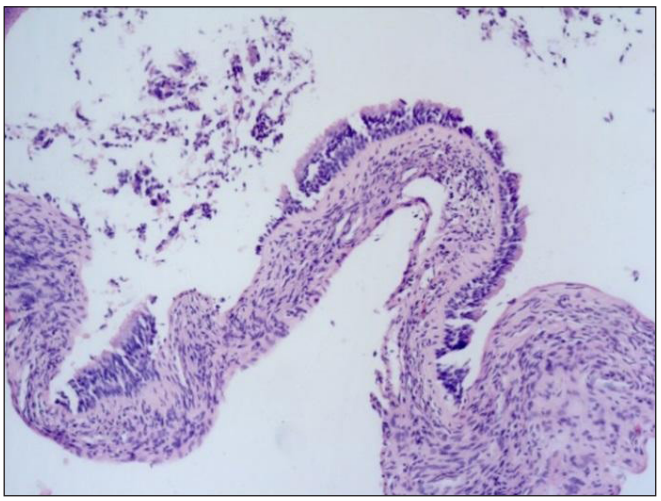


Fig. 2. Cyst wall is lined with cylindrical epithelium, areas of epithelial desquamation, the connective tissue of various degrees of maturity, and areas of sclerosis. Hematoxylin and eosin staining. Magnification: x50.

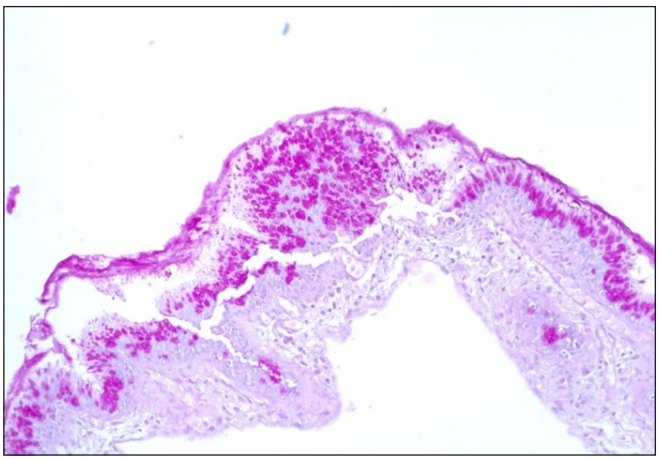


Fig. 3. Cyst wall with areas of epithelial metaplasia into multi-layered non-keratinized, with marked mucus production. PAS reaction – positive. Magnification: x50.

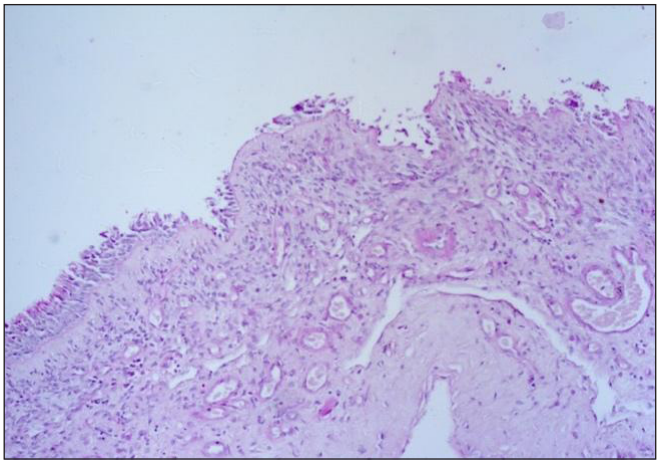


Fig. 4. Cyst wall with areas of epithelial desquamation, proliferation of connective tissue of various degrees of maturity, neoangiogenesis, and pleurisy. PAS reaction – negative. Magnification: x50.

layer of the epithelium, indicating the influence of inflammatory factors (Figure 5). In retention cysts, positive expression was observed in two layers of the cyst wall (Figure 6).

To establish the presence and severity of inflammatory changes in the wall thickness of the removed cysts, IHC with immunophenotyping was performed using MAB to CD68 and CD3, which identify macrophages and T-lymphocytes.

An insignificant number of T-lymphocytes was detected in the retention cyst walls in IHC with MAB to CD3 (Figure 7). The amount and density of cellular infiltrate were significantly higher (Figure 8.)

In the walls of both retention and pseudocysts, clusters of macrophages of various sizes were detected, which gave positive expression from MAC to CD68. It should be noted that in retention cysts separate clusters of positively expressing macrophage cells were observed (Figure 9), while in pseudocysts the number of marked macrophages was significantly higher (Figure 10).

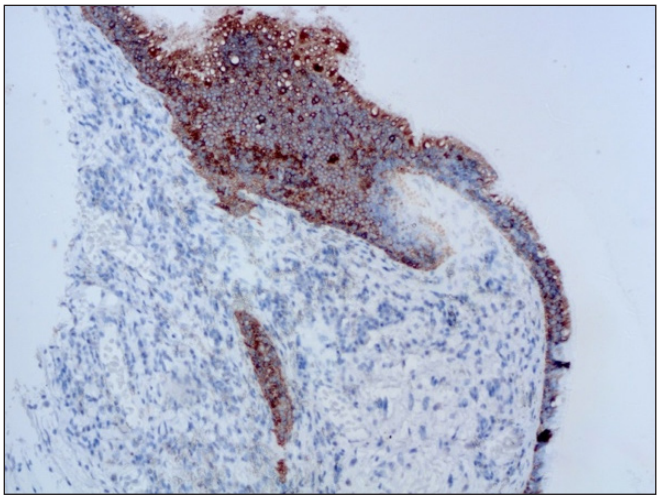


Fig. 5. Uneven positive expression in some cells in the areas of epithelial metaplasia of the cyst wall. IHC to PanCK AE1/AE2. Magnification: x100.

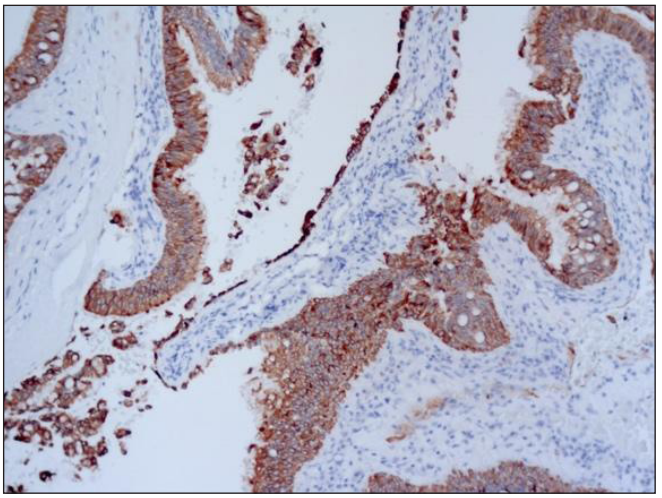


Fig. 6. Pronounced positive expression in the epithelium of the cyst wall, focal atrophy, and areas of marked epithelial metaplasia. IHC to PanCK AE1/AE2. Magnification: x100.

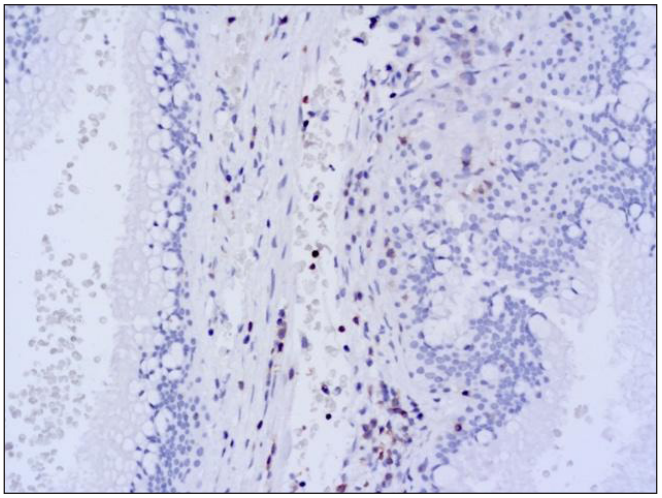


Fig. 7. An insignificant number of positive T-lymphocytes in the cyst wall. IHC with MAB to CD3. Magnification: x200.

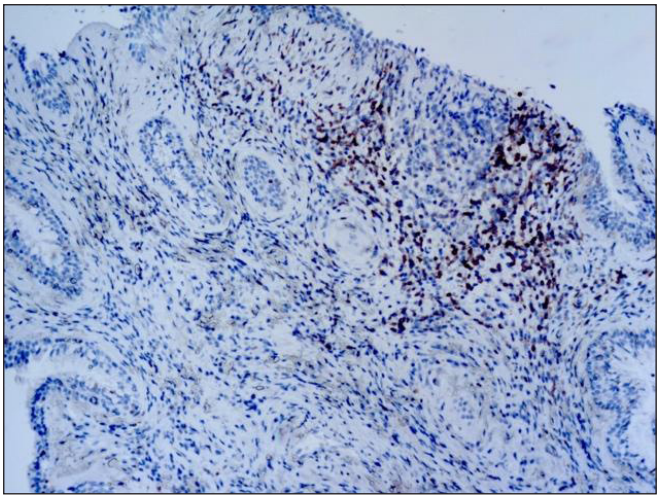


Fig. 8. Pronounced expression and a large number of positive T-lymphocytes in the cyst wall. IHC with MAB to CD3. Magnification: x200.

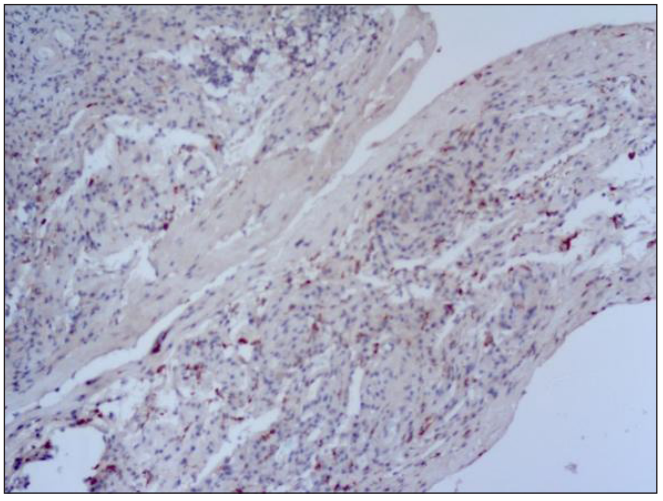


Fig. 9. A moderate number of positive macrophages is diffusely distributed in the cyst wall. IHC with MAB to CD68. Magnification: x100.

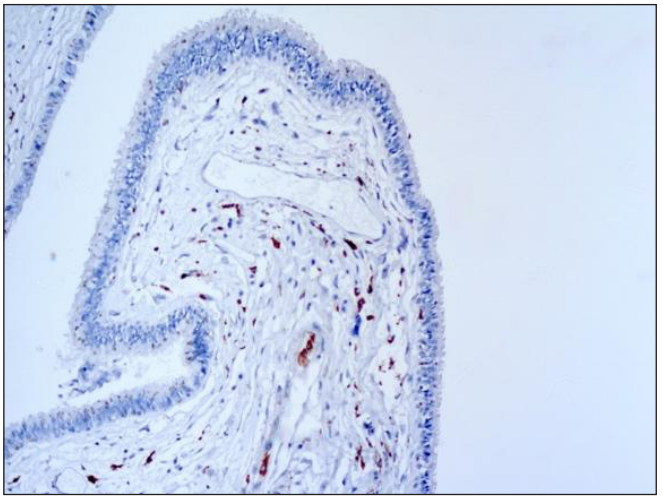


Fig. 10. A large concentration of positive large-sized macrophages in the cyst wall. IHC with MAB to CD68. Magnification: x100.

Table III. Results of PAS reaction and immunohistochemistry of inflammatory markers in biopsy samples of retention and pseudocysts

Study groups	PAS reaction	PanCK AE1/AE2	T-lymphocytes, CD3	Macrophages, CD68
Retention cyst (n =5)	2.8±0.2	2.8±0.2	1.4±0.24	1.6±0.24
Pseudocyst (n =5)	0.4±0.24	0.6±0.24	2.6±0.24	2±0.31
p	0.012	0.012	0.037	0.46

The assessment of the severity of the inflammatory reaction in biopsy samples of the maxillary sinus cysts according to individual markers is presented in Table III.

As can be seen from Table III, the retention cyst had a significantly higher percentage of cells that retained the function of mucus production (positive PAS reaction) compared to the pseudocyst (<0.05). At the same time, the degree of expression of epithelial cells (PanCK AE1/AE2) in retention cysts was significantly higher than in pseudocysts ($p<0.05$). Biopsy samples of false cysts showed a significantly higher expression of T-lymphocytes (CD3) than those of retention cysts ($p<0.05$). However, the number of macrophages (CD68) in the walls of retention and pseudocysts did not differ significantly ($p>0.05$).

DISCUSSION

Since the tactical issues of treatment of cystic formations of the maxillary sinus are still under development, especially in cases of small cysts (up to 1.5 cm) and the absence of specific symptoms, the tactics of their observation or treatment remain at the discretion of the attending doctor. The further course of this pathology is always unpredictable. The high rates of spontaneous regression of cysts described in the literature [3,6] suggest that there are certain pathomorphological features of their development that explain such a course of the disease.

Our studies using the PAS reaction showed that mucus formation in retention cysts is preserved not only when the cylindrical structure of the epithelium is preserved, but also in case of its metaplasia into a multi-layered non-keratinized epithelium and atrophy, so the mechanism of their regression is highly unlikely.

A small number of inflammatory cells infiltrating the connective tissue layer in retention cysts indicates the absence of active inflammation, but the presence of areas of polyp formation with epithelial metaplasia indicates the presence of residual signs of a chronic inflammatory process [14]. Similar changes in retention cysts are described by Pezato R, et al. [15] and they can be caused by the initiating factor of its formation – obstruction of the duct of the seromucous gland [7].

Inflammatory changes in the wall of pseudocysts are more pronounced than in retention cysts, as evidenced by the dense infiltration of the connective tissue layer of the cyst wall by T-lymphocytes and macrophages, as inflammatory cells positive for CD3 and CD68. Active polyp formation with metaplasia and epithelial degeneration indicates the duration of the inflammatory reaction.

Thus, the main difference between pseudocysts and retention cysts is the absence of an epithelial lining on the inner side of the cystic formation and the severity of inflammatory changes in the thickness of its wall. Taking into account that the content of the pseudocysts is represented by exudate or transudate [16], since there is no mucus formation, it can be assumed that the resolution of the inflammatory process in the pseudocyst and its elimination in the surrounding tissues, in particular in the adjacent bone, can contribute to the stabilization of the cyst size and its regression.

CONCLUSIONS

1. According to the morphological analysis of the walls of cystic formations of the maxillary sinus, 68.5% of cases were identified as pseudocysts, and their wall was represented by two layers – connective tissue and epithelial, and 31.5% were identified as retention cysts, which had three layers – 2 layers of the epithelium with connective tissue between them.
2. It was established that the epithelium of a retention cyst retains its function of mucus formation even in case of metaplasia and atrophy, while the epithelium of a pseudocyst almost completely loses it, which was confirmed histochemically using the PAS reaction.
3. IHC with MAB to CD3 and CD68 found that the inflammatory infiltrate in the wall of retention and pseudocysts is represented by T-lymphocytes and macrophages, while retention cysts were weakly infiltrated by these cells, and pseudocysts had pronounced inflammatory cell infiltration.

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ORIGINAL ARTICLE

ASSESSMENT OF THE EFFICIENCY OF ANALGETIC ACTION OF LAPAROSCOPICALLY ASSISTED TAP BLOCK AS A COMPONENT OF PERIOPERATIVE MULTIMODAL ANALGESIA PLAN IN OBESE PATIENTS UNDERGOING METABOLIC SURGERY

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ABSTRACT

The aim: To assess the effectiveness and feasibility of laparoscopically assisted TAP block utilization in the system of multimodal analgesia by comparing the severity of pain and associated postoperative recovery indicators in obese patients after laparoscopic sleeve gastrectomy

Materials and methods: The retrospective study included 39 patients, who underwent metabolic surgery from 2013-2022. All patients were divided into 2 groups depending on the chosen perioperative analgesia protocol. Group 1 included 19 patients who prior to skin incision a local infiltration of the trocar puncture areas of the abdominal wall. Group 2 included 20 patients, whom in addition to the above-described anaesthesia procedure after completion of the main stage of surgery, a laparoscopically assisted bilateral subcostal TAP block was additionally performed

Results: The need to use opioid analgesics in the rescue analgesia mode arose in 17.6% (3/17) of patients of the first group, and 5% (1/20) of patients in the second group Average duration of postoperative hospitalization in group 1 was 7.2±1.1 days, and in group 2 it was 6.2±1.4 days ($P < 0.05$).

Conclusions: Subcostal TAP block in obese patients is a safe and effective method of regional anaesthesia. Further study of this option of regional anaesthesia is required in order to be able to form clearer recommendations for its routine use in clinical practice.

KEY WORDS: obesity, laparoscopically assisted TAP block, metabolic surgery, multimodal analgesia

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INTRODUCTION

According to the WHO data, in 2016 the number of overweight adults in the world exceeded 1.9 bln persons (39% of the population of our planet aged over 18), among whom 650 mln (13%) were suffering from obesity. The above statistical data coupled with the catastrophic dynamics of this illness spread allowed professionals to characterize the problem of being overweight as a "non-infectious pandemic" of today's world [1].

Rapid evolution of metabolic surgery is driven by its proven effectiveness in the treatment of obesity, multiple concurrent conditions, and metabolic disorders [1]. As a result of such development, we observe not only improvement in surgical techniques but also a radical change in the basic principles of perioperative management of patients. In particular, the widespread use of laparoscopic access has created the necessary preconditions for the full implementation of the Enhanced Recovery After Surgery (ERAS) [2] protocols in metabolic surgery. ERAS is a system of multimodal integrated patient management, which aims to reduce perioperative stress, accelerate physical and psychological recovery, reduce hospitalization duration and, as a result, reduce the financial burden on national health systems [3].

In turn, one of the key and most important components of the ERAS is the system of multimodal analgesia (MMA), which is designed to minimize and effectively manage pain in the early postoperative period. This is achieved by utilizing a pre-emptive strategy (administering analgesia in advance) and the use of a synergistic combination of simultaneous systemic and regional mechanisms of pain control. This approach allows

significantly enhance the analgesic effect even with lower doses of each of the pharmacological agents (compared to other analgesic protocols) and reduces or avoids entirely the use of opiates and side effects caused by them [4].

According to modern research data, an important place in the system of multimodal analgesia is given to regional methods of anaesthesia. Even though until recently (during the "open" abdominal surgery era) thoracic epidural anaesthesia was obviously considered the gold standard, now with widespread utilization of laparoscopic technology, there has been a rapid increase in scientific and practical interest in alternative and less invasive options of afferent regional blocks of the abdominal wall [5]. One of the key techniques among the latter is the so-called transversus abdominis plane block (TAP block), the purpose of which is to administer a local anaesthetic into the space of the abdominal wall between the internal oblique and transverse abdominal muscles under ultrasound or laparoscopic control. Depending on the place of the anaesthetic administration, the planned effect of the technique is to block the parietal pain component at the level of Th6 – L1 [6].

Findings presented in contemporary publications on the assessment of the effectiveness and safety of different variants of TAP block contain certain contradictions [7]. This is why an objective assessment of the results of this technique in the system of multimodal analgesia necessitates additional research.

THE AIM

The aim of the study was to assess the effectiveness and feasibility of laparoscopically assisted TAP block utilization in the system of multimodal analgesia by comparing the severity of pain and associated postoperative recovery indicators in obese patients after laparoscopic sleeve gastrectomy with and without application of the specified method of regional anaesthesia.

MATERIALS AND METHODS

Our study was performed in line with the principles of the Declaration of Helsinki. Also, the Local Ethics Committee of State Scientific Institution Center For innovative Medical Technologies of the National Academy of Sciences of Ukraine approved this study. All participants signed informed consent. The retrospective study included 39 patients suffering from obesity and comorbid type 2 diabetes under the mandatory condition that they have given their voluntary informed consent, who underwent metabolic surgery from 2013–2022, namely, laparoscopic sleeve gastrectomy (19 patients from 2013 to 2018 and 20 patients from 2019 to 2021). Morbid obesity was the indication for surgery (body mass index (BMI) over 40 kg/m^2) or class II obesity (BMI over 35 kg/m^2) with type 2 diabetes and other concurrent diseases that are difficult to treat by conservative correction [8]. Patients with simultaneous or revision surgeries, severe pathology of the cardiovascular and respiratory systems, renal failure, upper abdominal organ surgeries in the past medical history, and postoperative complications were not included in the study. Patients with occurring complications during the postoperative period were excluded from the final analysis of the results.

All patients were divided into 2 groups depending on the chosen perioperative analgesia protocol. Group 1 included 19 patients who prior to skin incision a local infiltration of the trocar puncture areas of the abdominal wall with a 0.25% solution of bupivacaine – 25 ml (5 ml at the injection site of each trocar) was performed. Group 2 included 20 patients whom, in addition to the above-described anaesthesia procedure after completion of the main stage of surgery (before removal of the preparation from the abdominal cavity), a laparoscopically assisted bilateral subcostal TAP block with 0.25% solution of bupivacaine – 40 ml (20 ml of local anaesthetics on the right and left) was additionally performed. The postoperative analgesia procedure in both study groups was standardized and included intravenous administration of acetaminophen 3 g/day (1 g every 8 hours) and dexketoprofen 100 mg/day (50 mg every 12 hours) with the transition to oral administration of paracetamol after 36 hours after surgery.

