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Features of cerebral blood flow in patients with dyscirculatory encephalopathy and concomitant hypothyroidism at long-term follow-up

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ABSTRACT

Aim: To evaluate cerebral blood flow characteristics in patients with dyscirculatory encephalopathy (DE) and concomitant hypothyroidism in the long-term follow-up period.

Materials and Methods: A single-center cohort study consecutively included 60 patients with hypertensive DE and concomitant hypothyroidism (mean age 61±6 years; 95% women). In the long-term follow-up period (mean duration – 10 years), results of repeated clinical-neurological and instrumental examinations of 52 patients were analysed. Duplex scanning of extra- and intracranial vessels assessed peak systolic velocity (Vps) and end-diastolic velocity (Ved), and resistive index (RI) and pulsatility index (PI) were calculated.

Results: At baseline, patients with DE and concomitant hypothyroidism predominantly presented with cephalgic (67.3%), vestibular (61.5%), and cerebroasthenic (63.5%) syndromes. In the long-term follow-up period, an increase in the frequency of vestibular syndrome was observed, reaching 80.8% ($p=0.034$). Duplex scanning demonstrated an increase in Vps in the left common carotid artery (CCA) and bilateral internal carotid arteries (ICA), accompanied by a decrease in Ved in the middle cerebral artery (MCA) on both sides. Additionally, an increase in RI was observed in the right CCA and left MCA. At the same time, in the vertebrobasilar system, a decrease in flow velocity parameters was noted in the right vertebral artery (V4 segment) and basilar artery (BA), along with an increased RI in the right V4 segment of the vertebral artery.

Conclusions: Long-term follow-up demonstrated an increased frequency of vestibular syndrome, deterioration of cerebral blood flow predominantly in the carotid circulation due to reduced vascular elasticity, and decreased flow velocity in the vertebrobasilar system in patients with DE and concomitant hypothyroidism. These findings justify the need for timely diagnosis and correction of thyroid dysfunction in patients with chronic cerebral ischemia to optimize therapeutic, preventive, and rehabilitation strategies.

KEYWORDS: chronic cerebral ischemia, cardiovascular diseases, comorbidity

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INTRODUCTION

Cardiovascular pathology remains the leading cause of mortality worldwide [1], with cerebrovascular diseases (CVDs) occupying a significant place within its structure [2]. CVDs have also become a global medical and social problem in Ukraine. Over the past 10 years, the number of patients with CVDs in our country has doubled and exceeded 8200 per 100000 population. This increase is attributed to both a rise in chronic, slowly progressive forms of CVDs and stroke incidence. Chronic cerebral circulation insufficiency – dyscirculatory encephalopathy (DE) – holds a prominent position among cerebrovascular disorders. According to epidemiological data, DE accounts for up to 67% of CVD cases [3].

The issue of comorbidity in cardio-neurology is one of the most relevant challenges in the modern healthcare system. Comorbidity complicates disease progression, worsens prognosis, and increases the number of complications [4].

Thyroid disorders in Ukraine and other countries have become one of the most prevalent endocrine pathologies,

leading to a decline in quality of life and working capacity. Estimates of the prevalence of primary hypothyroidism in the general population usually do not account for aetiology and depend on several factors, including the type of studied population and the definition of the condition itself (e.g., whether subclinical hypothyroidism is included) [5]. Data from the National Health and Nutrition Examination Survey (NHANES) estimated the prevalence of hypothyroidism (both overt and subclinical) at 4.6% [6]. A screening study in the United States reported a prevalence of overt and subclinical hypothyroidism of 0.4% and 9%, respectively, with the latter increasing to more than 20% among women aged ≥75 years [7]. According to a European meta-analysis, the prevalence of overt and subclinical hypothyroidism was 0.37% and 3.8%, respectively, including both diagnosed and undiagnosed cases, while the incidence was estimated at 226 cases per 100000 persons per year [6, 7].

Hypothyroidism is associated with increased cardiovascular morbidity and mortality [8, 9]. The elevation of arterial blood

pressure (BP) in hypothyroidism is related to increased peripheral vascular resistance, reduced vascular relaxation capacity, impaired diastolic relaxation of the heart, and changes in renal haemodynamics [10, 11]. This predominantly results in diastolic hypertension (HTN). In a hypothyroid state, the density of alpha-1 adrenergic receptors increases, while beta-adrenergic receptor density decreases [10], leading to enhanced smooth muscle contractility and vasoconstriction. Plasma vasopressin levels increase, resulting in elevated sodium and water retention [12]. Stimulation of the sympathoadrenal system during reduced thyroid function helps maintain BP levels and compensates for decreased cardiac output. Relative increases in aldosterone and cortisol levels are also observed, both of which actively contribute to BP regulation [10].

Several studies have shown that cerebral blood flow and brain glucose consumption decrease in thyroid hypofunction. In hypothyroidism, cerebral blood flow may decrease by up to 38% below normal, while oxygen and glucose consumption decrease by approximately 27%. Vascular resistance in cerebral vessels increases twofold [13].

Neurological disorders in hypothyroidism represent a severe and widespread condition of the nervous system. Cerebral pathology, specifically DE developing due to metabolic and vascular disturbances in patients with hypothyroidism, reflects endothelial dysfunction, namely a breakdown in the compensatory capacity of the endothelium [14, 15].

Despite numerous studies addressing hypothyroidism and its neurological complications, certain aspects of the diagnosis and clinical course of neurological pathology in hypothyroidism require further investigation.

AIM

The study aimed to assess the characteristics of cerebral blood flow in patients with DE and concomitant hypothyroidism at long-term follow-up.

MATERIALS AND METHODS

A single-centre cohort study analysed the results of a comprehensive examination of 60 patients (mean age 61 ± 6 years; 57 women [95%], 3 men [5%]) with dyscirculatory encephalopathy (DE) in the setting of grade 1–2 HTN (hypertensive DE) and concomitant hypothyroidism, who were consecutively enrolled between 2010 and 2013 and were under outpatient follow-up at the State Institution of Science «Center of innovative healthcare technologies» State Administrative Department (until 07.07.2024 – State Scientific Institution «Scientific and Practical Centre of Preventive and Clinical Medicine» State Administrative Department). The presence of DE was confirmed based on clinical-neurological, neuropsychological, laboratory, and instrumental examination findings in accordance with generally accepted approaches [16].

Concomitant thyroid hypofunction due to autoimmune thyroiditis was present in 39 (65%) patients, post-surgical hypothyroidism in 9 (15%), and spontaneous hypothyroidism was recorded in 12 (20%) cases. The included patients were under regular follow-up by a neurologist and endocrinologist,

continuously received L-thyroxine replacement therapy, and regularly monitored thyroid hormone levels.

Patients with grade 3 HTN, malignant neoplasms of the thyroid gland or brain, decompensated somatic diseases, pregnant women, and patients with alcohol and/or psychoactive substance abuse were excluded from the study.

In the long-term follow-up period (2022–2024), a re-examination of patients from the initially formed cohort was conducted; the mean follow-up duration was 10 years. During the observation period, 2 patients died, and 6 discontinued medical care at the institution. Thus, the follow-up stage was completed by 52 patients, in whom repeated clinical-neurological and instrumental assessments were performed.

Duplex ultrasound scanning of extra- and intracranial vessels was carried out according to a standardised methodology. Peak systolic velocity (Vps) and end-diastolic velocity (Ved) were measured, and the resistive index (RI [Pourcelot index]) and pulsatility index (PI [Gosling index]) were calculated to assess vascular resistance [17]. The study included analysis of blood flow in the common carotid artery (CCA), internal carotid artery (ICA), middle cerebral artery (MCA), vertebral artery (V1–V3 and V4 segments) bilaterally, as well as in the basilar artery (BA).

Statistical processing of the obtained data was performed using the MedCalc software package v. 23.5.1 (MedCalc Software Ltd., Belgium) and EZR v. 1.68. Central tendency and variability of quantitative variables were expressed as median (Me) and interquartile range (IQR). Qualitative variables were presented as absolute values and relative frequencies (%).

In paired samples, quantitative variables were compared using the Wilcoxon signed-rank test. The results of comparisons of quantitative variables in paired samples included the Me difference, calculated using the Hodges–Lehmann method (ΔMeHL), with a 95% confidence interval (CI). The McNemar test was used to compare the frequency of qualitative characteristics in paired samples. A p-value < 0.05 was considered statistically significant.

ETHICS

The study was carried out in accordance with the fundamental principles of the Council of Europe Convention on Human Rights and Biomedicine, the World Medical Association's Declaration of Helsinki on ethical principles for medical research involving human subjects, and applicable national regulations. The study protocol received approval from the local ethics committee. Written informed consent was obtained from all participants.

FRAMEWORK

The study was conducted as a fragment of the scientific project of the Scientific Department of Internal Medicine (State Institution of Science «Center of innovative healthcare technologies» State Administrative Department) «Improvement of the strategy of personalized treatment and rehabilitation of patients with cardiovascular diseases and neurological disorders» (state registration number 0125U000319; term: 2025–2029).

RESULTS

Patients included in the study reported headache, reduced work capacity, unsteadiness while walking, general weakness, fatigue, memory impairment, decreased concentration, sleep disturbances, irritability, tearfulness, dizziness, and feelings of anxiety.

The structure of the studied patient cohort according to the main neurological manifestations is presented in Fig. 1. At baseline, patients with hypertensive dyscirculatory encephalopathy and concomitant hypothyroidism predominantly presented with cephalgic, vestibular, and cerebroasthenic syndromes. The study demonstrated a statistically significant increase in the frequency of vestibular syndrome in the long-term follow-up period – from 61.5% to 80.8% ($p=0.034$). At the same time, a decrease in the frequency of cephalgic syndrome was observed (from 67.3% to 34.6%; $p=0.002$). The frequency of other syndromes, including atactic, cerebroasthenic, and mnesic syndromes, did not show statistically significant changes over the 10-year period (Fig. 1).

According to the results of duplex scanning of extra- and intracranial arteries, changes in cerebral blood supply were identified (Table 1). In the carotid circulation, an increase in peak systolic velocity (Vps) was observed in the left common carotid artery (CCA) and bilaterally in the internal carotid arteries (ICA), accompanied by a decrease in end-diastolic velocity (Ved) in the middle cerebral artery (MCA) on both sides. In addition, a statistically significant increase in the resistive index (RI) was found in the right CCA and the left MCA. Moreover, an increase in the pulsatility index (PI) was recorded in the left MCA.

In the vertebrobasilar system, a decrease in flow velocity parameters was observed in the right vertebral artery (VA, V4 segment) and the BA, as well as an increase in RI in the right VA (V4 segment) (Table 1).

The obtained results are associated with the activation of compensatory mechanisms, in particular sympathicotonia, which contributes to increased arterial tone and reduced vascular elasticity, and is accompanied by pseudonormalisation of blood flow in the CCA. An increase in the RI in the carotid circulation arteries may indicate vascular remodelling in this vascular territory under conditions of increased haemodynamic load, aimed at maintaining adequate cerebral blood supply.

DISCUSSION

The results of the present study indicate the adverse role of concomitant hypothyroidism in the course of DE, manifested by an increase in neurological symptom severity and worsening of cerebral circulation disturbances.

The predominance of vestibular syndrome among the included patients corresponds to current understanding of the pathophysiology of chronic cerebral ischemia. It is known that damage to small cerebral vessels leads to diffuse injury of the white matter, particularly of the conduction pathways responsible for motor coordination and balance [18, 19]. Such changes are especially frequently localized in subcortical structures and the cerebellum, clinically manifesting as gait disturbance, instability, and dizziness. Similar findings have also been reported in studies of chronic cerebral hypoperfusion, which have demonstrated a relationship between reduced perfusion and the development of motor and coordination disorders [20].

The deterioration of cerebral blood flow in patients with concomitant hypothyroidism can be explained by the multifactorial influence of thyroid deficiency on the cardiovascular system. In particular, thyroid hormones play a key role in regulating vascular tone, cardiac output, and peripheral vascular resistance. Their deficiency is associated with reduced cardiac output, increased systemic vascular

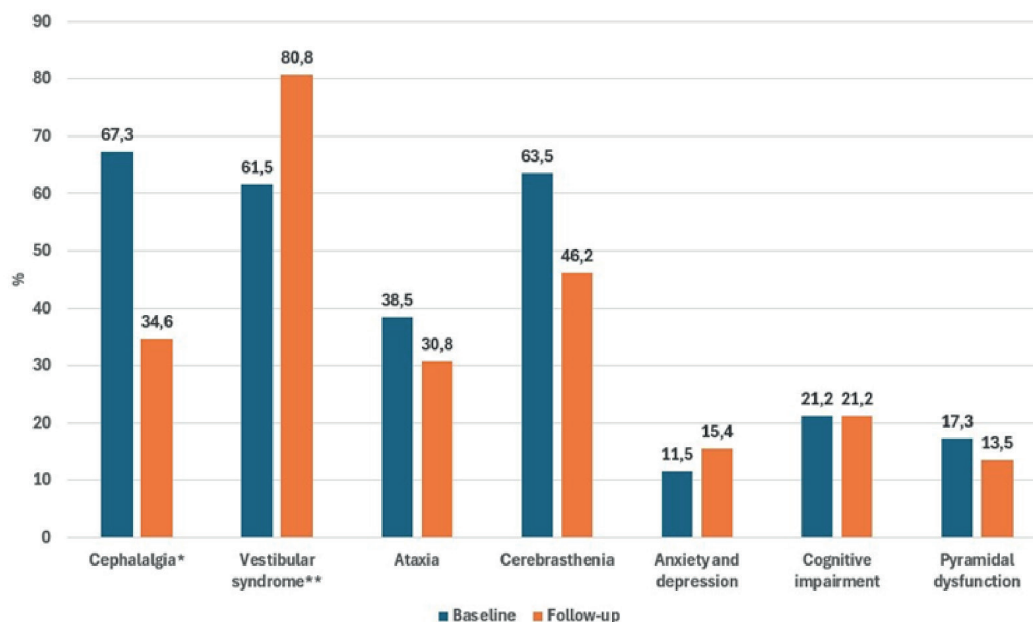


Fig. 1. The profile of the studied patients' neurological presentations at baseline and long-term follow-up ($n=52$). * – $p=0.002$; ** – $p=0.034$

Picture taken by the authors

Table 2. The parameters of extra- and intracerebral arteries duplex scanning of the studied patients at baseline and long-term follow-up (n=52), Me (IQR)

Vessels	Parameters	Baseline	Follow-up	Δ MeHL (95 % CI)	p
CCA	Vps (D), cm/s	74.0 (62.0...93.5)	83.5 (70.0...89.0)	4.3 (-3.0...11.5)	0.244
	Vps (S), cm/s	71.5 (61.5...86.0)	94.0 (87.5...95.0)	15.0 (8.5...22.0)	<0.001
	Ved (D), cm/s	19.0 (17.0...23.0)	20.0 (18.0...20.0)	0 (-2.0...2.0)	0.885
	Ved (S), cm/s	21.5 (18.0...26.5)	24.0 (20.0...31.0)	2.5 (0...5.5)	0.036
	RI (D), a.u.	0.70 (0.67...0.74)	0.72 (0.68...0.77)	0.035 (0.010...0.060)	0.010
	RI (S), a.u.	0.71 (0.68...0.76)	0.73 (0.69...0.76)	0.020 (-0.005...0.040)	0.159
ICA	Vps (D), cm/s	62.0 (53.0...70.0)	76.0 (63.0...97.0)	17.3 (10.5...31.5)	<0.001
	Vps (S), cm/s	63.0 (55.0...70.0)	74.0 (63.0...84.0)	10.0 (6.0...14.5)	<0.001
	Ved (D), cm/s	24.5 (21.0...33.0)	22.0 (20.0...22.0)	-5.0 (8.5...-2.5)	<0.001
	Ved (S), cm/s	27.0 (19.0...31.5)	21.0 (20.0...22.0)	-4.0 (-6.5...-2.5)	<0.001
VA (V1-V3 segment)	Vps (D), cm/s	38.0 (34.5...44.5)	38.0 (32.5...46.0)	1.8 (-4.0...8.0)	0.460
	Vps (S), cm/s	39.0 (34.5...45.5)	47.0 (35.5...51.5)	6.5 (1.5...11.5)	0.009
	Ved (D), cm/s	12.0 (10.0...14.0)	14.0 (11.0...18.0)	2.5 (1.0...4.0)	0.002
	Ved (S), cm/s	14.5 (12.0...17.0)	13.0 (11.0...21.5)	2.0 (-0.5...4.5)	0.131
	RI (D), a.u.	0.65 (0.63...0.68)	0.64 (0.62...0.67)	-0.010 (-0.030...0.015)	0.534
	RI (S), a.u.	0.62 (0.57...0.67)	0.62 (0.60...0.63)	0.010 (-0.015...0.040)	0.374
MCA	Vps (D), cm/s	90.0 (84.0...112.0)	99.0 (82.0...121.0)	2.0 (-10.0...11.5)	0.740
	Vps (S), cm/s	93.0 (86.0...115.0)	88.0 (78.5...97.0)	-10.5 (-21.5...-1.5)	0.023
	Ved (D), cm/s	41.0 (31.0...57.0)	33.0 (32.0...47.0)	-7.0 (-14.0...-1.0)	0.020
	Ved (S), cm/s	46.0 (35.5...61.0)	31.0 (30.0...42.0)	-13.0 (-20.5...-7.0)	<0.001
	RI (D), a.u.	0.56 (0.52...0.63)	0.60 (0.55...0.61)	0.020 (-0.005...0.050)	0.097
	RI (S), a.u.	0.56 (0.56...0.60)	0.60 (0.55...0.62)	0.030 (0.005...0.055)	0.010
	PI (D), a.u.	2.2 (2.0...2.8)	2.3 (2.3...2.6)	0.20 (0...0.50)	0.062
	PI (S), a.u.	2.2 (2.0...2.5)	2.2 (2.2...2.6)	0.25 (0.05...0.50)	0.005
VA (V4 segment)	Vps (D), cm/s	58.0 (44.0...75.0)	42.0 (37.5...62.0)	-11.5 (-19.5...-4.0)	0.004
	Vps (S), cm/s	59.0 (43.0...72.0)	53.0 (39.0...67.0)	-5.5 (-13.0...2.0)	0.132
	Ved (D), cm/s	25.5 (18.0...36.0)	20.5 (16.0...22.0)	-7.5 (-10.5...-3.5)	<0.001
	Ved (S), cm/s	23.0 (18.0...33.0)	23.0 (18.5...26.0)	-3.5 (-7.0...0)	0.051
	RI (D), a.u.	0.53 (0.52...0.60)	0.57 (0.53...0.60)	0.025 (0...0.045)	0.035
	RI (S), a.u.	0.55 (0.51...0.58)	0.55 (0.53...0.62)	0.015 (-0.010...0.040)	0.173
BA	Vps, cm/s	66.5 (51.0...79.0)	60.0 (43.5...63.0)	-9.5 (-18.5...-1.5)	0.023
	Ved, cm/s	30.0 (23.0...37.5)	26.0 (17.5...27.0)	-4.0 (-8.5...-0.5)	0.018
	RI, a.u.	0.57 (0.54...0.60)	0.56 (0.52...0.61)	0 (-0.025...0.025)	0.919

Note: CCA – common carotid artery; ICA – internal carotid artery; MCA – middle cerebral artery; VA – vertebral artery; BA – basilar artery; D – right; S – left; a.u. – arbitrary unit

Source: compiled by the authors of this study

resistance, and decreased blood flow, including cerebral perfusion [9, 10, 21–25].

In addition, an important pathophysiological mechanism of cerebral blood flow impairment is the development of endothelial dysfunction. Current research has shown that hypothyroidism is accompanied by reduced bioavailability of nitric oxide (II), increased levels of pro-inflammatory cytokines, and oxidative stress, leading to impaired vasodilation and vascular wall remodeling [26]. In turn, endothelial dysfunction

is a key component in the pathogenesis of atherosclerosis, including cerebrovascular disease [15].

Our findings regarding the predominant involvement of the carotid circulation also have a pathophysiological basis. It has been established that hypothyroidism is associated with increased arterial wall stiffness and thickening of the carotid intima-media complex, which is an early marker of atherosclerosis [27, 28]. Additionally, even minor thyroid function deviations within reference ranges are associated

with an increased risk of stroke [22]. This explains our findings of reduced vascular elasticity, specifically in the carotid circulation and impaired cerebral perfusion.

The interaction between HTN, hypothyroidism, and cerebrovascular pathology deserves special attention. It is well known that HTN is a leading factor in the development of DE, and its coexistence with hypothyroidism significantly amplifies adverse vascular effects. Such comorbidity contributes to faster progression of small vessel disease, development of chronic cerebral ischaemia, and cognitive impairment [29, 30].

The obtained results are also consistent with systematic reviews demonstrating an increased risk of cardiovascular and cerebrovascular complications in patients with hypothyroidism [24]. This allows hypothyroidism to be considered an independent risk factor for the progression of chronic cerebral ischemia.

Certain limitations of the present study include a relatively small sample size, which limits the generalizability of the findings, as well as incomplete adjustment for comorbid factors that may have influenced cerebral hemodynamics. Moreover, given the observational design of the study, the results should be interpreted with caution when assessing potential causal relationships between concomitant hypothyroidism, severity of DE clinical manifestations, and cerebral blood flow disturbances.

Thus, despite these limitations, the results of the present study are consistent with current evidence and expand the understanding of clinical and hemodynamic features of DE in patients with concomitant hypothyroidism. The findings indicate the importance of considering thyroid dysfunction as a factor associated with more pronounced cerebral circulation impairment and progression of neurological symptoms in chronic cerebral ischemia. The practical significance of this work lies in increased attention to early detection and correction of hypothyroidism in patients with DE.

CONCLUSIONS

Based on the results of long-term follow-up, an increased frequency of vestibular syndrome was observed in patients with DE and concomitant hypothyroidism, as well as a deterioration of cerebral blood flow, predominantly in the carotid circulation, associated with reduced vascular elasticity. In addition, decreased cerebral blood flow velocity parameters were identified in the vertebrobasilar system, which may indicate impaired perfusion of the posterior cerebral regions. The obtained results justify the need for timely diagnosis and correction of thyroid dysfunction in patients with chronic cerebral ischaemia to optimise therapeutic, preventive, and rehabilitation strategies.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Selective metabolic and hepatic biochemical alterations in breast cancer patients receiving different treatment protocols: A comparative cross-sectional study

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ABSTRACT

Aim: To study biochemical changes in women with breast cancer according to treatment protocols, with emphasis on liver and metabolic markers.

Materials and Methods: A descriptive comparative cross-sectional study of 141 women including chemotherapy only (n=50), newly diagnosed n=46 and chemotherapy + metformin n=45 was conducted. The glucose, albumin, ALP, AST, ALT, creatinine and total bilirubin were determined in venous samples of blood by standard enzymatic methods. Data were presented as mean±SD and analyzed with one-way ANOVA.

Results: Glucose and ALP levels were significantly different. Compared with chemotherapy-only (86.38±15.96 mg/dL) and newly diagnosed groups, increased glucose (197.15±58.15 mg/dL) in the chemotherapy + metformin group p<0.001. Higher ALP was also noted in the metformin group (127.35±58.88 U/L) compared with chemotherapy alone (105.02±30.96 U/L) and newly diagnosed patients (108.81±40.84 U/L), p=0.039. Albumin, AST, ALT, creatinine and total bilirubin were not statistically different. AST was moderately correlated with ALT (r=0.524) and strongly correlated with total bilirubin r=0.752, p<0.001.