All surgeries were performed by one surgeon with a standard placement of 5 trocars [9]. The level of carboxy pneumoperitoneum was 12 mm Hg. Mobilization of the greater gastric curvature and the fundal part of the stomach was performed with the LigaSure Blunt Tip Laparoscopic Sealer/Divider LF1844 instrument (manufactured by Medtronic). Gastric tube formation was performed on a 36 Fr gauging probe using an Endo GIA Universal XL linear stapler and 60 mm disposable replaceable purple cartridges with Tri–Staple technology (manufactured by Medtronic) without peritonization of the resection line. Removal of the resected part of the stomach was performed through an optical trocar placed in the midline at the same distance from the navel and the xiphoid process. Intraoperative management of all patients included in the study was performed according to the anaesthesia protocol standardized in the clinic.

The standard technique of laparoscopically assisted TAP block was used (the so-called bulge technique) [10]. Local anaesthetic was injected between the midclavicu-

Table I. Characteristics of patients in the study groups by age, sex, comorbid pathology and anthropometric data

Variables	Group 1 (N=19)	Group 2 (N=20)	p
Age, (years)	49.2±9.9	50.6±12.1	0,68
Dyslipidemia, n (%)	17 (89.5%)	18 (90%)	0,95
Arterial hypertension, n (%)	15 (7%)	17 (85%)	0,62
Sleep apnoea syndrome, n (%)	3 (15.7%)	5 (25%)	0,47
Body weight, (kg)	143.2±34.5	153.5±29.1	0,32
Body mass index, (kg/m^2)	49.5±11.2	51.2±10.4	0,61
Excess body weight, kg	80.2±34.4	85.5±28.8	0,6
Surgery duration, (min)	171.7±60.1	137.7±54.3	0,03

Table II. Parameters of the level of postoperative pain for VAS in the first 48 hours after surgery.

Postoperative hours	level of postoperative pain		p
	Group1 (n=17)	Group2 (n=20)	
3 h	3,5±1,5	2,4±1,3	0,023
6h	2,7±1,4	1,7±1,3	0,03
12 h	2,6±1,5	1,5±1,0	0,013
24 h	1,8±0,52	1,1±0,9	0,005
48 h	1,4±1,2	0,5±0,7	0,007

lar and anterior inguinal lines 1.5 – 2 cm below the costal arch through a Stimuplex A needle manufactured by B. Braun during laparoscopic imaging of the transverse abdominal muscles area. The first portion (0.1-0.2 ml) of anaesthetic was administered preperitoneally, and the main volume (second portion) was administered after pulling up the needle by 3-4 mm, i.e., in the space between the transverse and internal oblique muscles of the abdomen. Ultrasound procedure control was used to ensure the correct injection of the anaesthetic into the required intermuscular space (before the start of the research, at the stage of mastering the laparoscopically assisted TAP block technique). The technique was considered mastered after 5 consecutive ultrasound-confirmed correct injections of the anaesthetic.

For the purpose of comparative analysis, the following was assessed in the study groups: surgery duration, frequency of postoperative complications and mortality, and dynamics of pain severity on a 10-point pain numerical rating scale (NRS), which is a digital version of the visual-analog scale [11], need for administration of narcotic analgesics during the first 48 hours after surgery and compliance with the discharge criteria adopted in the clinic 48 hours after surgery, actual duration of the postoperative hospitalization. In the second group of patients, the duration of performance of the laparoscopically assisted subcostal bilateral TAP block was assessed.

Patient discharge from the hospital was deemed possible under the following conditions: the possibility of effective pain management with the use of oral analgesics, normal tolerance to liquid food, ability to drink at least 1 liter of liquid per day, restoration of normal motor activity (up to prehospital level), knowing and understanding by a patient of the postoperative complication symptoms and his/her actions in case of occurrence thereof.

Statistical data processing was performed using methods of variation and descriptive statistics using the statistical analysis package SPSS Statistics, version 23. Before starting the data analysis, all indicators were checked for normal distribution using the Shapiro-Wilcoxon test. Statistical indicators of mean values (M) and standard deviation (SD) were used in the study. To assess statistically significant differences in the mean values of quantitative traits subject to the law of normal distribution, parametric assessment methods were used in the dependent groups (Student's t-test). Pearson's test ($\chi 2$) was used in the comparative analysis of qualitative parameters (frequency distributions) between groups of patients. Differences in the results obtained were deemed statistically significant at $p < 0.05$, which provides a 95% probability level.

RESULTS

Among 39 patients included in the study, 21 were women (53.8%) and 18 were men (46.2%). The average age of patients was 49.9±11.0 years, average body mass

index was 50.4 ±10.7 kg/m^2. The average patient body weight was 148.4±31.9 kg, and the average excess body weight was 82.9±31.3 kg. The average duration of the surgery was 145.2±56.4 minute

Carbohydrate metabolism indicators in the study groups did not differ significantly and were the following: the average level of C-peptide was 3.96±1.47 ng/ml, the average level of glycated hemoglobin was 7.7±1.5%, the average level of fasting glucose was 8.9±2.4 mmol/l, an average level of insulin was 27.9±13.1 mU/l, an average level of leptin was 24.2±16.6 ng/ml, the average level of the HOMA-IR index was 10.9±6.7.

Groups of patients included in the study by age, sex, body weight, body mass index, severity and nature of an obesity-associated pathology were comparable (table I).

The average surgery duration in the first study group was 171.7±60.1 minutes, in the second group – 137.7±54.3 minutes (P=0,03). The average duration of performing the laparoscopically assisted subcostal bilateral TAP block in patients of the second group was 1.4±0.3 minutes. Significantly longer surgery duration in the first study group was probably due to the "learning curve" of the surgical team at the stages of mastering the laparoscopic sleeve gastrectomy technique. No complications directly associated with the performance of the TAP block were observed. There were no fatalities.

Pain intensity according to the NRS during the first 48 hours after surgery was significantly lower in study group 2 (table II).

In the early postoperative period, 2 cases of complications were observed in patients of the study group 1: iatrogenic damage to the urethra during insertion of an urinary catheter due to stricture of the urethra – 1 male patient, and acute renal failure – 1 female patient. These patients were excluded from the final analysis of the results. No postoperative complications in the study group 2 were observed.

Thus, pain and related pain indicators were studied in a total of 37 patients – 17 patients from group 1 and 20 patients from group 2.

The need to use narcotic analgesics in the rescue analgesia mode arose in 17.6% (3/17) of patients of the first group, and 5% (1/20) of patients of the second group (with a level of pain 6 or more points under the NRS). In this case, 2 patients of the first group required a single intramuscular injection of opiates, and 1 patient of the first group and a patient of the second group required a double injection of opioid analgesics. 48 hours after the surgery, 52.9% (9/17) in the first group and 75% (15/20) of patients in the second group met the above-mentioned hospital discharge criteria, and 47.1% (8/17) of the patients of the first and 25% (5/20) of patients in the second group. Among the main causes (nausea, vomiting, pain, insufficient food intake per os) of non-compliance with the discharge criteria 48 hours after surgery, insufficient pain management due to oral administration of analgesics was observed in 4 (23.5%) patients in the first group, while in the second group there were no such cases.

Among the main reasons for non-compliance with discharge criteria in the first and second groups of the study, insufficient pain control was noted in 4 (23.5%) and 0 (0%) patients, nausea - in 2 (11.7%) and 3 (15%) patients, inability to consume a sufficient daily volume of liquid - in 3 (17.6%) and 2 (10%) patients, respectively.

The actual average duration of postoperative hospitalization in group 1 was 7.2±1.1 days, and in group 2 it was 6.2±1.4 days (P <0.05).

DISCUSSION

Data provided by contemporary research show that in the "structure" of the pain syndrome after laparoscopic interventions 50-70% are attributable to the parietal pain component, 10-20% to visceral, and 20-30% are associated with carboxypneumoperitoneum [13]. It follows from the above that the use of regional methods of abdominal wall anaesthesia in the perioperative period is an important and prospective technique [12]. However, there are debatable and sometimes controversial issues that require further critical re-evaluation. They are primarily associated with the assessment of the actual effectiveness and safety of regional anaesthesia options and differences in views on the feasibility of combining local infiltration anaesthesia of trocar wounds area and abdominal blocks (or the use of these techniques as alternatives) [14]. There is no agreement of opinion on the optimal imaging technique for performing the TAP block [15]. Even though presently ultrasound control of the procedure is considered the "gold standard", however, according to some authors, it also has a number of disadvantages, namely: the need for ultrasound equipment to be located in the operating room as well as specially trained anaesthesiologist; it does not always allow to identify clearly and correctly the necessary space for anaesthesia injection in obese patients; prolongs patient's stay on the operating table; does not completely eliminates the possibility of "unnoticed" iatrogenic damage to the abdominal wall vessels and abdominal organs. That is why laparoscopically assisted TAP block is now considered by some authors as an effective and safe alternative to the procedure performed under ultrasound control and is increasingly used in clinical practice [15]. This is also confirmed by the results of our research.

On 24th of February 2022, Russia illegally crossed the borders of our country for the second time, after 2014, and without warning started a full-scale war against Ukraine. The provision of elective and emergency surgical and anesthetic care to the civilian population during military operations has certain features. First of all, it is necessary to reduce the operation time and lay of stay as much as possible. Reduction of the patient's stay in the operating room depends, among other things, on the intraoperative dose of opioids and the need for mechanical ventilation. Laparoscopically assisted TAP block reduced intra- and postoperative doses of opioids and early recovery time. The absence of the need for an ultrasound machine, the special skills of the anesthesiologist, the speed of execution, and a good opioid-sparing effect make the laparoscopically assisted TAP block a promising method of perioperative analgesia for obese patients in wartime conditions.

We are aware that our research contains a number of limitations. They are, in particular, associated with a small number and non-randomized selection of patients during the formation of the comparison groups, the lack of clearly defined criteria for locations (levels) of anaesthetic injections when performing operations in the upper abdominal cavity area, the likelihood of bupivacaine solution injection in the wrong location in some part of patients, which in turn cannot be verified without the use of ultrasound equipment.

However, given the importance of pain management in abdominal surgery, and especially in the enhanced recovery after surgery system, the study of those outlined issues and the search for optimal options for analgesia is certainly relevant and necessitates further research.

CONCLUSIONS

1. The use of laparoscopically assisted bilateral subcostal TAP block in the study population has been shown to be effective, resulting in a statistically significant ($P < 0.05$ compared with no-patient) reduction in pain during the first 48 hours after sleeve gastrectomy.
2. Minimum time (1.4 ± 0.3 min) of the procedure, absence of related iatrogenic injuries, the possibility of regional anaesthesia without additional involvement of specialists and equipment for ultrasound imaging, a statistically significant reduction in hospital stay in the group of patients using laparoscopic assisted TAP-block indicate the feasibility of using this technique in metabolic surgery.
3. Further study of this option of regional anaesthesia is required in order to be able to form clearer recommendations for its routine use in clinical practice.

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2. *"Comprehensive development of innovative minimally invasive methods in surgery with utilization in practical and training programmers", registration number: 0120U105160, period 01.01.2021- 31.12.2023*

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ORIGINAL ARTICLE

ASSOCIATION OF CASPASE-8 LEVELS WITH RESPIRATORY PARAMETERS AND PRESENCE OF HYPERTENSION IN COPD PATIENTS

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ABSTRACT

The aim: To investigate the association between hypertension and serum Caspase-8 levels in COPD patients.

Materials and methods: 95 COPD patients (GOLD 2nd grade, group B) were included in the study: 47 non-hypertensive COPD patients formed the main group, and 48 patients with concomitant COPD and hypertension formed the comparison group. Patients underwent examination according to GOLD 2022 Guidelines. Caspase-8 serum levels were measured by ELISA.

Results: Performed analysis showed that an increase in Caspase-8 serum levels was significantly associated with the presence of concomitant hypertension in both univariate and multivariate analyses. A significant association was also found regarding FEV1 levels but not FVC.

Conclusions: Both presence of concomitant hypertension and spirometry parameters, which indicate the severity of COPD, can be considered strong predictors of the intensification of apoptosis in COPD patients.

KEY WORDS: COPD, hypertension, Caspase-8, apoptosis

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death with rising trends year by year [1, 2]. COPD includes violations in all parts of the bronchopulmonary tract: bronchitis, airway narrowing, and emphysema [1]. COPD is a heterogeneous disease with smoking being the predominant modifiable risk factor. Data on the particular mechanisms of COPD development are still controversial, but violations of immune regulation due to subclinical inflammation are considered the main pathophysiological mechanisms of the disease [3]. Moreover, novel data suggest that age and genetics play a crucial role in COPD predisposition and development [2].

In conditions of wartime and continuous warfare, soldiers are exposed to various vapors and gases, which can increase the risk of developing COPD [3]. Moreover, maintaining a healthy lifestyle during military operations is an impossible task for both military personnel and civilians, which increases the possible harm and speeds up the progression of chronic diseases such as hypertension [4]. Due to such changes, we can expect a significant drop in overall health rates and an increase in the number of non-communicable diseases or a worsening of their course. As such, Hussain et al. [5] state that the relative increase in some non-communicable diseases in Iraq reached 3–5 times, with hypertension and diabetes being the primary causes. These factors further contribute to socio-economic changes and can lead to an increased burden on healthcare. Therefore, assessing novel pathogenetic chains and possible predictors of non-communicable diseases is an important scientific problem, especially in conditions of war.

Smoking, along with occupational hazards, air pollution, and biomass fuels, is considered to be a major risk factor for COPD [6, 7]. In the long-term course of the disease, continuous smoking results in damage to the airways and the development of fibrosis. However, in COPD, airway narrowing is not reversible even after removing the hazardous factors [2]. Chronic local and systemic inflammatory reactions lead to subsequent progressive airway remodeling, eventually causing their narrowing [2]. On the other hand, smoking causes intensive reactive oxygen species (ROS) production, which eventually depletes the antioxidative system and induces cellular apoptosis [2].

Release of interleukin-1 as a result of smoke-induced inflammasome activation initiates both early and chronic inflammatory reactions [7]. Apoptosis, as a consequent process of chronic inflammation and hypoxia, accompanies COPD pathogenesis. Data show increased apoptosis rates in both epithelial and endothelial cells in COPD patients compared to normal lung tissue. Especially fast rates are observed in cigarette-mediated lung disease. This suggests an imbalance between lung tissue destruction and repair [1].

Caspases (Cas) family includes 12 described specific cysteine-aspartate proteases, which take part in immunity and apoptosis regulation. It is noted that Cas-1, Cas-4, and Cas-5 predominantly take part in immunity, on the other hand, Cas-2, Cas-8–10 are initiator and Cas-3, Cas-6–7 are effector caspases, which regulate both intrinsic and extrinsic apoptosis pathways. Cas-8 is a key player in the extrinsic apoptotic mechanism [8].

Data suggest [6, 9] that Caspase-8 (Cas-8) is involved not only in apoptosis, but also in inflammation development. Rong et al. [6] note that Cas-8 is involved in the production of pro-IL-1β, which in part is associated with numerous cardiopulmonary conditions.

THE AIM

To investigate the association of concomitant hypertension on levels of serum Caspase-8 levels in COPD patients.

MATERIALS AND METHODS

This study included 95 COPD patients (GOLD 2nd grade, group B). The main group consisted of 47 non-hypertensive COPD patients. The comparison group included 48 patients with concomitant COPD and hypertension. The median age, gender, duration of COPD, and hypertension are presented in Table I.

Diagnosis of hypertension was made according to ESC/ESH guidelines (2018) [10]. Diagnosis of COPD was made according to GOLD guidelines (2022) [8]. All patients provided written consent to participate in research in accordance with the recommendations of the Ethics Committees for Biomedical Research, Ukrainian Health Legislation, and the Declaration of Helsinki of 2000, European Community Directive 86/609 On Human Participation in Biomedical Research.

For continuous variables, we calculated the median (Me), lower (Lq), and upper quartiles. Differences between unrelated samples were calculated using Mann-Whitney U-test [11-14]. Categorical variables were presented in absolute and percent values. Pearson's Chi-squared test was used to assess differences between groups [12]. Linear regression was used to calculate associations between independent variables and dependent continuous variables. Beta-coefficients and respective 95 % confidence intervals (CI) were calculated. Categorical variables were coded as K-1 according to the proposed method by Hardy [13]. The coding of groups in regression models was as follows: COPD-only — reference group; COPD+HTN — comparison group. The gender reference group included female patients. Significance level in the study was considered as p=0.05. Statistical calculations were performed in IBM SPSS 25.0 for Windows.

RESULTS

COPD-only patients were older compared to COPD+HTN patients: 62.0 [52.3; 65.8] years vs. 60.0 [58.0; 62.8] years (p=0.026). No significant differences were found regarding gender distribution in studied groups (p=0.426) (table I).

Table I. Characteristics of patients included into study

Index		COPD (n=47)	COPD+HTN (n=48)	p
Age, years, Me [Lq; Uq]		62.0 [52.3; 65.8]	60.0 [58.0; 62.8]	0.026
Gender	Females, %	14 (29,8)	18 (37,5)	0.426
	Males, %	33 (70.2)	30 (62.5)	
Duration of COPD, years, Me [Lq; Uq]		7.0 [6.0; 9.0]	8.5 [7.0; 10.0]	0.014
Duration of HTN, years, Me [Lq; Uq]		—	7.0 [6.0; 8.0]	—

Table II. Spirometry parameters and Caspase-8 serum levels in studied patients, Me [Lq; Uq]

Index	COPD (n=47)	COPD+HTN (n=48)	p
FVC, % of predicted	67.0 [64.0; 68.0]	65.0 [63.0;67.0]	0.078
FEV_1, % of predicted	61.0 [58.0; 65.0]	57.0 [54.0; 60.0]	0.001
FEV_1/FVC, %	73.0 [71.0; 77.0]	72.0 [69.0; 75.0]	0.014
Cas-8, ng/ml	3.48 [2.99; 3.72]	3.79 [3.56; 3.84]	<0.001

Table III. Univariate and multivariate linear regression analysis of Cas-8 levels

Predictor	Univariate			Multivariate		
	B	95.0 % CI	p	B	95.0 % CI	p
Concomitant HTN	0.406	0.225–0.587	<0.001	0.197	0.025–0.369	0.025
Male gender	-0.024	-0.234–0.187	0.824	0.014	-0.147–0.174	0.867
Age, years	0.007	-0.012–0.026	0.464	0.010	-0.005–0.025	0.190
COPD duration, years	0.090	0.059–0.122	<0.001	0.048	0.015–0.081	0.005
FVC, % of predicted	-0.048	-0.075–-0.021	0.001	-0.118	-0.235–-0.002	0.047
FEV_1, % of predicted	-0.061	-0.070–-0.044	<0.001	0.061	-0.059–0.180	0.317
FEV_1/FVC, %	-0.023	-0.040–-0.007	0.006	0.070	-0.033–0.174	0.182

Table IV. Designed linear models for predicting Cas-8 levels in hypertensive and non-hypertensive COPD patients

Predictor	Model 1			Model 2			Model 3		
	B	95.0 % CI	p	B	95.0 % CI	p	B	95.0 % CI	p
HTN	0.345	0.176–0.514	<0.001	0.198	0.024–0.372	0.026	0.306	0.128–0.484	0.001
Male gender	-0.003	-0.174–0.169	0.974	0.008	-0.150–0.166	0.920	-0.031	-0.200–0.138	0.984
Age, years	0.005	-0.011–0.021	0.538	0.012	-0.003–0.028	0.117	0.010	-0.007–0.026	0.830
COPD duration, years	0.067	0.034–0.100	<0.001	0.052	0.021–0.084	0.001	0.075	0.044–0.106	<0.001
FVC, % of predicted	-0.022	-0.047–0.003	0.087	—	—	—	—	—	—
FEV_1, % of predicted	—	—	—	-0.041	-0.062–-0.021	<0.001	—	—	—
FEV_1/FVC, %	—	—	—	—	—	—	-0.012	-0.027–0.003	0.110
Constant	3.573	1.429–5.717	<0.001	4.478	2.903–6.053	<0.001	2.646	1.284–4.009	<0.001

Model 1 predictors: concomitant HTN, male gender, age, COPD duration, FVC;
Model 2 predictors: concomitant HTN, male gender, age, COPD duration, FEV1;
Model 3 predictors: concomitant HTN, male gender, age, COPD duration, FEV1/FVC.

Table V. Linear regression with backward exclusion of variables for Model 1 and model 2

Predictor	Model 1			Model 2		
	B	95.0 % CI	p	B	95.0 % CI	p
Concomitant HTN	0.330	0.171–0.488	<0.001	0.172	0.001–0.343	0.049
COPD duration, years	0.069	0.037–0.101	<0.001	0.060	0.031–0.090	<0.001
FVC, % of predicted	-0.023	-0.047–0.001	0.065	—	—	—
FEV_1, % of predicted	—	—	—	-0.039	-0.058–-0.019	<0.001
Constant	3.954	2.215–5.694	<0.001	5.039	3.627–6.450	<0.001

Model 1 predictors: concomitant HTN, male gender, age, COPD duration, FVC;
Model 2 predictors: concomitant HTN, male gender, age, COPD duration, FEV1;

Overall median duration of COPD after diagnosis was significantly (p=0.014) lower in the COPD-only group than in patients with concomitant hypertension: respectively 7.0 [6.0; 9.0] years and 8.5 [7.0; 10.0] years. The median duration of hypertension was 7.0 [6.0; 8.0] years in COPD+HTN patients (table I).

Forced vital capacity was slightly higher in COPD-only patients than in COPD+HTN patients: 67.0 [64.0; 68.0] % vs. 65.0 [63.0; 67.0] % (p=0.078). A significant difference was found in FEV_1 in the COPD group: 61.0 [58.0; 65.0] % vs 57.0 [54.0; 60.0] % (p=0.001). Median FEV_1/FVC ratio was significantly higher in COPD-only patients than in the COPD+HTN group: respectively 63.0 [61.0; 67.0] % and 62.0 [59.0; 65.0] % (p=0.014) (table II).

Univariate analysis (table III) showed direct association of concomitant HTN with increase in Caspase-8 levels in COPD patients: mean increase was by 0.406 [95.0 % CI 0.225–0.587] ng/ml (p<0.001). COPD duration was also directly associated with increased levels of Cas-8: 0.090 [95.0 % CI 0.059–0.122] ng/ml (p<0.001). All studied parameters of respiratory function were negatively associated with Cas-8 levels in univariate analysis.

Noteworthy, in multivariate analysis significant association with increased Cas-8 levels were found only with concomitant hypertension (0.197 [95.0 % CI 0.025–0.396] ng/ml, p=0.025) and COPD duration (0.048 [95.0 % CI 0.015–0.081] ng/ml, p=0.005). Among respiratory function parameters only FVC (-0.118 [95.0 % CI -0.235–-0.002], p=0.047) showed significant association, but not FEV_1 and FEV_1/FVC (table III).

Three linear models were built, each including different respiratory parameters: FVC, FEV_1 and FEV_1/FVC. Model 1 included concomitant HTN, male gender, age, COPD duration, FVC; Model 2 — concomitant HTN, male gender, age, COPD duration, FEV_1; and Model 3 — concomitant HTN, male gender, age, COPD duration, FEV_1/FVC.

In Model 1 both concomitant HNT and duration of COPD were significant predictors of Cas-8 levels increase: 0.345 [95.0 % CI 0.176–0.514] ng/ml (p<0.001) and 0.067 [95.0 % CI 0.034–0.100] ng/ml (p<0.001). However, FVC did not show significance: -0.022 [95.0 % CI -0.047–0.003] ng/ml (p=0.087) (table IV).

Regarding Model 2, presence of concomitant HTN showed weaker but still significant association with increase of Cas-8 levels: 0.198 [95.0 % CI 0.024–0.372] ng/ml (p=0.026). As in Model 1 COPD duration showed strong direct association with Cas-8 levels increase: 0.052 [95.0 % CI 0.021–0.084] ng/ml (p=0.001). Noteworthy, FEV_1 showed significant inverse association with Cas-8: -0.041 [95.0 % CI -0.062–-0.021] ng/ml (p<0.001) (table IV).

Regarding Model 2, presence of concomitant HTN showed weaker but still significant association with increase of Cas-8 levels: 0.198 [95.0 % CI 0.024–0.372] ng/ml (p=0.026). As in Model 1 COPD duration showed strong direct association with Cas-8 levels increase: 0.052 [95.0 % CI 0.021–0.084] ng/ml (p=0.001). Noteworthy, FEV_1 showed significant inverse association with Cas-8: -0.041 [95.0 % CI -0.062–-0.021] ng/ml (p<0.001) (table IV).

In Model 3 presence of concomitant HTN and duration of COPD were significantly associated with increased Cas-8 levels: 0.306 [95.0 % CI 0.128–0.484] ng/ml (p=0.001) and 0.075 [95.0 % CI 0.044–0.106] ng/ml (p<0.001). FEV_1/FVC was inversely associated with Cas-8 but association was nonsignificant: -0.012 [95.0 % CI -0.027–0.003] ng/ml (p=0.110) (table IV).

Further analysis with backward exclusion of variables was applied to Model 1 and Model 2 regarding the strongest association of respiratory parameters and Cas-8 levels in them. As a result, in both models age and gender of patients were excluded as being non-significantly associated with Cas-8 levels (table 5).

In both models, concomitant hypertension and COPD duration were strong predictors of Cas-8 levels increase. However, FEV1 showed a significant reverse association with Cas-8 levels, and the association of FVC was weaker: -0.039 [95.0 % CI -0.058–-0.019] ng/ml (p<0.001) and -0.023 [95.0 % CI -0.047–0.001] ng/ml (p=0.065), respectively (Table 5).

DISCUSSION

Apoptosis, or regulated cell death, is mediated by two mechanisms: intrinsic and extrinsic pathways. While the extrinsic pathway is initiated by extracellular signaling, the intrinsic pathway depends on the violation of cellular homeostasis [1]. Caspases play a vital role in both processes, as they are involved in the initial and executive stages, and regulate inflammation, immunity, and apoptosis interplay. It is noted that Cas-1, Cas-4, and Cas-5 predominantly take part in immunity, while other caspases mostly regulate apoptosis. Moreover, Cas-2, Cas-8–10 are initiator caspases, and Cas-3, Cas-6–7 are effector caspases that regulate both intrinsic and extrinsic apoptosis pathways. Caspase-8, a member of the cysteine protease family, is an initiator caspase of the extrinsic pathway [10], which further activates executioner caspases promoting subsequent apoptosis processes. On the other hand, data suggest [6, 11] that Caspase-8 is involved not only in apoptosis, but also in the development of inflammation. Rong et al. [6] note that Cas-8 is involved in the production of pro-IL-1β, which is associated with numerous cardiopulmonary conditions and can be a link to their comorbidities.

Number of processes are also involved in triggering apoptosis in lung tissue, such as the release of inflammatory cytokines, oxidative stress, long-term exposure to environmental factors, and smoking, among others [1, 15]. Notably, oxidative stress, induced mainly by cigarette smoking, hypoxia, and release of reactive oxygen species, plays a key role in the development of apoptosis.

Strong associations between COPD and cardiovascular diseases have been shown in different studies. The data indicate not only symptom aggravation but also violations of clinical course. COPD and hypertension are very frequent comorbidities as cardiovascular risks increase due to hypoxia, persistent oxidative stress, and chronic inflammation [16]. Genetic factors and aging are also considered significant factors in COPD development and course nowadays. The results of this study showed a direct association between increased Cas-8 levels and the duration of COPD. Although the incidence of hypertension development in COPD patients was not evaluated due to study design limitations, the

results show a direct association between concomitant hypertension and increased Cas-8 levels, which suggests a strong impact of cardiac function violation on COPD course.

Research [5] shows that the increasing prevalence of hypertension leads to higher morbidity and mortality rates during and after wartime. Additionally, the presence of comorbid conditions almost doubles these indices, which subsequently increases disability and healthcare burden. Continuous war operations have led to the adaptation of current socio-economic and medical resources in Ukraine, especially in regions with active combat actions [20]. This requires the study of novel challenges and realities caused by war on non-communicable diseases.

To the best of our knowledge, there is a lack of data on the study of initiator caspases in the comorbidity of COPD and hypertension. However, various studies provide data on impaired cardiac and vascular function in COPD, considering inflammation as the core of its pathogenesis. For example, the research by Fisk et al. [18] showed that COPD patients had higher systolic blood pressure and heart rate compared to non-smokers, although the differences were not significant. On the other hand, COPD patients had significantly higher indices of arterial stiffness, which is the initial trigger of cardiovascular pathology development. Arslan et al. [19] also found that both systolic and diastolic nighttime blood pressure were increased in COPD patients compared to controls. The authors also noted significantly higher heart rates and pulse pressure in COPD subjects. Such findings suggest the presence of violations of cardiovascular function in COPD, which can further trigger heart function and morphology impairment.

In all developed models, concomitant hypertension showed a significant association with an increase of Cas-8 levels in COPD patients, suggesting an aggravation of apoptotic processes induced by increased systemic blood pressure. On the other hand, the duration of COPD, an indirect marker of its worsening, was also significantly associated with an increase in Cas-8 levels. This finding can indicate that irreversible changes in the bronchopulmonary tree with the duration of the disease directly stimulate apoptotic activity. The age and gender of examined patients were not associated with an increase in Cas-8 in both univariate and multivariate analyses and developed models.

Among studied respiratory parameters, the strongest association with Cas-8 levels was observed with FEV_1. This index is directly related to the severity and stability of the COPD course and can reflect the grade of inflammation in the bronchial wall. Noteworthy, is that FVC showed a nonsignificant association with Cas-8 levels. This may be due to known gradual ageing-related decline in FVC, which is observed irrespectively of the presence of lung conditions. Moreover, FEV_1/FVC ratio did not show a significant association with Cas-8 levels in COPD patients.

STUDY LIMITATIONS

To the best of our knowledge, there are a few studies, which assessed activity of apoptosis in COPD patients. However, our study has some limitations such as relatively small sample of patients and involvement of one hospital. Only stable COPD patients were included in study, which limits usage of results in patients with COPD exacerbations. In addition, sample included only COPD GOLD 2nd grade group B patients, which limits application of results for patients with more severe COPD.

CONCLUSIONS

The war in Ukraine presents novel challenges in medical practice and underscores the need for accurate and rapid non-invasive diagnostic tests for non-communicable diseases. Our study found that the presence of concomitant hypertension and the duration of COPD is significantly associated with increased Cas-8 levels in COPD patients. Both the presence of concomitant hypertension and spirometry parameters indicate the severity of COPD, and higher Cas-8 levels can be considered as additional strong predictors of disease severity and intensification of apoptosis in COPD patients. These findings suggest the need for proper medical support and education for such patients to maintain a stable course of both diseases.

Among respiratory function parameters, the strongest association with increased Cas-8 levels was found with FEV_1, but not with FVC and FEV_1/FVC, in both univariate and multivariate models.

However further studies are required in order to investigate additional clinical and anamnestic factors of apoptosis aggravation in COPD patients.

FURTHER STUDIES

Regarding continuing war in Ukraine and changes in the structure of non-communicable diseases, the assessment of novel predictors of COPD and hypertension progression can be an actual medical task in order to strengthen prophylactics of this comorbidity. Dynamic evaluation of changes in the apoptosis state of studied patients is planned in perspective.

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Scientific-research task: «Improving the diagnosis and prevention of cardiorespiratory pathology in patients with chronic obstructive pulmonary disease based on the study of markers of systemic inflammation and cardiohemodynamics» (0119U002895, 2019–2021)

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ORIGINAL ARTICLE

ASSESSMENT OF THE CONSEQUENCES OF THE DETERIORATION OF THE EPIDEMIOLOGICAL SITUATION DURING HOSTILITIES

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ABSTRACT

The aim: Scientific substantiation of the methodology for predicting the consequences of the worsening of the epidemic situation on the territory of Ukraine during military operations for the timely adoption of measures for the medical protection of military personnel in conditions of biological contamination.

Materials and methods: Determination and generalization of the impact of biological contamination due to the use of biological weapons were carried out considering the main determinants of the epidemic process using the index and coefficient of medical protection. Applied methods of scientific research: epidemiological, system, and information approach.

Results: The authors proposed indicators that consider the pathogenicity of the infectious agent, contagiousness, the degree of non-specific protection of servicemen, specific protection of servicemen, and the sanitary-epidemiological state of the area of operations of troops (forces). Relevant epidemic situations were simulated, and the index and coefficient of medical protection were calculated to predict the consequences of the worsening of the epidemic situation to make timely decisions regarding the implementation of medical protection measures for military personnel in conditions of biological contamination during the repulsion of armed aggression.

Conclusions: In the conditions of biological contamination, when biological weapons and biological terrorism are used, the epidemic process in the army is intensified, which requires timely decisions regarding the implementation of medical protection measures for military personnel in conditions of biological contamination.

KEY WORDS: military medicine, biological weapons (terrorism), medical protection, forecasting the consequences of biological contamination

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INTRODUCTION

Today, in the conditions of the armed aggression of the Russian Federation against Ukraine, the use of various types of weapons, in particular weapons of mass destruction (WMD), creates prerequisites for a sharp deterioration in the sanitary and epidemiological condition of the troops [1]. In addition, the probability of the occurrence of mass infectious diseases is increasing, not only as a result of the use of biological weapons but also as a consequence of the deterioration of the sanitary and epidemic situation in the area of operations due to the activation and change of the boundaries and structure of previously studied natural foci of particularly dangerous infections (PDI), newly emerging dangerous infectious diseases and loss of control over some previously managed infections [2, 3].

In addition, when repelling Russia's armed aggression on the territory of Ukraine and defending its territory, the risk territory is the territory of operational-strategic directions of actions of the troops (forces), where the sanitary-epidemiological condition worsens because of the specified actions. Time of risk – the corresponding period of the task (within two months or more), considering the epidemiological features of the development of the epidemic process (seasonality, cyclicity, periodicity) of individual nosological forms, relative to which the specified territory is epidemically unfavorable; the risk group is servicemen of the interspecies operational and operational-tactical group of troops who are susceptible and not protected against the relevant infections. The risk factors for the development of epidemic problems in military groups are the deterioration of

the sanitary-epidemiological condition of the relevant territory of Ukraine as a result of damage to communal networks (water supply, sewage, electricity supply) during hostilities; complicating the organization of water supply, food, accommodation of personnel, population; accelerated evacuation of the population to the middle of the country from the relevant border regions of Ukraine, the territory of the enemy's active operations; conscription and replenishment of military teams to wartime states in conditions of full deployment of the Armed Forces of Ukraine with personnel who are not protected against relevant infectious diseases. In such conditions, the epidemic process in the troops is intensified, which affects their fighting capacity, and the high efficiency of medical protection measures of the troops in conditions of biological contamination is achieved only when predicting the consequences of the worsening of the epidemic situation [4-6].

This determines the relevance of measures for the medical protection of troops in the conditions of biological contamination and the scientific justification of the methodology of forecasting the consequences of the worsening of the epidemic situation (the use of biological weapons, biological terrorism) in the conditions of biological contamination during the repulsion of armed Russian aggression on the territory of Ukraine.

THE AIM

Scientific substantiation of the methodology for forecasting the consequences of the worsening of the epidemic situation (the use of biological weapons, biological terrorism) during the repulsion of Russia's armed aggression on the territory of Ukraine to take timely measures for the medical protection of military personnel in conditions of biological contamination.

MATERIALS AND METHODS

Determination and generalization of the impact of biological contamination due to the use of biological weapons (biological terrorism) were carried out considering the main determinants of the epidemic process using the index and coefficient of medical protection. Applied methods of scientific research: epidemiological, system, and information approach.

RESULTS

To ensure the protection of military personnel in conditions of biological contamination, it is necessary to take into account the multifactorial determinants of the epidemic process. The most significant factors are pathogenicity of the infectious agent, contagiousness, degree of non-specific protection of servicemen (depends on the level of equipment and training of personnel), specific protection of servicemen (depends on the type of pathogen, implementation of vaccination and its effectiveness, use of emergency prevention), lethality. Thus, for example, the degree of danger to personnel in the event of isolated cases of typhoid and paratyphoid, shigellosis, viral hepatitis A (VHA), and cholera during the implementation of the relevant actions of troops (forces) is moderate and low, respectively, several cases

Table I. Degree of the danger of infectious diseases

Nosoform	The number of those who fell ill		
	a single case	several cases	dozens of those who fell ill
Pneumonic plague	very high	very high	very high
Viral hemorrhagic fevers (Lassa, Marburg, Ebola)	very high	very high	very high
Bubonic plague	high	high	very high
Anthrax (generalized form)	average	high	very high
Cholera	average	high	very high
Tularemia	average	high	very high
Tick-borne encephalitis	low	average	high
Brucellosis	low	average	high
Yellow fever	low	average	high
Diphtheria	average	high	very high
Meningococcal infection	low	average	high
Typhoid	low	average	high
Shigellosis	low	low	average
Hepatitis A	low	low	average

Table II. Index of medical protection taking into account the determinants of the epidemic process of infectious diseases

Nosological form	Conducting medical protection measures	Index of medical protection
Typhoid fever and paratyphoid fever	carried out promptly and in full	0,08
	carried out late and partially	0,2
Shigellosis	carried out promptly and in full	0.08
	carried out late and partially	0,2
Viral hepatitis A	carried out promptly and in full	0,072
	carried out late and partially	0,2
Cholera	carried out promptly and in full	0,24
	carried out late and partially	0,3
Meningococcal infection	carried out promptly and in full	0,045
	carried out late and partially	0,1
Diphtheria	carried out promptly and in full	0,08
	carried out late and partially	0,1
Viral hemorrhagic fevers	carried out promptly and in full	0,05525
	carried out late and partially	0,35
Yellow fever	carried out promptly and in full	0,125
	carried out late and partially	0,2
Tularemia	carried out promptly and in full	0,1125
	carried out late and partially	0,25
Tick-borne encephalitis	carried out promptly and in full	0,06
	carried out late and partially	0,25
Malaria	carried out promptly and in full	0,05
	carried out late and partially	0,25
Brucellosis	carried out promptly and in full	0,0375
	carried out late and partially	0,1
Pneumonic plague	carried out promptly and in full	0,2
	carried out late and partially	0,4
Bubonic plague	carried out promptly and in full	0,05
	carried out late and partially	0,1
Anthrax (generalized)	carried out promptly and in full	0,1
	carried out late and partially	0,2

are average, low, and high, dozens of patients - high, moderate and very high, (Table I).

In the event of single cases of brucellosis during combat operations of troops (forces), the degree of danger to personnel is low, viral hemorrhagic fevers are very high, anthrax (generalized form) is average, several cases of brucellosis are average, viral hemorrhagic fevers are very high, anthrax (generalized form) – high, a dozen patients with brucellosis – high, viral hemorrhagic fevers and anthrax (generalized form) – very high (table I).

The degree of danger for the personnel in the event of single cases of diphtheria, meningococcal infection, or pneumonic plague during the implementation of the specified forms of actions when using troops (forces) - average, low, very high, respectively, several cases - high, average, very high and a dozen sick - very high and high, in the event of isolated cases of yellow fever, tick-borne encephalitis, malaria, the degree of danger to personnel is low, tularemia is average, bubonic plague is high, several cases of yellow fever, tick-borne encephalitis, malaria are average, tularemia is high, bubonic plague is high, a dozen patients with yellow fever, tick-borne encephalitis, malaria - high, tularemia and bubonic plague - very high, Table I.

To ensure effective interaction between command posts and units of the medical service to take timely measures for the medical protection of servicemen in conditions of biological contamination, based on the epidemic characteristics of various nosoforms, the characteristics of non-specific protection and the effectiveness of specific protection for various infections, we simulated the corresponding epidem-

Table III. The coefficient of medical protection, considering the dynamics of the sanitary-epidemiological state of the area of operations of troops (forces)

Nosological form	Conducting medical protection measures	Coefficient of medical protection in the sanitary-epidemiological state of the district		
		unstable	unfavorable	emergency
Typhoid fever and paratyphoid fever	carried out promptly and in full	0,16	0,24	0,32
	carried out late and partially	0,4	0,6	0,8
Shigellosis	carried out promptly and in full	0,16	0,24	0,32
	carried out late and partially	0,4	0,6	0,8
Viral hepatitis A	carried out promptly and in full	0,144	0,216	0,288
	carried out late and partially	0,4	0,6	0,8
Cholera	carried out promptly and in full	0,48	0,72	0,96
	carried out late and partially	0,6	0,9	1,2
Meningococcal infection	carried out promptly and in full	0,09	0,135	0,18
	carried out late and partially	0,2	0,3	0,4
Diphtheria	carried out promptly and in full	0,16	0,24	0,32
	carried out late and partially	0,2	0,3	0,4
Viral hemorrhagic fevers	carried out promptly and in full	0,105	0,1575	0,21
	carried out late and partially	0,7	1,05	1,0
Yellow fever	carried out promptly and in full	0,25	0,375	0,5
	carried out late and partially	0,5	0,75	1,0
Tularemia	carried out promptly and in full	0,225	0,3375	0,45
	carried out late and partially	0,5	0,75	1,0
Tick-borne encephalitis	carried out promptly and in full	0,12	0,18	0,24
	carried out late and partially	0,5	0,75	1,0
Malaria	carried out promptly and in full	0,1	0,15	0,2
	carried out late and partially	0,5	0,75	1,0
Brucellosis	carried out promptly and in full	0,075	0,1125	0,15
	carried out late and partially	0,2	0,3	0,4
Pneumonic plague	carried out promptly and in full	0,4	0,6	0,8
	carried out late and partially	0,8	1,0	1,0
Bubonic plague	carried out promptly and in full	0,1	0,15	0,2
	carried out late and partially	0,2	0,3	0,4
Anthrax (generalized)	carried out promptly and in full	0,2	0,3	0,4
	carried out late and partially	0,4	0,6	0,8

ic situation and calculated index and coefficient of medical protection.

The medical protection index was calculated according to the formula: Imp = C×(1-P)×E, where Imp is the medical protection index; C – index of contagion; P is the coefficient of specific protection (tension of collective immunity); E is the coefficient of emergency prevention (antibiotic prophylaxis, etc.).

Taking into account the pathogenicity of the corresponding infectious agent, its contagiousness, the degree of non-specific protection of the serviceman (depends on the degree of equipment and training of the personnel), and the specific protection of the servicemen (depends on the type of pathogen, vaccination, and its effectiveness, the use of emergency prevention) we determined the index of medical protection for a specific infectious nosology. Thus, in the case of the emergence and spread of infectious diseases with a fecal-oral transmission mechanism - typhoid and paratyphoid, cholera, shigellosis, and viral hepatitis A, based on the contagiousness, the effectiveness of specific protection and emergency prevention of these infections, the index of medical protection was 0,08, 0,24, 0,08 and 0,072, Table II.