Conclusions: The consumption of breast cancer therapy caused metabolic changes especially on glucose and ALP. Normal biochemical markers are still useful in surveillance for metabolic derangements due to treatment.

KEY WORDS: breast cancer, biochemical markers, Liver enzymes, metabolic profile, metformin therapy

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INTRODUCTION

BC (Breast Cancer) is the most prevalent malignancy diagnosed worldwide in women and poses a significant public health concern because the number of women diagnosed with this type of cancer as well as the number of women that die from breast cancer is large. The process of breast cancer development is not completely clarified at this time but it is characterized by the unregulated growth of breast epithelial cells; this type of cancer develops as the result of a multi-stage process in which cells develop several molecular and cellular abnormalities that allow for neoplasia, invasion and metastasis. There have been improvements made by advancing early diagnosis and developing new approaches to treating BC that have led to increasing survival, however, the systemic effects of the disease and the treatments for the disease continue to present a clinical challenge [1-2]. The multimodal treatment plan for breast cancer most often involves a combination of surgery, chemotherapy and/or targeted biological therapies. Although these strategies have significantly improved patient outcomes, they can also cause systemic physiological adaptations that disrupt metabolic and biochemical homeostasis [3]. In particular, cytotoxic chemotherapy and have the potential to change

liver function, renal metabolism and systemic biochemical markers as a direct result of their actions on rapidly dividing cell populations and their general metabolic demands on the individual [4]. Biochemical parameters such as liver and kidney function tests, and metabolic markers are essential for the baseline assessment and monitoring of cancer patients receiving treatment. Evaluation of liver enzymes including aspartate aminotransferase (AST) and alanine-aminotransferase (ALT), and metabolic markers like glucose, albumin, alkaline-phosphatase (ALP), creatinine and bilirubin is critical to assess organ function and global metabolic regulation in therapy. The modification in these markers can reflect treatment-related toxicity, metabolic adaptation or systemic stress related to the malignancy [5-6]. Recently, growing interest has focused on the potential use of metformin as an adjunctive drug in cancer treatment. Metformin is mainly used to treat type 2 diabetes mellitus; it activates AMP-activated protein kinase (AMPK) and inhibits mTOR signaling pathway in the cells [7], thus affecting cellular metabolism. Such actions have been linked with decrease cellular growth, increased metabolic control, and potential anti-tumor activity. Consequently, metformin is investigated as an adjuvant therapeutic

drug for a broad range of malignancies, including breast cancer [8-9]. And one of the strongest knowledge is that metformin manipulates systemic metabolic control, mainly influences glucose metabolism, liver enzymatic activities and cellular energetics homeostasis. These metabolic interactions can modify the biochemical landscape of cancer patients in treatment, which is dependent not only upon the response to treatment but also reflects systemic physiologic adaptation. Monitoring standard biochemical markers for patients receiving metformin combined with traditional cancer treatments may thus provide important information concerning the metabolic and physiological modifications induced by therapy [9-10]. Although interest in the oncologic applications of metformin has grown, few studies have specifically evaluated its impact on common biochemical parameters in breast cancer patients receiving combination treatment regimens. An understanding of these biochemical alterations may allow for improved clinical assessment, assist in the diagnosis of metabolic derangement, and provide insight into the physiological impact and efficacy of various treatment protocols [11-12]. The purpose of the current study was to evaluate the overall biochemical and metabolic characteristics (biochemical variables including liver or metabolic biomarkers) of women diagnosed with breast cancer that receive various therapeutic regimens predominantly involving available serum-based (biochemical) profile tests. The study was intended to use data derived from routine laboratory testing performed on patients undergoing treatment to identify possible biochemical profiles (biochemical biomarkers) associated with treatment that included metformin-based therapies in addition to identifying mechanisms responsible for producing systemic metabolic changes during breast cancer treatment.

MATERIALS AND METHODS

STUDY DESIGN AND PARTICIPANT SELECTION

Between July & December 2024, researchers accrued 141 histologically proven breast cancer patients through the oncology center at Mansoura University, Egypt. There were three study groups based on treatment regimen; Chemotherapy (n=50), newly diagnosed with no prior treatment (n=46), and Chemotherapy + Metformin (n=45). Study inclusion criteria included patients with breast cancer (any stage), aged greater than or equal to ($\geq$) 18 years and on one of the above listed chemotherapy plus metformin protocols at time of recruitment. Even though people were included in a research project at the same level of operation, there were potential differences as a result of people's backgrounds and histories (e.g., how long they had been treated). Therefore, we can prepare for this potential increase in variability by recognizing that there will be differences among the groups that are created.

Participants who were not eligible for study inclusion included those with any of the following criteria; Pre-existing liver disease (e.g. hepatitis, cirrhosis); Pre-existing kidney disease; any other malignancy; or any of the medical records missing. Inclusion into this study included membership into

the Metformin subgroup, that included diabetic patients only, was by report and available for subgroup reporting.

ETHICAL APPROVAL

The Institutional Review Board (IRB) of Mansoura University Faculty of Medicine approved the study (Approval No: MDP. 24. 05. 152) and in compliance with ethical standards issued by the Egyptian Ministry of Health. All patients had provided written informed consent before enrollment.

CHEMOTHERAPY TREATMENT REGIMEN

Subjects received conventional chemotherapy regimens calculated according to standard breast cancer protocols. The treatment was mainly anthracycline-based (doxorubicin, cyclophosphamide) and taxane-based (paclitaxel, docetaxel) regimens given either in combination or sequentially per institutional guidelines.

GROUPING

Group 1 included patients receiving chemotherapy as standard care n=50. Group 2 was composed of newly diagnosed breast cancer patients with no history of treatments n=46. Patients from Group 3 were treated with metformin plus standard chemotherapy n=45.

BLOOD SAMPLING AND BIOCHEMICAL ANALYSIS

We obtained peripheral venous blood specimens (approximately 5 mL) from all participants through usual aseptic venipuncture approach into plain tubes with no anticoagulant. Blood was allowed to clot at room temperature for 30 min and serum was separated by centrifugation (3000 rpm for 10 min). Serum levels for glucose, albumin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine and total bilirubin were measured by commercial diagnostic kits (Randox Laboratories, Crumlin, UK) on a semi-automated analyzer according to the manufacturers' protocols. The following methods were applied: Glucose: Glucose GOD-PAP (Enzymatic Colorimetric method). Albumin: Albumin BCR (Bromocresol Green Colorimetric method). AST: AST (GOT) (Kinetics UV method). ALT: ALT (GPT) (Kinetic UV method). Alkaline Phosphatase (ALP) AMP method, Colorimetric Kinetic. Creatinine: Creatinine (Jaffé method, Colorimetric Kinetic); Total Bilirubin: Bilirubin, Total (Jendrassik-Grof method, Colorimetric). All assays were conducted via standardized enzymatic and colorimetric methods. Routine quality control was carried out with commercial control sera, and intra-assay coefficients of variation were kept below 5%.

STATISTICAL ANALYSIS

SPSS version 26 was used for statistical analysis. The Shapiro-Wilk test showed whether the data met normality. Data that fit the normal distribution were summarized with descriptive statistics, mean ($\pm$ SD). The chemical data, for all three treatment groups, were analyzed with one-way analysis of variance (ANOVA). Where ANOVA showed significant differences, post hoc comparisons were made using Tukey's Honestly Significant Difference (HSD) test to find out which treatment groups differed. The Pearson correlation coefficient was calculated as a measure of

Table 1. Demographic and clinical characteristics of breast cancer patients across groups

Parameter	Chemotherapy (n=50)	Newly diagnosed (n=46)	Chemotherapy + metformin (n=45)	p-value
Age (years)	47.58±10.49	49.96±11.84	57.93±10.32	0.06
Family history of breast cancer				0.247
Yes	20 (40.0%)	21 (45.7%)	13 (28.9%)	
No	30 (60.0%)	25 (54.3%)	32 (71.1%)	
Menopausal status				0.001
Premenopausal	29 (58.0%)	24 (52.2%)	10 (22.2%)	
Postmenopausal	21 (42.0%)	22 (47.8%)	35 (77.8%)	

Note: Continuous variables are presented as Mean ± SD and categorical variables as number (percentage)

One-way analysis of variance (ANOVA) was used to compare continuous variables, and the Chi-square test was used for categorical variables

Statistical significance was defined as a p-value ≤ 0.05

Source: Compiled by the authors of this study

association between the continuous chemical data (e.g. AST with ALT, AST with total bilirubin). A p-value of <0.05 was used for all tests as a statistically significant result.

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE STUDY GROUPS

The demographic and clinical characteristics at baseline are shown in Table 1 for all study participants who were recruited. The age of patients receiving chemotherapy/metformin was greater than the age of patients receiving chemotherapy alone and the age of patients who were newly diagnosed, although these age-related differences were not statistically significant (p=0.06). The frequency distribution of breast cancer family history was similar across groups (p=0.247). However, menopausal status was the only demographic that showed that postmenopausal women were more prevalent in the chemotherapy/metformin group (77.8%) versus the chemotherapy (42.0%) and newly diagnosed (47.8%) groups (p=0.001). This data is consistent with the greater average age of patients in the metformin chemotherapy cohort.

COMPARATIVE ANALYSIS OF BIOCHEMICAL PARAMETERS ACROSS TREATMENT GROUPS HEPATIC FUNCTION PROFILE

Comparison of hepatic function markers among the three groups are shown in Table 2 and Figs 1-2. Although serum levels of AST and ALT individually showed no significant differences between groups, the AST/ALT ratio (De Ritis ratio) was significantly higher in the chemotherapy with metformin group compared with the chemotherapy group and newly diagnosed group (1.61±1.02 vs. 1.25±0.49 vs. 1.18±0.44; p=0.009). The levels of alkaline phosphatase (ALP) differed significantly between groups (p=0.039), with the highest mean level in the chemo- with metformin-treated group. The total bilirubin concentration was comparable among all groups (p=0.468), indicating that liver excretory function remained stable despite the difference in enzyme profile

RENAL AND METABOLIC MARKERS

Renal function and metabolic biomarkers are summarized in Table 3 and Figure 3. Serum glucose levels were significantly higher (p<0.001) in the chemo- with metformin group than those of both the new diagnosis (86.38±15.96 mg/dL) and

Table 2. Comparison of hepatic function markers among groups

Parameter	Chemotherapy (n=50)	Newly diagnosed (n=46)	Chemotherapy + metformin (n=45)	p-value
AST (U/L)	29.72 ± 12.49	25.65 ± 13.40	34.52 ± 31.40	0.128
ALT (U/L)	26.80 ± 14.92	23.93 ± 15.63	23.49 ± 14.29	0.500
ALP	105.02 ± 30.96	108.81 ± 40.84	127.35 ± 58.88	0.039
AST/ALT ratio	1.25 ± 0.49	1.18 ± 0.44	1.61 ± 1.02	0.009
Total Bilirubin (mg/dL)	0.58 ± 0.24	0.56 ± 0.21	0.75 ± 1.40	0.468

Note: Values are expressed as Mean ± SD

Statistical comparisons were performed using one-way ANOVA

Source: Compiled by the authors of this study

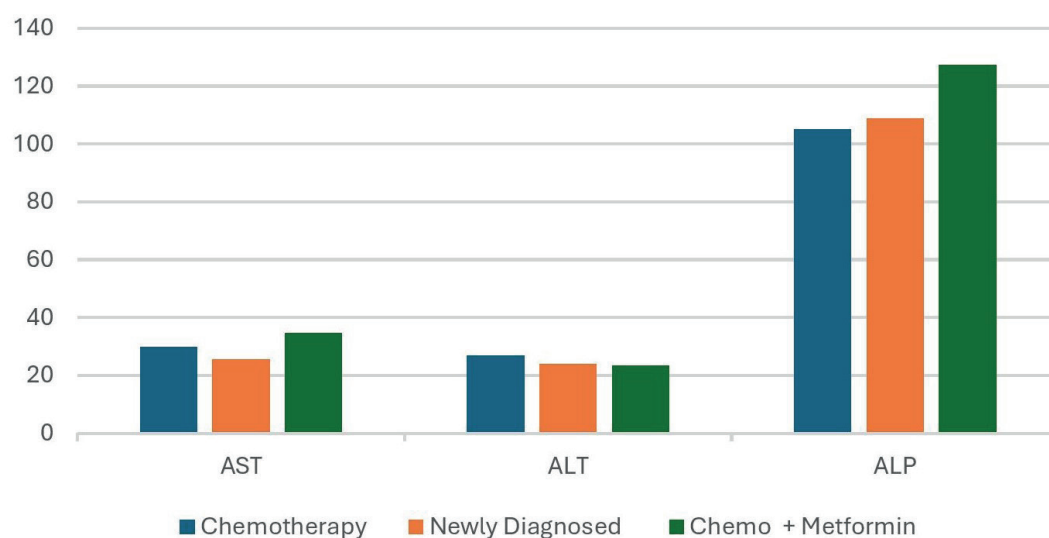


Fig. 1. Comparative mean levels of AST, ALT and ALP among the three groups: chemotherapy, newly diagnosed, and chemo-combined with metformin

Source: Own materials

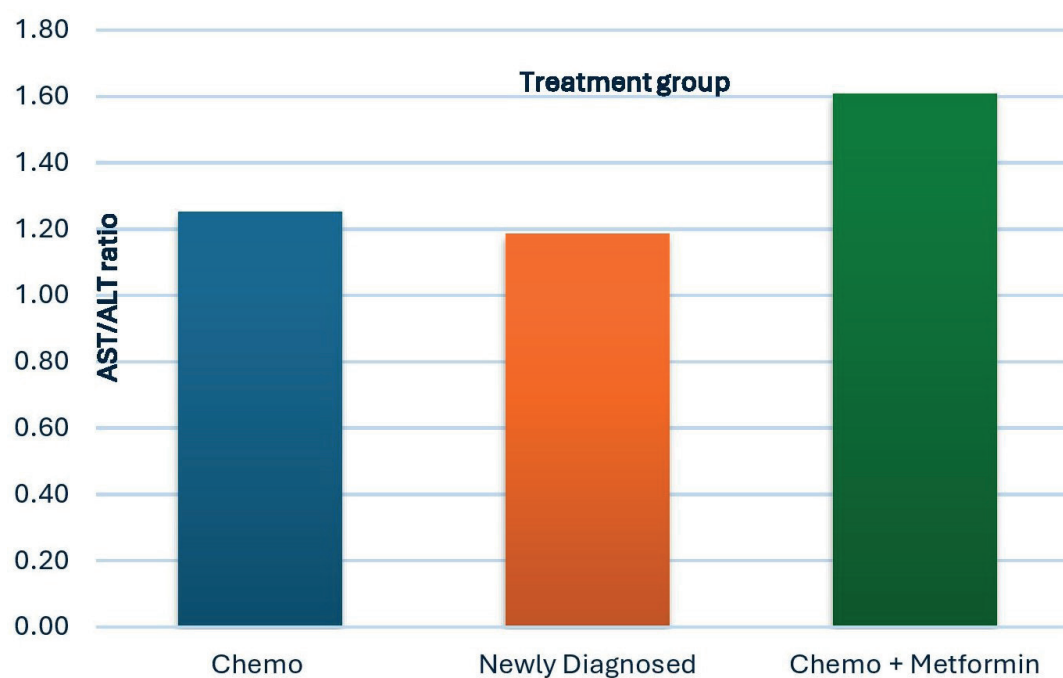


Fig. 2. Distribution of AST/ALT ratio within treatment groups studied

Source: Own materials

Table 3: Comparison of renal and metabolic biomarkers between treatment groups

Parameter	Chemotherapy n=50	Newly diagnosed n=46	Chemotherapy + metformin n=45	p-value
Glucose (mg/dL)	86.38±15.96	93.27±19.22	197.15±58.15	<0.001
Creatinine (mg/dL)	0.88±0.17	0.87±0.17	1.05±0.64	0.057
Albumin (g/dL)	4.22±0.44	4.13±0.36	4.12±0.75	0.569

Notes: Values are presented as Mean ± SD

Statistical comparison was performed using one-way ANOVA

A p-value ≤ 0.05 was considered statistically significant

Source: Compiled by the authors of this study

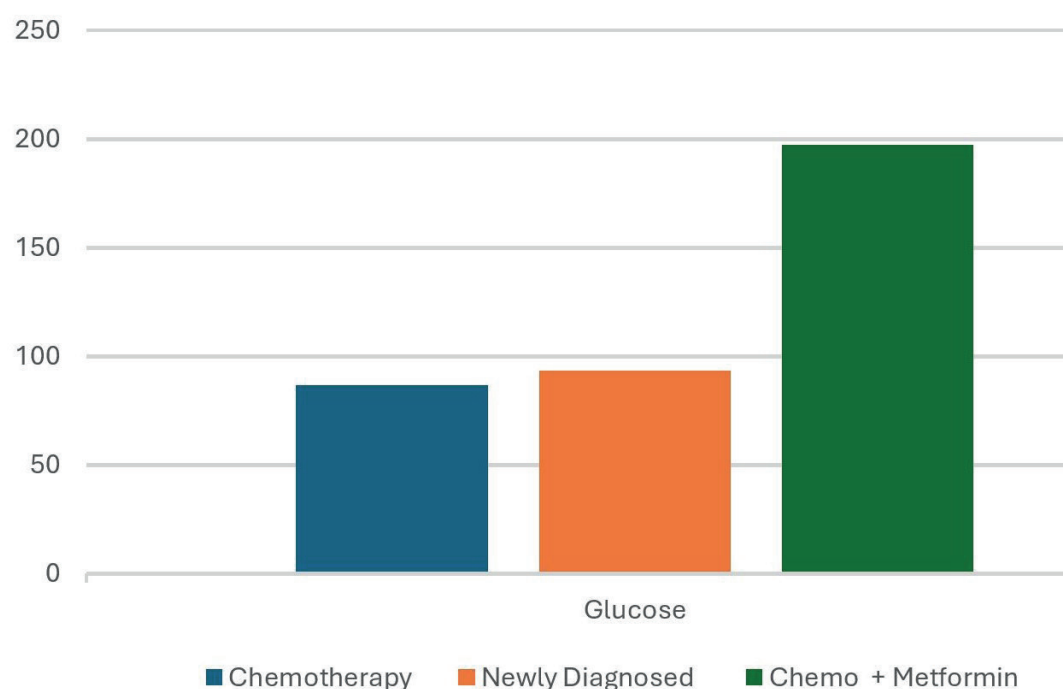


Fig. 3. Comparative mean levels of glucose among the three groups: chemotherapy, newly diagnosed, and chemo-combined with metformin
Source: Own materials

the chemo- groups (197.15 ± 58.15 mg/dL vs. 93.27 ± 19.22 mg/dL). This result is not surprising considering that metformin is used as an antidiabetic agent for glycemic control, and the presence of this drug in this population indicates these patients likely have underlying T2DM or impaired glucose tolerance.

CORRELATION ANALYSIS OF KEY BIOCHEMICAL MARKERS

The relationships between multiple biochemical parameters were assessed in the entire study population using Pearson correlation analysis as shown in Table 4. There was a moderate to strong positive correlation between aspartate transaminase (AST) and total bilirubin ($r=0.752$, $p<0.001$), a moderate positive relationship between AST and alanine transaminase (ALT) ($r=0.524$, $p<0.001$), and a low positive association between AST and alkaline phosphatase (ALP) ($r=0.381$, $p<0.001$). The correlation between serum creatinine and age of patients was also found to be significantly positive ($r=0.192$, $p=0.022$).

Table 4. Correlation analysis of selected hepatic and renal parameters

Variable Pair	Pearson Correlation (r)	p-value
AST vs. ALT	0.524	<0.001
AST vs. bilirubin	0.752	<0.001
AST vs. ALP	0.381	<0.001
Creatinine vs. age	0.192	0.022

Source: Compiled by the authors of this study

DISCUSSION

The purpose of this study was to assess changes in blood biochemistry in patients receiving various treatments for breast cancer, focusing on 'hepatic and metabolic markers' or biomarkers having 'dynamic variability' (ie, indicating relatively high) during treatment. We believe that our research suggests that cancer treatment induces selective biochemical changes and not general organ dysfunction. Specifically, we found significant differences between both glucose metabolism and selective hepatic enzyme activity; however, renal function along with 'hepatic synthetic capacity markers' generally remained unchanged [13-14]. The most remarkable finding was the significantly elevated serum levels of glucose in chemo- with metformin (197.15 ± 58.15 mg/dL) compared to patients receiving chemotherapy only (86.38 ± 15.96 mg/dL) and newly diagnosed patients (93.27 ± 19.22 mg/dL) ($p<0.001$). Metformin is widely used to treat patients with multiple conditional manifestations of known pre-existing metabolic disorder as seen in type-2 diabetes mellitus or insulin resistance. Therefore, the hyperglycemia we observed may represent a reflection of baseline metabolic status rather than a direct pharmacodynamic effect of metformin per se [15-16]. In addition, metabolic reprogramming related to malignancy and stress due to treatment may cause abnormal glucose homeostasis among cancer patients [17-18]. This explanation is in line with the demographic data indicating that the metformin-treated population had a greater age and was overwhelmingly postmenopausal, conditions typically linked with an increased risk of metabolic dysfunction. In addition, metabolic reprogramming associated with cancer and the physiological stress of treatment may further worsen glucose homeostasis in these patients [19-20]. Hepatic

biomarker assessment showed a trend that is consistent with treatment-related metabolic effects. Although there was no significant difference in AST and ALT levels between the groups, when expressed as the De Ritis ratio (AST/ALT) this was significantly increased in the metformin-augmented therapy group ($p=0.009$). The AST/ALT ratio has recently been appreciated as a sensitive index of systemic metabolic stress and liver surrogacy in response to different pathologic conditions including malignancy, systemic inflammation and metabolic disease [21–23]. A higher ratio with low levels of bilirubin and albumin indicates a change in hepatic metabolic programming instead of cellular damage [24]. This observation is consistent with accumulating evidence that the metabolic landscape of the liver can be altered by cancer per se and concomitant therapies [25]. ALP was significantly different ($p=0.039$) among the groups with the highest mean value in metformin treatment. ALP is an indicator of hepatobiliary function and bone metabolism. In cancer patients, high ALP may be due to increased skeletal turnover (especially in bone metastasis), liver metabolic stress or a physiological response to therapy [21]. Lack of concomitant elevation in total bilirubin ($p=0.468$) or ALT indicates that the observed ALP increase is more likely metabolic or bone-related rather than cholestatic liver injury [19–21]. Analysis of renal and metabolic parameters also supports the idea of selective biochemical change amongst the groups studied. Serum creatinine levels were similar across groups ($p=0.057$), reflecting overall preservation of renal function within each treatment cohort [26]. Likewise, albumin levels remained constant ($p=0.569$), suggesting that hepatic synthetic capacity and nutritional status were unaffected by the therapeutic regimens investigated [25–26]. These observations strengthen the interpretation that the biochemistry changes were limited to particular metabolic processes, and not systemic organ toxicity [27]. Significant correlations between biochemical parameters were also assessed via correlation analysis, which provided insight into the interrelationships of the various elements. A moderate positive correlation between AST and ALT was found ($r=0.524$, $p<0.001$), a finding that is consistent with their similar hepatic origin [28]. Total bilirubin also correlated strongly with AST ($r=0.752$, $p<0.001$), consistent with a coupled process between hepatocellular enzyme activity and bilirubin metabolism that may be affected by treatment for cancer [29–30]. The study also further supports the notion that hepatic biochemical markers are interrelated and operates through metabolic pathways [31]. Findings indicate that there is no obvious association between glucose levels and AST level ($r=0.103$, $p=0.224$), which demonstrates there is a strong dissociation between both liver functioning

and overall glucose metabolism in these subjects, which suggests there are disconnects between how well the liver is functioning and how well the rest of the body is using glucose. A significant positive correlation was found between age and creatinine ($r=0.192$; $p=0.022$). This reinforces previous physiology findings stated in previous studies showing the reduction in glomerular filtration from aging [32–33].

There are many limitations to note in this study. The most important limitation is that patients from all stages of disease were entered into the study without stratification by stage of disease. The literature clearly demonstrates that biochemical parameters related to both organ-specific and metabolism differ greatly based on the stage of cancer, how long the patient has had the disease, and how long the patient has been treated. This variation due to differences in the stages may have altered the starting points of the biochemical measurements and likely impacted the variability within each group. Subsequent studies will need to determine if there is any difference in biochemical levels based solely upon the length of time that the patient has been on treatment, as opposed to as a function of disease progression, thus developing a clearer interpretation of the biochemical relationship with clinical response to therapy.

CONCLUSIONS

This research shows that various treatment plans for breast cancer can lead to notable differences in the baseline biochemical makeup within the underlying tissues where glucose, metabolic or metabolic-related markers, liver function measures are also being measured. The increased level of glucose (very elevated) within the metformin-treatment group was likely due to concurrent metabolic issues rather than from the effects of metformin. The elevated AST:ALT ratio and elevated ALP levels while retaining normal bilirubin, albumin, and creatinine leading to the conclusion that the adjustments seen in metabolic function and liver function tests were likely adaptive responses rather than indications of generalized organ injury. These biochemical changes, which are selective in their specificity to glucose metabolism, their marker ALP, and their AST/ALT ratio, are indicative of the specific markers being specific protocol indicators of the metabolic adaptation of animals rather than generalized organ toxicity; thus, when interpreting clinically, close attention must be paid to the disease stage, duration of the treatment, and underlying comorbid conditions (e.g., pre-existing insulin resistance). Future longitudinal prospective studies should attempt to correlate these biochemical changes with treatment outcomes and disease progression in order to more clearly delineate their role in protocol-specific metabolic monitoring.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Significance of Epstein-Barr Virus and Human Papillomavirus type 16 in the development of pleomorphic adenomas of the salivary glands

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ABSTRACT

Aim: The aim of the study was to determine the role of Epstein-Barr virus and human papillomavirus (HPV) type 16 in the development of pleomorphic adenoma of the salivary gland by identifying the viruses in tumor tissue, oral mucosal epithelium, oral fluid, and blood.

Materials and Methods: The study included 30 patients with a morphologically confirmed diagnosis of pleomorphic adenoma of the parotid salivary glands, who were assigned to group 1. The control group (group 2) consisted of 10 patients who had no tumor or non-tumor salivary gland pathology either during life or at autopsy examination. To identify Epstein-Barr virus and HPV type 16, an immunohistochemical examination of tumor tissue fragments in group 1 and salivary gland tissue fragments in group 2 was performed, as well as polymerase chain reaction (PCR) analysis of blood, buccal scraping, and oral fluid. Statistical analysis of the obtained data was performed using the PAST software (version 4.15, Natural History Museum, University of Oslo, Norway). Mean values of indicators were compared using the Mann-Whitney U test.

Results: The immunohistochemical reaction with mouse monoclonal antibody (MMA) to HPV type 16 was positive in a significantly greater ($p < 0.05$) number of cases in group 1 (26 cases, 86.7%) compared with group 2 (3 cases, 42.9%). The number of cases with a positive immunohistochemical reaction with MMA to anti-Epstein-Barr virus was significantly higher ($p < 0.05$) in group 1 (8 cases, 26.7%) compared with group 2 (1 case, 14.3%). PCR study of buccal scraping, blood and oral fluid samples from patients in group 1 revealed a lower number of cases with a positive reaction compared with the immunohistochemical examination of tumor tissue. In group 2, this analysis did not detect any positive cases at all. In group 1 PCR enabled the detection of Epstein-Barr virus DNA in buccal scraping in 2 cases, accounting for 6.7%; in oral fluid samples in 4 patients (13.3%); in blood samples in 4 patients (13.3%). The study of buccal scraping, oral fluid and blood by PCR in patients from group 1 enabled the detection of HPV type 16 DNA, respectively, in 1 case (3.3%), 2 cases (6.7%), 2 cases (6.7%).

Conclusions: HPV type 16 appears to play a greater role in the genesis of pleomorphic adenomas of the parotid salivary glands compared with Epstein-Barr virus. Immunohistochemical examination of tumor tissue is an effective method for demonstrating the role of HPV type 16 and Epstein-Barr virus in the development of pleomorphic adenomas of the salivary glands. PCR analysis of oral fluid, blood, and buccal scraping is not a sufficiently sensitive or reliable method for identifying the investigated viruses in patients with pleomorphic adenomas.

KEYWORDS: Epstein-Barr virus, human papillomavirus type 16, pleomorphic adenoma, salivary gland, immunohistochemistry, polymerase chain reaction

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INTRODUCTION

Salivary gland tumors are uncommon lesions that account for approximately 3% to 6% of all head and neck tumors. The annual incidence of salivary gland tumors reaches 4-13.5 cases per 100 000 people in the world [1, 2]. They are characterized by clinical and biological complexity, histopathologic diversity [2, 3]. In the fifth edition of the World Health Organization classification of head and neck tumors, salivary gland tumors are represented by more than 20 malignant variants and more than 15 benign variants [4]. These tumors can develop in major or minor salivary glands; however, they are more frequently diagnosed in the parotid gland [4]. The most common malignant tumors

of salivary glands are mucoepidermoid carcinoma and adenoid cystic carcinoma. Pleomorphic adenomas are the most common benign tumors, accounting for 85% of all salivary gland neoplasms and 60% of benign tumors [5, 6].

Pleomorphic adenomas are found mainly in the superficial lobe of parotid gland (90% cases). The deeper lobe of parotid gland is involved in pathological process in less than 10% of cases [7]. This tumor mainly develops in women (female-to-male ratio of 1.6 to 1) at a mature age (30-50 years), characterizes by slow growth, scant clinical symptoms and can relapse with recurrence rates of up to 6.8% [7, 8]. The transformation of pleomorphic adenoma into a malignant tumor, according to various researchers, occurs in 3.3-6.2%

of cases [9]. Morphologically pleomorphic adenoma is characterized by structural diversity and heterogeneity, which is due to the different ratio of the epithelial (parenchymal) and mesenchymal (stromal) components, forming this tumor; the complexity and multicomponent structure of the parenchyma itself and the stroma of the tumor [8].

Understanding the etiopathogenesis of pleomorphic adenomas is important for improving existing treatment approaches, developing new therapeutic methods, and predicting recurrence and malignant transformation of these tumors. Studies investigating the etiopathogenesis of pleomorphic adenomas remain rather limited, which is due to the relatively low incidence of these tumors within the overall structure of oncological diseases. According to various researchers, the development of pleomorphic adenomas may be associated with harmful habits (alcohol consumption and tobacco smoking), unbalanced nutrition, exposure to ionizing radiation and chemical agents, hazardous working conditions, genetic factors, autoimmune diseases, and immunodeficiency states [1, 10].

Recently, an increasing number of studies have appeared in the literature demonstrating the role of viruses, particularly the HPV type 16 and Epstein-Barr virus, in the genesis of tumor development [11]. Thus, the role of HPV type 16 in the development of cervical, oropharyngeal, and anal cancers, among others, has been proven. Epstein-Barr virus is associated with the development of lymphoproliferative disorders and nasopharyngeal carcinoma [12]. The role of Epstein-Barr virus and HPV type 16 in the development of pleomorphic adenomas of the salivary glands remains controversial and unresolved. This highlights the relevance of conducting a comprehensive study aimed at identifying HPV type 16 and Epstein-Barr virus in patients with pleomorphic adenomas, which may help to confirm the virus-associated genesis of this benign salivary gland tumor.

AIM

The aim of the study was to determine the role of Epstein-Barr virus and HPV type 16 in the development of pleomorphic adenomas of the salivary glands by identifying the viruses in tumor tissue, oral mucosal epithelium, oral fluid, and blood.

MATERIALS AND METHODS

The study included 30 patients with a morphologically confirmed diagnosis of pleomorphic adenoma of the parotid salivary gland (mesenchymal variant in 15 cases, mixed variant in 10 cases, and epithelial variant in 5 cases), who were assigned to group 1. The control group (group 2) consisted of 10 patients who had no tumor or non-tumor salivary gland pathology either during life or at autopsy examination. The causes of death in group 2 patients were acute heart failure and dislocation of the brain stem.

To identify Epstein-Barr virus and HPV type 16, an immunohistochemical examination of tumor tissue fragments in group 1 and salivary gland tissue fragments in group 2 was performed, as well as PCR analysis of blood, buccal scraping, and oral fluid.

Immunohistochemical examination was performed on adhesive Super Frost Plus slides (Menzel, Germany) using MMA to HPV type 16 (clone CAMVIR-1, Diagnostic BioSystems, USA) and anti-Epstein-Barr virus (LMP, clone CS.1-4, Dako, Denmark). The Master Polymer Plus Detection system (Peroxidase, DAB chromogen) (Master Diagnostica, Spain) was used, while citrate buffer (pH 6.0) and EDTA buffer (pH 8.0) were applied for high-temperature antigen epitope retrieval. The histological specimens were examined using a ZEISS Primostar 3 microscope (Carl Zeiss, Germany) equipped with an integrated color digital camera.

In group 1, blood and oral fluid samples, as well as buccal scraping, were collected from patients after surgical treatment for pleomorphic adenoma of the salivary glands, whereas in group 2 these samples were obtained during hospitalization. Peripheral blood samples were collected into sterile closed-system tubes with a volume of 2.5 mL containing ethylenediaminetetraacetic acid. Oral fluid samples were collected into a special sterile container. Buccal scraping was obtained using a sterile disposable probe from the inner surface of both cheeks and placed into a sterile tube containing a special transport medium. DNA extraction from the obtained biological samples was performed using the commercial Sansure Biotech kit (S50016E, China) based on magnetic particles, according to the manufacturer's instructions. A commercial Sansure Biotech test system (S3015E) was used for the detection of Epstein-Barr virus DNA, while Sansure Biotech test system (S3019E) was used for the detection of HPV type 16 DNA. Real-time PCR was carried out using the Applied Biosystems™ 7500 Real-Time PCR System (Life Technologies Corporation, USA).

Statistical analysis of the obtained data was performed using the PAST software (version 4.15, Natural History Museum, University of Oslo, Norway). Mean values of indicators were compared using the Mann-Whitney U test. Differences were considered statistically significant at $p < 0.05$.

RESULTS

The immunohistochemical reaction with MMA to HPV type 16 was positive in a significantly greater ($p < 0.05$) number of cases in group 1 (26 cases, 86.7%) compared with group 2 (3 cases, 42.9%) (fig. 1). In group 1, it was noteworthy that the parenchymal component of pleomorphic adenoma demonstrated more pronounced expression of the studied MMA compared with the stromal component. In patients with the epithelial variant of the tumor, a positive reaction was detected in all cases (5 cases, 100%); in the mixed variant, in 9 cases (90%); and in the mesenchymal variant, in 12 cases (80%) (table 1).

The number of cases with a positive immunohistochemical reaction with MMA to anti-Epstein-Barr virus was significantly higher ($p < 0.05$) in group 1 (8 cases, 26.7%) compared with group 2 (1 case, 14.3%) (fig. 1). In group 1 patients, light microscopy revealed more pronounced expression in the parenchymal component of the tumor compared with the stromal component. In patients with the epithelial variant of pleomorphic adenoma, a positive reaction was

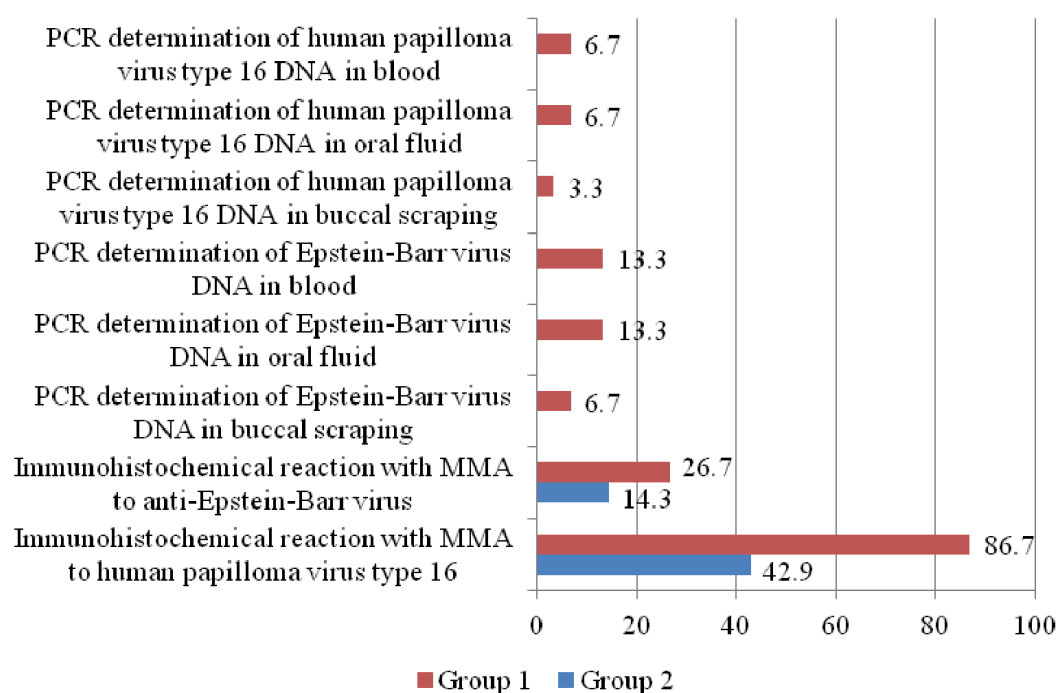


Fig. 1. Total number of cases with positive immunohistochemical reaction and PCR in groups 1-2.

Source: Own materials

Table 1. Results of immunohistochemical studies and PCR in group 1

Study name	Histological variant of pleomorphic adenoma					
	Mesenchymal (n=15)		Mixed (n=10)		Epithelial (n=5)	
	Number of cases with a positive reaction					
	Abs.	Rel., %	Abs.	Rel., %	Abs.	Rel., %
Immunohistochemical reaction with MMA to HPV type 16	12	80	9	90	5	100
Immunohistochemical reaction with MMA to anti-Epstein-Barr virus	1	6.7	3	30	4	80
PCR determination of Epstein-Barr virus DNA in buccal scraping	-	-	1	10	1	20
PCR determination of Epstein-Barr virus DNA in oral fluid	-	-	2	20	2	40
PCR determination of Epstein-Barr virus DNA in blood	-	-	2	20	2	40
PCR determination of HPV type 16 DNA in buccal scraping	-	-	1	10	-	-
PCR determination of HPV type 16 DNA in oral fluid	-	-	2	20	-	-
PCR determination of HPV type 16 DNA in blood	-	-	2	20	-	-

Source: Compiled by the authors of this study

observed in 4 cases (80%); in the mixed variant, in 3 cases (30%); and in the mesenchymal variant, in 1 case (6.7%).

PCR study of buccal scraping, blood and oral fluid samples from patients in group 1 revealed a lower number of cases with a positive reaction compared with the immunohistochemical examination of tumor tissue. In group 2, this analysis did not detect any positive cases at all. In group 1 PCR enabled the

detection of Epstein-Barr virus DNA in buccal scraping in 2 cases (1 patient with the mixed variant of the tumor and 1 patient with the epithelial variant), accounting for 6.7%; in oral fluid samples in 4 patients (2 cases with the mixed variant and 2 cases with the epithelial variant); and in blood samples in 4 patients (2 patients with the mixed variant and 2 patients with the epithelial variant), accounting for 13.3%.

The study of buccal scraping, oral fluid and blood by PCR in patients from group 1 enabled the detection of HPV type 16 DNA, respectively, in 1 case (3.3%) with a mixed variant; in 2 cases (6.7%) with a mixed variant; in 2 cases (6.7%) with a mixed variant.

DISCUSSION

The evidence supporting the role of viruses in oncogenesis is based on the detection of viral particles, viral DNA or RNA, as well as viral proteins using both classical and modern research methods. The detection and analysis of viruses remain complex and challenging issues [13]. In the present study, in order to determine the role of Epstein-Barr virus and HPV type 16 in the development of pleomorphic adenomas of the salivary glands, an immunohistochemical examination of tumor tissue was performed, along with PCR study of buccal scraping, oral fluid, and blood samples.

Immunohistochemical examination, as is well known, is based on the detection of viral antigens in biopsy specimens using specific antibodies. In the present immunohistochemical study, MMA to HPV type 16 and anti-Epstein-Barr virus were used. Analysis of the immunohistochemical findings revealed a greater number of cases with a positive reaction with MMA to HPV type 16 in patients with pleomorphic adenomas (26 cases, 86.7%) compared with the control group (3 cases, 42.9%). The number of cases with a positive immunohistochemical reaction with MMA to anti-Epstein-Barr virus was also higher in group 1 (8 cases, 26.7%) compared with group 2 (1 case, 14.3%). Detailed characteristics of the expression of the studied MMA in patients with pleomorphic adenomas have been previously described and published [12]. The results of the immunohistochemical study suggest a greater role of HPV type 16 in the development of pleomorphic adenomas compared with Epstein-Barr virus.

The involvement of HPV type 16 in tumor development occurs through classical oncogenic mechanisms. The viral oncoproteins E6 and E7 induce the inactivation and degradation of the tumor suppressor proteins p53 and pRb, leading to loss of cell cycle control, inhibition of apoptosis, and uncontrolled proliferation of epithelial cells [14, 15]. E6 activates the telomerase enzyme (hTERT), promoting cellular immortalization, that is, the loss of limitations on the number of cell divisions, thereby enabling cells to proliferate almost indefinitely [14, 15]. E7, in turn, stimulates the expression of S-phase factors, thereby enhancing the replicative activity of cells [16]. Some studies have also reported the involvement of HPV type 16 in the epigenetic reprogramming of tumor cells. This epigenetic remodeling includes hypermethylation of tumor suppressor gene promoters, modification of histones and microRNAs, which results in the functional «silencing» of genes responsible for the regulation of the cell cycle and apoptosis [17, 18].

The potential oncogenic mechanisms of Epstein-Barr virus are mainly associated with latent infection and the expression of viral proteins such as LMP1 and EBNA2. LMP1 functions as a «pseudo-receptor» that activates intracellular signaling pathways, thereby stimulating cell proliferation, inhibiting apoptosis, and promoting the production of

pro-inflammatory cytokines [19]. EBNA2 functions as a transcriptional regulator that activates the expression of both viral and cellular genes involved in the proliferation and transformation of infected cells [20].

Epstein-Barr virus is also capable of inducing the above-mentioned epigenetic changes (DNA methylation and histone modifications), which affect the expression of cellular genes [21], as well as promoting immune evasion, that is, the ability of tumor cells or viruses to avoid recognition and destruction by the immune system [22, 23]. Numerous studies have failed to detect a stable concentration of the investigated virus in different biological media, or have identified it in tissues only in low quantities, which suggest that it may act as a modifying factor of the tumor microenvironment rather than as a direct trigger of transformation [24].

Modern and accurate methods for the diagnosis of viral infections include PCR, which allows the identification of the virus within a short period after infection [25]. In the present study, PCR was used to identify the DNA of HPV type 16 and Epstein-Barr virus in buccal epithelium, oral fluid, and blood samples obtained from patients who underwent surgery for pleomorphic adenomas of the salivary glands. Using this method, Epstein-Barr virus DNA was detected in the buccal epithelium of 2 patients (6.7%), in oral fluid samples of 4 patients (13.3%), and in blood samples of 4 patients (13.3%). PCR also enabled the detection of HPV type 16 DNA in the buccal epithelium of 1 patient (3.3%), in oral fluid samples of 2 patients (6.7%), and in blood samples of 2 patients (6.7%).

The comparative analysis performed by the authors revealed discrepancies between the results of PCR study of blood, oral fluid, and buccal scraping and the immunohistochemical examination of tumor tissue. These discrepancies may indicate, first, the low effectiveness of PCR or of the investigated biological media for viral identification; second, the absence of viral replication or viral DNA in the studied media despite the presence of viral antigens in tumor tissue. The observed discrepancies may also be explained by the fact that the viral load in the investigated biological media was below the sensitivity threshold of the applied test systems. When HPV type 16 and Epstein-Barr virus enter the oral cavity or bloodstream from the salivary gland, they may alter their morphofunctional properties, which may prevent their complete detection by PCR and could account for the identified discrepancies.

Some studies have reported low sensitivity and specificity (16-27%) for the detection of human papillomavirus in oral fluid and oral mucosal epithelium using PCR [26]. According to some studies, the difficulty of detecting human papillomavirus in the oral cavity is associated with the presence of a large number of bacteria (approximately 50-100 billion) [27].

CONCLUSIONS

HPV type 16 appears to play a greater role in the genesis of pleomorphic adenomas of the parotid salivary glands compared with Epstein-Barr virus. Immunohistochemical examination of tumor tissue is an effective method for

demonstrating the role of HPV type 16 and Epstein-Barr virus in the development of pleomorphic adenomas of the salivary glands. PCR analysis of oral fluid, blood, and

buccal scraping is not a sufficiently sensitive or reliable method for identifying the investigated viruses in patients with pleomorphic adenomas.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Analysis of vestibular disorders after stapedotomy depending on the method of stapes footplate fenestration

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ABSTRACT

Aim: To compare the severity of early postoperative vestibular disorders after stapedotomy using two techniques of stapes footplate fenestration: the Skeeter microdrill and the manual perforator.

Materials and Methods: Sixty patients with otosclerosis who underwent stapedotomy in 2024-2025 were included in the study. The patients were randomly divided into two equal groups: Group A-stapedotomy performed using a Skeeter microdrill; Group B-stapedotomy performed using a manual perforator. Audiological assessment included pure-tone audiometry (air conduction, bone conduction, air-bone gap) and speech perception tests. Vestibular function was evaluated preoperatively and on postoperative day 7 using electronystagmography, as well as positional and static-coordination tests. An integrated clinical-instrumental vestibular scale (0-3 points), combining clinical symptoms, Romberg and Fukuda tests, and objective ENG parameters, was applied.

Results: Spontaneous nystagmus on postoperative day 7 was detected in 26.7% of patients in Group A and in 40% of patients in Group B ($p=0.59$). The mean postoperative increase in the vestibular score was significantly lower in Group A (0.73 vs 1.23; $p=0.02$). Both groups demonstrated significant improvement in air-conduction thresholds and reduction of the air-bone gap, with no statistically significant intergroup differences in audiological outcomes.