If foci of infectious diseases with an airborne transmission mechanism, such as diphtheria, meningococcal infection, pneumonic, or plague, occur in the area of operation, the index of medical protection for these

infections will be 0,012, 0,045, 0,2. Taking into account the contagiousness effectiveness of specific protection and emergency prevention of such infectious diseases with the main transmission mechanism of transmission, such as yellow fever, tick-borne encephalitis, tularemia, malaria, and the bubonic form of the plague, in the conditions of their occurrence and spread, the index of medical protection of troops, primarily in endemic, natural focal areas, was 0,125, 0,06, 0,1125, 0,05 and 0,05, respectively, Table. II.

When such infectious diseases with the leading contact mechanism of transmission occur in the area of action, such as brucellosis, viral hemorrhagic fevers (Lassa, Marburg, Ebola), and anthrax (generalized form), taking into account their contagiousness, the effectiveness of specific protection and emergency prevention for these infections, in the conditions their occurrence and distribution in the troops, the index of medical protection of personnel, primarily in endemic, naturally concentrated territories, was 0,0375, 0,0553, 0,1, respectively, Table. II.

To take timely measures for the medical protection of servicemen in the conditions of biological contamination, we suggest using the coefficient of medical protection, which takes into account the effectiveness of medical protection measures taking account the dynamics of the sanitary and epidemiological state of the area of operations of troops (forces): Cmp = Imp×A, where Cmp is the coefficient of medical protection; Imp - index of medical protection; A - assessment of the sanitary-epidemiological state of the area where the troops are located (unstable, unfavorable, emergency). Thus, for example, the coefficient of medical protection in the event of the occurrence and spread of typhoid and paratyphoid, cholera, shigellosis, and viral hepatitis A in the case of a healthy sanitary-epidemiological state of the area of operations, in the case of an unstable sanitary-epidemiological state of the area of operations will be 0,16, 0,48, 0,16, 0,144, with an unfavorable sanitary-epidemiological state of the area of operations, the coefficient of medical protection in the foci of the specified infections was 0,24, 0,72, 0,24, 0,216, with an extraordinary sanitary-epidemiological state of the area of operation – 0,32, 0,96, 0,32, 0,288, respectively, Table III.

The coefficient of medical protection of servicemen against diphtheria, meningococcal infection, and pneumonic plague in the case of unstable sanitary and epidemiological conditions in the area of operations will be 0,024, 0,09, 0,4, in conditions of unfavorable sanitary and epidemiological conditions in the area of operations, the index of loss of combat capability will be 0,036, 0,135, 0,6, with an extraordinary sanitary-epidemiological condition in the area of operations of the troops - 0,048, 0,18, 0,8. The coefficient of medical protection of military personnel against yellow fever, tick-borne encephalitis, tularemia, malaria, and the bubonic form of the plague in the case of an unstable sanitary-epidemiological condition in the area of operations will be 0,25, 0,12, 0,225, 0,1 and 0,1, in case of an unfavorable sanitary-epidemiological condition the state of the area of operations at the appearance and spread of diseases of the personnel for yellow fever, tick-borne encephalitis, tularemia, malaria and the bubonic form of the plague, the coefficient was 0,375, 0,18, 0,3375, 0,15 and 0,15, in the case of an emergency sanitary-epidemiological state of the action area - 0,5, 0,24, 0,45, 0,2 and 0,2. The coefficient of medical protection against brucellosis, viral hemorrhagic fevers (Lassa, Marburg, Ebola), and anthrax (generalized form) in the case of unstable sanitary and epidemiological conditions in the area of operations will be 0,075, 0,105, 0,2, in the case of unfavorable sanitary and epidemiological conditions in the area of operation, the coefficient will be 0,1125, 0,1575, 0,3, in the case of an extraordinary sanitary-epidemiological state of the area of operations, the coefficient in the foci of the specified infections will be 0,15, 0,21, 0,4, Table III.

It should be noted that under the most unfavorable conditions - when implementing medical protection measures without taking into account the peculiarities of the development of the epidemic process of the specified infections, for example, if such measures as the creation of specific protection of the body of a military serviceman (immunoprophylaxis, vaccination), timely use of emergency preventive measures against the specified infections, were not carried out, then the negative impact of the conditions of biological contamination on the combat capability of personnel increases significantly, Table III.

DISCUSSION

We dare to assert that the high efficiency of measures for the medical protection of troops (forces) in the conditions of biological contamination is achieved only when forecasting the consequences of the worsening of the epidemic situation. It is also necessary to take into account the multifactorial determinant of the epidemic process when using biological weapons (biological terrorism). Important are the proposed indicators that take into account the pathogenicity of the infectious agent, contagiousness, the degree of non-specific protection of servicemen (depends on the level of equipment and training of personnel), specific protection of servicemen (depends on the type of pathogen, implementation

of vaccination and its effectiveness, use of emergency prevention) and sanitary the epidemiological state of the area of operations of the troops (forces). It should be added that relevant epidemic situations were simulated, and the index and coefficient of medical protection were calculated to predict the consequences of the worsening of the epidemic situation (the use of biological weapons, biological terrorism) to make timely decisions regarding the implementation of medical protection measures for military personnel in conditions of biological contamination during the repulsion of armed aggression of Russia on the territory of Ukraine [2].

Thus, the goal of the research has been achieved, scientifically based methodological approaches to forecasting the consequences of the worsening of the epidemic situation (use of biological weapons, biological terrorism) during the repulsion of armed aggression of Russia on the territory of Ukraine, directions for its improvement are proposed. The results of the work are original. In further work, it will be necessary to calculate indicators taking into account the types and methods of use of troops (forces). The implementation of the presented proposals into practice will ensure the adoption of timely measures during the combat use of troops (forces) regarding the medical protection of servicemen in conditions of biological contamination [5].

CONCLUSIONS

1. It has been proven that the long-term armed aggression on the territory of Ukraine and the presence of a constant threat from Russia, a terrorist country, to use biological weapons and the deliberate destruction of critical infrastructure, determine the high probability of biological contamination of the territory of Ukraine.
2. In the existing conditions, the role of forecasting the consequences of the deterioration of the epidemic situation in order to achieve high efficiency of measures for the medical protection of troops (forces) in the conditions of biological contamination is increasing.
3. The need to use indicators that consider the multifactorial determinants of the epidemic process when predicting the consequences of the deterioration of the epidemic situation in the conditions of biological contamination is determined.
4. The relevant epidemic situations and calculated indicators of the effectiveness of medical protection for forecasting the consequences of the worsening of the epidemic situation (use of biological weapons, biological terrorism) when decisions are made regarding the implementation of measures for the medical protection of military personnel in conditions of biological contamination during the repulsion of armed aggression of Russia on the territory of Ukraine are simulated.

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ORIGINAL ARTICLE

PSYCHOLOGICAL FACTORS OF STUDENTS' VITALITY DURING THE WAR IN UKRAINE

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ABSTRACT

The aim: A theoretical analysis of the problem of the hardiness of a person who suddenly found himself in extreme conditions and an empirical study of his individual and psychological factors that contribute to the strengthening of this personal characteristic and mobilize the internal reserve of student youth.

Materials and methods: The following psychodiagnostic methods were used in the empirical study: "Methodology for the diagnosis of hardiness" by S. Muddy, "Test for the diagnosis of properties of the nervous system" by Y. Strelyau, "Methodology for the diagnosis of character accentuations" by K. Leonhard, "Mini-Mult Test", "Psychological Stress Scale", "Coping Behavior Questionnaire" by R. Lazarus, S. Folkman, "Test of Meaningful Life Orientations" by D. Leontiev, Life orientation test C. Scheyer, M. Carver. The study was conducted from September 2022 to January 2023.

Results: It was established a direct connection of hardiness with a strong and mobile nervous system, hyperthymic and demonstrative accentuations of character. Inversely related to hardiness are pedantic, unbalanced, dysthymic, and exalted accentuations of character, all personality disorders. People with a high level of hardiness are characterized by expressed optimism, the meaningfulness of life, and the use of adaptive coping strategies.

Conclusions: The study showed the high importance of hardiness for the full functioning of student youth during martial law and its conditioning by the properties of the nervous system and individual psychological characteristics. This emphasizes the need for making efforts to increase their level of vitality.

KEY WORDS: hardiness, student youth, psychological properties of personality

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INTRODUCTION

The problem of hardiness is becoming relevant for modern Ukrainian youth, who found themselves in wartime conditions of danger and uncertainty about their future. The life experience of young people has expanded to the ability to recognize by the sound of an object in the sky the level of its danger and which military object carries this danger (missile, drone, plane, etc.), as well as by the sounds of explosions: is the object on the ground hit whether the air defense forces of Ukraine worked. This is a small list faced by modern youth, who before the war were distracted by gadgets and dreams of ending the COVID quarantine and returning to their usual lifestyle. However, with the beginning of the war, with the chaotic rocket attacks on the civilian population, it was necessary to instantly change life priorities, assess the conditions of stay and plan life for the near term (at least from the sound of the air-raid alarm siren to its cancellation, and there could be many such sirens during the day, or they could last several hours).

Such tension and dangerous conditions affected the self-organization of time and space, which affected the changes in people's daily life, including young people. That is why the statements of the WHO representative that "a quarter of Ukraine's population is at risk of developing a severe mental health condition as the country grapples with the year-long Russian invasion" [1] are not groundless. It should be noted that the conditions in which Ukrainian citizens are in their country

carry a hidden threat to every individual. Citizens see, experience, and realize the results of Russian missiles hitting residential and cultural buildings, universities, schools, and public stops. In addition to the threat from the air, there is a threat to life on the ground - these are streamers, masked mines, and unexploded grenades, which most often maim children and farmers. Ukrainian mass media widely cover the facts of destruction, mass tragic deaths of citizens in various regions of Ukraine, stories about being in occupation, captivity, etc.

All these tragic phenomena and facts, constant stay in life-threatening conditions affect the emotional state of the individual. And at the same time, it is impossible to act constructively, to adapt, and to survive such tests without internal strength, which is embodied in the concept of "hardiness", introduced by S. Kobeis and S. Muddy [2]. The ideas of these scientists about the importance of hardiness and vitality for the life of an individual are confirmed by various studies, where hardiness is defined: as a concept of an individual who steadfastly meets problems, has a goal, controls in achieving goals, and is always ready to accept a challenge [3], as a dedication to the formation of active behavior concerning the environment and neutralization of stressful situations [4], as an important component of the life activities of elderly people, in whom the levels of vitality are related to the degree of formation of the cognitive construct "personal exclusivity of existential experience" [5]. This testifies to the versatility of this phenomenon and the uniqueness of its manifestation in individuals of different ages and different conditions, who strive for a meaningful and fulfilling life, showing existential courage, despite adverse circumstances [6].

Currently, there is no unambiguous definition of the concept of hardiness, so we started from the understanding of the authors of this construct - S. Kobeis and S. Muddy [2, 6-8]. Hardiness includes three relatively autonomous components: involvement, control, and risk acceptance, which allow a person to withstand the weight of a stressful situation, maintain internal balance, and not reduce the success of activities. In our opinion, each of the components of hardiness adds a certain feature of the ability to overcome the difficulties of life, emphasizing the individuality of everyone in adapting to the uncertainty of his future existence in conditions of war. In one of his works, S. Muddy [7] proposed to consider the model of hardiness, distinguishing negative factors (acute and critical stressors; mental and physical stress; disruption of well-being: ineffectiveness, diseases, psychological problems) and components of hardiness: sustainable beliefs (involvement, control, risk-taking); sustainable mastery; social support and sustainable health practices (exercise, relaxation, diet, treatment). This model of hardiness prompted us to conduct an empirical study on the participation of youth in wartime conditions.

THE AIM

The purpose of the study was to analyze the current state and approaches to the problem of personal hardiness in extreme conditions, which are currently extrapolated in domestic and foreign psychology, to establish individual and psychological factors of hardiness that contribute to the strengthening of this personal characteristic and mobilize the internal reserve of student youth during martial law in Ukraine.

To realize the goal and our assumption about the direct connection of the features of the nervous system and individual psychological characteristics with the levels of hardiness, the following research tasks were identified: to diagnose the level of hardiness and its components among students during the war; to establish correlations of hardiness with psychological properties of the individual; using regression analysis to establish psychological factors of hardiness.

MATERIALS AND METHODS

The peculiarity of our sample is that psychology students who have been in Ukraine since the beginning of the war took part in the study. The study was conducted over four months (from September 2022 to January 2023), when student youth experienced intense periods of rocket attacks, long blackouts, and Internet unavailability. Such ambiguous dynamics of shelling of the civilian population create conditions of uncertainty, in which the individual mentally hardens his internal resources and balances thanks to hardiness in the artificially created danger.

The sample consisted of 112 students of the National Aviation University, psychology major, 3-4 years, average age: 19.5 years; young women - 80%, young men - 20%.

During the research, the following psychodiagnostic methods were used: "Methodology of diagnosis of hardiness" by S. Maddi in the adaptation by D. Leontiev, "Test of diagnosis of properties of the nervous system" by Yan Strelyau, "Methodology of diagnosis of character accentuations" by K. Leonhard in the adaptation by H. Shmyshek, "Mini-Mult Test" (an abbreviated version of the MMPI), PSM-25 "Psychological Stress Scale", "Coping Behavior Questionnaire" by R. Lazarus, S. Folkman, "Test of Meaningful Life Orientations" by D. Leontiev, "Optimism Test" LOT (Life orientation test) C. Scheyer, M. Carver.

Table I. Significant correlations of hardiness with properties of the nervous system, accentuations of character, and personal traits of students

	Hardiness	Involvement	Control	Acceptance of risk
Properties of the nervous system (Y. Strelyau test)				
Power of excitation processes	0,585**	0,501**	0,558**	0,468**
Power of braking processes	0,360*	0,323**	0,323**	0,259**
Mobility	0,473**	0,465**	0,360**	0,477**
Character accentuations (K. Leongard test)				
Hyperthymic	0,373**	0,329**	0,420**	0,218*
Pedantic	-0,262**	-		-0,377**
Demonstrative	0,332**	0,256*	0,306**	0,335**
Unbalanced	-0,244*	-0,287**	-0,224*	
Dysthymic	-0,327**	-0,277**	-0,373**	-0,210*
Exalted	-0,239*	-	-0,265**	-0,262**
Personality Traits and Disorders (MMPI test)				
Hypochondria (Hs)	-0,216*	-0,214*	-0,312**	-
Depression (D)	-0,508**	-0,506**	-0,468**	-0,363**
Hysteria (Hy)	-0,386**	-0,433**	-0,354**	-
Psychopathy (Pd)	-0,300**	-0,334**	-0,289**	-
Paranoia (Pa)	-0,455**	-0,513**	-0,327**	-0,373**
Psychasthenia (Pt)	-0,229*	-0,233*	-0,304**	-
Schizoid (Se)	-0,228*	-0,229*	-0,248*	-

Notes: * Correlation is significant at the 0.05 level
** Correlation is significant at the 0.01 level

Table II. Significant correlations of hardiness with the level of psychological stress and coping strategies of students

	Hardiness	Involvement	Control	Acceptance of risk
Coping strategies (R. Lazarus test)				
Acceptance of responsibility	-0,344**	-0,283**	-0,319**	-0,322**
Escape	-0,532**	-0,489**	-0,488**	-0,426**
Planning a solution to the problem	0,448**	0,408**	0,451**	0,304**
Positive reassessment	0,377**	0,393**	0,345**	0,258**
Finding social support	-	0,205*	-	-
Psychological stress (PSM-25 test)				
Psychological stress	-0,391**	-0,374**	-0,411**	-0,236*

Notes: * Correlation is significant at the 0.05 level
** Correlation is significant at the 0.01 level

Correlation analysis was used to establish correlations between hardiness and the individual psychological properties of respondents. The Pearson correlation coefficient was used for correlation analysis. Linear regression analysis was used to determine the psychological determinants of hardiness. Vitality was the dependent variable, those individual psychological characteristics that had significant correlations with vitality were selected as independent variables. Based on the data of the regression analysis, a regression equation is derived, which allows to estimate the influence of each independent variable on the predicted values. Statistical processing was carried out using the IBM SPSS Statistics 26 program.

RESULTS

Based on the results of hardiness diagnostics, it was established that only 11% of students have a high level of hardiness, 63% have an average level of hardiness, and 27% have a low level of hardiness. Among individual components of hardiness, a high level of involvement was diagnosed in 8% of students, an average level in 57%, and a low level in 35%. Control at a high level is

Table III. Significant correlations of hardiness with the level of optimism and meaningful life orientations of students

	Hardiness	Involvement	Control	Acceptance of risk
Meaningful life orientations (D. Leontiev test)				
Meaningfulness of life	0,414**	0,490**	0,230*	0,347**
Goals in life	0,312**	0,463**	-	-
The process of life	0,608**	0,648**	0,430**	0,510**
The result of life	0,319**	0,429**	-	-
Locus of control of yourself	0,435**	0,517**	0,280*	0,410**
Locus of life control	0,253*	0,250*	-	0,262*
Optimism (Ch. Scheyer, M. Carver LOT test)				
Optimism	0,378**	0,434**	0,209*	0,395**

Notes: * Correlation is significant at the 0.05 level
** Correlation is significant at the 0.01 level

found in 8% of students, at an average level in 61%, and at a low level is diagnosed in 31%. The most pronounced component of hardiness is "aspiration to risk": its high level was diagnosed in 45%, average - 49%, and low - in 6% of students.

One of the assumptions of the study was the conditioning of high hardiness by the properties of the nervous system (strength and mobility of nervous processes) and its connection with the characterological and personal characteristics of young people. Correlation analysis of properties of the nervous system, accentuations of character, and personality traits with hardiness showed that the closest connection was established between the strength of nervous system excitation processes and hardiness (table I). There is a direct connection between a strong and mobile nervous system and hardiness, which indicates that the individual's ability to withstand stressful situations and maintain internal balance is determined by the properties of the nervous system.

Among character accentuations, hyperthymic and demonstrative have a direct connection with hardiness. It should be noted that both accentuations are manifested by high energy, an active life position, and sociability. Pedantic, unbalanced, dysthymic, and exalted accentuations of character are inversely related to hardiness. Low mood, imbalance, and tendency to get stuck reduce the adaptive potential and hardiness of students.

Regarding personality disorders diagnosed by the Mini-multi method, we can see that all connections with hardiness and its components are exclusively reversed. The closer the subjects are to the pole of psychopathology, the less pronounced hardiness and its components are. Similar results were obtained in the study of the dependence of social and psychological adaptation on personal characteristics and personality disorders [9]. Pronounced personality disorders reduce the possibility of effective adaptation and coping with stress.

Significant correlations were established between hardiness, stress level, and coping strategies used by students to master difficult life situations during the war (Table II). We can see the inverse relationship of hardiness and its components with psychological stress, which proves its significant contribution to overcoming stressful situations.

Coping strategies that increase the level of hardiness include problem-solving planning and positive reassessment of the situation. A direct connection was also established between the hardiness component "engagement" and the search for social support. These coping strategies are adaptive and contribute to effective coping with stressful situations. Inverse correlations were established between hardiness and coping strategies of escape and acceptance of responsibility.

It was established that optimism and the level of meaningfulness of life are directly related to hardiness and its components (Table III). Moreover, the greatest contribution to an optimistic attitude is involvement, that is, delight in the actual life process, a sense of one's contribution to important life events. Likewise, involvement has the closest correlations with indicators of overall meaningfulness of life, goals in life, and life processes. It can be concluded that a person's enthusiasm for his work, the feeling of his need for others, and being in the center of events fill life with meaning and brings satisfaction to the present period of life, and contributes to setting goals for the future.

A linear regression analysis was conducted to establish the most important psychological factors of hardiness. The value of R-square is 0.805, that is, the specified predictors explain 80% of the dependent variable, which characterizes the regression model as quite effective. Fisher's test significance is F=0.000, indicating that the regression model is statistically significant.

Hardiness = 61.057 + 0.643 (power of excitation processes) - 1.719 (escape) - 0.518 (paranoia) + 0.769 (life process) + 0.806 (optimism)

The greatest contribution to the prediction of the dependent variable "hardiness" is the strength of nervous system's excitation processes, the escape coping strategy, the sixth scale of the Mini-Mult methodology, "paranoia" or rigidity, satisfaction with the life process, and optimism. So, we can conclude that both typological and purely psychological properties turned out to be important predictors of hardiness. The leading factor of high hardiness is the strength of the nervous system's excitation processes and its mobility (the inverse relationship with paranoia/rigidity confirms the importance of this characteristic of the nervous system). Optimism and the meaningfulness of the current period of life also have a significant impact on the formation of life hardiness. The application of the "escape" coping strategy, which excludes involvement in activities and life in general, significantly reduces the hardiness.

DISCUSSION

Each of the components of the hardiness model [7], based on which our research was conducted, in a complex demonstrates the variability of manifestations due to the expansion of experience in ways of responding and interacting with others and the environment, which can have both positive and negative effects. Since a person is naturally vulnerable, the mechanisms of hardiness can act as a buffer, reducing the effect of negative factors on the individual [7].

Among such survival mechanisms, the most valuable is the search for social support, especially in the context of terrorist attacks [10], although social support did not reduce the relationship between a stressful event and coping [11], it is defined as information that makes the subject believe that he is cared for, loved, respected and is a member of a network of mutual obligations [11]. Actually, in our study, the scale "seeking social support" has a direct correlation with the component "involvement". Evidence that supportive interpersonal interactions protect against the health effects of life stress are reviewed [12].

These facts testify in favor of the correct actions of the Ukrainian government regarding the organization of social information on the behavior of adults and children in case of danger (for example, about the location of bomb shelters, safe places in the house, places of humanitarian and medical aid, centers of "invincibility", places with free water, first aid courses, etc.) through mass media, chatbots, SMS messages, even when the Internet is not working, which in the complex can be called elements of the "culture of survival". The importance of such a culture, in conditions of limited time for cognitive processing of information for making the right decisions, prevents the effect of "freezing" [13].