Conclusions: Both stapedotomy techniques effectively restore hearing in patients with otosclerosis. However, stapedotomy performed with a Skeeter microdrill is associated with less pronounced early postoperative vestibular disturbances compared with the manual perforator. The proposed integrated vestibular scale enables objective assessment of vestibular dysfunction in the early postoperative period and is suitable for routine clinical practice.

KEY WORDS: otosclerosis, stapedotomy, vertigo, vestibular disorders

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INTRODUCTION

Otosclerosis is a pathological bone remodeling process within the otic capsule that leads to stapes ankylosis and conductive or mixed hearing loss. Stapedotomy is considered the treatment of choice, as it provides significant improvement in hearing outcomes and social communication. However, even when optimal audiological results are achieved, postoperative vestibular disorders – such as vertigo, dizziness, and nausea – may substantially impair quality of life, prolong rehabilitation, and negatively affect patient satisfaction with treatment [1, 2]. Recent reviews emphasize that contemporary stapes surgery outcomes depend not only on the choice of fenestration instrument, but also on the standardization of surgery, prosthesis characteristics, and the control of intraoperative technical factors [3].

According to Singh et al., the incidence of vertigo after stapedotomy, as reported in the literature, varies widely, ranging from 3.4% to 55% [4]. This variability is partly explained by differences in the diagnostic criteria for vertigo, heterogeneous follow-up intervals, and variations in surgical techniques.

In addition to early postoperative symptoms, vestibular dysfunction may also occur in the late postoperative period and, in some cases, require revision surgery. Borysenko et

al. reported the results of a retrospective analysis of 787 stapedoplasty procedures, in which 43 patients (5.5%) underwent revision surgery. Among these patients, vertigo was the primary indication for revision surgery in 6 of 43 cases (14%) [5]. These findings indicate that vestibular complications are not limited to the early postoperative phase and may result in long-term clinical consequences, including the need for additional surgical intervention.

A key factor that may determine the risk of vestibular disorders is fenestration of the stapes footplate. At this stage, mechanical impact, vibrational load, and/or thermal effects may be transmitted to the inner ear structures, initiating transient or persistent cochleovestibular symptoms [1]. Therefore, the choice of stapedotomy techniques that minimize labyrinthine trauma remains a relevant area of clinical research.

In everyday clinical practice, when laser systems are unavailable, stapedotomy is commonly performed using either a Skeeter microdrill or a manual perforator. Therefore, a comparison of these two methods is of practical relevance. The Skeeter microdrill enables more controlled fenestra formation, particularly when operated at low rotational speeds, facilitating adherence to a standardized surgical technique [6]. In contrast, the manual perforator minimizes

the energy (vibrational and thermal) component of impact. Given the wide variability in reported postoperative vertigo rates [4] and the inconsistent data regarding the advantages of laser techniques in routine clinical practice [2], an objective analysis of vestibular disorders after stapedoplasty, depending on the stapedotomy method (using a Skeeter microdrill or a manual perforator), with subsequent assessment of vestibular function based on vestibulometric data, is warranted.

AIM

To compare the severity of postoperative vestibular disorders between two groups of patients with otosclerosis: those undergoing stapedoplasty using a Skeeter microdrill and those undergoing stapedoplasty using a manual perforator.

MATERIALS AND METHODS

The study included 60 patients with otosclerosis who underwent surgery in 2024-2025 at the State Institution «O.S. Kolomyichenko Institute of Otolaryngology of the National Academy of Medical Sciences of Ukraine». All procedures were performed by a single surgeon.

INCLUSION CRITERIA

All consecutive patients with a diagnosis of otosclerosis who underwent primary stapedoplasty during the study period were included, irrespective of postoperative vestibular symptoms.

EXCLUSION CRITERIA

Patients requiring revision surgery, those with a history of vestibular dysfunction, and patients with neurological or vascular disorders affecting vestibular function were excluded.

Audiological assessment was performed preoperatively and on postoperative day 7 using Interacoustics AC-40 and AD 629 audiometers in a controlled acoustic environment. Pure-tone audiometry included air-conduction (AC) and bone-conduction (BC) thresholds measured at frequencies of 0.25, 0.5, 1, 2, and 4 kHz. The air-bone gap (ABG) was calculated at the corresponding frequencies. Mean AC, BC, and ABG values across these frequencies were analyzed preoperatively and postoperatively, as well as frequency-specific changes.

Speech audiometry was performed to assess functional hearing outcomes using standardized recorded Ukrainian speech material presented monaurally through headphones. Speech recognition performance was evaluated by determining the minimal sound intensity level (dB HL) required to achieve 50% and 100% correct word recognition for each patient. The 50% recognition level was determined using standardized digit-based speech material, whereas the 100% recognition level was assessed using phonetically balanced word lists. These parameters reflected the sound intensity required to achieve partial and complete speech intelligibility, respectively, with lower intensity levels indicating better speech perception performance. Preoperative and postoperative values (postoperative day 7) were compared to quantify surgical effects on speech perception.

Vestibular function was assessed using electronystagmography (ENG), performed with the Dx-Systems M-Test-4 hardware-software complex (Ukraine). The examination included registration of spontaneous nystagmus at rest and during positional testing, as well as evaluation of static and dynamic balance.

Preoperative vestibular assessment comprised rotational testing using a Bárány chair, with analysis of vestibulo-ocular reflex parameters, presence of nystagmus, and its quantitative characteristics, including reaction duration (seconds), nystagmus frequency (Hz), mean amplitude (degrees), mean fast-phase angular velocity ($^{\circ}/s$), mean slow-phase angular velocity ($^{\circ}/s$), and the ratio of fast- to slow-phase angular velocities (K coefficient). In addition, static-coordination tests were performed, including the Romberg test and the Fukuda stepping test, to assess postural stability and balance control.

In the early postoperative period (postoperative day 7), evaluation of vestibular function was limited to non-provocative tests. These included assessment of spontaneous nystagmus during head movements without rotational stimulation, positional testing, and static-coordination tests (Romberg and Fukuda tests). Rotational testing was not performed postoperatively to avoid excessive vestibular stimulation in the early recovery phase.

To standardize and objectify balance assessment, an integrated clinical classification was proposed, incorporating the results of positional tests, the Romberg test, the Fukuda stepping test, and ENG parameters. Balance function was graded on a 0-3-point scale as follows: 0 – no balance disturbance; 1 – mild disturbances (Grade I); 2 – moderate disturbances (Grade II); and 3 – severe disturbances (Grade III). The vestibular grading scale is presented in Table 1.

The balance score was determined preoperatively and reassessed on postoperative day 7. An increase in the balance score was interpreted as a worsening of vestibular disorders in the early postoperative period. Application of this integrated scale enabled conversion of descriptive clinical and instrumental findings into quantitative values and allowed statistical comparison between the study groups.

All patients were examined on postoperative day 7. Preoperative ENG data were obtained from routine preoperative assessment and used for comparison.

The study population included 60 patients: 47 women (78.3%) and 13 men (21.7%), resulting in a female-to-male ratio of 3.6:1. The mean age of the patients was 45 years (range, 24-72 years). Using randomization, patients were divided into two equal groups of 30 patients each. Group A underwent stapedotomy performed with a Skeeter microdrill (Medtronic). Group B underwent stapedotomy performed using a conventional manual perforator.

All other surgical steps were identical in both groups and included an endomeatal approach, removal of the stapes superstructure, and fixation of a Teflon prosthesis to the long process of the incus with placement of its shaft into the fenestra. Teflon prostheses with diameters of 0.4 mm or 0.6 mm were used depending on fenestra size and

Table 1. Integrated clinical–instrumental scale for assessment of vestibular disorder severity

Score	Symptoms	Static coordination tests (Romberg / Fukuda)	Instrumental nystagmus recording (ENG)	Interpretation
0	None	Stable performance without instability	No nystagmus	Vestibular function preserved
1	Minimal dizziness or nonspecific unsteadiness (episodic sway without true vertigo and without limitation of daily activity)	No significant deviations (patient maintains upright posture; no clinically significant axis deviation or pronounced trunk rotation)	No nystagmus	Mild clinical manifestations without objective signs
2	Vertigo, imbalance	Pronounced instability without falling; deviation or rotation	Positional nystagmus or isolated nystagmus beats	Moderate vestibular disorders
3	Intense vertigo, marked balance impairment	Inability to maintain position or interruption of the test	Pronounced spontaneous nystagmus	Severe vestibular deficit

Source: compiled by the authors of this study

individual anatomical features. Tympanic and mixed forms of otosclerosis were equally represented in both groups.

The initial dataset was prepared in Microsoft Excel (Microsoft Corp., Redmond, WA, USA). Statistical analysis and data visualization were performed using Python and the Matplotlib library. Quantitative data are presented as mean (M) $\pm$ standard deviation (SD). Differences between the study groups were analyzed using Student's t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Within-group comparisons of preoperative and postoperative values were performed using the paired Student's t-test for normally distributed data and the Wilcoxon signed-rank test for

non-normally distributed data. Qualitative variables, such as the presence or absence of nystagmus, were analyzed using Fisher's exact test. A p-value <0.05 was considered statistically significant.

ETHICS

The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion in the study. The study protocol was approved by the Local Ethics Committee of the State Institution «O.S. Kolomiychenko Institute of Otolaryngology of the National Academy of Medical Sciences of Ukraine».

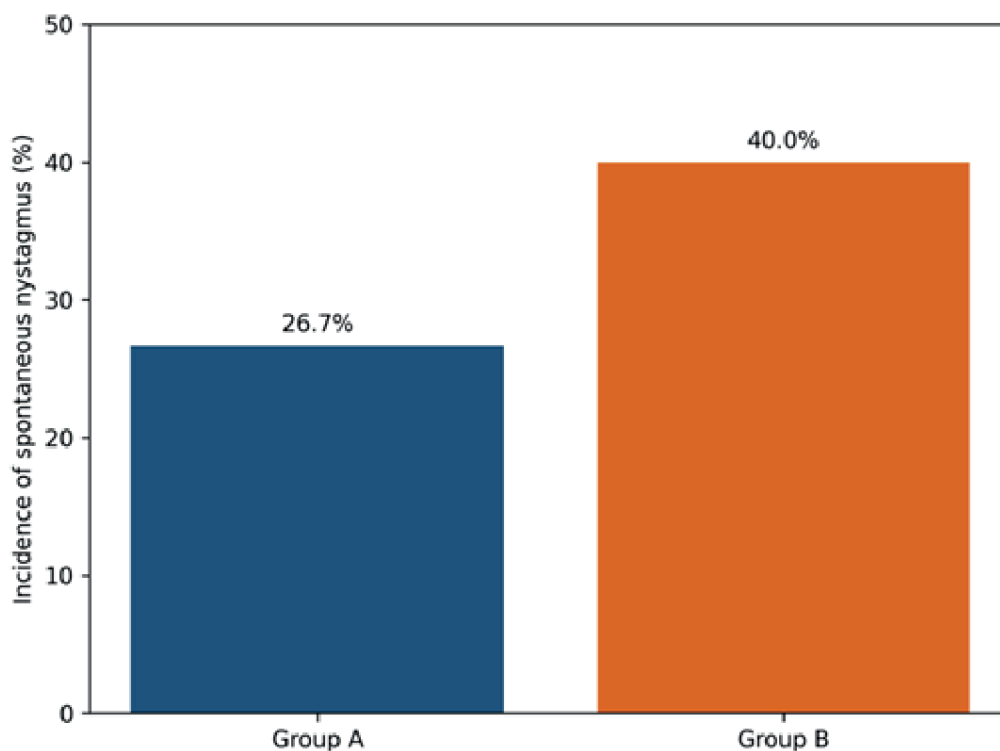


Fig. 1. Incidence of spontaneous nystagmus in the early postoperative period in patients after stapedotomy

Picture taken by the authors

FRAMEWORK

The study was carried out within the framework of a research project «Improving rehabilitation methods for patients with acquired blast injury and congenital pathology of the temporal bone area» conducted at the State Institution “O.S. Kolomiychenko Institute of Otolaryngology of the National Academy of Medical Sciences of Ukraine” (state registration number: 0125U000346; study period: 2025-2027).

RESULTS

The study results demonstrated the following findings. In the early postoperative period, all patients exhibited signs of vestibular dysfunction; however, the severity of these disorders differed between the study groups.

On postoperative day 7, spontaneous nystagmus was recorded in 20 of 60 patients (33.3%). In Group A, nystagmus was observed in 8 of 30 patients (26.7%), whereas in Group B it was more frequent, occurring in 12 of 30 patients (40%) (Fig. 1). According to Fisher’s exact test, the difference between the groups did not reach statistical significance ($p = 0.59$). The incidence of nystagmus was numerically higher in patients operated on using the manual perforator.

The mean postoperative increase in the balance score on postoperative day 7 compared with preoperative values was 0.73 in Group A and 1.23 in Group B, indicating less pronounced vestibular impairment in patients operated on using the Skeeter microdrill. The difference remained statistically significant when analyzed using both parametric and nonparametric methods ($p=0.02$ and $p=0.031$, respectively).

Tympanic and mixed forms of otosclerosis, as well as the diameter of the Teflon prosthesis (0.4 or 0.6 mm), were equally distributed between the two groups and were therefore not included in the statistical analysis. Hearing improvement was observed in all patients in both groups. Air-conduction thresholds improved by 20-25 dB, with reduction of the air–bone gap to ≤ 10 dB in the majority of patients, findings that were corroborated by speech audiometry. No statistically significant differences in audiometric parameters were observed between the groups.

A statistically significant improvement in speech recognition performance was observed in both study groups after surgery. In Group A, the sound intensity level required to achieve 50% word recognition decreased from 71.33 ± 15.53 dB preoperatively to 51.17 ± 19.28 dB on postoperative day 7 ($p<0.0001$). Likewise, the level required to achieve 100% word recognition decreased from 87.67 ± 16.70 dB to 68.17 ± 14.53 dB ($p<0.0001$).

In Group B, the sound intensity level required to achieve 50% word recognition decreased from 63.00 ± 11.79 dB preoperatively to 45.17 ± 15.67 dB postoperatively ($p<0.0001$). Similarly, the level required to achieve 100% word recognition decreased from 83.00 ± 11.79 dB to 65.17 ± 15.67 dB ($p<0.0001$).

Between-group comparison of the magnitude of postoperative change demonstrated no statistically significant differences for either the 50% or 100% word recognition thresholds (Fig. 2 and Fig. 3). These findings indicate that both surgical techniques provide comparable postoperative improvement in functional speech perception.

Preoperative intergroup comparison revealed a borderline difference between the groups ($p=0.023$ for Student’s t-test;

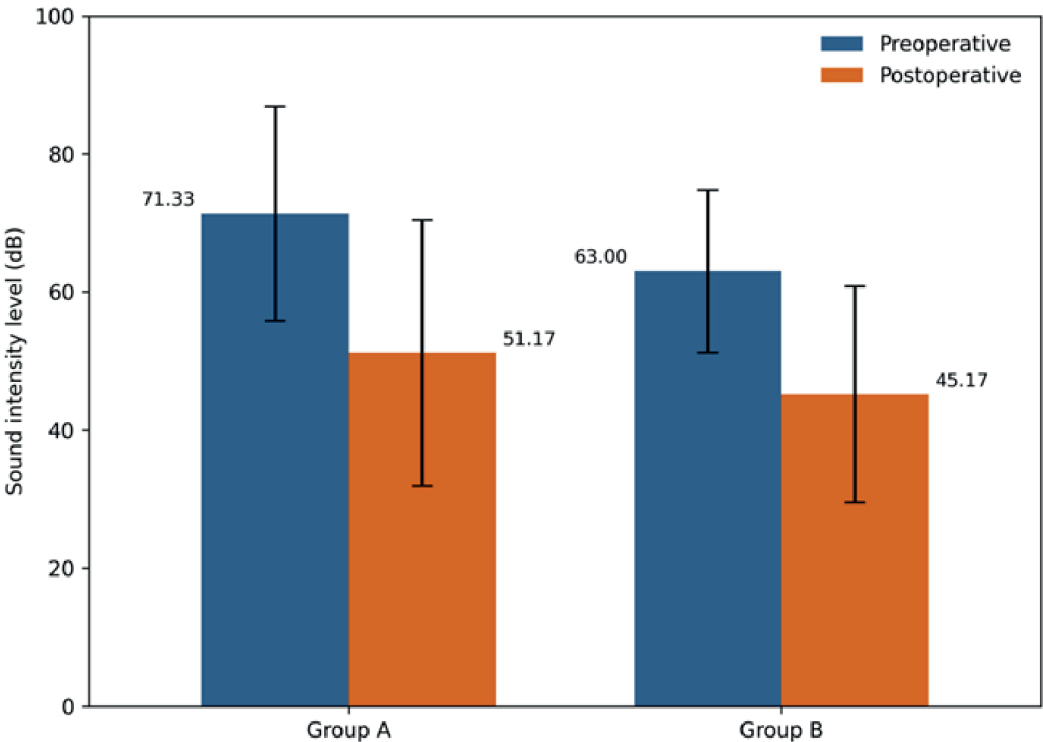


Fig 2. Preoperative and postoperative sound intensity levels required to achieve 50% word recognition in Group A and Group B ($M \pm SD$)
Picture taken by the authors

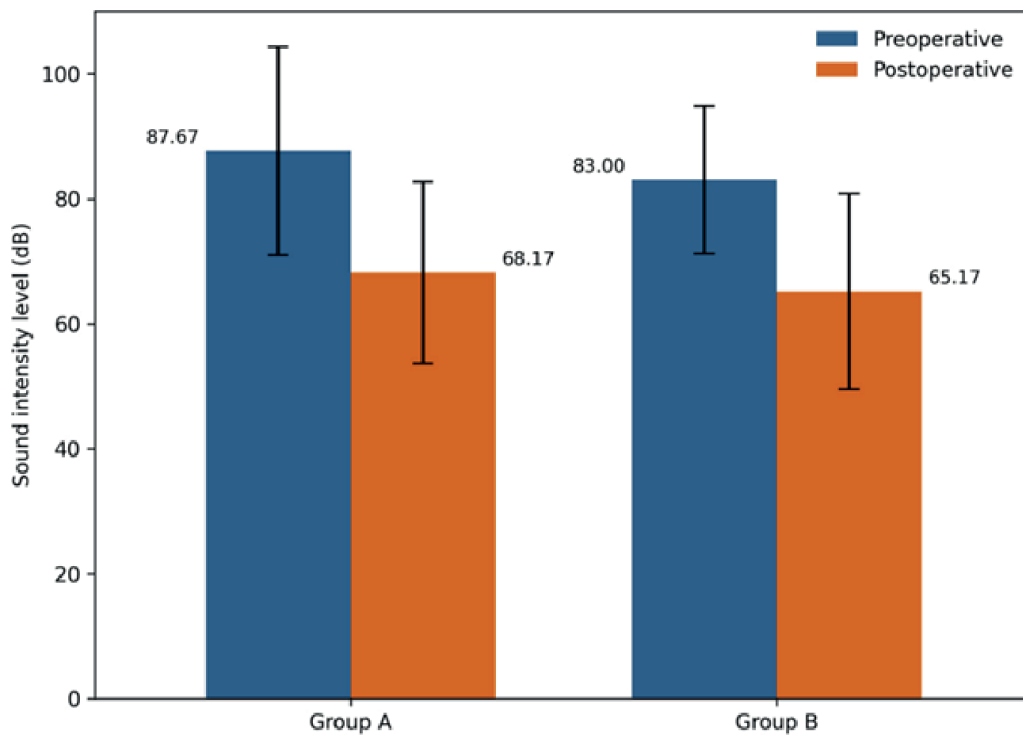


Fig. 3. Preoperative and postoperative sound intensity levels required to achieve 100% word recognition in Group A and Group B ($M \pm SD$)

Picture taken by the authors

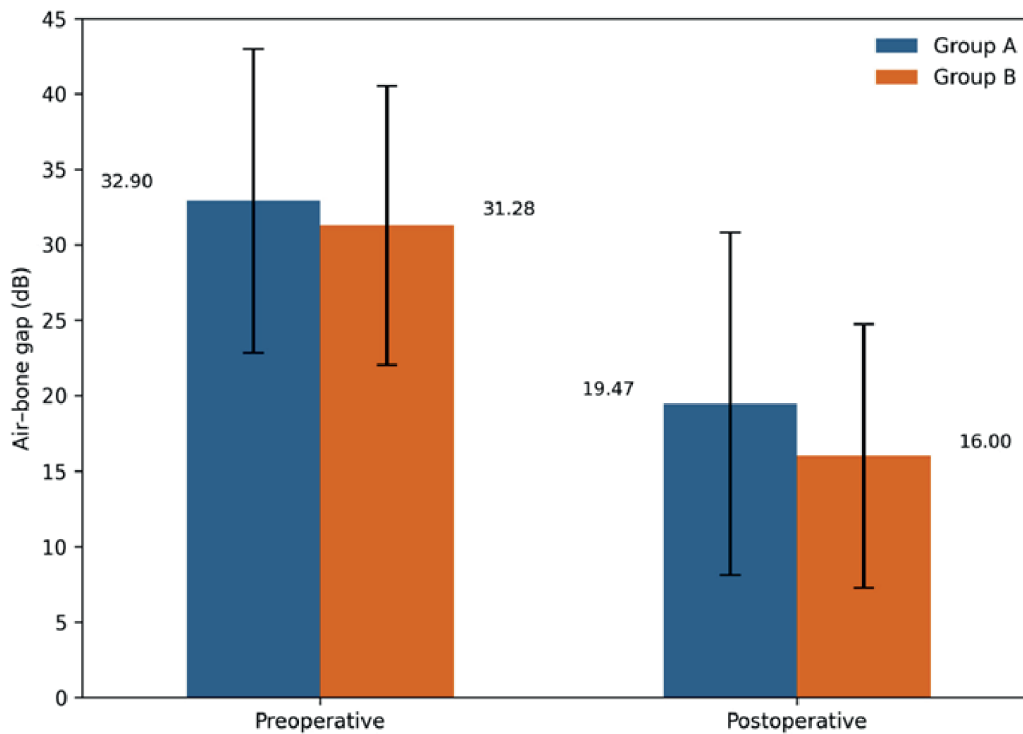


Fig. 4. Air-bone gap before and after stapedotomy in Group A and Group B ($M \pm SD$)

Picture taken by the authors

$p=0.059$ for the Mann-Whitney U test). No statistically significant differences were observed between the groups after surgery ($p=0.19$ for Student's t-test; $p=0.20$ for the Mann-Whitney U test). Within-group comparisons demonstrated significant improvement in both groups ($p<0.0001$).

Intergroup comparisons revealed no statistically significant differences either before surgery ($p=0.22$ for Student's

t-test; $p=0.20$ for the Mann-Whitney U test) or after surgery ($p=0.45$ for Student's t-test; $p=0.35$ for the Mann-Whitney U test). Within-group comparisons demonstrated significant improvement in both groups ($p<0.0001$).