We consider hardiness as a personal characteristic, the foundation of whose strength relates to the peculiarities of the nervous system, and the ability to respond constructively to difficult life circumstances, using appropriate coping strategies, which confirm the results of the correlation analysis. The constancy of hardiness as a personality trait that exists regardless of time and types of adversity has been proven in studies involving student youth [14].

CONCLUSIONS

Summarizing the results of the conducted research, we would like to note the importance of hardiness for the full functioning of student youth during the war. The established individual and psychological factors of hardiness show their dependence on the properties of the nervous system and psychological characteristics that can be developed and formed during training in institutions of higher education. The level of hardiness is most increased by the strength of the nervous system excitation processes, satisfaction with the life process and optimism, and the use of the "escape" coping strategy and personality rigidity are significantly reduced.

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ORIGINAL ARTICLE

DYNAMICS OF INDICATORS IN PLATELET HEMOSTASIS IN POLYTRAUMA AND ENLARGED BODY MASS INDEX

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ABSTRACT

The aim: Analyze the dynamics of indicators in platelet hemostasis in polytrauma and enlarged body mass index.

Materials and methods: A comprehensive study of hemostasis was performed in 224 sick with polytrauma and high body mass index within a month and on the 360th day.

Results: In Group I, the aggregation time was shortened during stimulation of ristomycin by 25% from day 1 to day 3. In patients in the II group, with the addition of ADP, the presence of hyperaggregation of platelets was determined from the 1st to the 3rd day and from the 30th to the 360th (a 36% reduction in time compared to the control was determined). In patients in the III group, ADP-aggregation was reduced on the 1st day (by 34%), after which hypoaggregation was noted (from the 3rd to the 14th and on the 360th day) with an increase in the rate of approximately 33% compared to the control group, after which there was a persistent hyperaggregation from 30 to 360 day with a 25% reduction in aggregation time.

Conclusions: An individual response of platelets to damage was established depending on the severity of polytrauma and increased body mass index.

KEY WORDS: platelet hemostasis, increased body mass index, polytrauma

Wiad Lek. 2023;76(5 p.2):1285-1289

INTRODUCTION

The system of hemostasis is one of the fluorescent systems of the body. Changes in its functional state occur under the influence of various stimuli, particularly polytrauma provokes the reaction for homeostasis restoration [1]. At the same time, the nature of the disorders that develop can be both adaptive and pathological [2].

Increased coagulation and abnormal fibrinolysis both can be found in patients with increased body mass index (IBMI) [3]. Endothelial dysfunction is observed in patients with an increased body mass index (IBMI) due to a significant increase in fat mass, impaired dilatation and vascular proliferation, impaired thrombosis, fibrinolysis, and impaired anti-inflammatory and antioxidant functions [4, 5].

In recent years, it has been confirmed that impaired lipid and carbohydrate metabolism accompany the IBMI and is often combined with anomalies of the thrombosis/fibrinolysis system. Thus, an increased level of fibrinogen appears in many cases of a combination of IBMI and hyperinsulinemia and IBMI with type 2 diabetes, together with an increase in the activity of factor VII of blood coagulation [6].

Cell hemostasis is known to be an aggregation of blood cells between them, adhesion – sticking them to the vascular wall or other surface and releasing factors from blood cells that contribute to the activation of plasma hemostasis [7]. Platelets are central to these processes.

In patients with polytrauma on the background of IBMI, the course of the traumatic disease is complicated due to the presence of excess weight, which requires special attention.

THE AIM

Analyze the dynamics of indicators in platelet hemostasis in polytrauma and enlarged body mass index.

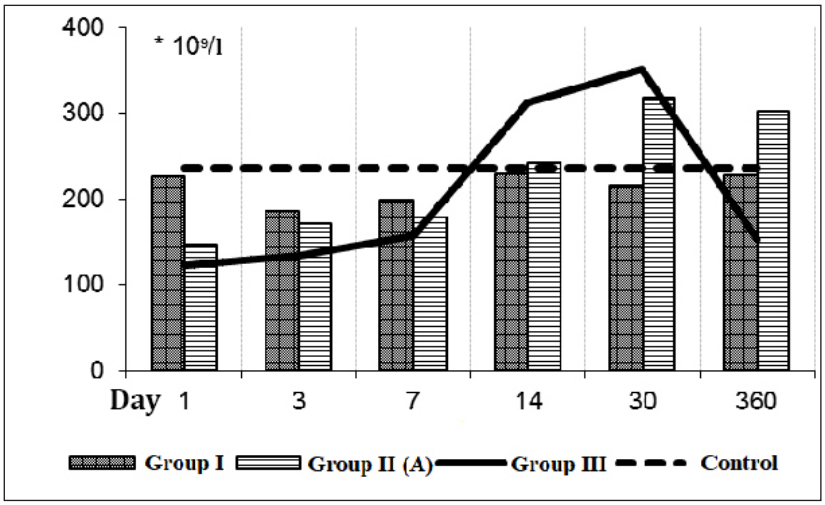

Fig. 1. The number of platelets in patients with the polytrauma depends on BMI.

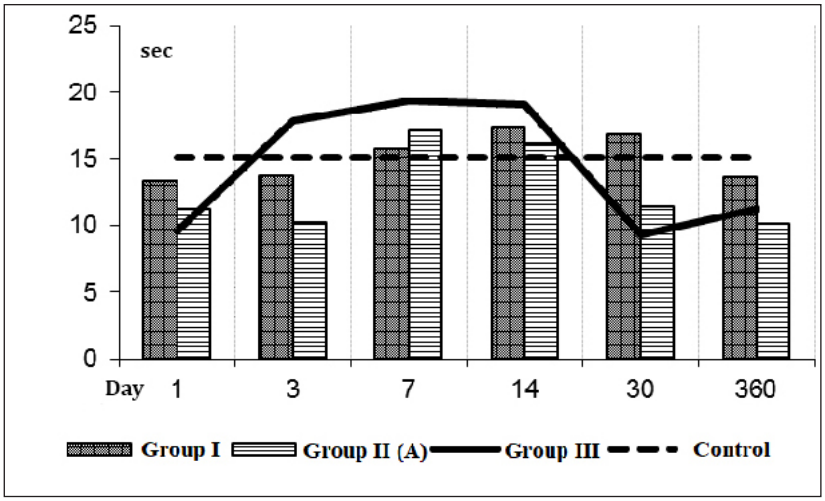

Fig. 2. The time of aggregation of platelets with the addition of ADP in patients with polytrauma depends on BMI.

MATERIALS AND METHODS

A comprehensive study of hemostasis was performed on 224 sick with polytrauma and high body mass index within a month and on the 360th day. Studied: platelet count, Adenosine Diphosphate (ADP)-aggregation, ristomycin-aggregation. The study was conducted for the period 2021-2023.

The patients had the same severity of the condition at the time of hospitalization on the APACHE-II scale (14.0 ± 5.8). All patients were divided into 3 groups depending on the BMI. Group I: 88 sick with a BMI at the time of admission under 29.9 (26.1 ± 3.1), Group II: 84 patients with a BMI at the time of admission 30.0 - 39.9 (35.2 ± 3,8), Group III: 52 patients with a BMI at the time of admission above 40.0 (46.2 ± 5.8). The control group: 60 volunteers. Platelet hemostasis indicators in polytrauma and increased BMI were analyzed on 1, 3, 7, 14, 30, and 360 days after polytrauma

The medical-statistical calculation of the obtained research results was performed using a package of application programs: Microsoft Excel 2016, Statsoft Statistica 10.0 for Windows, IBM SPSS 25.0 for Windows, etc. When characterizing the central tendency and variability of quantitative (continuous or interval) traits, the mean value (M) and standard deviation (SD) were determined. The probability of differences in the obtained quantitative characteristics in two mutually independent groups was analyzed using of the Mann-Whitney U-test and in mutually dependent groups - the Wilcoxon matched-pairs signed-ranks T-test.

RESULTS

The number of platelets obtained upon admission to the clinic varied ambiguously depending on the degree of BMI. So in patients of group I (BMI ≤ 29.9) in all periods of the examination, the level of platelets in the blood did not go beyond the limits of physiological values (Fig. 1).

In group II (BMI 30.0-39.9), their decrease was probably determined in the first week of the disease by an average of 30-35% compared with the control. In the future, their dynamics had a positive direction. Between 30-360 days, the number of platelets in these patients was near the upper limit of normal values - 30% higher than the control (Fig. 1).

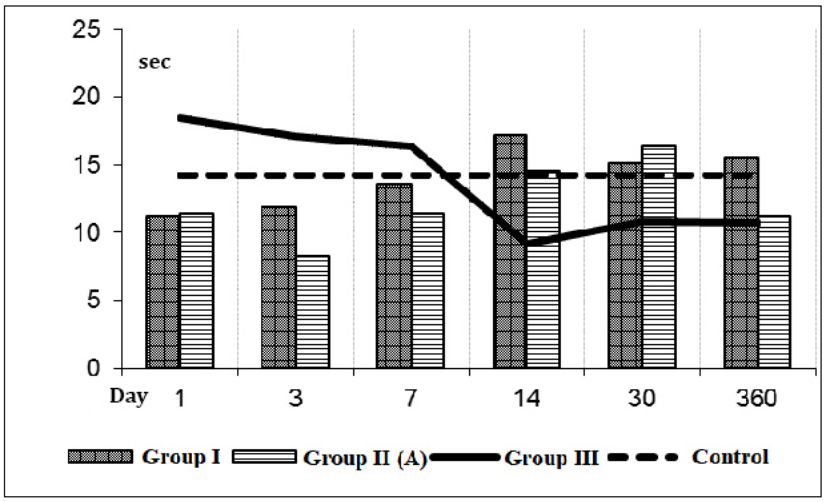

Fig. 3. The time of aggregation of platelets with the addition of Ristomycin in patients with the polytrauma depending on BMI.

In group III (BMI ≥ 40.0), thrombocytopenia in the first week of hospital stay was also quite pronounced. Their minimum number was determined from the 1st to the third day and was 122.8 ± 15.2 • 10^9/l and 134.3 ± 8.2 • 10^9/l, respectively ($p < 0.05$). Later, a gradual increase in their number was noted – from the 14th to 30th day, an increase in the quantitative composition of platelets was determined (313.4 ± 10.3 • 10^9/l and 352.3 ± 16.3 • 10^9/l, respectively), after which a decrease in the number of platelets was observed until the 360th day of observation.

In the post-traumatic period of aregation, the properties of platelets were intensively changed in all examined patients. In Group I (BMI ≤ 29.9), this process was the least pronounced (Fig. 2, 3): a shortening of the aggregation time was observed during stimulation of ristomycin by 25% from day 1 to day 3.

Later, we noted a slight (by 10%) lengthening on the fourteenth day after stimulation of ADP and ristomycin, then the index was fully restored.

In the II group (BMI 30.0 – 39.9), platelet hyper aggregation was ascertained when adding ADP for the period 1-3 days and 30-360 days, when a 36% reduction in time was determined compared to the control; Ristomycin – from the 1st to the seventh day with a minimum on the 3rd day – 8.2 ± 1.2 * s ($p < 0.05$), after which from the 30th day to the 360 th with a minimum on the 360 days examination – 11.2 ± 2.7 * s ($p < 0.05$).

In patients in the III group (BMI ≥ 40), a different dynamic was noted. So ADP-aggregation was reduced on the first day by 34%. Then there was a period of hypo aggregation from the 3rd to 14th day, when the indicator increased by 33% compared to the control group, after which stability was established hyper aggregation from the 30th to the three hundred and sixtieth day (25% time reduction). Aggregation of ristomycin lasted from the 1st to the 7th day with a maximum on the third day of – 17.2 ± 1.2 * s ($p < 0.05$), after which a stable one was noted hyper aggregation from the 14th to the 360- a day with a reduction time by an average of 35%.

DISCUSSION

Similar results were obtained during other studies. Thus, a study [8] of trauma patients established increased force of contraction of platelets compared to the control group (6390 ± 2340 versus 4790 ± 470 μN, P = 0.043). to start platelet contraction reduction occurred faster in trauma patients compared to controls (660 ± 467 and 1130 ± 140 s, P = 0.0022).

In turn, Verni C. C. et al. [9] proved that Trauma-induced coagulopathy was present in 25% of injured patients and caused 10% of deaths. They pointed to upon injury, a decrease in hemostatic function occurs due to coagulation factor deficiency, vascular dysfunction and hyperfibrinolysis and platelet dysfunction. When exposed to agonists over the first 24 hr post-injury, in patients with polytrauma, platelets mobilized significantly less calcium compared to healthy patients. Partial restoration of platelet activity was present in a third of the examined after 120 hr (not fully obtaining healthy baseline function). They indicated, that platelet dysfunction in polytrauma was characterized by a weak response to agonists of the hemostatic function.

Rimaitis M. et al. [10] analysis of coagulogram and rotational thromboelastometry was performed, the results of which were obtained within 72 hours in patients after craniotomy for hematoma removal and/or brain decompression at four time points (T0–T3). As a result, levels of hypocoagulation and increased clotting time and coagulation parameters were determined between those who died and those who survived. In addition, the limit values of coagulation parameters in the deceased were established. A decrease from 35.8% to 15.9% of hypocoagulation was established. Also, a decrease in fibrinogen levels and the presence of hyperfibrinolysis

with early cessation of fibrinolysis after TBI were noted. This was associated with increased mortality rates. In addition, the authors established optimal levels of threshold values of indicators that increased the probability of mortality: fibrin polymerization thromboelastometry (FIBTEM) clot amplitude ≤ 13 mm in the T0 period and FIBTEM ≤ 16.5 mm in the T1 period increased the probability of a fatal outcome by 6.0, respectively (95 % confidence interval [CI] 1.54–23.13, p = 0.010) and 9.7 (95% CI 2.06–45.36, p = 0.004). In addition, maximum FIBTEM clot hardness ≤ 14.5 mm at T0 and ≤ 18.5 mm at T1 increased such odds by 6.3 (95% CI 1.56–25.69, p = 0.010) and 9,1 (95% CI 1.88–44.39, p = 0.006) respectively. Fibrinogen < 3 g/L on the 1st day after surgery (T1) increased the probability of in-hospital mortality by 9.5 times (95% CI 1.72–52.98, p = 0.01). In addition, increased blood coagulation was not associated with the development of death.

CONCLUSIONS

An individual response of platelets to damaged was established depending on the severity of polytrauma and increased body mass index.

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Compliance with Ethics Requirements. The ethical approval was obtained from Bioethics Committee of the Kharkiv National Medical University. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008, as well as the national law. Informed consent was obtained from all the patients included in the study.

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ORIGINAL ARTICLE

FUNCTIONAL CHARACTERISTICS OF THE CARDIOVASCULAR SYSTEM OF PATIENTS WITH ISCHEMIC HEART DISEASE WITH OBESITY

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ABSTRACT

The aim: To determine the features of the functional characteristics of the cardiovascular system of patients with ischemic heart disease with obesity.

Materials and methods: Examined 130 persons (mostly military personnel and persons who were in the zone of active hostilities): 65 patients (the main group, 62,67±8,93 years) with coronary heart disease and obesity and 45 people of the control group (virtually healthy people, randomized by age and sex, 58,76±14,6 years).

Results: Coronary heart disease and obesity compared to healthy individuals probably the exceed all values of the functional state of the cardiovascular system: systolic blood pressure (152.72±14.61 and 119.03±7.94 mmHg; $p<0.001$); diastolic blood pressure (90.74±7.36 and 80.36±6.74 mmHg; $p<0.001$); end-diastolic volume (103.17±40.84 and 52.48±8.58 mm^3; $p<0.001$); end-systolic volume (47.98±29.92 and 31.47±8.42 mm^3; $p=0.001$); end-diastolic size (4.74±0.81 and 4.12 ± 0.27 cm; $p<0.001$); end-systolic size (3.34±0.76 and 3.17±0.59 cm; $p=0.014$).

Conclusions: The identified functional disorders of the heart in the comorbid course of coronary heart disease and obesity can be used for early diagnosis of cardiovascular complications in such patients and for the development of adequate therapeutic schemes.

KEY WORDS: structural and functional state, coronary heart disease, obesity

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INTRODUCTION

A large number of studies indicate that depression, insomnia, and obesity are significantly threatening and highly prevalent public health problems (especially in patients who took part in active combat) [1, 2], which quite often occurring simultaneously [3, 4] and provoke risks of occurrence and the development of many chronic diseases leading to high levels of economic burden for healthcare systems [5, 6].

Depressive conditions are found to be the third most common of all chronic conditions in both men and women and affect about 23 % of veteran participants [7]. At the same time, the vast majority (more than 90 %) of patients with depressive conditions complain of sleep disturbances (including insomnia, which occurs in 30–40 % of civilians and 24–54 % of veterans during 6–8 years after returning from the zone of active hostilities). Scientists point to the possibility of depressive states and sleep disorders provoking the development of obesity [8, 9], which is quite relevant for our country in view of the large-scale conduct of active hostilities in Ukraine. In addition, several pathways have been identified through which depression and insomnia can influence the development of overweight and obesity, among which the most influential are circadian changes, which have a negative effect on appetite regulation and increase food consumption [10].

Obesity is a complex, adiposity-based chronic disease, where management targets both weight-related complications and adiposity to improve overall health and quality of life [11]. It is a chronic polyetiological disease associated with the influence of a number of genetic and neurological factors, changes in the functions of the endocrine system, the lifestyle and eating behavior of the patient, and not solely with energy imbalance.

From 1975 to 2016, the number of obese people around the world more than tripled. Such diseases as arterial hypertension (2.9 times more often), type

2 diabetes mellitus (3 times more often), and hypercholesterolemia (2.1 times) [12] accompany obesity. Annually about 2.5 million people die worldwide of diseases related to obesity.

It is known that obesity is one of the main risk factors for Noncommunicable diseases such as cardiovascular diseases (coronary artery disease, arterial hypertension, ischemic stroke). Type 2 diabetes mellitus, musculoskeletal system disorders, some cancer (including cancer of the endometrium, breast, ovary, prostate, liver, gall bladder, kidney and colon). The risk of non-infectious diseases increases with the increase of the body mass index (BMI).

THE AIM

The aim was to determine the features of the functional characteristics of the cardiovascular system of patients with ischemic heart disease with obesity.

MATERIALS AND METHODS

Examined 65 patients (the main group) with coronary heart disease (CHD) and obesity and 45 people from the control group (virtually healthy people, randomized by age and sex). The subjects of the main group were 62.67 ± 8.93 years old, and the control group was 58.76 ± 14.6 years old. The majority of the surveyed both the main and control groups included military personnel and persons who were in the zone of active hostilities.

The diagnosis of CHD was established according to the recommendations American College of Cardiology Foundation, American Heart Association, Task Force on Practice Guidelines, American College of Physicians, and other organizations. The diagnosis of obesity was established according to the recommendations European Association for the Study of Obesity and National Health Institute. The study was conducted for the period 2021-2023.

The medical-statistical calculation of the obtained research results was performed using a package of application programs: Microsoft Excel 2016, Statsoft Statistica 10.0 for Windows, IBM SPSS 25.0 for Windows, etc. When characterizing the central tendency and variability of quantitative (continuous or interval) traits, the mean value (M) and standard deviation (SD) were determined. The probability of differences in the obtained quantitative characteristics in two mutually independent groups was determined using the Mann-Whitney U-test, and in mutually dependent groups - the Wilcoxon matched-pairs signed-ranks T-test.

RESULTS

The main values of the functional state of the cardiovascular system (CVS) of patients with coronary artery disease and obesity were analyzed in comparison with individuals of the control group (Table I). Were defined the levels of SBP (systolic blood pressure), DBP (diastolic blood pressure), HR (the heart rate), and pulse. The obtained results indicate quite significant disorders of the functional state of the CVS in patients with CHD against the background of obesity.

It was determined that with CHD and obesity compared to the control group the superiority of all values of the functional state of the CVS, which characterizes the presence of significant complications of obesity, was probably determined. So, the corresponding predominance of values was determined SBP (152.72 ± 14.61 mm Hg and 119.03 ± 7.94 mm Hg; $p < 0.001$); DBP (90.74 ± 7.36 mm Hg and 80.36 ± 6.74 mm Hg; $p < 0.001$); HR (82.31 ± 11.34 beats/min and 71.34 ± 7.36 beats/min; $p < 0.001$) and Pulse (80.92 ± 9.75 beats/min and 71.34 ± 7.36 beats/min; $p < 0.001$) with CHD and obesity compared to the control group.

In addition, echocardiographic abnormalities of the CVS were determined in patients with CHD and obesity compared to healthy individuals, which also confirms significant functional disorders in the comorbid course of CHD and obesity (Table II). Were defined the levels of EDV (end-diastolic volume), ESV (end-systolic volume), EDS (end-diastolic size), ESS (end-systolic size), EF (ejection fraction), CO (cardiac output).

Probable was established advantage of the values of echocardiographic examination indicators of the state of the heart in CHD with obesity compared to the control group was established. So, the corresponding indicators in the main group and the control group were equal: EDV – 103.17 ± 40.84 mm^3 and 52.48 ± 8.58 mm^3; $p < 0.001$; ESV – 47.98 ± 29.92 mm^3 and 31.47 ± 8.42 mm3; $p = 0.001$; EDS – 4.74 ± 0.81 cm and 4.12 ± 0.27 cm; $p < 0.001$; ESS – 3.34 ± 0.76 cm and 3.17 ± 0.59 cm; $p = 0.014$; EF – 55.48 ± 7.75 % and 60.57 ± 3.57 %; $p = 0.003$ and CO – 91.47 ± 15.24 ml and 70.24 ± 12.48 ml; $p < 0.001$.