After stapedotomy, bone-conduction thresholds changed only minimally in both groups. In Group A, the mean bone-conduction threshold increased from 21.63 ± 9.26 dB to

22.73±8.75 dB, while in Group B it increased from 17.69±8.80 dB to 19.93±10.41 dB. These findings indicate the absence of clinically significant sensorineural deterioration.

Both groups demonstrated significant improvement in air-conduction thresholds following surgery. In Group A, the mean air-conduction threshold decreased from 54.53±14.08 dB to 42.20±15.38 dB ($p<0.0001$), whereas in Group B it decreased from 48.38±13.68 dB to 35.52±13.51 dB ($p<0.0001$), reflecting comparable audiological efficacy of the two techniques.

In the early postoperative period, the air–bone gap decreased significantly in both groups, indicating effective restoration of sound-conduction function. In Group A, the mean air–bone gap decreased from 32.90±10.06 dB to 19.47±11.36 dB, while in Group B it decreased from 31.28±9.26 dB to 16.00±8.73 dB. No statistically significant intergroup differences were observed either before or after surgery, whereas within-group comparisons demonstrated significant improvement in both groups (Fig. 4.).

Intergroup comparisons revealed no statistically significant differences either before surgery ($p=0.52$ for Student's *t*-test; $p=0.61$ for the Mann–Whitney *U* test) or after surgery ($p=0.19$ for Student's *t*-test; $p=0.37$ for the Mann–Whitney *U* test). Within-group comparisons demonstrated significant improvement in both groups ($p<0.0001$).

DISCUSSION

Manual perforators, microdrills, and lasers are commonly used to create a fenestra in the stapes footplate. In the present study, both techniques demonstrated comparable audiological outcomes, while differences were observed in the severity of early postoperative vestibular disturbances.

With regard to hearing results, a prospective observational study by Palacios-García et al. demonstrated that low-speed microdrill fenestration and manual perforation provide similar short-term audiological improvement [6]. Our findings are consistent with these data, as no significant intergroup differences were observed in air–bone gap closure or speech recognition outcomes in the early postoperative period.

The interaction between fenestration instruments and the labyrinth differs in terms of mechanical characteristics. A manual perforator involves direct mechanical contact, whereas a microdrill introduces controlled rotational movement that may include vibrational and thermal components. Although such factors could theoretically influence the vestibular response, clinical evidence remains inconsistent.

In laser-assisted surgery, the “no-touch” principle has been proposed as a means of reducing mechanical trauma. Singh et al. reported improved vestibular outcomes with CO₂ laser fenestration compared with conventional techniques [4], and Matković et al. also highlighted the advantages of CO₂ laser use, particularly regarding early postoperative vertigo [7]. However, these findings are not universally supported. In a multicenter retrospective study, De Vito et al. did not demonstrate statistically significant differences in postoperative vertigo rates between CO₂

laser and conventional techniques [2]. These discrepancies underscore the importance of standardized vestibular assessment and objective instrumental evaluation.

Diode lasers represent a potentially more accessible alternative to CO₂ systems. Plodpai reported the safe application of diode laser in endoscopic stapedotomy with transient early postoperative vertigo [8], while Wang et al. demonstrated comparable audiological outcomes and no significant difference in postoperative vertigo frequency between diode laser and microdrill techniques [9]. Recent clinical data also suggest that postoperative vestibular symptoms may persist despite satisfactory audiological improvement, which further supports the need for focused vestibular assessment after stapedotomy [10].

Taken together, the available evidence suggests that the type of fenestration instrument alone does not determine the postoperative vestibular outcome. Rather, surgical precision, technical execution, and control of intraoperative parameters may play a decisive role. The significant difference in the integrated balance score observed in our study, despite the absence of differences in audiological outcomes, suggests that early vestibular response may represent a more sensitive indicator of surgical impact than pure-tone thresholds.

Unlike widely used scales such as DHI, CTSIB, and BESS, which primarily assess subjective symptoms or static balance under standardized conditions, the integrated clinical–instrumental scale applied in this study combines static-coordination tests with objective ENG parameters and is specifically tailored to the early postoperative period after stapedoplasty. This approach enables objective quantification of vestibular dysfunction and may be suitable for routine clinical practice.

This study has several limitations. The sample size was relatively small, which may limit the generalizability of the findings. Vestibular function was assessed only in the early postoperative period, and long-term vestibular outcomes were not evaluated. Furthermore, potentially relevant factors such as individual anatomical variability, exact fenestra size, prosthesis characteristics, and intraoperative parameters were not analyzed separately. These variables may influence vestibular responses and should be considered in future research.

Prospective studies with extended follow-up and multivariable analysis are warranted to better define predictors of vestibular outcomes after stapedoplasty and to optimize surgical techniques in the management of otosclerosis.

CONCLUSIONS

Both stapedotomy techniques – using the Skeeter microdrill and the manual perforator – proved effective in restoring hearing in patients with otosclerosis, with no significant differences in audiological outcomes between the groups in the early postoperative period.

However, analysis of postoperative vestibular function demonstrated a statistically significant intergroup difference in the increase of the integrated balance score, with lower

postoperative values observed in the Skeeter microdrill group. These findings suggest less pronounced early vestibular impairment associated with the use of the Skeeter microdrill compared with that of the manual perforator.

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CONFLICT OF INTEREST

The authors declare no conflict of interest

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Investigating the psychosocial and financial burden and perceived social support of parents with hospitalized children in Greece

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ABSTRACT

Aim: The present cross-sectional study aimed to investigate the psychosocial and financial burden, as well as the perceived social support experienced by parents of hospitalized children in Greece.

Materials and Methods: The sample consisted of 100 parents or legal guardians of children hospitalized in various departments of the General Hospital of Corinth, using a convenience sampling method. The Bakas Care Outcomes Scale (BCOS), the Multidimensional Scale of Perceived Social Support (MSPSS), and the Index of Personal Economic Distress (IPED) were used as measurement tools (pp. 4-6). Data analysis was performed using descriptive statistics and Spearman's rho correlation coefficient.

Results: The mean score on the BCOS was 51.34 (SD=5.79), indicating a moderate to negative perception of the caregiving experience. On the IPED scale, the mean score was 17.67 (SD=2.17), with 82% of participants experiencing severe financial hardship (score >15). The mean MSPSS score was 4.24 (SD=0.39), indicating moderate to high perceived social support =1. A significant positive correlation was observed between perceived social support and financial hardship ($p=0.324$, $p=0.001$), suggesting that those experiencing greater financial hardship received more support.

Conclusions: The findings highlight the need for comprehensive, family-centered interventions within the hospital setting. Provision of psychosocial support, financial assistance, and accommodation facilities is imperative to alleviate the significant burden faced by caregivers and improve the overall hospital experience for families.

KEYWORDS: burden, social support, parents of hospitalized children, caregiver

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INTRODUCTION

The concept of caregiver burden encompasses the overall impact on individuals who care for persons with increased needs, including both objective and subjective dimensions. Objective burden refers to measurable, practical consequences, such as loss of time, financial expenses, disruption of daily routines, and changes in social or professional roles, whereas subjective burden reflects the caregiver's personal perception of the emotional and psychological strain of caregiving [1, 2].

Hospitalization of a child, particularly in cases of chronic, severe, or life-threatening illness, constitutes a highly stressful experience that affects parents' emotional, physical, social, and professional functioning [3, 4]. The child's clinical and nursing characteristics, including diagnosis, severity, complexity of care, duration of hospitalization, and need for specialized or repeated procedures, are strongly associated with elevated parental stress, anxiety, depressive symptoms, emotional exhaustion, and post-traumatic stress [1, 3-6]. Sudden or acute admissions provoke intense psychological shock and adaptation difficulties, while even scheduled hospitalizations elicit stress, particularly in parents of young children [4, 7]

Physical burden is a central but often overlooked aspect of caregiving, resulting from inadequate rest, prolonged uncomfortable positions, constant noise, exposure to medical interventions, and lack of privacy. These factors contribute to chronic fatigue, musculoskeletal pain, headaches, gastrointestinal symptoms, and immunosuppression, which may extend beyond hospitalization [1, 3, 5].

Psychological burden arises from exposure to the child's pain, medical uncertainty, and caregiving demands, often manifesting as secondary traumatic stress, anxiety, depression, and post-traumatic stress disorder [6, 8]. Contributing factors include poor communication with healthcare staff, insufficient information, lack of control, and repeated exposure to stressful hospital environments, which intensify feelings of guilt, isolation, and inadequacy, impair decision-making, concentration, family functioning, and professional performance [9-10]

Hospitalization also imposes significant social, financial, and occupational burdens. Caregiving responsibilities necessitate redistribution of time and resources, disrupting daily life, social interactions, and work commitments, and may lead to professional burnout in the absence of

supportive structures [3, 6, 10]. Financial strain arises from direct medical expenses, transportation, accommodation, and indirect income loss, with more severe impacts for chronic or complex conditions and prolonged care needs [4].

Parental stress is further influenced by the child's emotional and behavioral responses, which can trigger secondary trauma and heightened feelings of failure [6, 8, 11, 12]

Sociodemographic factors-such as age, gender, educational level, family structure, socioeconomic status, and occupational stability-shape resilience, access to resources, and coping abilities. Younger parents, mothers, single parents, those with additional dependents, low income, or insecure employment tend to experience higher burden, whereas older parents, those with higher education, and those with stable work environments demonstrate better adaptation and more active caregiving engagement [2-5, 13]

Parents' cognitive and subjective interpretation of the child's illness-including expectations of treatment outcomes, probability of relapse, and perceived manageability-strongly affects their psychological burden. Inconsistent information, uncertainty, catastrophizing, and excessive personal responsibility amplify distress and psychosomatic symptoms, while resilience and adaptive coping strategies are protective [3, 5, 9] Sociocultural factors and prevailing social narratives around parental adequacy and caregiving further shape emotional responses, with stigma or limited support intensifying guilt, isolation, and perceived failure [2, 13].

Social support is a critical protective factor, encompassing emotional, informational, and practical resources from family, friends, professional networks, and healthcare staff. Adequate social support, particularly when empathetic and participatory, mitigates stress, enhances resilience, and improves adaptation to caregiving demands, while its absence exacerbates psychological distress, loneliness, and burnout [14-19]

Overall, pediatric hospitalization presents parents with complex, multi-dimensional challenges, encompassing emotional, physical, social, financial, and occupational domains. Understanding these factors is essential for developing targeted interventions that enhance parental resilience, ensure access to support resources, and improve the hospitalization experience for both children and families. In Greece, empirical data systematically examining the burden on parents and its connection to social support remain limited, highlighting the need for further research [20, 21].

AIM

The aim of this study was to examine the psychosocial and financial burdens experienced by parents of hospitalized children in Greece, as well as the role of their perceived social support.

MATERIALS AND METHODS

PARTICIPANTS

The sample of this study was composed of a total of 100 parents or legal guardians of children (n=100) who

were hospitalized in various clinics and departments of the General Hospital of Corinth, with only one pediatric clinic. Participant selection was based on convenience sampling, a non-random method often used in healthcare research. The study was conducted from November 21, 2025, to January 31, 2026.

Respondents met the pre-determined eligibility criteria in the study, which included:

- Hospitalization of the child for more than one week, regardless of age and diagnosis
- Daily presence in the hospital and primary care of the child by the parent or legal guardian
- Sufficient knowledge of the Greek language to ensure proper understanding and accurate completion of the research tools
- Consent to participate, after full oral and written information about the purpose and nature of the study

EXCLUSIVE CRITERIA

Inadequate Cognitive or Emotional State: Parents or legal guardians with known cognitive impairment, active severe psychiatric disorders, or intense emotional distress that would hinder their ability to provide informed consent or objective responses.

Illiteracy or Language Barriers: Parents or legal guardians with an inability to read or write in Greek, which would prevent the independent and accurate completion of the research tools.

Incomplete Responses: Participants who failed to complete more than 20% of the research tools or withdrew their consent during the data collection process.

MEASURES

The self-administered questionnaire included questions on the demographic characteristics of the participants, information on the child's hospitalization, as well as the Bakas Caregiving Outcomes Scale, Multidimensional Scale of Perceived Social Support, and Index of Personal Economic Distress questionnaires [16-18]

QUESTIONS REGARDING THE DEMOGRAPHIC CHARACTERISTICS OF THE PARTICIPANTS AND INFORMATION ABOUT THE CHILD'S HOSPITALIZATION

Participants answered questions regarding their demographic characteristics (such as gender, age, place of residence, family and professional status, level of education, existence of other children, etc.), and questions related to the child's hospitalization (such as duration of hospitalization, perceived level of severity of the condition, and degree of understanding of the disease by the parent). In addition, there were questions regarding their personal needs as caregivers during the current period and self-assessment of their current health status.

BAKAS CAREGIVING OUTCOMES SCALE (BCOS) (BAKAS ET AL., 2006)

It is designed to measure life changes in family caregivers of persons with chronic illness. The scale was originally developed to measure life changes in family caregivers of

stroke survivors but has also been used in family caregivers of those with heart failure and a variety of other chronic conditions. It includes 15 items that assess areas such as social and occupational functioning, physical well-being, and overall quality of life. The 16th item is a general item assessing the degree to which a caregiver's life has changed because of taking care of the patient, but it is not included in the overall score. Responses are given on a seven-point Likert scale, ranging from 3 (negative change) to +3 (positive change), with 0 indicating no change, e.g., "As a result of providing care, my time for family activities: changed for the worse, did not change, changed for the better". The ratings ranging from -3 to +3 are converted to a scale of +1 to +7 to ensure all scores are positive for analysis. Scores above +4 suggest that the caregiver's life has improved, while scores of +4 or below reflect negative views of the caregiving experience. A total BCOS score is obtained by adding up the individual item scores, with possible totals ranging from 15 to 105. Higher overall scores represent more favorable outcomes for the caregiver. The updated BCOS can be completed either as a self-report questionnaire or via an interview. This scale has demonstrated high internal reliability (Cronbach's $\alpha = 0.90$) and has been applied to a variety of caregiver populations, including parents of children with chronic or acute conditions [16]. In the present study, the Greek version was used [19], and Cronbach's α value was 0.84.

MULTIDIMENSIONAL SCALE OF PERCEIVED SOCIAL SUPPORT (MSPSS) (ZIMET ET AL., 1990)

It consists of 12 items and measures perceptions of support from 3 sources: Family, e.g. "I get the emotional help and support I need from my family", Friends, e.g. "I can count on my friends when things go wrong" and significant other, e.g. "There is a special person in my life who cares about my feelings" [17]. A seven-point Likert scale is used for the rating, and the total score is the sum of all items divided by 12. There is also a mean score for each subscale. Higher scores on any subscale or the total score indicate higher levels of perceived social support. Alternatively, according to another rating system. Any mean scale score ranging from 1 to 2.9 could be considered low support; a score of 3 to 5 could be considered moderate support; a score from 5.1 to 7 could be considered high support. The questionnaire has been translated into many languages and has been shown to have good to excellent psychometric properties [18]. The scale has proven particularly useful in mental health research and has been associated with lower levels of anxiety, depression, and psychological distress, particularly in populations experiencing stressful situations, such as caregivers of hospitalized children. In this study, the Greek translation of MSPSS was used, and Cronbach's α was 0.88 [20].

INDEX OF PERSONAL ECONOMIC DISTRESS (IPED) (MADIANOS ET AL., 2010)

The scale includes 8 questions and assesses the financial difficulties experienced by a person in meeting basic daily needs (bills, nutrition, transportation, etc.), e.g., "I cannot pay for food or necessities". The importance of the scale lies in its ability to record objective manifestations of financial

insecurity, which is a critical factor in predicting psychosocial burden [3]. Each question has three answer options (rarely, sometimes, or often), and the total score ranges from 8 to 24. Values above 15 are considered indicative of serious financial hardship.

The scale exhibits satisfactory internal consistency (Cronbach's $\alpha = 0.5-0.8$) and has been developed specifically for the socioeconomic conditions of the Greek population. In this study, Cronbach's α value was 0.82.

PROCEDURE

RESEARCH DESIGN AND DATA COLLECTION

A cross-sectional study lasting three months (September - November 2025) was conducted in the following clinics and departments of the General Hospital of Corinth, Greece: Pathology, Oncology, Surgery Department, Pediatric Clinic, Emergency Department (ED), and outpatient clinics. Parents of children hospitalized or examined in the above clinics and departments participated. The questionnaires were personally delivered by the researcher to the participants during their stay in the hospital, in the context of their daily presence in the areas where their children were hospitalized. This specific method allowed for the approach of a representative sample of parents who directly experienced the experience of pediatric hospitalization, thus ensuring the relevance and validity of the data collected in relation to the objectives of the study.

DATA ANALYSES

Statistical analysis of the data was performed using IBM SPSS Statistics software, version 29.0. The analysis initially included descriptive statistics to record the sociodemographic characteristics of the participants and the characteristics of the hospitalized children and their hospitalization. For qualitative variables, frequencies and percentages were presented, while for quantitative variables, measures of central tendency and dispersion (mean, median, standard deviation, minimum, and maximum value) were calculated. The normality of the data was tested with the Kolmogorov-Smirnov and Shapiro-Wilk tests. Regarding the psychometric scales (BCOS, MSPSS, and IPED), measures of central tendency and dispersion were calculated per question and overall, for the questionnaires and their subscales. At the same time, the internal reliability of the scales was examined with the Cronbach's alpha coefficient, in order to determine the consistency of the responses within each tool. Subsequently, the correlations between the key variables (BCOS, MSPSS, and IPED) were investigated using the non-parametric Spearman's rho coefficient, as most variables did not exhibit a normal distribution. Furthermore, possible differences were examined based on the sociodemographic characteristics of the participants and the characteristics of the hospitalized children and their hospitalization performing t-test and ANOVA.

ETHICS

To conduct this study, all principles of research ethics and the principles of the Declaration of Helsinki were strictly adhered to. The necessary approval was requested and

secured from the competent scientific and administrative committees of the nursing units where the study was carried out. The study was approved by the Scientific Council of the General Hospital of Corinth under protocol numbers 2085 and 2044, at its 14th session held on November 20, 2025.

Participants were fully informed about the purpose, methodology, and use of the data that would result from the research. They were assured about the anonymity and confidentiality of the information provided, and that they had the option to withdraw at any time without any consequences. In the case of withdrawal, their personal data was immediately destroyed and not included in the analysis. The data was used only for this research and was

stored securely, in accordance with the principles of personal data protection (GDPR). Access to the data was limited exclusively to members of the research team.

RESULTS

Of the total of 100 questionnaires distributed, all were returned adequately completed, ensuring a 100% response rate. The mean age of the caregivers was 36.59 years old ($SD=8.62$, $Min=21$, $Max=60$, $Range=39$) and the mean age of the child was 7.12 years old ($SD=3.70$, $Min=1$, $Max=15$, $Range=14$). In addition, the mean hospitalization time of the child was about 4 days ($M=3.96$, 3.32 , $Min=1$, $Max=17$, $Range=16$) (Table 1).

Table 1. Demographic characteristics of the participants and information about the child's hospitalization

Variable	Frequency	Percentage (%)
Origin		
Greek	70	70.0
Stranger	30	30.0
Marital/relationship status		
Married	53	53.0
Single	8	8.0
Widow/er	5	5.0
Divorced	28	28.0
Living with a partner	6	6.0
Job		
Housewife	33	33.0
Civil servant	26	26.0
Private employee	29	29.0
Unemployed	8	8.0
Other	4	4.0
Residence		
City of Corinth	29	29.0
Wider area of Corinth	69	69.0
Other	2	2.0
Education		
Primary school	26	26,0
Secondary school	23	23,0
High School	30	30,0
University	21	21,0
Having received information about the child's illness		
Not at all	5	5.0
A little	15	15.0
Quite a bit	52	52.0
A lot	28	28.0
HospitalizationWard		
Internal Medicine Department	3	3.0

Table 1. Cont.

Oncology Department	4	4.0
Surgical Department	7	7.0
Emergency Department (ED)	23	23.0
Pediatric Ward	46	46.0
Outpatient Department	17	17.0
Relationship to the child		
Father	27	27.0
Mother	70	70.0
Other (e.g., grandparents, siblings, uncles)	3	3.0
Age group of the child		
Up to 1 years old	4	4.0
1-5 years old	34	34.0
6-11 years old	47	47.0
12-15 years old	15	15.0
16-18 years old	0	0.0
Caregiver of the rest children		
Relative/friend	11	11.0
Employed person	5	5.0
Nurse/school	1	1.0
Grand parents	18	18.0
Other	1	1.0
Needs requiring support (Multiple choice / Multiple responses allowed)		
Assistance with all activities	35	35.0
Financial Support	47	47.0
Emotional Support	55	55.0
Respite	37	37.0
Having other children		
Yes	64	64.0
No	36	36.0
Number of children in the family (including the hospitalized child)		
1	64	64.0
2	28	28.0
3	8	8.0

Source: compiled by the authors of this study

In the BCOS the possible total score ranges from 15 to 105, and higher overall scores represent more favorable outcomes for the caregiver. In the study, the mean score was 51.34 (SD=5.79), indicating negative changes and moderate to negative views of the caregiving experience (Table 2).

Moreover, scores above 4 suggest that the caregiver's life has improved, while scores of 4 or below reflect negative views of the caregiving experience. According to the above table, the caregiver's life has improved in only four dimensions: self-esteem, relationship with friends, relationship with family, and relationship with the child.

On the contrary, the caregiver's life has been worse in all the other dimensions (physical health, time for family activities, general health, etc.).

The mean score in the MSPSS was 4.24 (SD=0.39, Min=3.08, Max=5, Range=1.92). The above scores indicate moderate to high perceived social support. Moreover, based on their scores on the scale, all participants (100%) were classified in the category "moderate perceived social support" (overall total mean score=3-5). The total score in the IPED ranges from 8 to 24, and values above 15 are considered indicative of serious financial hardship. In this study, the mean score was 17.67 (SD=2.17, Min=13.00, Max=23.00, Range=10.00).

Table 2. Descriptive statistics for the Bakas Caregiving Outcomes Scale (BCOS)

	N	Range	Minimum	Maximum	Mean	Std. Deviation
BCOS overall total score	100	26.00	38.00	64.00	51.34	5.79
My self esteem	100	6	1	7	4.10	1.84
My physical health	100	4	1	5	3.14	1.03
My time for family activities	100	4	1	5	2.38	0.98
My ability to cope with stress	100	6	1	7	3.00	1.24
My relationship with friends	100	6	1	7	4.18	1.73
My future outlook	100	6	1	7	3.72	1.68
My level of energy	100	5	1	6	3.33	1.20
My emotional well-being	100	6	1	7	3.11	1.20
My roles in life	100	4	1	5	3.16	0.97
My time for social activities with friends	100	6	1	7	3.00	1.28
My relationship with my family	100	6	1	7	4.30	1.29
My financial well-being	100	6	1	7	3.07	1.08
My relationship with the care recipient	100	6	1	7	4.60	1.23
My physical functioning	100	5	1	6	3.09	1.15
My general health	100	5	1	6	3.16	1.17

Source: compiled by the authors of this study

Moreover, most of the participants (82%) were experiencing serious strain (values above 15), and the rest 18% were experiencing low strain. The above result indicates that the caregivers in this study were experiencing serious financial hardship.

No significant differences were found in the BCOS total score and in the IPED total score, based on the demographic characteristics of the participants and the characteristics of the child's hospitalization.