DISCUSSION

The data obtained by us regarding the increase in normative values of the structural and functional state of the CVS in obesity, which characterize the presence of significant complications of obesity, were also confirmed by other conducted studies. So, Koo H. C. et al. [13] analyzed the nationally representative data from 14,025 Malaysian adults who participated in the NHMS 2015 and demonstrated that overweight/obese was associated with an increased risk of undiagnosed high blood pressure (odds ratio (aOR): 3.08; 95 % confidence interval (CI): 2.60–3.63; p: 1.37×10^{-36}) after adjustment for sociodemographic characteristics, lifestyle factors, and health conditions. In addition, they proved that central obesity was associated with an increased risk of undiagnosed high blood pressure (aOR: 2.83; 95 % CI: 2.45–3.26; p: 5.28×10^{-41}).

Table I. Functional state of the CVS, M ± SD

State of the CVS	Research groups		p
	the main (n = 65)	**the control** (n = 45)	
SBP, mm Hg	152,72 ± 14,61	119,03 ± 7,94	< 0,001
DBP, mm Hg	90,74 ± 7,36	80,36 ± 6,74	< 0,001
HR, beats/min	82,31 ± 11,34	71,34 ± 7,36	< 0,001
Pulse, beats/min	80,92 ± 9,75	71,34 ± 7,36	< 0,001

Notes: the probability of differences in the comparison of the indicators of the main and control groups.

Table II. Results of echocardiographic examination of the heart of patients with CHD and obesity, M ± SD

State of the heart	Research groups		p
	the main (n = 65)	**the control** (n = 45)	
EDV, mm^3	103,17 ± 40,84	52,48 ± 8,58	< 0,001
ESV, mm^3	47,98 ± 29,92	31,47 ± 8,42	0,001
EDS, cm	4,74 ± 0,81	4,12 ± 0,27	< 0,001
ESR, cm	3,34 ± 0,76	3,17 ± 0,59	0,014
EF, %	55,48 ± 7,75	60,57 ± 3,57	0,003
CO, ml	91,47 ± 15,24	70,24 ± 12,48	< 0,001

Notes: the probability of differences in the comparison of the indicators of the main and control groups.

Tabib A. et al. [14] evaluate the association between obesity and hypertension among Iranian children and adolescents. They determined, that the prevalence of hypertension was higher among obese compared to healthy weight subjects ($p < 0.001$). Hypertension had the strongest association with central obesity by waist circumference (OR 4.098; 95 % CI 3.549–4.732), generalized obesity by BMI [OR 3.000; 95 % CI 2.749–3.274], and central obesity by waist-to-height ratio (OR 2.683; 95 % CI 2.451–2.936).

Lewis A. J. M. et al. [15] determined the effects of World Health Organization class III obesity (BMI > 40 kg/m2) vs. healthy weight (BMI < 25 kg/m2) upon right ventricles (RV) volumes, energetics, and systolic function. Obesity was associated with remodeling of both the RV and left ventricles (LV). Obesity was associated with a 17 % increase in RV end-diastolic volume (163 ± 30 mL vs. 139 ± 28 mL; $p < 0.0001$), a 26 % increase in RV end-systolic volume (62 ± 17 mL vs. 49 ± 16 mL; $p < 0.001$), and a 3 % absolute reduction in RV ejection fraction (62 ± 6 % vs. 65 ± 7 %; $p = 0.01$).

Gao Y., Zeng J., Zou F., et al. [16] established that in the inverse-variance weighted analysis, every 1-standard deviation higher waist-to-hip ratio adjusted for BMI was significantly associated with higher LV mass-to-end-diastolic volume ratio (β = 0.4583; 95 % CI: 0.2921 to 0.6244; p = 6.418 × 10–8) and lower LV end-diastolic volume (β = -0.2395; 95 % CI: -0.3984 to -0.0807; p = 0.0031) after Bonferroni adjustment.

CONCLUSIONS

In the case of coronary heart disease and obesity, a corresponding predominance was probably determined in systolic blood pressure values, diastolic blood pressure, heart rate, and pulse compared to the control group. In patients with coronary heart disease and obesity, a probable advantage was established in end-diastolic volume, end-systolic volume, end-diastolic size, end-systolic size, ejection fraction, and cardiac output compared to the control group

Identified functional disorders of the heart in the comorbid course of coronary heart disease and obesity can be used for early diagnosis of cardiovascular complications in such patients and the development of adequate therapeutic schemes.

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ORIGINAL ARTICLE

APPLICATION OF PROBIOTIC ANTISEPSIS FOR PURULENT COMPLICATIONS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

The aim: To improve the results of surgical treatment of patients with type 2 diabetes and purulent-necrotic wounds by using probiotic antiseptics.
Materials and methods: 66 patients with type 2 diabetes and purulent-necrotic complications took part in this study. Probiotic antiseptics were used for local treatment in the experimental group (n=31), and traditional antiseptics were used in the control group (n=35). The levels of pro-inflammatory markers in the blood (IL-6, TNF-a, CRP) were studied; microscopic material was taken to study the type of cytogram during bandaging, before wound treatment with antiseptics or debridement on admission to the hospital (1st day), on the 3rd day and on the 7th day.
Results: Analysis of dynamic changes in pro-inflammatory markers between the first and seventh days proved that only in the experimental group there was a statistically significant difference (IL-6 (P=0.004), TNF-a (P=0.001), CRP (P=0.018)). Detection of regenerative-inflammatory and regenerative cytogram types on the 7th day in the experimental group had a statistically significant difference compared to the control group (p=0.002 and p<0.001, respectively).
Conclusions: the use of probiotic antisepsis accelerates wound healing in patients with type 2 diabetes and purulent-necrotic complications.

KEY WORDS: Diabetes Mellitus 2 type, *Bacillus subtilis*, Interleukin-6, TNF-alpha, C-Reactive Protein

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INTRODUCTION

Every year, the number of patients with type 2 diabetes mellitus (T2DM) in the world increases by 5–7%, and every 12–15 years it doubles. According to WHO statistical materials, in 2005 there were 200 million patients with diabetes in the world, in 2013 – more than 382 million, in 2014 – 422 million, in 2019 – 462 million, in 2021 – 532 million, in 2045 they predict their growth to 700 million people [1]. T2DM has now reached the scale of a pandemic.

According to the data of the Public Health Center of Ukraine, the incidence of T2DM has doubled over the past 10 years. In 2016, more than 1.2 million people in Ukraine suffered from T2DM causes more than 3% of primary disability of the working population of Ukraine [2].

Along with the increase in T2DM incidence, the mortality rate from its complications also increases. According to WHO data, the mortality rate increased by 3% between 2000 and 2019 [3].

The constant increase in the number of patients with T2DM leads to an increase in the number of its complications. One of its most frequent complications is diabetic foot syndrome (DFS), which develops in 6-11% of patients, and 40-70% of them require surgical treatment with the use of antibacterial drugs. 30% of hospitalizations of patients with T2DM are related to DFS [4].

In 40% of patients, a recurrence of purulent-necrotic processes of the lower extremities occurs within the first year after treatment, and in 60% – within three years [5].

In patients with purulent-necrotic processes of soft tissues, aerobic gram-positive cocci are the most common causative agents, among which *Staphylococcus aureus* and streptococci are most often isolated. Patients with a long course and relapse have a combined flora that often acquires antibiotic-resistant properties [6].

In patients with purulent-necrotic wounds of soft tissues, a "circulus vitiosus" is formed, which is caused by a violation of wound healing in diabetes, as well as an increase in the level of blood glucose in the presence of an inflammatory focus [7].

Analysis of procalcitonin, interleukin-6, and fibrinogen levels is used to diagnose complications of purulent-necrotic soft tissue processes in T2DM [8].

Taking into account the trends in the incidence of T2DM and the development of its purulent complications, the issue of finding and developing new anti-

microbial agents for the treatment of this category of patients has become extremely urgent.

THE AIM

The purpose of the work was to improve the results of surgical treatment of patients with T2DM and purulent-necrotic wounds by using probiotic antiseptics.

MATERIALS AND METHODS

This study was conducted at the clinical base of the Department of General Surgery No. 2 of the Bogomolets National Medical University in the Kyiv City Clinical Hospital No. 3. The criteria for inclusion in the experiment were: men and women, aged from 18 to 75 years, the presence of purulent-necrotic wounds of various localization and (on the background) T2DM. All included patients (n=66) were randomly divided (randomized) into two groups by the method of closed envelopes. The research group included 31 patients, where probiotic antiseptics were used as a local treatment, and the control group - 35 patients - with the use of traditional antiseptics (Table I).

The above data indicate that the control and experimental groups are comparable to each other ($p>0.05$).

The use of probiotic antiseptics included the use of a combination of antiseptics based on lactic acid bacteria (LAC), which are pathogenic for humans.

To treat the skin around the wound, a gel was used, the composition of which included: ethyl alcohol 60.0%, 2-propanol 5.0%, *Bacillus megaterium*<5%, *Bacillus subtilis* 5.0%, enzymes 5-10%. A gel was used to clean the wound, which included: purified water,

Fig. 1. Dynamics of macroscopic changes in the wound of Patient S., 54 years old: 1a. State before admission to the hospital; 1b. The 3rd day in the hospital; 1c. The 7th day in the hospital

Fig. 2. Dynamics of macroscopic changes in the wound of Patient S. 58 years old: 2a. State before admission to the hospital; 2b. The 3rd day in the hospital; The 7th day in the hospital

Table I. Characteristics of patients included in the experiment

Indicator	Group distribution		
	Control (CG)	Experimental (EG)	p
Age, years	53,5±5,7	54,8±5,3	0,658 #
Female/male, abs. (%)	18(51,4 %) / 17(48,6%)	16(51,6 %) / 15(48,4%)	0,913 ##
Upper extremity lesions, abs (%)	26 (74,3%)	25 (80,7%)	0,936 #
Lower extremity lesions, abs. (%)	6 (17,1%)	5 (16,1%)	0,873 #
Other body parts, abs. (%)	3 (8,6%)	2 (3,2%)	0,921 #
Duration of type 2 diabetes, years	10,3	9,8	0,737 #
Glycosylated hemoglobin levels, %	6,7±0,23	6,9±0,26	0,862 #
Prior administration of antibacterial agents, days	57,1±6,9	56,25±4,8	0,811 ##
The number of co-morbid conditions, n	2,4	2,6	0,683 #
IL-6 level, pg/ml	37,2±6,1	48,1±10,6	0,767 #
TNF-a level, pg/ml	14,5±0,97	13,9±1,4	0,138 #
CRP level, mg/l	48,5±5,9	61,3±9,2	0,375 #

Note: # – Student's T –test, ## – Wilcoxon T-test.

Table II. Average values of the levels of pro-inflammatory markers

	The first day			The third day			The seventh day			p#	p##
Group	CG	EG	p	CG	EG	p	CG	EG	p		
IL-6	37,2	48,1	0,767	26,6	24,0	0,610	27,5	23,9	0,031	0,317	0,004
TNF-a	14,5	13,9	0,138	13,7	15,1	0,904	14,1	10,3	0,525	0,803	0,001
CRP	48,5	61,3	0,375	47,2	49,9	0,428	40,1	36,9	0,048	0,119	0,018

Note: # – comparison of indicators between the first day and the seventh in the control group;
– comparison of indicators between the first day and the seventh in the experimental group.

Table III. Changes in cytogram types

Cytogram type (%)	The first day			The third day			The seventh day		
	CG	EG	p	CG	EG	p	CG	EG	p
Necrotic	12,5	6,25	<0,001	0	0	-	0	0	-
Degenerative-inflammatory	50	43,75	0,865	43,75	12,5	0,045	0	0	-
Inflammatory	37,5	50	0,572	56,25	56,25	0,597	28,125	0	<0,001
Inflammatory and regenerative	0	0	-	0	25	<0,001	62,5	37,5	0,083
Regenerative-inflammatory	0	0	-	0	6,25	<0,001	9,375	43,75	0,002
Regenerative	0	0	-	0	0	-	0	18,75	<0,001

Note: comparison of changes in cytogram types was performed using Fisher's F-test.

anionic surfactant 5-15%, amphoteric surfactant, nonionic surfactant, ethoxylated alcohols, sodium chloride, enzymes, *Bacillus megaterium*, *Bacillus subtilis*, citric acid, preservative. For the final stage of wound treatment, 2-3 doses of spray were used, which included *Bacillus subtilis* > $5*10^7$ CFU/ml, *Bacillus megaterium* > $5*10^7$ CFU/ml, didecyldimethylammonium chloride 0.1%.

The main mechanism of probiotic antiseptics is to create antagonism in the wound between mycobacteria and pathogenic microorganisms, which caused and maintained inflammation. The creation of colonies of *Bacillus subtilis* when using the spray forms a biofilm, which also has protective properties against the penetration of other pathogenic microorganisms into the wound and prevents their reproduction in the wound.

The control group used antiseptics based on octenidine dihydrochloride (0.001%) and 2-phenoxyethanol (2%), or antiseptics based on decamethoxine.

All patients received the treatment of concomitant pathology with the participation of specialists, symptomatic treatment and empiric (at the beginning of treatment) antibiotic therapy, and etiological - after

Fig. 3. Dynamics of macroscopic changes in the wound of Patient S., 52 years old: 3a. When admitted to the hospital; 3b. The 3rd day in the hospital; 3c. The 7th day in the hospital, secondary surgical treatment, autodermoplasty according to Thirsch; 3d. The 7th day in the hospital, secondary surgical treatment, autodermoplasty according to Thirsch

determining antibiotic sensitivity, daily debridement with wound dressing and control of laboratory indicators with the determination of cytogram types.

To study the levels of pro-inflammatory markers, blood was taken from the peripheral vein on an empty stomach, and microscopic material was taken for cytogram-type research during bandaging, before wound treatment with antiseptics or debridement. The material was collected from patients during admission (1st day) to the hospital, on the 3rd day, and on the 7th day.

Wound healing processes were analyzed based on the types of cytograms according to Steinberg: type I – "necrotic", type II – "degenerative-inflammatory", type III – "inflammatory", IV – "inflammatory-regenerative", V – "regenerative-inflammatory", VI - "regenerative".

The statistical analysis of the levels of pro-inflammatory markers and the study of their results were carried out in IBM SPSS Statistics Base (version 28). Statistically significant results were considered when a value of $p<0.05$ was obtained. Quantitative data were presented as arithmetic mean ± standard deviation (SD). The Chi-square test was used to check the normality of the data distribution. The criteria for normal distribution were $p>0.05$. When obtaining data that corresponded to a normal distribution, the Student's T-test for related and unrelated samples was used to compare the data. When data that differed from a normal distribution were obtained, the Wilcoxon W-test for related and unrelated samples was used to analyze the data. The analysis of cytogram types and their changes was carried out using Fisher's exact method, which made it possible to compare the frequency of symptoms.

Modern principles of bioethics were followed during the conduct of this experiment. Commission of the Bogomolets National Medical University issues of bioethics approved this research design. The conducted research did not carry risks of deterioration of the patients' health, the research was conducted with the inclusion of bioethical norms and biostatistical standards. Before the start of the study, all patients signed an informed consent to participate in this study and further use and publication of their data. All used medicinal products are registered and authorized for use in Ukraine.

RESULTS

The increased glycosylated hemoglobin level testified to the long course of T2DM and the insufficient level of glycaemia correction, which forms the background for the purulent-necrotic complications of T2DM development. The increased level of IL-6, the level of CRP, and the level of TNF-a significantly exceeded normal values, which indicates a pronounced inflammatory process.

After analyzing the obtained data, it was found that on the 7th day there was a statistically significant difference between the levels of Interleukin-6 and C-reactive protein between the control and experimental groups (27.5 and 23.9 ($p=0.031$) respectively). The level of tumor necrosis factor, in turn, did not have a statistically significant difference in the control and experimental groups (40.1 and 36.9 ($p=0.048$), respectively). In both groups, a unidirectional positive trend towards a decrease in pro-inflammatory cytokines was observed, which, in our opinion, is due to the effectiveness of the prescribed treatment. However this effect in the experimental group became statistically significant only on the 7th day, which is directly related to the duration of the wound process, with a decrease the degree of systemic inflammation against the background of local wound treatment (Table II).

In the control group, the average level of IL-6 on the first day was 37.2, on the seventh day – 27.5 ($p=0.317$),

TNF-a on the first day was 14.5, on the seventh day – 14.1 (p=0.803), CRP on the first day – 48.5, on the seventh day – 40.1 (p=0.119). In the experimental group, the average level of IL-6 on the first day was 48.1, on the seventh day – 23.9 (p=0.004), TNF-a on the first day was 13.9, on the seventh day – 10.36 (p=0.001), CRP on the first day – 61.3, on the seventh day – 36.9 (p=0.018) (Table II).

During the analysis of dynamic changes in the indicators of pro-inflammatory markers between the first and seventh days, we found a statistically significant difference only in the experimental group. In comparison, there was no statistically significant difference between the first and seventh day in the control group. The obtained result testified to the higher effectiveness of the use of probiotic antiseptics in patients with purulent-necrotic wounds of various localization in T2DM.

The obtained data show that there was a statistically significant difference between the first type of cytogram (p<0.001) in the control and the experimental group of patients upon admission to the hospital, and there was no statistically significant difference between the detection of the second and third types of cytograms (p=0.865 and p=0.572, respectively) (Table III).

On the third day, a statistically significant difference was found between the second, fourth, and fifth types of cytogram (p=0.045, p<0.001, p<0.001, respectively). The obtained result shows that on the 3rd day, the majority of patients with active inflammatory processes remained in the control group, while patients with the regenerative phase of inflammation began to appear in the experimental group.

On the seventh day, there were no patients with the first and second types of cytograms, but in the control group, there were still patients with the third type of cytogram, which indicates a longer period of transition to the regenerative phase of the inflammatory process. Analysis of the results of detection of the fourth type of cytogram on the seventh day had no statistically significant difference (p=0.083). When analyzing the fifth and sixth types of cytograms, a statistically significant difference was obtained (p=0.002 and p<0.001, respectively) (Table III).

Having analyzed the above data, it can be concluded that the healing processes occurred faster in patients from the experimental group, which testified to the effectiveness of the use of probiotic antiseptics in comparison with chemical antiseptics.

The data obtained by us indicate a higher efficiency, acceleration of regenerative processes in the wound in patients who were treated with the use of probiotic antiseptics, compared to patients treated with traditional chemical antiseptics.

DISCUSSION

At the moment, there is no "gold standard" for the purulent-necrotic wounds treatment in patients with T2DM. The magnitude of pathogenetic mechanisms, the severity and duration of diabetes, irrational antibiotic therapy, frequent relapses or incomplete recovery lead to the need for repeated treatment, which in turn cause the continuation of the pathological process with higher resistance to the prescribed treatment, the appearance of antibiotic-resistant strains of bacteria in wounds.

The main methods of local treatment of patients with purulent-necrotic wounds in T2DM are surgical treatment with the use of antiseptics, hydrogel and collagen-based bandages, the use of VAC therapy, phototherapy, ultrasonic cavitation, and laser wound cleaning [9].

In addition to local treatment, hypoglycemic, antibacterial, anti-inflammatory therapy, epithelial growth factors, and endothelial growth factor are used [9]. Higher levels and risks of antibiotic resistance in patients with foot infection in T2DM are being described each year, and during the COVID-19 pandemic, this rate has exceeded previous levels [10]. Tao YW and others in their study describe the positive effect of the use of systemic probiotics in patients with T2DM, which led to the normalization of the intestinal microflora and improved response to insulin therapy [11].

Probiotic antiseptics have been successfully used in patients with wounds in critical ischemia with detection of multiresistant pathogens such as *Enterococcus Faecalis, Klebsiella pneumonia, Proteus mirabilis*. In this study, no bacterial growth was detected after 21 days of use [12]. S. Martínez-Pizarro describes the positive results of treatment of patients with wounds caused by *A. baumannii, Pseudomonas aeruginosa* [13]. There are also a number of publications in the medical literature that describe the results of treatment of patients with atopic dermatitis, acne, psoriasis, and erysipelas with probiotics based on *S. thermophiles, V. filiformis, B. longum, B. subtillis* [14-16].

Regarding the use of a probiotic antiseptic based on *Lc. chungangensis*, a study was conducted on mice with T2DM and purulent wounds and results were obtained, indicating a positive effect in reducing IL-4, IL-6, IL-10, and TNF-α, growth factors (TGF-β1 , VEGF, PDGF, and FGF), and chemokines (CCL2 and CXCL4) [17].

Regarding the use of probiotic antiseptics based on *B. Subtilis in vitro*, a positive effect on the formation of biofilms and the displacement of *Pseudomonas aeruginosa, Escherichia coli, Salmonella enterica* from the nutrient medium was proven [18].

CRP, IL-6, TNF-α, and Procalcitonin are recommended for diagnosing the level of inflammation [19, 20].

Therefore, one of the promising areas of probiotics use is the development of probiotic antiseptics for the treatment of long-term purulent-necrotic lesions of soft tissues in patients with T2DM.

CONCLUSIONS

1. Local use of probiotic antiseptics leads to faster statistically significant positive dynamics of changes in systemic inflammation indicators in patients with purulent-necrotic wounds in T2DM. ($p=0.001$).
2. Probiotic antiseptic accelerates the healing of wounds in these patients, compared to the use of chemical antiseptics. ($p<0.001$).
3. Implementation of the latest methods and treatment schemes into clinical practice requires detailed study, but has great potential for development. Probiotic antiseptics can be a new direction in local treatment of patients with purulent-necrotic wounds in T2DM.

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ORIGINAL ARTICLE

WAYS OF IMPROVING THE QUALITY OF PROSTHETICS OF MILITARY PERSONNEL

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ABSTRACT

The aim: Justify the choice of the construction material of dental prostheses, taking into account the clinical picture and concomitant diseases in military personnel and the study of the dynamics of military personnel seeking orthopedic dental care.

Materials and methods: 185 military personnel were examined and fitted with prosthetics in the period from March 2022 to March 2023. Methods: general clinical, content analysis, bibliosemantic, medical and statistical.

Results: All patients who came to us for dental care had previously been replaced with fixed metal structures. Of them, 121 people indicated problems related to the use of metal prostheses. From these patients, a risk group of intolerance to prosthesis materials was formed and a search was made for base materials that would be biologically indifferent. For the manufacture of partial removable prostheses, we chose the basic thermoplastic material Acron, manufactured by Roko (Poland), which has high biocompatibility with the tissues of the prosthetic bed. When choosing the structures of partial removable prostheses in patients with various defects of the dentition, we were guided by a small number of clinical visits, which is relevant for military personnel who are on rotation and treated in the hospital.

Conclusions: Our careful selection of structural material made it possible to prevent complications and produce high-quality removable prostheses in a short period of time. An analysis of the reasons for orthopedic care showed low awareness of the servicemen regarding the need for timely orthopedic treatment.

KEY WORDS: military stomatology, periodontal disease, acrylic polymers, thermoplastic materials, biocompatibility

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INTRODUCTION

The repulsion of Russia's full-scale aggression against Ukraine is taking place against the backgr1ound of high dental morbidity among the servicemen of the Armed Forces of Ukraine. Numerous studies that were conducted before its beginning established a high level of dental morbidity among the personnel of the units that participated in the ATO/OS in the east of Ukraine (2014-2021) [1-3]. In the structure of diseases of the oral cavity of military personnel, caries and its complicated forms (pulpitis, periodontitis) prevailed (88.7%), periodontal diseases make up 3.9%, others (mucous membrane diseases of the oral cavity, non-carious lesions, etc.) - 7.4% [4]. The authors also established that a large part of military personnel who needed oral cavity rehabilitation was 57.47%, and the number of those who needed orthopedic treatment (dental prosthetics) was 9.36% of the number of those examined during preventive examinations [4, 5]. These preliminary data indicate significant problems with dental health in military personnel who are now resisting a full-scale Russian invasion of Ukraine.

Due to the specific conditions of life and combat activity of the personnel of the Armed Forces, connected with the peculiarities of the military profession, military dentistry has always occupied a special place in the dental service of Ukraine. To provide all types of dental care to military personnel in full, specialized units are organized in military medical institutions, namely offices, departments, clinics [6].

In 2015, in order to optimize the organization of providing dental care to servicemen of the Armed Forces of Ukraine, on the basis of a number of legal acts, the «Instructions on the procedure for providing dental care in health care facilities and medical units of the Armed Forces of Ukraine» was created, approved by order of the Ministry of Defense of Ukraine No. 1071/27516 of September 7, 2015 [7], which regulates the provision of dental care to military personnel. Since the beginning of the full-scale invasion, the Ministry of Health of Ukraine has also made numerous changes to legal acts related to assistance to the military and law enforcement officers, as well as issued a number of new documents [8].

According to the above-mentioned Instruction, dental orthopedic care for military personnel is defined as restoration of the functions of the chewing apparatus, elimination of congenital and acquired deformities of the face and jaws through the use of various types of special prostheses, devices, which are divided into: dental prosthetics (replacement of defects of teeth and dentition and effective influence on teeth to improve their functioning); maxillofacial prosthetics (replacement of defects of bones and soft tissues of the face during the provision of surgical assistance in connection with injuries, wounds, congenital and acquired defects of the maxillofacial area); orthodontics (correction of bite anomalies and the position of individual teeth) [7]. The scope of free orthopedic dental care includes prosthetics with dental devices and prostheses made of steel, chrome-cobalt alloys and plastic. In the case of use of precious metals, electroplating and porcelain in dental prosthetics by the categories of persons specified in clause 6 of this section, only the cost of such materials is paid [7].

There are various reasons why military personnel seek orthopedic dental care: removal of an orthopedic structure for the purpose of further treatment by a dentist-therapist, manufacture of new dental orthopedic structures, complaints about unpleasant sensations in the oral cavity due to prostheses, etc. [9].

THE AIM

The purpose of our work was to substantiate the choice of the construction material of dental prostheses, taking into account the clinical picture and concomitant diseases in military personnel who required orthopedic treatment, as well as to study of the reasons and dynamics of the servicemen's request for orthopedic dental care.

MATERIALS AND METHODS

Special medical orthopedic care of level 3-4 is provided in specialized military medical departments and civilian dental institutions. The clinical and scientific base of the research was the department of post-graduate education of dentists-orthopedics, which is located on the basis of the communal enterprise "Poltava Regional Center of Stomatology - Dental Clinical Polyclinic" and provides consultative and specialized orthopedic care of various levels of complexity.

Examination and prosthetic fitting of 185 military personnel who were treated in a hospital and on rotation in the Poltava region and who sought help on their own between March 2022 and March 2023 were carried out, of which 121 people indicated problems related to the use of metal prostheses, which made it possible to assign them to the risk group of intolerance to dental materials of prostheses. In turn, this group was divided into three clinical subgroups taking into account their somatic status and the presence/absence of complaints and referrals to clinics due to prosthetics for the selection of appropriate treatment and materials.

Methods: general clinical and special methods of examination of patients; content analysis for the analysis of regulatory and legal provision of dental care for military personnel; bibliosemantic for the analysis of literary sources; medical and statistical for the calculation of derived values.

RESULTS

Employees of the department carried out an examination and prosthetics of 185 military men who were being treated in a hospital and on rotation in the Poltava region, in the period from March 2022 to March 2023.

At the first stage of the research, we studied the distribution of patients who sought dental care by referral. The largest number of patients for orthopedic treatment were sent by the Poltava Military Hospital - 144 (77.8%). the number of servicemen who applied to the polyclinic registry - 28 (15.1%), self-referrals to the doctors of the department of orthopedics - 13 (7.0%) (Fig 1).

We also studied the dynamics of the number of requests during the year: self-referrals for dental care almost did not change), but the number of people referred by the military hospital increased monthly (from 4 people in March 2022 to 20 people in March 2023 (table I, fig 2).

The insignificant number of self-referrals is most likely due to the fact that patients are not fully aware of the need to maintain oral health (including through timely prosthetics), or do not consider it so necessary to waste time. The reason for this is the low awareness of the population about the importance of restoring the integrity of the tooth rows for the normal functioning of the gastrointestinal tract [10].

A significant number of patients sent by the hospital for treatment is explained, firstly, by the active hostilities on the territory of our country and the monthly increase in the number of military personnel who need specialized help, and secondly, by the fact that the patients undergo a comprehensive examination at the hospital, revealing including dental problems and, if necessary, they are sent to a dentist for treatment, as well as the fact that in the field conditions of military stay, the occurrence or exacerbation of existing diseases of the mucous membrane and periodontal tissues is possible.

Table I. Distribution of patients by referral

Month	Referral from the military hospital	Self-referral to the polyclinic	Self-referral to the specialists of the Department of Orthopedic Dentistry
March, 2022	4	1	-
April, 2022	8	1	-
May, 2022	9	2	1
June, 2022	11	2	1
September, 2022	12	2	2
October, 2022	13	2	2
November, 2022	15	3	1
December, 2022	16	3	2
January, 2023	18	4	2
February, 2023	18	4	1
March, 2023	20	4	1
In total	144	28	13

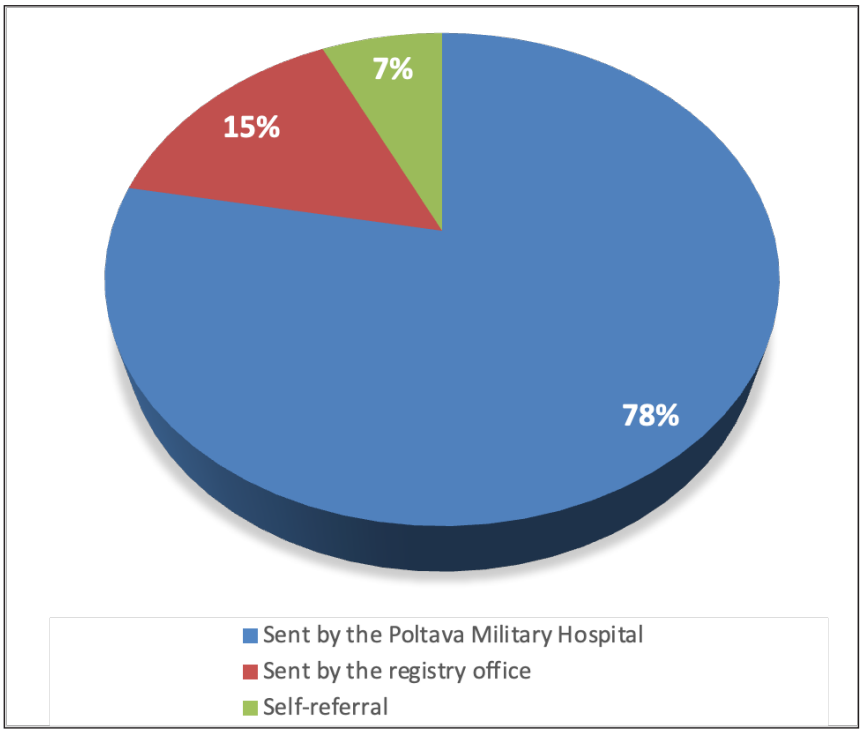

Fig. 1. The ratio of the number of patients by referral

All patients who came to us for dental care had previously been fitted with fixed metal prostheses. Among them, 121 people indicated problems related to the use of metal prostheses: a bitter taste in the mouth, increased salivation, dryness of the mucous membrane, burning of the tongue, lips, cheeks, palate, difficulties during swallowing, "fatigue" of the chewing muscles. , decreased appetite. The presence of such complaints allowed us to single out these patients in the risk group of intolerance to dental materials of prostheses. These patients were invited for examination. Out of 121 patients, 32 (26.5%) had a complicated somatic status (all of them had a history of the following diseases: pathology of the gastrointestinal tract, endocrine system, vegetative-vascular disorders, diseases of the cardiovascular system), 89 (73.5%) were with somatically uncomplicated status.

Next, taking into account the somatic status of patients and the presence/absence of complaints and appeals due to the quality of prosthetics, we formed three clinical groups.

The first group, somatically complicated, included 32 people (26.5%). In these patients, we observed changes in the mucous membrane of the oral cavity: hyperemia of the gingival margin, dryness of the mucous membrane, and a decrease in the amount of saliva.

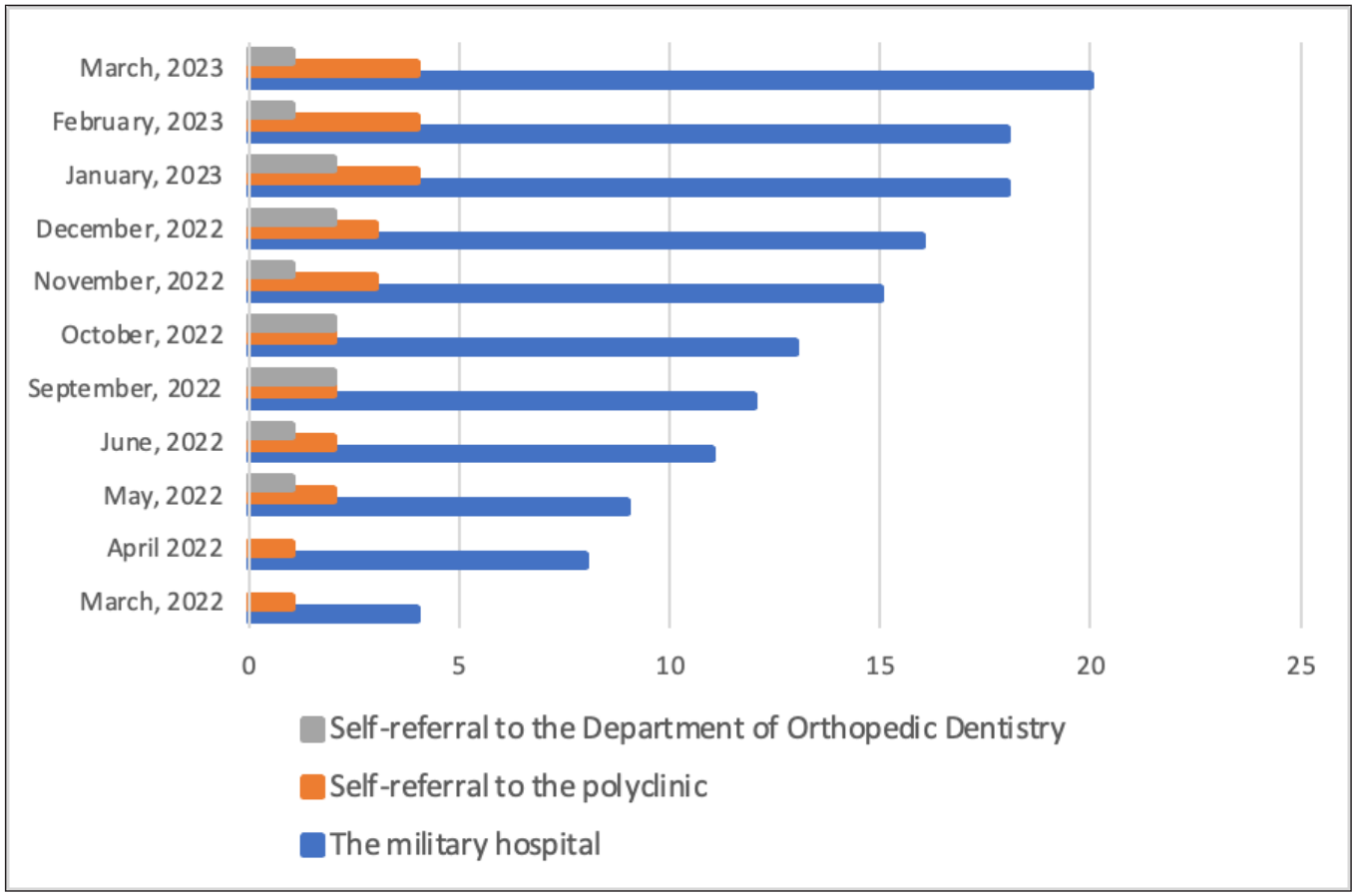

Fig. 2. Dynamics of the number of referrals to the hospital and independent appeals of the military for orthopedic help

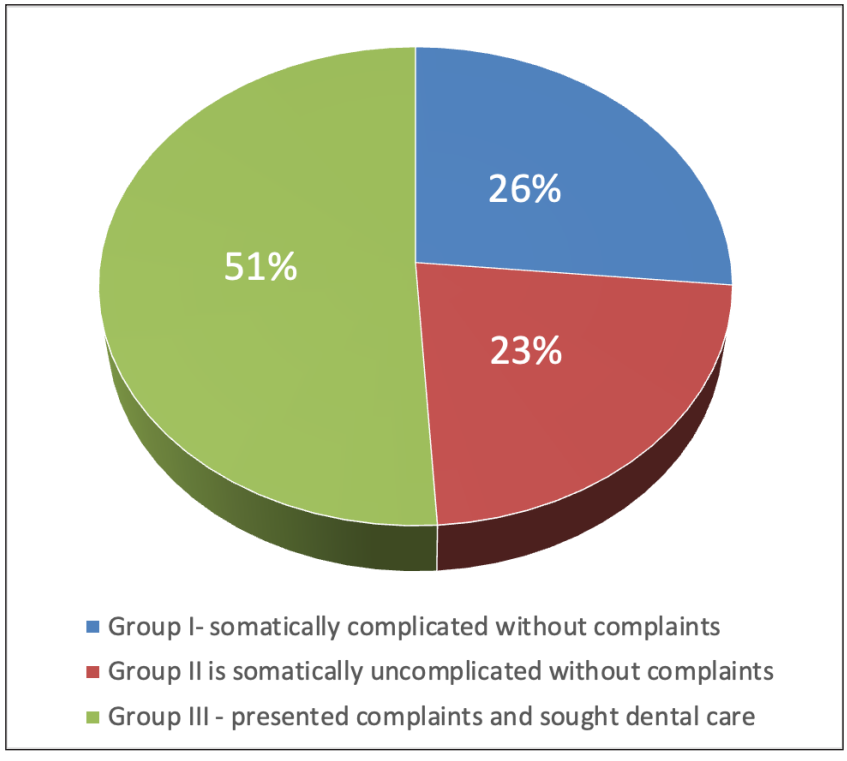

Fig. 3. The ratio of the number of patients of the risk group

The second group, 27 patients (22.3%), consisted of individuals with similar objective tissue changes of the prosthetic bed, but somatically uncomplicated status.

Patients of the first and second groups did not apply to dental clinics with complaints about the quality of prosthetics after fixing the metal structures on cement.

The third group, 62 patients (51.2%) with a somatically uncomplicated status, included persons who had previously turned to dentists with complaints about the specified symptoms or about problems with dental prostheses. Objectively: the presence in the oral cavity of acute, in some patients - chronic inflammatory periodontal diseases, tooth mobility of the 3rd degree (Fig 3).

Based on the above, it can be assumed that the somatic status of patients did not have a significant impact on the consequences of prosthetics with metal structures and the presence/absence of patient complaints.

However, this division into groups was determined by different clinical approaches to prosthetics and material selection.

Thus, from the formed risk group, 51.2% of patients complained about the quality of prosthetics, and the objective picture of their oral cavity met the criteria of patients diagnosed with "intolerance of dental prostheses". The given data prove the relevance of the problem of biocompatibility of materials for the manufacture of orthopedic structures with tissues of the prosthetic bed, especially in patients with chronic periodontitis and related diseases.

In connection with the fact that 121 military personnel were included in the risk group of intolerance to dental materials, we conducted an active search for basic materials that would be biologically indifferent to the tissues of the prosthetic bed. These requirements are met by thermoplastics: nylon, polyoxymethylene, polypropylene, polyethylene, which, according to the manufacturer, are characterized by the absence of a toxic-allergic irritant and have high biocompatibility. Thus, all our patients were made partial removable prostheses made of thermoplastic material Acron, manufacturer Roko (Poland).

When choosing the designs of partial removable prostheses in patients with various dentition defects, we were guided by the need for a small number of clinical visits, which is relevant for military personnel who are on rotation and receiving treatment in the hospital.

DISCUSSION

The analysis of literary sources allowed us to monitor the toxic effect of polymeric materials on the tissues of the prosthetic bed and the body as a whole, which makes it impossible to use acrylates in patients with diseases of the mucous membrane of the oral cavity and gastrointestinal tract [11].

Any orthopedic treatment must be scientifically based, therefore 21st century dentistry uses biologically compatible materials in its arsenal. Dental prosthetics is considered effective when restoring aesthetics and function, taking into account the biocompatibility of structural dental materials. Most of the failures in prosthetics are related to the nature of the intolerance of structural materials [12]. Unfortunately, metal dental prostheses have disadvantages associated with the increased sensitivity of some patients to their components, which is confirmed by the presence of signs of intolerance to metal structures in 77.8% of the examined. The mechanism of occurrence of this pathology is multipathogenetic and largely depends on the condition of the patient's body. Galvanosis phenomena are quite often observed in patients with gastrointestinal pathology, which worsens the course of the underlying disease and makes it impossible to use most metal alloys for the manufacture of dental prostheses [13].

One of the most significant negative factors of acrylic polymers is microporosity, which leads to a change in the quantitative and qualitative composition of the microflora of the oral cavity and the emergence of dysbacteriosis. On the surface of acrylic prostheses, as a result of impaired self-cleaning of the mucous membrane, the growth and reproduction of pathogenic microflora occurs: Staphylococcus aureus, Pseudomonas aeruginosa, fungi of the genus Candida. It has been established that acrylic plastic is most susceptible to their destructive action, and structures made of it become a permanent depot for microorganisms [4, 14]. As a result, the acrylic base of the prosthesis is an inducer of the reproduction of microorganisms and the appearance of an unpleasant odor from the oral cavity [15, 16].

Even with the most careful observance of the technology of manufacturing structures based on polymethyl methacrylate, residual monomer is noted in the base, which is released from the prosthesis for 5 years and causes the appearance of a number of toxic-allergic reactions in the oral cavity [17].

From the basic dental materials that would be biologically indifferent to the tissues of the prosthetic bed, we settled on thermoplastics, which, according to the manufacturer, are characterized by the absence of a toxic-allergic irritant and have high biocompatibility, which, as noted by a number of authors, is especially relevant for patients with diseases mucosa of the oral cavity, gastrointestinal tract, immune, endocrine, and nervous systems [17, 18].

CONCLUSIONS

1. The percentage of complications of permanent prosthetics with metal structures with signs of bioincompatibility remains quite high - 65.4% of the total number of examined servicemen, which is manifest-

ed by the complaints of patients and the results of the examination.
2. Among 121 patients with clinical signs of intolerance to denture materials, 51.2% had a more severe course of the reaction of the tissues of the oral cavity, which prompted them to turn to the dental clinic with complaints.
3. Prosthetics of such patients should be performed with basic materials that would be biologically indifferent to the tissues of the prosthetic bed. The material of choice in our case was thermoplastics.
4. The somatic status of the patients had no significant effect on the course of the reaction of intolerance to the materials of the prostheses.
5. The insignificant number of self-referrals for help is explained by the fact that patients are not fully aware of the need to maintain the health of the oral cavity (including due to timely prosthetics), or do not consider it so necessary to waste time, which occurs due to low awareness..