There was a significant positive correlation between MSPSS total score and IPED total score (Spearman's $\rho=0.324$, $p=0.001$), indicating that greater perceived social support is associated with greater economic hardship (Table 3).

DISCUSSION

This study aimed to investigate the psychosocial and financial challenges faced by parents of hospitalized children in Greece, as well as the impact of their perceived social support. It seeks to provide reliable data that can be used to develop targeted interventions by healthcare professionals, social services, and health policy organizations.

The primary finding was that caregivers experienced negative changes and held moderate to negative perceptions of their caregiving role, as measured by the Bakas Caregiving Outcomes Scale (BCOS). This result aligns with numerous other studies showing that a child's hospitalization, especially in cases of chronic, severe, or life-threatening conditions, is a highly stressful event that affects parents' emotional, physical, social, and professional well-being [3, 4].

Specifically, the caregiver's life has improved in only four areas: self-esteem, relationships with friends, relationships with family, and relationships with the child. The improvement

in the caregiver's self-esteem and relationships with friends, family, and the child indicates that caregiving does not only have negative effects. On the contrary, it can lead to strengthening the caregiver's relationships and self-esteem as they take on an additional demanding role. This aspect is particularly important since most studies focus on the negative impacts of caregiving.

Conversely, the caregiver's life has worsened in all other areas (physical health, time for family activities, overall health, etc.). Similarly, other research has found a decline in physical health and an increased physical burden among parents of hospitalized children, which manifests as chronic fatigue, musculoskeletal pain, headaches, gastrointestinal symptoms, and immunosuppression, effects that may persist beyond the hospitalization period [1, 3, 5].

The most frequently mentioned need was emotional support, accounting for 55%. This finding highlights the profound psychological burden experienced by caregivers due to anxiety about the child's health, uncertainty regarding the course of hospitalization, and the overall exhaustion caused by constant vigilance and care. This need emphasizes the importance of psychological reinforcement through mental health interventions, counseling support, or parent support groups. This result aligns with similar findings from numerous studies that emphasize the high psychological strain on caregivers of hospitalized children [6, 8, 9, 10].

The need for rest and assistance with daily tasks indicates that physical fatigue and overload of responsibilities are also significant challenges. Caregivers often must pause or limit other social and family obligations without having alternative support options, which increases the caregiving burden and can lead to both physical and mental exhaustion.

Table 3. Spearman's correlations

Variable		BCOS Total score	IPED Total score	MSPSS Total score
BCOS total score	Spearman's rho	—		
	p-value	—		
IPED total score	Spearman's rho	-0.100	—	
	p-value	0.324	—	
MSPSS total score	Spearman's rho	0.082	0.324	—
	p-value	0.418	0.001	—
Parentage score	Spearman's rho	0.068	0.033	-0.022
	p-value	0.501	0.747	0.829
Childage score	Spearman's rho	0.214	-0.077	0.079
	p-value	0.033	0.449	0.433
Hospital_days	Spearman's rho	0.086	0.089	-0.083
	p-value	0.397	0.378	0.414
Number of children	Spearman's rho	-0.100	-0.039	0.095
	p-value	0.324	0.698	0.346

Source: compiled by the authors of this study

Regarding the composition of the sample, most of the hospitalized children were of school age (6–11 years), who are likely more exposed to infections or injuries requiring hospitalization. The high participation of preschool-aged children (2–5 years) also highlights a vulnerable group that relies entirely on their caregivers to address health issues. The small proportion of children under 1 year old (4%) may be related to the fact that infants are more often admitted to specialized units, which might not have been included in this study.

Most participants (18%) reported that grandparents were responsible for caregiving, indicating the central supportive role of the extended family. Grandparents appear to play an important role as consistent caregivers, especially in times of crisis or need, such as a child's hospitalization. Following this, 11% mentioned relatives or friends as alternative caregivers, reflecting the use of the families' social networks. Similarly, 5% hired a paid caregiver, which may suggest both financial means and a lack of available family support.

Therefore, there is a strong reliance on family relationships, particularly on the older generation, which should be considered in support interventions by recognizing the expanded caregiving needs that arise from a child's hospitalization.

In this study, the proportion of foreign caregivers was significant (30%). The presence of many foreign caregivers highlights the need to provide culturally sensitive care and possibly language assistance to ensure equal access to information and support. This multicultural composition emphasizes the importance of incorporating interpretation, intercultural mediation, and tailored communication tools into the design of caregiver support interventions, as linguistic or cultural barriers can negatively affect both the understanding

of the child's condition and the accompanying person's hospitalization experience.

Most participants (80%) reported being fairly or very well informed about their child's illness. This finding is particularly encouraging, as it demonstrates effective communication between healthcare professionals and parents/caregivers. Such information significantly helps reduce uncertainty, enhances the sense of control, and lowers anxiety, as supported by international literature [21–24]. Caregiver information is not only a right but also an empowering factor that facilitates emotional adjustment and strengthens trust in the healthcare system. Maintaining a consistent, clear, and accessible communication channel between medical staff and the family is essential for managing psychological stress.

Regarding the economic burden, the total score on the IPED ranges from 8 to 24, with scores above 15 indicating significant financial hardship. In this study, the average score was 17.67 (SD=2.17, Min=13.00, Max=23.00, Range=10.00). Furthermore, most participants (82%) were experiencing serious financial strain (scores above 15), while the remaining 18% were experiencing low strain. These results suggest that the caregivers in this study were facing considerable financial difficulties. Similarly, according to the Bakas Caregiving Outcomes Scale (BCOS) questionnaire, the financial well-being of parent caregivers had worsened. Forty-seven percent of participants reported that caring for a hospitalized child was burdensome not only psychologically but also financially. The deterioration in financial well-being reflected in the BCOS scores (almost one out of two burdened) aligns with Bakas et al. [16], confirming that caregiving responsibilities extend beyond psychological strain to tangible economic consequences

for the family unit. Caregivers face both direct and indirect costs, such as transportation, accommodation, medication expenses, and loss of income due to time away from work. This highlights the need for government support and programs to assist vulnerable families, especially when hospitalization is long-term.

From the above, it is evident that financial and emotional needs often coexist, creating a significant burden for the caregiver. Financial insecurity can increase mental stress, while the lack of emotional support intensifies the feeling of having no help. The combination of these two needs indicates a vulnerable population group that requires support through measures that include both financial relief and the provision of psychosocial services, both within and outside the hospital setting.

The mean score on the Multidimensional Scale of Perceived Social Support (MSPSS) was 4.24 (SD=0.39, minimum=3.08, maximum=5, range=1.92), indicating a moderate to high level of perceived social support. Additionally, all participants (100%) were categorized as having “moderate perceived social support” based on their overall total mean scores falling between 3 and 5.

No significant differences were observed in the total scores of the Bakas Caregiving Outcomes Scale (BCOS) or the Index of Personal Economic Distress (IPED) when considering the participants’ demographic characteristics or the details of the child’s hospitalization.

The positive correlation between social support and economic distress found in our study mirrors the observations of Economou et al.[15] and Madianos et al. [14], where was suggested that in the Greek cultural context, the perception of support is often ‘mobilized’ by the presence of severe financial or health crises, such as a child’s hospitalization, reinforcing the family’s role as a primary safety net.

This study’s strengths lie in its originality within the Greek population. However, it has several limitations. Being a cross-sectional study, it cannot establish causal relationships. Additionally, a convenience sampling method was employed at a single small regional hospital, which limits the generalizability of the findings. Furthermore, the use of self-reported questionnaires may lead to social desirability bias.

The study emphasizes the need for family-centered, institutional support for caregivers of hospitalized children. Key priorities include addressing caregivers’ psychosocial, emotional, physical, and financial burdens through targeted interventions such as mental health screening, stress reduction, improved communication with healthcare professionals, psychosocial support within hospitals, and financial and accommodation assistance. Supporting caregivers’ physical well-being, offering respite care, flexible work arrangements, and strengthening social support systems are essential to improving both caregiver well-being and the overall hospitalization and recovery experience of children.

Future research could explore the topic using a larger sample from various hospitals across Greece. It could also focus on parents of children hospitalized in pediatric hospitals or parents of children with specific medical diagnoses. Additionally, conducting a comparative study between caregivers who are parents of children and caregivers of adult patients using the same measurement tools would be of interest. Finally, specific demographic variables and caregiving characteristics could be examined to identify the factors that significantly contribute to caregiver burden.

CONCLUSIONS

This study highlights the significant and multifaceted burden borne by parents of hospitalized children at the General Hospital of Corinth, emphasizing the need for targeted interventions. The results show that caregivers face negative changes in almost all areas of their lives, with a predominant need for emotional support. The most striking finding concerns the disproportionately high level of financial hardship, which, although it seems to mobilize the informal social support network, highlights the inadequacy of institutional safety nets. The lack of formal financial assistance and facilitating arrangements exacerbates the psychological and physical burden, leading to severe stress. The study concludes that family-centered health policies should be implemented, which would incorporate the measurement of caregiver burden and the provision of practical and financial relief.

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CONFLICT OF INTEREST

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CREATIVE COMMONS 4.0

The efficacy of 755 nm Alexandrite laser in the treatment of hirsutism

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ABSTRACT

Aim: To evaluate the efficacy and safety of the 755 nm Alexandrite laser in the treatment of facial hirsutism.

Materials and Methods: 50 patients with facial hirsutism underwent 4 to 6 treatment sessions using the 755 nm Alexandrite laser, spaced three to four weeks apart. Clinical assessment was performed using the Ferriman-Gallwey scoring system prior to treatment. Patient response was assessed by their self-reported reduction in hair growth at the end of the protocol.

Results: Most of the patients experienced excessive hair growth on the cheeks, chin, and upper lip. Following treatment, 50% of patients reported a 50-75% reduction in hair growth, 30% reported a reduction greater than 75%, 10% reported a 25-50% reduction, and 10% reported a reduction of less than 25%. Mild erythema and slight discomfort were observed in a few patients.

Conclusions: The 755 nm Alexandrite laser appears to be a safe and effective option for long-term facial hair reduction in suitable patients. However, further studies are recommended.

KEYWORDS: hirsutism, Alexandrite laser therapy, erythema

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INTRODUCTION

The definition of hirsutism is the excessive growth of terminal hair in androgen-dependent areas of the body in women, including the face, chest, back, abdomen, and thighs. It results from increased androgen production (of ovarian or adrenal origin) or increased sensitivity of hair follicles to normal blood androgen levels [1]. According to the Ferriman-Gallwey classification system, hirsutism is diagnosed at a grade ≥ 8 , and its prevalence among women of reproductive age is approximately 5% [2]. The quantity and distribution of hair that is considered normal for a female differs based on her race as well as her understanding of societal, cultural, and familial standards. For example, women of Asian descent have very little face and body hair, while Mediterranean women often have moderate amounts [3]. With age, androgen-dependent hair growth patterns change. While facial hair grows more with age, terminal hair development in the pubic and axillary regions decreases. Because hirsutism is difficult to define, patients' terms such as „unwanted hair“ are used to assess the need for treatment [4]. For clinical and therapeutic aims, hirsutism can be classified according to the underlying causes into constitutional (dermatological), endocrine-based, iatrogenic (drug-induced), and ectopic-production. In one study, hormonal and ultrasound tests showed the most prevalent causes were polycystic ovary syndrome (60.8%), hyperprolactinoma (7.2%), idiopathic hirsutism (28.9%), and undetermined (3.1%) [5]. Hair can be removed by different methods, including mechanical (shaving or waxing), chemical (depilatory creams), electrolysis,

medication, and laser therapy. Among these, laser hair removal is fast, minimally invasive, and can achieve long-term reduction. Multiple treatment sessions are typically required at 4-8-week intervals to achieve optimal long-term hair reduction [6].

Laser parameters, including power, spot size, and pulse duration, determine the ultimate outcome of therapy. The outcomes are also impacted by skin parameters such as absorption, scattering, heat conduction, and density [7]. The laser hair removal fundamental concept depends on selective photothermolysis of the hair follicle while sparing the surrounding epidermis. It involves delivering a substantial amount of energy in a period of time equal to or less than the target's thermal relaxation time (TRT) [7]. Furthermore, the primary chromophore is melanin, which absorbs laser energy and translates it to heat that destroys the hair follicle. So, higher eumelanin absorption of the wavelengths caused greater damage to the darker hair [8]. Skin types are divided into 6 types (Fitzpatrick skin types I-VI) according to the density, size, and activity of melanosomes in the melanocytes. Darker hair and lighter skin (Fitzpatrick skin types I-IV) provide a perfect combination for successful laser hair removal. There is less likelihood of injury to the epidermis since absorption occurs more at the levels of follicular melanin than epidermal melanin [9]. By focusing on melanin in hair follicles, unwanted hair growth can be effectively reduced by various types of laser that have wavelengths within the red-infrared spectrum, including ruby, Alexandrite, diode, and Nd:YAG lasers. The

Alexandrite laser is a solid-state laser with a wavelength of 755 nm, which lies in the middle of the melanin-absorbing spectrum. The Alexandrite laser is frequently used on individuals with light skin types I-III. For individuals with a darker complexion, this wavelength is safer to use than ruby lasers [10]. After several treatments, the effectiveness rate of hair removal using Alexandrite has been observed to range from 40% to 80% after six months [11].

AIM

The aim of this study is to evaluate the efficacy and safety of the 755 nm Alexandrite laser in the treatment of facial hirsutism.

MATERIALS AND METHODS

STUDY DESIGN

From September 2024 to March 2025, a prospective, single-arm interventional medical study was conducted to assess the effectiveness and safety of Alexandrite lasers for hirsutism with each patient receives the service as their own control. Written informed consent was obtained from each patient. The target area was identified and documented. The Fitzpatrick skin phenotypic scale and the Ferriman-Gallwey scoring system were used to assess skin type and the severity of hirsutism, respectively.

EXCLUSION CRITERIA

Patients were excluded if they met any of the following: pregnant and lactating females, inflammatory skin diseases, active infection at the site of treatment, a history of hypertrophic or keloid scar formation, and females with clinical signs of hyperandrogenism.

TREATMENT PROTOCOL

Four to six treatment sessions spaced at 4-8 week intervals were conducted using an Alexandrite laser operating at 755 nm (Motus AXE, DEKA, Calenzano, Italy). A unique handpiece (Moveo, TM) with an integrated cooling system was attached to the laser. With respect to skin phenotype and hair thickness, the laser parameters were selected with a spot size of 6 mm, a pulse duration of 8.0 ms, and a fluence of 5 J/cm². All patients were instructed to avoid hair removal methods other than shaving or depilatory creams during the study period. They were asked to refrain from shaving for 10 days prior to the first session to allow proper clinical assessment and to shave approximately 24 hours before each laser session. They were additionally cautioned not to remove their hair using any kind of hair removal technique other than shaving or depilatory cream between sessions. Protective eyewear was worn by both the patient and medical staff during each treatment session. Following the laser session, all patients received post-operative care, including ice application for a few minutes immediately after laser sessions, prophylactic topical antibiotics, avoiding the sun, and using sunscreen cream.

CLINICAL ASSESSMENT

Clinical assessment was performed using the Ferriman-Gallwey scoring system at baseline and one month after

the final session. Standardised digital photographs were obtained under identical lighting and positioning conditions before and after treatment. Two independent dermatologists, blinded to the treatment session number, evaluated the photographs to assess improvement. Treatment response was categorised as poor (<25%), fair (25-50%), good (50-75%), and excellent (>75%) based on both photographic evaluation and patient self-assessment.

STATISTICAL ANALYSIS

Data were analysed using SPSS software version 26. Descriptive statistics were used to summarise demographic and clinical data. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequencies and percentages.

ETHICAL APPROVAL

The article focused on the ethical tents articulated in the Declaration of Helsinki and has ethical approval of Hammurabi College of Medicine, University of Babylon.

RESULTS

This study included fifty female participants with an age range from 20 to 40 years old (a mean age $\pm$ SD of 30 $\pm$ 5.6 years). Skin phenotype III, with dark, coarse hair, was present in all of them. Excessive hair growth was observed on the cheeks, chin, upper lip and upper forehead in 20 patients, while 20 patients had involvement of the cheeks, chin, upper lip, and neck. 10 patients had isolated chin involvement (Table 1).

The assessment of the severity of hirsutism in the face (cheeks, chin, upper lip, and forehead) and neck was evaluated according to the Ferriman-Gallwey scoring system. When there was no excessive terminal hair, the scale was zero; when there was significant hair, the scale was 4. The mean score for both cheeks and chin was 4; for the neck, it was 3; for the upper lip, it was 2; and for the forehead, it was 1 (Table 2).

All patients received between four and six treatment sessions depending on clinical severity and response to therapy. In this study, 40% of the patients showed favourable results with only 4 sessions, however 20% of them had 5 sessions and another 20% of the patients required up to 6 (Table 3).

The successful outcomes of the therapy were evaluated by calculating the hair reduction (comparing the fraction of terminal hairs before and after laser treatment). The results showed that 50% of the patients reported 50-75% hair reduction, 30% showed >75% hair reduction, 10% showed 25-50% hair reduction, and another 10% of the patients showed <25% hair reduction (Table 4, Fig. 1). The post-treatment Ferriman-Gallwey scores demonstrated a marked reduction compared with baseline values, supporting the clinical improvement observed in photographic analysis.

Regarding the adverse effects, some participants noticed a slight erythema, with mild pain reported, especially in those patients who did not shave well enough before the time of the session.

Table 1. Area of hirsutism treated with alexandrite laser

Site of hirsutism	Number of patients	Percentage
Cheeks, chin, upper lips and forehead	20	40%
Cheeks, chin, upper lips, and neck	20	40%
Chin only	10	20%

Source: compiled by the authors of this study

Table 2. Severity of hirsutism in the treated areas

Site of hirsutism	Grading of severity
Cheeks	4
Chins	4
Neck	3
Upper lip	2
Forehead	1

Source: compiled by the authors of this study

Table 3. Number of sessions needed for treatment

Number of sessions	Number of patients	Percentage
1	0	0.0 %
2	4	8%
3	6	12%
4	20	40%
5	10	20%
6	10	20%

Source: compiled by the authors of this study

Table 4. Hair reduction after laser treatment

Hair reduction	Number of patients	Percentage
<25%	5	10%
25-50%	5	10%
50-75%	25	50%
>75%	15	30%

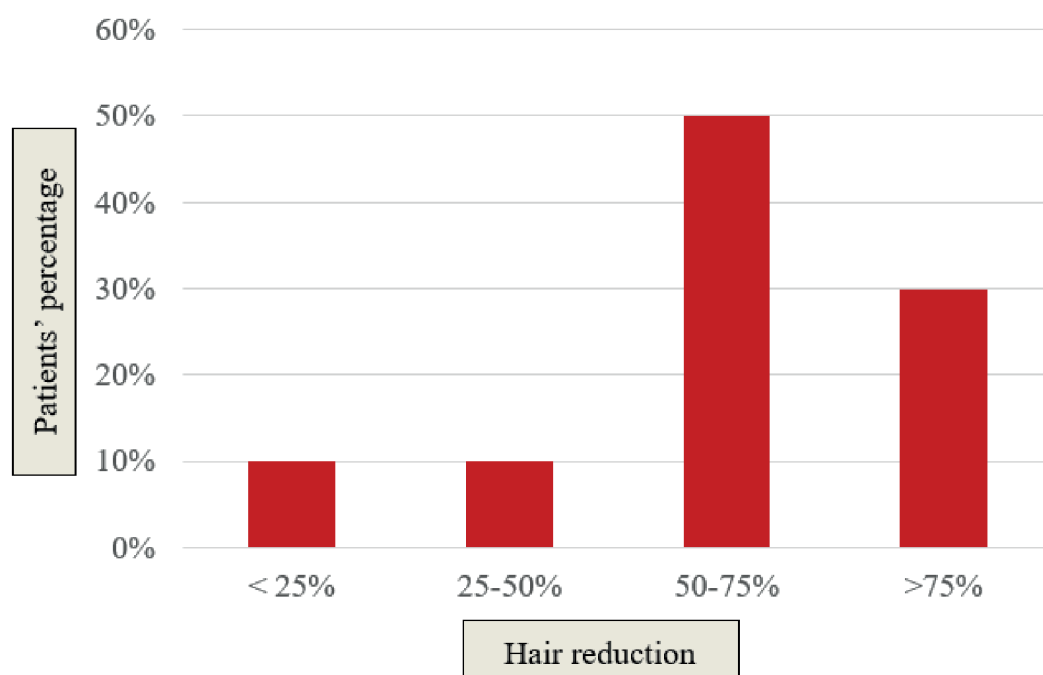
Source: compiled by the authors of this study

DISCUSSION

Currently, the majority of hair removal treatments are performed using Alexandrite lasers, diode lasers, and intense pulsed light devices. The long-pulse (755 nm) Alexandrite laser has been reported to be effective in hair reduction since 1997. The devices' physical properties exhibit notable variations with respect to the wavelength of light, pulse duration, spot size, and fluence [12].

When selecting the treatment settings, Fitzpatrick skin type and hair colour are the primary clinical criteria to consider [9]. Despite its ability to penetrate deeply into the dermis, the laser can effectively treat both fair and black hair. However, due to the competition with melanin, the long-pulse (755 nm) Alexandrite laser is mostly utilised for skin types II-IV because of the risk of hyper- or hypopigmentation. Additionally, to avoid this problem, we utilised a specific handpiece with a cooled sapphire cylinder tip that reduces epidermal injury [13, 14].

When compared to other lasers or light-based methods, several studies have shown Alexandrite and diode laser systems are effective option in long-term hair reduction.

**Fig. 1.** Percentage of hair reduction response after laser treatment

Source: compiled by the authors of this study

A study evaluating the effectiveness of three laser systems found mean hair reduction rates of 59.5%, 70.3%, and 47.4% with diode, Alexandrite, and Nd:YAG lasers, respectively [15, 16]. Another study compared the efficacy of Alexandrite and intense pulsed light systems, reporting that six sessions of Alexandrite laser treatment led to longer hair-free intervals compared to IPL. Hair count reduction was significantly larger on the Alexandrite side compared to the intense pulsed light, 46% and 27%, respectively [17].

About the efficacy of therapy, 80% of the patients enrolled in the current study showed more than 50% hair reduction. These results were comparable with the findings of the Mustafa FH et al. study, which reported 40-80% hair reduction after treatment sessions within six months [11]. Moreover, the study findings were comparable with the Nistico SP et al. study that evaluated a total of 49 patients with a mean age of 32.6 years and Fitzpatrick skin types of II to IV treated with Alexandrite laser on the face, limbs, and inguinal and axillary areas. A marked reduction in hair regrowth was noted 3 months after the final treatment in all areas studied, with the face showing a 76-90% reduction of the hair [18].

Regarding the safety of the Alexandrite laser, the current study reported only slight adverse effects, mainly slight erythema and transient discomfort, particularly in those who did not properly shave before the session. Signs of paradoxical hypertrichosis, cutaneous infection, dyspigmentation, or scarring were not reported. These outcomes were comparable with the findings of the Chen C et al. study, which reported less than 4.5% of adverse effects were likely

to occur, including hyper- and hypopigmentation [19].

Another prospective trial by Nistico SP et al. evaluated the efficacy of the Alexandrite laser for 16 patients with hirsutism. The study reported only mild erythema and pain following the treatment sessions in 7 patients (57% had skin type V), which persisted for 3-4 days and faded away [20].