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ORIGINAL ARTICLE

CLINICAL AND IMMUNOLOGICAL FEATURES OF THE COURSE OF CARIES IN YOUNG PEOPLE WHO HAVE SUFFERED A CORONAVIRUS INFECTION

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ABSTRACT

The aim: To establish the clinical and immunological features of the course of caries in young people who have suffered from the coronavirus disease.

Materials and methods: The main group consisted of 30 people aged 20,6±2,4 years who suffered from the Covid19 coronavirus infection 6,1±1,2 months ago. All patients underwent a dental and immunological examination.

Results: The analysis of the indicators of the dental status revealed the possibility of the existence of a relationship between the signs of the transferred acute viral infection SARS-Cov2 and the development of dental caries, first, under the condition of reduced caries resistance. In the immune system of the examined patients were found significant changes, which definitely played a pathogenetic role in the development and progression of the carious process. They were manifested by changes of varying degrees of severity, which were both unidirectional and opposite in nature: T-lymphocyte deficiency, in particular, mainly due to T-cytotoxic lymphocytes/suppressors, an increased level of B-lymphocytes and an increased level of activated CD54+ cells of T-lymphocytes.

Conclusions: In young people with dental caries who have suffered a coronavirus infection during the last 6 months, the prevalence of caries and its intensity are significantly higher than in the comparison group. Violations in the cellular and humoral links of the immune system, which combined with the pro-inflammatory profile of the blood serum, the phenomenon of immunotoxicosis, contributed to the further progression of the carious process in the oral cavity.

KEY WORDS: caries, coronavirus disease, young age, immunological parameters, cytokines, circulating immune complexes

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INTRODUCTION

A large-scale problem in the world is the SARS-CoV-2 coronavirus, which causes coronavirus disease (COVID-19), characterized by a large number of complications - "post-COVID syndrome" [1-5]. Analysis of the protective value of humoral immunity and the duration of its intensity is important for scientists because of the need to indicate the level of antibodies to SARS-CoV-2 for laboratory diagnosis and prevention of the recurrence of coronavirus disease [3, 6, 7]. One of the pathogenetic strategies of the virus is the ability to provoke the aggression of the immune system against its own tissues in the form of autoimmune and autoinflammatory processes, which is considered a unique feature of the survival of β-CoV in the body of an infected person [4].

Zinchuk O.M. and co-author Velavan T.P. and the co-author note that «activity of the synthesis of anti-coronavirus antibodies is directly proportional to the intensity of the infectious process. Therefore, in severe cases of the disease, antibody production indicated at the highest level and antibodies detected in the blood serum longer, while in mild cases and with an asymptomatic course of the infectious process, antibodies to SARS-CoV-2 often have a minimal level or not defined at all» [6, 8]. Also, Velavan T.P. and the co-author note that «level of anti-coronavirus antibodies usually decreases within a few months after infection, and the neutralizing activity of antibodies after symptomatic cases of COVID-19 in most patients persists for 6-8 months. In addition to disease severity, the duration of humoral immunity is likely to depend on baseline antibody levels» [8]. Data from the US Centers for Disease Control and Prevention (CDC) shows that there is a high probability of the simultaneous presence of IgM and IgG in patients who has just been infected with the coronavirus. This is a feature of COVID-19 [1,2]. In addition to various examination methods, laboratory indicators also help in assessing the degree of severity, diagnosing complications, and predicting the course of the disease [9, 10].

It is well known that dental caries is a multifactorial

disease, the elimination of this disease is the main task of dentistry [11-13]. The non-specific resistance of the organism has an indirect effect on mineralization processes [12]. There are many oral symptoms in COVID-19 [14-16], but the coexistence with the underlying disease is not fully established. It is still not clear whether oral symptoms are manifestations of the disease or arise from a loss of immune response [14,17].

There is evidence that immune functioning associated with periodontitis and (less studied) dental caries changes with age. In both cases, age-related mechanistic changes in the functioning of the immune system are complex and not fully studied, and it is not clear how they correlate with disease susceptibility [18]. Study have shown that caries affects the inflammatory and oxidative status of the periodontium, while its treatment appears to restore periodontal homeostasis [19]. Also needed studies with longer follow-up in order to assess the impact of the pandemic on dental caries [20].

THE AIM

To determine the clinical and immunological features of the course of caries in young people who have suffered from coronavirus disease.

MATERIALS AND METHODS

The main group consisted of 30 people who had Covid19 infection, mostly of mild and moderate severity, and had caries. The comparison group consisted of 20 people who had caries but did not have coronavirus infection. The control group consisted of 35 people, randomized by age and gender, who did not have signs of caries and did not have a coronavirus disease. The mean age of the examined patients was 20,6 ± 2,4 years. In the main group of patients, the duration from the moment when there was a disease with coronavirus disease to the moment of inclusion in the study was 6,1±1,2 months.

The patients selected for this study underwent a dental examination. Determination of the prevalence and intensity of dental caries, the state of oral hygiene and periodontal tissues was determined using the following indexes: Average of Decayed, Missing, and Filled Teeth index (DMFT); Standard Deviation of Decayed, Missing, and Filled Teeth index (SD of DMFT); Average of Oral Hygiene Index Score (OHIS) (OHI-S); Interdental Hygiene Index (IDHI) and Gingival Index (GI), Löe and Silness.

The immunological status studied of the studied cohort of patients, namely: quantitative assessment of the main populations and subpopulations of lymphocytes, determination of their functional activity, concentration of circulating immune complexes of various molecular sizes, serum immunoglobulin levels, phagocytic activity of neutrophils, and cytokine status by level I and II tests according to requirements WHO Memorandum [21].

The following were evaluated: phenotype of lymphoid cells, lymphocyte subpopulations – CD3+ lymphocytes (T cells); CD4+ lymphocytes (T-helpers); CD8+ lymphocytes (T-cytotoxic lymphocytes/suppressors); CD16+ lymphocytes (NK cells), CD22+ lymphocytes (B cells), CD54+ lymphocytes (activated lymphocytes that express the adhesion molecule ICAM-1), CD95+ lymphocytes (activated lymphocytes that express the FAS receptor) - by indirect immunofluorescence method using monoclonal antibodies manufactured by CJSC "Sorbent-Service" against lymphocyte antigens CD 3, CD 4, CD 8, CD 16, CD 22, CD 54, CD 95 with a final count of 200 cells of each phenotype on a «Lumam I3" fluorescent microscope; the functional activity of T-lymphocytes by the morphological method of the proliferative activity of lymphocytes in the reaction of blast transformation of lymphocytes (RBTL) with the mitogen phytohemagglutinin (PHA-M) of the "Wellcome Burroughs" company; phagocytic activity of neutrophils according to the degree of absorption of latex particles with the calculation of Hamburg's phagocytic index and Wright's phagocytic number; the functional state of B-lymphocytes by examining the level of the main classes of serum immunoglobulins Ig G, Ig A, Ig M by the method of simple radial immunodiffusion in a gel according to G. Mancini et al., 1965; the concentration of circulating immune complexes (CIC) in blood serum - by the method of precipitation in a solution of polyethylene glycol (PEG-6000) on a microspectrophotometer "Specol-21" (Germany) at a wavelength of 450 nm [21].

Descriptive analysis results presented as percentage distribution, mean and standard deviation (SD), or median and interquartile range (IQR). Chi-square and Fisher's exact test is used to determine any differences in the distribution of categorical variables. Because continuous variables did not follow a normal distribution, Kruskal–Wallis analysis of variance and Mann–Whitney U-test is used to detect differences in means between two or three groups. All exposure variables were included in a multivariable regression model. Results of regression analysis presented as unadjusted and adjusted odds ratios (ORs) with their 95% CIs. The level of significance was set at $p < 0.05$. Statistical data processing was also determined by the method of variational statistics using the Microsoft XP "Excel" application program package and the specialized "STATGRAPHICS Plus version 2.1" program.

Table I. Dental status of persons who have suffered from the coronavirus disease

	Main	Control
Average of DMFT	3.2	2.1
SD of DMFT	2.1	1.4
Average of OHI-S	1.44	1.1

The average and standard deviation of DMFT in main group from control group was 3.2 and 2.1, respectively, the average and standard deviation of DMFT was 2.1 and 1.4, for main group from control (P<0.01).

Table II. Index indicators of the dental status of persons with caries who suffered from the coronavirus disease (M±m)

	Main	Control
IDHI	1,55 ± 0,28	0,82 ± 0,43
GI, Löe та Silness	1,81 ± 0,36	0,79 ± 0,64

Table III. The content of the main and activated subpopulations of lymphocytes in the examined persons (M±m)

Immunological indicators	Main group (n=30)	Comparison group (n=20)	Control group (n=35)
Leukocytes, x 10^9/л	6,13±0,41	5,70 ± 1,20	7,76 ± 0,82
Lymphocytes, %	43,15±1,27	44,25± 1,14	32,14 ± 3,70
$CD3^+$ lymphocytes, %	53,4±1,3*	61,6±1,2x	64,31 ± 4,03
$CD4^+$ lymphocytes, %	33,8±1,2	34,8±1,7	33,23 ± 3,90
$CD8^+$ lymphocytes, %	14,8±0,9*	18,6±0,8x	20,50 ± 2,05
$CD4^+/CD8^+$	2,92±0,1*	1,8±0,1*x	1,61 ± 0,29
$CD22^+$lymphocytes,%	32,6±1,4*	25,2±1,2x	21,06 ± 1,17
$CD16^+$lymphocytes,%	12,3 ±1,1*	16,8±1,1 x	16,7 ± 1,11
$CD95^+$lymphocytes,%	11,21±0,32 *	6,77±0,23 x	5,04±0,02
$CD54^+$lymphocytes,%	21,2±1,03 *	13,4±1,05 x	13,8±0,81

Notes:
*– the difference between the indicator and the control group is significant (p<0.05);
x - the difference in the indicator between the groups is significant (p<0.05);
n - the number of patients.

Table IV. Indicators of functional activity of immunocompetent cells in the examined persons (M±m)

Immunological indicators	Main group (n=30)	Comparison group (n=20)	Control group (n=35)
RBTL spontaneous, %	2,42±0,12*	1,98±0,08x	1,77 ± 0,22
RBTL from PHA-M, %	76,41±2,75	79,27±2,11	78,3 ± 3,97
Phagocytic number	3,47±0,12*	3,48±0,09*	5,97 ± 0,34
Phagocytic index, %	49,73±2,13 *	48,44±3,05*	67,53 ± 4,41
NBT-test, spontaneous, %	36,12±2,21*	38,03±1,95*	24,69±1,89

Notes:
*– the difference between the indicator and the control group is significant (p<0.05);
x - the difference in the indicator between the groups is significant (p<0.05);
n - the number of patients.

RESULTS

DENTAL STATUS OF THE EXAMINED PATIENTS

The assessment of the dental status of the examined young persons with dental caries who suffered corona virus disease is given in Tables I and II.

The average and standard deviation of DMFT in main group from control group was 3.2 and 2.1, respectively, the average and standard deviation of DMFT was 2.1 and 1.4, for main group from control (P<0.01).

During the examination were primarily diagnosed deep caries of the molars and caries in the area of the tooth neck. Complaints were mainly about short-term,

Table V. Serum concentration of the main classes of immunoglobulins and CIC in the examined persons (M±m)

Immunological indicators	Main group (n=30)	Comparison group (n=20)	Control group (n=35)
Ig G, g/l	17,31±1,03*	12,45 ± 0,98 x	12,73±1,25
Ig A, g/l	2,56 ± 0,16*	1,32 ±0,17 x	1,59±0,11
Ig M, g/l	0,99 ± 0,02	80,93±0,11	1,01±0,07
CIC of large size (>19S), c.u.	33,08 ± 2,21*	47,24±2,13x	52,5±4,02
CIC of medium size (11-19S) c.u.	42,26 ± 2,16*	34,11±1,96 x	30,96±3,52
CIC of small size (<11 S), c.u.	32,22 ± 1,82*	20,16±2,31*x	15,23±1,07

Notes:
*– the difference between the indicator and the control group is significant ($p<0.05$);
x - the difference in the indicator between the groups is significant ($p<0.05$);
n - the number of patients.

Table VI. Concentration of pro- and anti-inflammatory cytokines in blood serum of examined patients (M±m)

Immunological indicators	Main group (n=30)	Comparison group (n=20)	Control group (n=35)
TNF-α, пг/мл	82,6 ±3,1*	64,9±2,4*x	51,3±4,1
IL-1β, пг/мл	82,6±2,4 *	57,2±3,6 *x	46,9±2,98
IL-6, пг/мл	12,3±0,9	11,4±0,7	12,94±1,2
IL-4, пг/мл	19,1±1,3 *	23,5±1,2 x	22,41±1,4

Notes:
*– the difference between the indicator and the control group is significant ($p<0.05$);
x - the difference in the indicator between the groups is significant ($p<0.05$);
n - the number of patients.

involuntary pain from sweets in the examined teeth. The patients indicated that they had not visited a dentist from the time they had a coronavirus disease to the time of inclusion in the study for 6.1±1.2 months. The main reason is the unavailability of dental clinics during the pandemic. In addition, according to the respondents, they were periodically in a state of stress due to the uncertainty of the future due to the pandemic, fear for the health of their relatives, and perhaps began to consume more sweet carbonated drinks and sweets. As can be seen from the data presented in Table 2, significantly higher values of hygienic indices were found in the patients of the main group, which indicates a much deeper character of periodontal tissue damage and tooth pathology with the formation of dentition defects.

INDICATORS OF SYSTEMIC IMMUNITY IN YOUNG PEOPLE WITH CARIES WHO HAVE SUFFERED A CORONAVIRUS INFECTION

The main indicators of the cellular link of the immune system in the examined young people are presented in the Table. III.

The data shown in Table 3 demonstrate that the total number of leukocytes and the percentage of lymphocytes in the peripheral blood in both groups of examined persons were preserved and corresponded to the normative values.

The results of the study of the cellular link of immunity showed that the level of CD3+ cells in the primary patients was probably lower than the similar indicator in the comparison group by 13.3% ($p<0.05$), and the content of T-cytotoxic lymphocytes/suppressors (CD8+ lymphocytes) - by 20.4% ($p<0.05$). In both groups of patients, an imbalance of immunoregulatory subpopulations revealed, while the level of CD4+ lymphocytes corresponded to normative indicators, and the percentage level of CD8+ lymphocytes was significantly lower than the indicator of the control group in the comparison group.

At the same time, a probable increase in the percentage of CD22+ cells in the examined main group was found, which indicates a significant activation of the B-cell link of the immune system in response to the chronic persistence of infectious antigens on the mucous membrane and transferred coronavirus infection. Also, in both groups of patients, was detected a probable increase in the content of activated lymphocytes that express the FAS receptor and ready for apoptosis, however, in patients of the main group, the level of CD95+ lymphocytes was higher than that of the comparison group. This is due to greater activity of inflammatory changes in the oral cavity and probably higher serum concentration of TNF-α, the main cytokine of inflammation. It should be noted that in the main group of examined patients was found a probably high-

er level of CD54+ lymphocytes, which participate in the adhesion process and express the adhesion molecule ICAM-1. Which is a consequence of impaired adhesion and cooperation of immunocompetent cells for a long time after the coronavirus infection.

The study of the functional activity of immunocompetent cells in the examined individuals of the main group (Table IV) showed high indicators of spontaneous proliferative activity of lymphocytes compared to the data of the control group ($p<0.05$), while the stimulated PHA-M proliferative activity of lymphocytes had no significant differences from normative values.

A significant decrease in phagocytosis indicators observed in the examined persons of both groups. Studies have shown that the index of phagocytic number and phagocytic index in the main group of patients was lower ($p<0.05$) than the values in healthy individuals and patients of the comparison group.

In the data of patients, it was determined that long-term persistence and antigenic stimulation by various bacteria caused an increase in the metabolic activity of neutrophils.

Table V shows data on the serum concentration of the main classes of immunoglobulins and CIC.

During the study of indicators of humoral immunity in the examined persons, a probable increase in the serum concentration of IgG and IgA was found in the main group of patients ($p<0.05$).

It should be noted that in the main group of patients there was an imbalance in the level of CICs in the blood serum, which was manifested by an increase in the content of pathogenic medium and small molecular CICs with a significant decrease in physiological CICs of large size, which is associated with the development of subclinical inflammation as a consequence of the transferred coronavirus infection.

Therefore, more pronounced phenomena of immunotoxicosis were observed in the main group of patients, which requires further dynamic monitoring.

The analysis of the data presented in Table VI showed a high activity of pro-inflammatory cytokines in the blood serum of examined caries patients, which was probably higher in persons who had undergone a coronavirus infection. Thus, in patients of the main group, the level of TNF-α and the content of IL-1β in blood serum exceeded the indicator in the comparison group, with therefore, the level of IL-6 in both groups of patients had no significant differences between them ($p>0.05$) and corresponded to normative values ($p>0.05$). TNF-α is a key starting pro-inflammatory cytokine that triggers an inflammatory reaction, participates in disturbances in the cellular link of the immune response, and increases the level of activated lymphocytes. IL-1β has the same properties. IL-6 is a cytokine that ends the inflammatory response, but since all subjects taken into the study before treatment, its level remained within the range of healthy individuals. In the main group of patients was found decrease in the level of anti-inflammatory IL-4, which was compensatory in nature.

DISCUSSION

Thus, we conducted a clinical and immunological examination of young people with dental caries who suffered mild and moderate coronavirus infection. 6,1±1,2 months passed from the moment of contracting the coronavirus disease to the moment of inclusion in the study.

Analysis of indicators of dental status revealed that within 6 months after experiencing the coronavirus disease in the examined patients, its indicators significantly worsened: the prevalence of caries was significantly higher than in the comparison group. The indicator of the intensity of dental caries was also higher than that of patients in the control group. From the above data, it follows that the intensity of dental caries is approximately 2 times higher in patients with a history of coronavirus infection than in the examined persons in the control group ($p<0.05$). It was shown that the values of the resistance of hard tissues to the effects of caries-causing factors are related to the intensity of dental caries damage. This indicates the existence of a relationship between the signs of an acute SARS-Cov2 viral infection and the development of dental caries, first of all, under the condition of reduced caries resistance.

Similar results were found in Matsuyama Y. et al. (2022): in children previously infected with COVID-19, dental caries was more common than in those who escaped the lesion and slightly increased after the pandemic [20]. Due to the tropism of the virus to mucous membranes, Paradowska-Stolarz (2021) was attempted to describe the oral manifestations of SARS-CoV-2 infection: «Angiotensin-converting enzyme 2 (ACE-2), which ensures the attachment of the virus, is also present in the oral cavity.» The analysis of the scientific study showed that the most common oral symptoms are dysgeusia (disturbance of taste), toothache, exacerbation of autoimmune diseases, as well as infection with herpes simplex and chickenpox viruses. Ulcers and aphthous stomatitis are also often mentioned. The author emphasizes that there are many oral symptoms in COVID-19, but the coexistence with the main disease is not fully established [14]. To assess the impact of the pandemic on dental caries in children, studies with longer follow-up are needed [20]. At the same time, studies assessing the impact of the global

pandemic on the prevalence of caries were almost impossible to find [17].

Significant changes in the immune system were found in the examined patients, which definitely played a pathogenic role in the development and progression of the carious process. They were manifested by changes of varying degrees of severity, which were both unidirectional and opposite in nature: T-lymphocyte deficiency, in particular, mainly due to T-cytotoxic lymphocytes/suppressors, an increased level of B-lymphocytes and an increased level of activated CD54+ cells of T-lymphocytes .

Violations in the cellular and humoral links of the immune system, which were combined with the pro-inflammatory profile of the blood serum, the phenomenon of immunotoxicosis, contributed to the further progression of the carious process in the oral cavity with the formation of a «vicious circle» of the combined pathology.

CONCLUSIONS

1. In young people with dental caries who have suffered a coronavirus infection during the last 6 months, the prevalence of caries and its intensity are significantly higher than in the comparison group, significantly higher values of the bleeding index, PMA index and hygiene index are found, which indicates deeper tissue damage and tooth pathology with the formation of dentition defects.
2. In the immune system of young people with dental caries who suffered from coronavirus infection during the last 6 months, signs of immunodeficiency were detected, primarily a decrease in the level of T-lymphocytes and T-cytotoxic lymphocytes/suppressors, which are accompanied by B-lymphocytosis and manifestations of hyperimmunoglobulinemia and activation pro-inflammatory changes with an increase in serum concentrations of TNF-α and IL-β.

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The Authors declare no conflict of interest.

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"WYZWANIA WSPÓŁCZESNEJ MEDYCYNY UZDROWISKOWEJ"

Drogie Koleżanki i Koledzy

W imieniu Zarządu Głównego Polskiego Towarzystwa
Balneologii i Medycyny Fizykalnej mamy zaszczyt zaprosić wszystkich Państwa do Ciechocinka,
do uczestnictwa w kolejnym Zjeździe PTBiMF.
Będzie to wydarzenie szczególne ponieważ odbędzie się po kilkuletniej przerwie
wywołanej przez pandemię COVID-19.

Zjazd odbędzie się w dniach 7-9 września 2023,
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Po ponad dwudziestu latach Zjazd PTBiMF powraca do Ciechocinka,
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- Leczenie uzdrowiskowe i balneorehabilitacja pacjentów z LONG COVID
- Nowoczesne zarządzanie obiektami uzdrowiskowymi w świetle wyzwań wynikających z sytuacji ekonomicznej oraz planowanych zmian w organizacji finansowania lecznictwa uzdrowiskowego w Polsce.

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