Several local studies in Iraq revealed that hirsutism was a common symptom in women, with idiopathic hirsutism being the most common cause among young females, followed by polycystic ovary syndrome. Laser treatment of unwanted hair is a safe, well-tolerated, and effective therapeutic option, which leads to high patient satisfaction [21].

Although a parallel control group was not included, each patient served as her own control through pre- and post-treatment comparison. Spontaneous reduction of terminal hair in established hirsutism is unlikely without hormonal or pharmacologic intervention. Therefore, the observed reduction is reasonably attributable to the laser treatment. Objective evaluation using standardised photography and blinded dermatologic assessment was also performed to minimise subjective bias.

CONCLUSIONS

Laser hair removal using a 755 nm Alexandrite laser achieves a significant and long-lasting reduction in facial hair growth in women with hirsutism. The procedure has been generally well-received, with only minor temporary side effects.

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CONFLICT OF INTEREST

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ORIGINAL ARTICLE

Legal and bioethical aspects of euthanasia: A comparative analysis of international practice and the Ukrainian experience

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ABSTRACT

Aim: To define the legal and bioethical aspects of the euthanasia problem in comparison with existing international practices and Ukrainian experience.

Materials and Methods: A descriptive and comparative study of the regulatory frameworks of seven jurisdictions (2020-2026). A sociological survey (N=540) of healthcare workers and medical students at the Bogomolets National Medical University and the National Cancer Institute (2025) was conducted using an adapted End-of-Life Attitude Scale.

Results: The global legal trend of 2024-2026 is characterised by an expansion of criteria for access to euthanasia (France, the United Kingdom, Ecuador). The proportion of healthcare workers who categorically reject euthanasia was only 15.0% (95% CI: 12.2-18.3%). The level of rejection of euthanasia among believers (religious persons) (15.9%) did not statistically differ from that of non-believers (non-religious persons) (12.9%) ($p=0.37$).

Conclusions: The Ukrainian medical community demonstrates a significantly higher level of openness to discussing euthanasia (85.0%) than current conservative legislation assumes. Religious identity is not a statistically significant predictor of a negative attitude toward euthanasia. The results substantiate the need for legislative dialogue on palliative care and the right to a dignified end of life in Ukraine.

KEY WORDS: euthanasia, legalization, sociological research, bioethics, dignity

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INTRODUCTION

The issue of legal regulation of euthanasia and assisted suicide is one of the most acute dilemmas of modern jurisprudence and bioethics, situated at the intersection of criminal law, constitutional guarantees, and bioethical standards. Over the past decades, a clear trend has emerged toward rethinking the classical concept of the «sanctity of life» [1, 2] in favour of the individual's right to autonomy and dignity in the dying process, which also aligns with one of the principles of bioethics [3]. International practice demonstrates a profound diversification of approaches: from the full legalization of active forms of euthanasia in the Benelux countries and Canada [4] to the strict prohibition and criminal prosecution of any form of assistance in dying in countries with established religious or conservative legal traditions. The global legal landscape today is shaped by the development of medical technologies that allow for the artificial maintenance of life over extended periods, which in turn brings to the forefront the question of the human right to a «good death» [5].

The relevance of this research is determined by the global transformation of bioethical standards and legal paradigms regarding end-of-life issues [6, 7]. At the current stage, an evolution in the criteria for access to euthanasia is observed: whereas previously the decisive factor was exclusively the terminal stage of a disease, the newest practice (Spain, the Netherlands) shifts the focus to the

category of «unbearable and constant suffering», which encompasses not only somatic but also severe psychological states [8]. A separate role in this process is played by judicial practice; in particular, the experience of Italy (2024-2025) demonstrates how Constitutional Court decisions legitimise assistance in ending life on the condition of a patient's dependence on life-sustaining means [7].

In Ukraine, however, a conservative approach persists: current legislation (Part 4, Art. 281 of the Civil Code of Ukraine [9] and Art. 52 of the Fundamentals of Healthcare Legislation [10]) contains an imperative prohibition of any form of accelerating death.

AIM

To define the legal and bioethical aspects of the euthanasia problem in comparison with existing international practices and the Ukrainian experience.

MATERIALS AND METHODS

The study is based on a comprehensive methodological approach combining methods of theoretical-legal analysis and empirical sociological research. A descriptive and comparative study was conducted of the legislation of Ukraine and the legislation of selected countries (France, Spain, Italy, Slovenia, the United Kingdom, and Ecuador) as of 2024-2026. Both legislative acts and constitutional court decisions were analysed. A systematic review of scientific publications for

the period 2020–2026 was carried out. A sociological survey was conducted. A total of 540 respondents were included in the study sample. Data collection was carried out in 2025 at the Bogomolets National Medical University and the National Cancer Institute. The study used an anonymous questionnaire based on an adapted End-of-Life Attitude Scale [11].

The statistical processing was performed using IBM SPSS Statistics v. 29. Qualitative variables are presented as absolute frequencies (n) and relative frequencies (%) with 95% confidence intervals (Wilson method). Pearson's χ^2 test was used for comparing frequencies between groups (believers [religious persons] vs. non-believers [non-religious persons]). Differences were considered statistically significant at $p < 0.05$.

ETHICS

The study was conducted in accordance with the principles of the Declaration of Helsinki and bioethical standards for conducting sociological surveys in the medical field. All survey participants (N=540) were informed of the research objectives and provided voluntary informed consent to participate. Participation was fully anonymous, guaranteeing the protection of personal data and the professional reputation of respondents. Data processing was carried out in a depersonalized form. Results are presented in summary tables and charts, which makes it impossible to identify specific individuals. The research protocol and instrument (questionnaire) underwent peer review and received approval from the local Bioethics Committees of the Bogomolets National Medical University.

FRAMEWORK

The study was conducted within the framework of a research project of the Bogomolets National Medical

University 2023–2025: «Human Life, Health, and Death in the Context of the Development of Biomedical Technologies: Philosophical, Bioethical, Sociological, and Historical Aspects» № 0123U101123.

RESULTS

Any form of euthanasia in Ukraine is prohibited. The main regulatory legal acts are: the Civil Code of Ukraine (Part 4, Art. 281), which explicitly prohibits granting a natural person's request to terminate their life [9]; and the Fundamentals of Healthcare Legislation (Art. 52), which prohibits medical workers from intentionally accelerating the death of a patient [10]. Despite past attempts to legalize passive euthanasia, the draft new Civil Code of Ukraine (the Code of Private Law) maintains the existing approach (Part 3, Art. 300): granting a natural person's request to terminate their life, including all forms of euthanasia and measures of assisted suicide, is prohibited [9].

There are studies [12] demonstrating that the right to life, enshrined in Art. 27 of the Constitution, should logically include the individual's right to determine the moment of its ending [12, 15]. Research also attests to the existence of a «latent» practice in which physicians or relatives, with unofficial consent, discontinue intensive care for terminally ill patients, which is legally classified as «failure to provide assistance» but is de facto passive euthanasia [12].

To visualise the differences in global approaches to the regulation of end-of-life issues and to determine Ukraine's position in this system, we systematised data according to key bioethical and legal parameters (see Table 1) [2, 6, 8].

Table 1 presents a systematic comparison of global models of euthanasia regulation with an emphasis on the specifics of Ukrainian legislation. The analysis reveals a profound

Table 1. Typology of Legal Models and Bioethical Dominants

Comparison Parameter	Liberal Model (Belgium, Netherlands)	Assisted Suicide Model (Switzerland, Oregon – USA)	Conservative Model (Ukraine, Poland, France)
Legal Classification	Legalized active euthanasia: direct administration of a drug by a physician	Decriminalization of assistance: the physician provides the means, but the patient self-administers	Strict prohibition: active actions are treated as premeditated murder
Bioethical Dominant	Personal autonomy: the right of a person to control their own body and death	Right to dignity: minimizing suffering while preserving the patient's subjectivity	Sanctity of life: life is the highest value, over which a person has no disposal
Role of Physician	Active executor of the patient's will	Intermediary (expert and provider of means)	Guardian of life; acts on the principle of Non-maleficence (do no harm)
Status of Passive Euthanasia	Permitted and regulated	Permitted (refusal of treatment)	Ukraine: formally prohibited, but de facto exists through the right to refuse medical care
Public Discourse in Ukraine	Perceived as a threat of abuse due to corruption in medicine	Viewed as a «lesser evil», but not legislatively supported	Dominant model, supported by religious communities and legislation
Key Risk (per Scopus)	«Slippery slope» – expansion of practice to the mentally ill and children	Commercialization («suicide tourism» in Switzerland)	«Latent euthanasia» – uncontrolled cessation of treatment without legal protection for the physician

Source: compiled by the authors based on [2, 6, 8]

dichotomy between the liberal model (Benelux) [13], where the principle of personal autonomy dominates, and the conservative model to which Ukraine belongs [1, 2].

A key aspect of comparison is the transformation of the physician’s role: from an active subject executing the patient’s will in liberal-model countries to strict adherence to the principle of non-maleficence (do no harm) in domestic practice [2, 4]. Of particular scholarly interest is the problem of «latent euthanasia» in Ukraine. Unlike countries with developed assisted suicide (Switzerland) [6, 14], where risks are associated with the commercialisation of procedures, in Ukraine the primary danger lies in the absence of legal immunity for physicians when discontinuing ineffective treatment for terminally ill patients. Decriminalisation for physicians or other persons must be accompanied by appropriate and adequate safeguards to prevent abuse and thereby ensure respect for the right to life.

The main conflict in Ukraine revolves around the principle of the «sanctity of life» (traditional and religious ethics) versus the principle of the «quality of life» (liberal bioethics) [8, 12].

Table 2 demonstrates the dynamics of expanding criteria for access to end-of-life procedures in international practice and the inertia of national legislation [3, 7].

The comparative analysis indicates several critical trends:

1. Evolution of Grounds: While the Dutch experience is based on the evaluative category of «unbearable suffering» [13, 16], the newest Spanish legislation (LORE, 2021) introduces more precise criteria for chronic di-

sability, which expands the circle of subjects entitled to the right to death.

2. Sources of Legitimation: The Italian case (Constitutional Court Decision No. 135/2024) illustrates a model of legalization via a Constitutional Court ruling, based on the patient’s technological dependence on life-support systems [7]. This creates an intermediate link between passive and active forms of assistance.
3. The Static Nature of Ukrainian Law: Against the backdrop of gradual European liberalization in a number of European countries, Ukraine maintains a strict normative adherence to the Criminal and Civil Codes and specialized legislation. In Ukraine, the issue of palliative care is often viewed in the context of a type of medical care, rather than as comprehensive legal provision of the right to a dignified end of life. Even the practice of the European Court of Human Rights (cases of *Pretty v. the UK*, *Mortier v. Belgium*, *Lambert and Others v. France*, and others) is very cautious, leaving States a wide margin of appreciation on issues of assisted suicide, without obliging them to undertake radical liberalization. The various aspects of the euthanasia prohibition in Ukrainian legislation are presented in Table 3.

In 2025, at the Bogomolets National Medical University and the National Cancer Institute, a study was conducted among healthcare workers and persons with medical education regarding their attitudes toward the euthanasia

Table 2. Comparative Analysis of Regulatory Legislation

Country	Status	Key Document	Criterion (Health Condition)
Netherlands	Legal	Act 2002 [19]	Unbearable suffering without prospect of improvement.
Spain	Legal	LORE (2021) [18]	Serious, incurable disease or chronic disability.
Italy	De facto legal	Constitutional Court Decision №. 135/2024 [21]	Dependence on life-support systems + irreversibility.
Ukraine	Prohibited	Criminal Code of Ukraine, Civil Code of Ukraine [9]	Prohibition of active euthanasia (Art. 52 of the Public Health Fundamentals Act) [20]

Source: compiled by the authors based on [9, 18, 19, 20, 21]

Table 3. Barrier Matrix: Why Do Changes Not Occur?

Barrier Category	Core Argument	Potential Risk of Change
Constitutional	Art. 27: The State is a guarantor of life, not death [22]	Risk of any euthanasia law being declared unconstitutional
Ethico-Religious	„Sanctity of life”: Influence of the All-Ukrainian Council of Churches and Religious Organizations (AUCCRO) [23]	Loss of political support from the conservative electorate
Systemic-Criminal	Institutional weakness: the judicial and medical systems are perceived as corrupt	Use of euthanasia to conceal crimes or seize property

Source: compiled by the authors based on [22, 23]

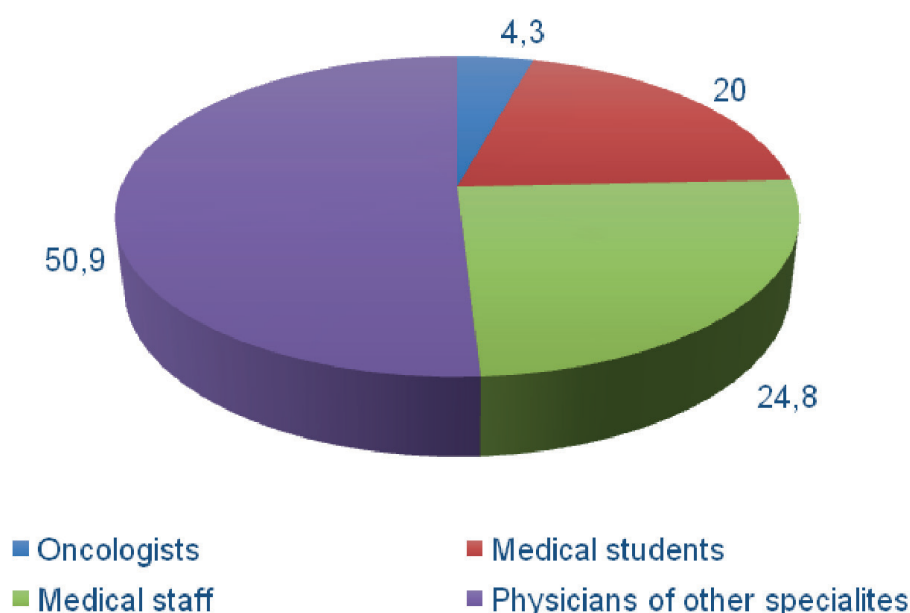


Fig. 1. The Profile (%) of the Enrolled Study Sample (N=540)

Picture taken by the authors

problem (N=540) (See Fig. 1). Among the respondents were oncologists (N=23; 4.3%), medical students (N=108; 20.0%), medical personnel (N=134; 24.8%), and physicians of other specialties (N=275; 50.9%) (Fig. 1). The sample was representative of the medical field, as it encompassed both experienced specialists (physicians of various profiles comprised over 50%) and the future generation of physicians (students – 20%). The smallest but most critical group consisted of oncologists (4.3%), who daily faced palliative conditions.

Among those surveyed, the vast majority identified themselves as religious (N=377; 69.8% [95% CI: 65.8-73.5%]), of whom Christianity was indicated as the denomination (N=355; 65.7%). The study records a high degree of religiosity among Ukrainian medical professionals. In the context of the research, this is an important argument, as it refutes the stereotype that religiosity is an absolute barrier to consideration of the euthanasia issue [5].

Only 15.0% (n=81; 95% CI: 12.2-18.3%) of respondents expressed the opinion that euthanasia is unacceptable under any circumstances. This means that 85.0% (n=459; 95% CI: 81.7-87.8%) of surveyed medical professionals are potentially open to discussing certain forms of assistance in dying, or at least do not reject the idea a priori. This indicator reflects a serious gap between Ukrainian legislation and the views of the professional community [9].

Comparative analysis by religious identity revealed that among religious respondents (n=377), 15.9% (n=60) were categorically opposed to euthanasia, while among non-religious respondents (N=163) – 12.9% (N=21). The difference between the groups did not reach statistical significance ($\chi^2=0.82$; df=1; p=0.37), indicating the absence of any influence of religious identity on the basic openness to dialogue on euthanasia issues in the studied sample.

International experience in 2024-2026 demonstrates that the legalization of euthanasia has ceased to be a local experiment of individual countries and has become a global legal challenge [8, 13]. For Ukraine, the most relevant approaches are the British model (lengthy preparation and strict criteria) and the Ecuadorian experience of decriminalization through a body of constitutional jurisdiction, which allows for avoiding political populism when resolving fundamental bioethical questions (Table 4).

The experience of Ecuador (2024-2025) [17] confirms the global trend in which the Constitutional Court outpaces the parliament, recognising the right to death as derived from the right to a dignified life. This establishes an important precedent for Latin American countries and potentially for Ukraine, where the judicial path to resolving bioethical conflicts may prove more productive than the legislative one. The results of the referendum in Slovenia (November 2025) [8] are important for analysing the Ukrainian context. Citizens' rejection of the legalisation of assisted suicide underscores that, despite the general European trend towards liberalisation, society in countries with a particular socio-cultural background retains a high level of concern about the risks of abuse (Table 4).

DISCUSSION

The finding that only 15% of Ukrainian medical professionals categorically reject euthanasia is striking against the backdrop of a legal prohibition that admits no exceptions. It echoes patterns documented in Canada before the legalisation of Medical Assistance in Dying (MAID), where prolonged clinical exposure to terminal suffering proved a stronger driver of attitudinal change than legislative debate [4]. The parallel with France (2026) and the United Kingdom (2025) is also telling: in both countries, gradual shifts in

Table 4. Current Data on International Practices

Country / Region	International Practice	Legal Source
Slovenia	Rejected. In November 2025, citizens voted against legalizing assisted suicide in a referendum	Referendum 23.11.2025 [24]
France	Adopted. In January 2026, the Senate and National Assembly agreed on a law on «Assistance in Dying»	Law of 07.01.2026 [25]
United Kingdom	In progress. The House of Commons supported the bill in June 2025. Implementation expected by 2029	Terminally Ill Adults Bill [26]
Ecuador	Legal. The court decriminalized active euthanasia in 2024, and secondary regulations by the Ministry of Health were adopted in 2025	Constitutional Court Decision [17]

Source: compiled by the authors based on [17, 24, 25, 26]

professional opinion preceded and ultimately enabled parliamentary reform [3]. Our data suggest Ukraine may be at a similar inflection point – with professional attitudes already moving towards a quality-of-life and autonomy-centred model [1], while the legal framework remains anchored in a sanctity-of-life paradigm.

The religiosity finding deserves particular attention. Ukraine is a predominantly Christian society, and religious institutions have consistently been among the strongest voices against any discussion of euthanasia. Yet our data show that among believing physicians, the rejection rate is comparable to that among non-believers. This is not an isolated result: Smets et al. (2011) found a similar pattern among Belgian physicians practising within a Catholic cultural context [2], and Spain’s legalisation of euthanasia (LORE, 2021) proceeded despite strong Church opposition, reflecting a practical divergence between institutional doctrine and individual clinical judgment [8]. The implication for Ukrainian policy is important: framing the euthanasia debate primarily as a religious question may misrepresent the actual landscape of professional opinion [5].

The most pressing practical problem, however, is not legalization but the «grey zone» that already exists. Nesterenko & Lytvynenko (2024) documented a widespread informal practice of withdrawing life-sustaining treatment without any legal framework to protect the physicians involved [12]. This is not passive euthanasia in the legal sense – it is an uncontrolled, undocumented practice that carries criminal risk for clinicians and offers no procedural guarantees for patients or families. The Swiss experience is a cautionary reference here: even a well-established legal framework can generate unintended consequences such as commercialization and ‘suicide tourism’ if eligibility criteria are insufficiently precise [6, 14]. A more immediately achievable step for Ukraine would be the formal regulation of treatment withdrawal

– standardized protocols, ethics committee oversight, legal immunity for physicians acting in good faith. This would not require constitutional amendment and would directly address the harm caused by the current vacuum. A further-reaching reform, modeled on the Dutch [13, 16] or French [3, 7] frameworks, could follow once institutional trust and oversight capacity are established.

CONCLUSIONS

Global trends of 2024-2026 demonstrate a tendency towards expanding the criteria for access to euthanasia, where the primary measure is no longer the terminal nature of the condition but the intolerability of the patient’s suffering. The experience of France and Ecuador confirms that legalisation is possible both through parliamentary reforms and through judicial activism. The Ukrainian regulatory model remains among the most restrictive in Europe, creating a significant gap between the formal prohibition and the existing latent practice of passive euthanasia.

Empirical data from 2025 attest to a high readiness of the Ukrainian medical community for decriminalisation of certain forms of assistance in a dignified end of life: the majority of surveyed medical professionals do not consider euthanasia unacceptable under any circumstances, which creates a foundation for the revision of legislative norms. Religious identity is not a significant predictor of a negative attitude towards euthanasia, which refutes the widespread argument about the decisive role of the confessional factor in the conservatism of the Ukrainian medical environment.

A phased transition appears advisable for Ukraine: from the legalisation of clear protocols for the withdrawal of treatment (passive euthanasia) to the development of a strictly regulated model of assisted suicide for terminally ill patients, which will allow avoiding the risk of a ‘slippery slope’ and ensuring state control over the process.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Peculiarities of security-sector specialists' psychological adaptation to stressful conditions of professional activities

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ABSTRACT

Aim: To investigate indicators of psychological adaptation among security-sector specialists to the stressful conditions of professional activities during wartime.

Materials and Methods: The research, which lasted from 2023 to 2025, involved 120 male security-sector specialists: experimental group (EG, n=60) – specialists who performed their service duties in combat conditions; control group (CG, n=60) – specialists whose activities took place in conditions of relative safety. Research methods: theoretical analysis and generalization of literature, psychological methods, and statistical methods.

Results: A significantly higher level of both reactive (by 7.06 points; $p < 0.01$) and personal (by 4.29 points; $p < 0.05$) anxiety has been found in the CG specialists compared to the EG. It has been found that specialists in the EG, compared to the CG, demonstrated significantly worse indicators of satisfaction: with themselves, their mental state – by 7.32 points; the situation and its dynamics – by 6.19 points; the sphere of interpersonal relationships – by 2.37 points; their functional state – by 2.47 points; their life-sustaining activities in general – by 7.23 points.

Conclusions: It has been proven that unfavorable factors of combat conditions and excessive physical and mental stress in wartime lead to a gradual loss of satisfaction with life-sustaining activities, an increased risk of developing stress disorders accompanied by symptoms of avoidance, distress, exhaustion, and re-experiencing trauma. The intensity and excessiveness of psycho-traumatic influences, the inability to form psychological defense mechanisms, and the severity of psychosomatic components of the stress response significantly alter the adaptive capabilities of security-sector specialists.

KEYWORDS: adaptation, security-sector specialists, professional activities, stress, combat operations, psyche

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INTRODUCTION

The professional activities of security-sector specialists (SSSs) in conditions of active combat operations are not without negative consequences for their mental health [1, 2]. Fear for one's own life; physical injuries; encounters with situations involving the execution of uncomfortable orders that run counter to moral and ethical beliefs; often the lack of necessary every day, "peaceful" conditions; lack of adequate nutrition and sleep have a powerful impact on the SSS, placing increased demands on both the psychophysical state of the body and their individual indicators, which determine the success of their service activities in extreme conditions.

In the combat zone, SSS officers are subjected to constant stress [3]. Prolonged tension of biological, physical, and psychological functions naturally leads to the depletion of the body's defenses and psychological trauma. The formation of psychological readiness to work in combat conditions, associated with motivational, regulatory, cognitive, and communicative processes, increases the stress resilience and adaptation of the SSS in crises of war [4].

The successful adaptation of the SSS to specific working conditions is a complex phenomenon determined not only

by professional but also by socio-psychological factors. Researchers [5, 6] argue that the following factors are conducive to successful adaptation: satisfaction with interpersonal relationships, including professional ones, satisfaction with one's functional state, and life-sustaining activities in general. The modern professional reality of the SSS is an inexhaustible source of psycho-traumatic situations, which are understood as extreme critical events, threatening situations that have a powerful and negative impact on the individual and require extraordinary efforts to overcome the consequences of this impact [7, 8]. They take the form of unusual circumstances or events that expose specialists to extreme, intense, and extraordinary influences that threaten their lives and health and those of their loved ones and fundamentally violate their sense of security. Traumatic events during the SSS's service activities are stressors with strong negative potential [9]. Such events lead to traumatic stress experiences for police officers, the psychological consequences of which are diverse and unpredictable. Hence, the ability to counteract the impact of stressful phenomena on the individual and adapt to crisis conditions in service activities is of significant importance.

Scientists argue [10-13] that excessive exposure to complex psychogenic or somatic factors can exceed an individual's adaptive capacity; prolonged exposure to stressors can lead to exhaustion. In such circumstances, attention should be paid to the adaptation period that SSSs undergo while performing their functional duties in wartime conditions. According to experts [14-16], it is the control of the individual barrier of mental adaptation that allows reducing the impact of psycho-traumatic situations on the individual, lowering the risk of mental problems, and reducing feelings of alienation and social isolation. At the same time, understanding the meaning of events in the surrounding environment contributes to the specialist's faster adaptation to the social environment. It activates their personal growth after experiencing psychological trauma. In the long term, this requires the use of modern approaches when working with SSSs under constant stress in their professional activities.

AIM

The aim is to investigate indicators of psychological adaptation among security-sector specialists to the stressful conditions of professional activities during wartime.

MATERIALS AND METHODS

PARTICIPANTS

The research, which lasted from 2023 to 2025, involved 120 male security-sector specialists (law enforcement officers): experimental group (EG, $n=60$) – law enforcement officers who performed their service duties in combat conditions; control group (CG, $n=60$) – law enforcement officers whose professional activities took place in conditions of relative safety. Age and length of service were not taken into account, but they corresponded to the active phase of the law enforcement officers' professional activities. The criteria for respondent inclusion were as follows: research participants are law enforcement officers who perform their service duties; no contraindications related to mental or physical health. The exclusion criterion was the respondents' desire to withdraw from the research at any time. The ascertaining stage of the research was conducted at the Odesa State University of Internal Affairs (OSUIA, Odesa, Ukraine), where police officers attended advanced training. At this stage of the research, the key parameters of the SSS's adaptive capabilities were analyzed. The final stage was the generalization, statistical processing, and interpretation of the results obtained. Thus, the research was organized on the principles of gradualism and systematicity, which ensured a complete reproduction of the empirical picture of the SSS's adaptive characteristics under high levels of risk and stress.

RESEARCH METHODS

Theoretical analysis and generalization of literature, psychological methods, statistical methods. The method of theoretical analysis and generalization of literature was used to study scientific sources on the topic of research (30 sources from MedLine, Scopus and Web of Science databases were studied).

To determine the peculiarities of the SSS's adaptation to stressful conditions, a set of psycho-diagnostic techniques was used: the "Reactive and Personal Anxiety Scale" (RPAS), the "Adaptation Assessment Questionnaire" (AAQ), and the "Traumatic Stress Questionnaire" (TSQ).

The RPAS technique is one of the tools for studying the psychological phenomenon of anxiety. The questionnaire consists of 20 statements that refer to anxiety as a state (anxious state, reactive or situational anxiety) and 20 statements that define anxiety as a tendency, a personality trait (anxious trait) [17]. If the anxiety level does not exceed 30 points, it means that the respondent does not feel particularly anxious, i. e., they are not very anxious at the moment. If the score is between 31 and 45, this indicates moderate anxiety. Very high anxiety (46 points or above) is directly related to the presence of neurotic conflicts, mood, and neurotic disorders, and psychosomatic disorders. In contrast, low anxiety (12 points or below) describes a state of depression, lack of response, and low motivation. The use of the reactive and personal anxiety scale in the context of this research is methodologically justified, since this technique allows for the differentiated measurement of anxiety both as a personality trait and as a psycho-emotional state.

The Adaptation Assessment Questionnaire (AAQ) [18] was chosen to assess the level of personality adaptation under conditions of high psycho-emotional stress, characteristic of the SSS's activities during the war. The questionnaire consists of 5 scales: satisfaction with oneself and one's mental state; satisfaction with the situation and its dynamics; satisfaction with the sphere of interpersonal relations; satisfaction with one's functional state; satisfaction with life-sustaining activities. Each scale consists of 6 items. Each item has 4 answer options (a, b, c, d), corresponding to the numbers 0, 1, 2, 3. When calculating, the total score for each scale can range from 0 (all answers "a") to 18 (all answers "d") points. The following classifications are taken into account in the interpretation: 0-3 points – unreliable results due to ignorance, naivety of the current problem; 4-6 points – successful adaptation, no serious problems; 7-9 points – "normal" level of stress that does not pose a threat to human health and well-being; 10-12 points – sub-extreme stressful situation, possibly exhaustion, dissatisfaction with life (psychological counseling is needed); 13-15 points – difficult life situations (psychological help and psychotherapy are needed); 16-18 points – situations that threaten mental health (there is a risk of suicide; urgent psychological help is needed).

The Traumatic Stress Questionnaire (TSQ) allows conclusions to be drawn about the relative severity of individual symptom groups [19]. Scale values below 50 T-points are usually asymptomatic. In the 50-65 T-point range, individual symptoms may appear after stress and are relatively obvious. A T-indicator of 65-70 points usually corresponds to a diagnosis of "partial" post-traumatic stress disorder (PTSD) or acute stress disorder (ASD). A T-indicator above 70 points significantly increases the likelihood of a clinically manifest disorder, and a T-indicator above 80 points

requires a definitive clinical diagnosis of PTSD or "full-blown" ASD. The "threshold" values given in T-points are usually intended only for assessing the overall indicators of PTSD and ASD, as well as individual subscales and depression scales. However, the range of 50-65-70-80 and higher T-indicators is "valid" as operational criteria for assessing the severity of post-traumatic conditions. At the same time, the summation calculates the values of the control and main subscales of PTSD and ASD: L (lie), Ag (aggravation), Di (dissimulation), depres (depression); PTSD: A (traumatic event), B (re-experiencing the trauma – "intrusion"), C (avoidance symptoms), D (hyperactivity symptoms), F (distress and maladjustment); ASD: a (traumatic event), b (dissociative symptoms), c (re-experiencing the trauma – "intrusion"), d (avoidance symptoms), f (hypervigilance symptoms). This approach allows us to record the mental changes in participants after a traumatic experience. The use of the above-mentioned techniques provides a comprehensive assessment of an individual's adaptive potential, combining quantitative accuracy with in-depth qualitative interpretation.

STATISTICAL METHODS

Statistical methods were used to process the data obtained. The compliance of the sample data distribution with the Gauss' law was assessed using the Shapiro-Wilk W test. The reliability of the difference between the indicators was determined using the Student's t-test. The reliability of the difference was set at $p < 0.05$. All statistical analyses were performed using SPSS software, version 10.0, adapted for medical and biological research.

ETHICS

The procedure for organizing the study and the topic of the article were previously agreed with the Committee on compliance with Academic Integrity and Ethics of the OSUIA. Also this study followed the regulations of the World Medical Association Declaration of Helsinki. Informed consent was received from all cadets who took part in this study.

FRAMEWORK

The study was conducted within the framework of the Scientific Research Plan of the Department of Psychology and Pedagogy of the Odessa State University of Internal Affairs for 2022-2027 within the framework of the scientific research work «Psychology of the personal development of a police officer in professional activity and the recovery period». State registration number 0123U103782.

RESULTS

The unfavorable factors of the combat environment and excessive physical and mental stress lead to certain changes in the adaptive resources of the SSS individual, as well as to the manifestation of mental disorders, as demonstrated by our results (Table 1).

Comparing the obtained indicators, it can be stated that the CG and the EG differ in the severity of signs of professional stress and indicators of psychological adaptation.

Thus, analysis of anxiety indicators shows that SSSs who did not perform their service duties in combat conditions demonstrate a significantly higher level of both reactive (by 7.06 points; $p < 0.01$) and personal (by 4.29 points; $p < 0.05$) anxiety. The level of anxiety (both reactive and personal) among SSSs in the CG is assessed as moderate, while among the EG officers, it is assessed as low (no anxiety). This indicates that SSSs in the CG feel more anxiety about the possibility of finding themselves in crisis and unfavorable conditions of professional activities (tours of duty to combat zones, performing specific service duties during martial law). On the other hand, SSSs of the EG, who are constantly in a combat environment, are calmer because they have already "burned out." Therefore, this indicator is significantly lower for them. It can be assumed that SSSs in the EG are aware of their anxiety but try to hide it, including from their immediate professional and/or personal environment.

The analysis of psychological adaptation indicators using the AAQ technique shows that SSSs in the EG, compared to the CG, demonstrate significantly ($p < 0.05$ - 0.001) worse satisfaction indicators: with themselves, their mental state – by 7.32 points; the situation and its dynamics – by 6.19 points; the sphere of interpersonal relations – by 2.37 points; their functional state – by 2.47 points; their life-sustaining activities in general – by 7.23 points. This indicates that SSSs in the EG are less satisfied with their lives and professional activities under stressful combat conditions for various reasons. In contrast, SSSs in the CG underestimate the danger posed by events experienced by their colleagues in combat conditions. In SSSs of the CG, the level of adaptation in all components is assessed as a "normal" level of stress that does not pose a threat to health and well-being, while in the EG, the components "Satisfaction with interpersonal relations" and "Satisfaction with functional state" – a "normal" level of stress, and in terms of "Satisfaction with oneself, one's mental state," "Satisfaction with the situation, its dynamics," and "Satisfaction with life-sustaining activities" – a sub-extreme stressful situation, exhaustion, dissatisfaction with life.

The analysis of psychological adaptation indicators of SSSs using the Traumatic Stress Questionnaire (TSQ), which allows determining the severity of individual groups of stress symptoms, shows that the EG, compared to the CG, is characterized by significantly higher ($p < 0.05$ - 0.001) indicators of PTSD, ASD symptoms (by 18.57 points), re-experiencing trauma (by 25.81 points), hyperarousal (body exhaustion) (by 29.52 points), hypervigilance (by 20.18 points), avoidance (by 14.04 points), as well as distress and maladjustment (by 7.67 points). These data indicate that this is probably not only a matter of systematic acute stress and PTSD reactions as natural phenomena, but also a desire to elicit empathy using known data on stress and psychological sessions (common among military personnel). This is supported by the fact that although the representatives of this group belong to law enforcement units and do not perform direct combat functions as military personnel,

Table 1. Comparative characteristics of psychological adaptation indicators of security-sector specialists to stressful conditions of professional activities during war (n = 120, Mean ± m, points)

Psychological adaptation indicators	Groups		Significance of the difference	
	CG (n=60)	EG (n=60)	t	p
Reactive and Personal Anxiety Scale				
Reactive Anxiety	40.50±1.87	33.44±1.25	3.14	<0.01
Personal Anxiety	34.25±1.32	29.96±1.53	2.12	<0.05
Adaptation Assessment Questionnaire				
Satisfaction with oneself and one's mental state	6.11±0.47	13.43±0.65	9.13	<0.001
Satisfaction with the situation and its dynamics	6.52±0.58	12.71±0.59	7.48	<0.001
Satisfaction with the sphere of interpersonal relations	7.49±0.63	9.86±0.67	2.58	<0.05
Satisfaction with one's functional state	6.08±0.49	8.55±0.62	3.13	<0.01
Satisfaction with life-sustaining activities	7.24±0.52	14.47±0.61	8.93	<0.001
Traumatic Stress Questionnaire				
L – lie	13.54±1.42	19.28±1.51	2.77	<0.051
Ag – aggravation	6.17±1.32	12.41±1.39	3.26	<0.01
Di – dissimulation	7.25±1.06	11.25±1.24	2.34	<0.05
ITCP, TCP	84.16±2.57	102.73±2.61	5.07	<0.001
A – traumatic event	6.53±1.18	11.49±1.25	2.89	<0.05
B – re-experiencing the trauma	13.50±1.89	39.31±1.98	9.43	<0.001
C – avoidance symptoms	25.27±1.29	46.53±1.34	7.55	<0.001
D – hyperactivity symptoms	24.75±1.77	54.27±1.82	11.63	<0.001
E – hypervigilance symptoms	39.43±1.72	59.61±1.28	8.06	<0.001
F – distress and maladjustment	14.51±1.08	22.18±0.97	5.28	<0.001

Notes: Mean – arithmetic mean; m – error of arithmetic mean; t – Student's test value; p – reliability value

Source: compiled by the authors of this study

they still reflect the consequences of traumatic events and indicators of critical combat stress.

It should be noted that psychological trauma can manifest itself significantly through a conscious attitude towards psycho-traumatic events. The CG and the EG are defined by various indicators of experiencing a stressful situation, including changes in attitude towards the crisis and towards oneself. Thus, the representatives of the EG emphasize the presence of signs of acute stress and its negative consequences from working in combat conditions. As for the CG, on the contrary, such SSSs rule out the possibility of being in combat conditions (combat operations are taking place, but far away).

In general, the data obtained indicate that the actual indicators of PTSD and ASD can be a dynamic phenomenon, given the attitude towards the situation and oneself in it (for example, the inconsistency of the experience of fear with one's own "self-image" or the absence of the traits of a fighter in the "self-image", etc.). As a result, the specificity of traumatic combat stress significantly changes the dynamics of the adaptive capabilities of the SSS personality, which is associated with several factors:

the intensity and excessiveness of traumatic influences, insufficient time for the formation of psychological defense mechanisms, the severity of psychosomatic components of the stress response, etc.

DISCUSSION

The realities of modern warfare create extreme, highly unpredictable situations that endanger the lives and health of combatants [20, 21]. Hence, it is extremely important to ensure that every law enforcement officer is aware of the difficulties they may encounter while performing their duties under combat conditions, and to prepare them to ensure their own safety, etc. Often, security-sector specialists are forced to perform functions (military-related ones) that are not typical for law enforcement officers, feeling the strong impact of crises.

As researchers rightly point out [7, 14, 22], some specialists become focused and active in extreme conditions. However, in those who are insufficiently prepared, under the influence of strong emotions and tension arising during combat operations, sensitivity may decrease, the speed of reaction to external stimuli may slow down, coordination

of movements and actions may be impaired, and mental processes and attention may weaken, which reduces and jeopardizes the effectiveness of professional activities. At the same time, as the data obtained proves, the level of satisfaction with interpersonal relations, one's own functional state, etc., may decrease to a certain extent. Conversely, distance from systematic crisis conditions contributes to a stable functional state but determines the level of personal anxiety about the possibility of being in the unfavorable conditions of war. After all, rapid environmental changes, prolonged and often severe physical and mental stress, conflicting needs and motives, etc., all lead to considerable tension in the body and a loss of the SSS's adaptive potential.

At the same time, it should be noted that the SSS is currently influenced by many factors that contribute to the emergence of nervous and mental instability [23-25]. These may include, in particular, a different rhythm of life compared to the pre-war period, the requirements of professional discipline, significant physical and mental stress, the need to acquire special competencies, knowledge, skills, and abilities, and the difficulties that some law enforcement officers may experience when performing professional duties, mastering new atypical responsibilities, changes in the nature and mode of life-sustaining activities, etc. It is also worth noting that all this affects law enforcement officers' adaptive resources, slows the formation of psychological defense mechanisms, and contributes to the severity of stress response components, etc. As our results show, this list of personal changes is supplemented by symptoms of avoidance, distress, body exhaustion, and re-experiencing the trauma. As a result, in conditions of "unfair" treatment or conflict situations, excessive excitability, irritability, aggressive actions, and other forms of destructive behavior, etc., are violently manifested. That is why timely and qualified psychological assistance should be provided to restore constitutional and psychotypological mechanisms of compensation and adaptation. Under such conditions, it is possible to reduce the likelihood of alcoholism, prevent acts of conflict and aggression towards colleagues and citizens, suicidal manifestations, etc. Our standpoints and the data obtained complement the findings of scientists on this range of problems. [1, 5, 8, 13, 14, 26-30].

CONCLUSIONS

The level of psychological adaptation of security-sector specialists has been studied as a function of the

conditions of professional activities during the war. A significantly higher level of both reactive (by 7.06 points; $p<0.01$) and personal (by 4.29 points; $p<0.05$) anxiety levels was revealed in the CG specialists compared to the EG specialists, indicating that the CG specialists experience more anxiety about the possibility of encountering crisis conditions in their professional activities during wartime. It has also been found that the EG specialists, compared to the CG, demonstrate significantly ($p<0.05-0.001$) worse indicators of satisfaction: with themselves, their mental state – by 7.32 points; the situation and its dynamics – by 6.19 points; the sphere of interpersonal relations – by 2.37 points; their functional state – by 2.47 points; their life-sustaining activities in general – by 7.23 points. In addition, compared to the CG, the EG was diagnosed with significantly higher ($p<0.05-0.001$) indicators for PTSD and ASD symptoms (by 18.57 points), re-experiencing the trauma (by 25.81 points), hyperarousal (exhaustion of the body) (by 29.52 points), hypervigilance (by 20.18 points), avoidance (by 14.04 points), as well as distress and maladjustment (by 7.67 points). It has been proven that the adverse factors of combat situations and excessive physical and mental stress in wartime lead to a gradual loss of satisfaction with life-sustaining activities, an increased risk of developing stress disorders, accompanied by symptoms of avoidance (distancing oneself from one's immediate professional or social environment), distress, exhaustion of the body, and re-experiencing the trauma. The intensity and excessiveness of psycho-traumatic influences, the inability to form psychological defense mechanisms, and the severity of psychosomatic components of the stress response significantly alter the adaptive abilities of security-sector specialists.

The focus of modern medical and psychological attention should be on controlling the individual barrier to mental adaptation of security-sector specialists, which reduces the risk of mental health problems and decreases feelings of alienation and social isolation. At the same time, understanding the meaning of events in the surrounding environment contributes to the specialist's faster adaptation to the social environment, supports their personal growth after psychological trauma, and enables them to move forward and overcome professional and everyday crises.

PROSPECTS FOR FURTHER RESEARCH

Prospects for further research include examining potential changes in the personalities of law enforcement officers while performing their duties under martial law.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

Aspects of the use of artificial intelligence in medical education: Results of a cross-sectional survey conducted at Bogomolets national medical university

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ABSTRACT

Aim: To analyze the key aspects of artificial intelligence (AI) application in medical education and to assess related psychological attitudes among students and academic staff.

Materials and Methods: A cross-sectional study was conducted using an anonymous online survey. A total of 727 respondents participated, the majority of whom were involved in medical education. The questionnaire included demographic items, questions on frequency and purposes of AI use, self-assessment of AI proficiency, and a 40-item scale evaluating psychological attitudes. Data were analyzed using descriptive statistics and presented as relative frequencies (%).

Results: The findings demonstrated significant integration of AI into the medical education environment: 41.4% of respondents reported daily use, while 46.6% reported using these tools several times per week. Primary applications included learning support (79.6%), self-education (78%), and preparation of educational materials (30.1%). While 61.8% of participants rated their proficiency as high, the study raised concerns about the rapid pace of technological development and potential cognitive dependence.

Conclusions: The normalisation of AI in academic practice indicates its role as a cognitive extension. While it enhances efficiency and creativity, the risk of reduced autonomy and ethical challenges necessitates the development of structured educational strategies and methodological guidelines for its responsible use in medical training.

KEYWORDS: artificial intelligence, medical education, digital literacy

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INTRODUCTION

Today, Ukrainian society demonstrates a high level of openness to digital transformations, which have become an irreversible process and encompass all spheres of life and professional activity. The Ministry of Digital Transformation of Ukraine, in cooperation with partners, actively conducts analytical studies on the level of digital literacy of the population [1, 2].

An important component of this process is the development and promotion of digital competence frameworks for various groups of citizens. In particular, the Diia. The education platform provides access to the Digital Competence Framework for Citizens of Ukraine [3, 4], for Library Staff [5], and the Digital Competence Framework for Teaching and Academic Staff [6].

A significant recent step was the development and presentation in 2023 of the Digital Competence Framework for Healthcare Professionals (hereinafter referred to as the Framework), which was published both on the Diia.Education platform and on the official website of the Ministry of Health of Ukraine [7]. This Framework aims to systematise the digital skills and competencies of healthcare professionals, ensuring their effective adaptation to the digital environment and the integration of modern technologies into professional practice.

Digital competence in Ukraine is expanding across sectors, with artificial intelligence (AI) increasingly integrated into medical education to enhance learning, research, and professional training. While AI offers efficiency and personalised education, reliance on it raises concerns about critical thinking, ethics, and cognitive dependence. Limited empirical data on its use and psychological impact underscore the need for further research to balance benefits and risks [8].

AIM

To analyze the key aspects of AI application in medical education and to assess related psychological attitudes among students and academic staff.

MATERIALS AND METHODS

The empirical basis of the study consisted of survey responses collected from participants involved in medical education between 2025 and 2026. A total of 727 respondents, including students, interns, and academic staff, voluntarily and anonymously participated in the research.

Data were collected using a structured online questionnaire developed specifically for this study. The questionnaire included four main sections: socio-demographic

characteristics (age, gender, educational level); frequency and purposes of AI use in educational and professional activities; self-assessment of AI proficiency; and psychological attitudes toward AI, measured with a 40-item scale on a five-point Likert system ranging from “strongly disagree” to “strongly agree”. The study employed general scientific and psychological methods, including descriptive statistics, survey analysis, and assessment of cognitive and emotional attitudes toward AI in the context of medical education.

In the context of rapid digitalization, these technologies contribute to efficiency but generate new challenges related to algorithmic dependence and reduced critical thinking. The aim of this study was to investigate how AI systems influence psychological well-being and social interactions.

ETHICS

The study was conducted in accordance with the principles of the Declaration of Helsinki and bioethical standards for conducting sociological surveys in the medical field. All survey participants (N=727) were informed of the research objectives and provided voluntary informed consent to participate. Participation was fully anonymous, guaranteeing the protection of personal data and the professional reputation of respondents. Data processing was carried out in a depersonalized form. Results are presented in summary tables and charts, which makes it impossible to identify specific individuals. The research protocol and instrument (questionnaire) underwent peer review and received approval from the local Bioethics Committees of the National Medical University.

FRAMEWORK

The study was conducted as a part of the research project within the framework of the international ERASMUS+ UkraineDigiTrans project (GA number 101179494).

RESULTS

Fig. 1 illustrates various aspects of the perception and use of AI.

The perceived benefits of AI (Fig. 2) indicate an overall positive perception. The majority of participants reported that AI contributes to improved organisation (79.6%) and efficiency in achieving goals (61.6%). Regarding cognitive potential, 70.3% indicated that it inspires new ideas, and 59.9% reported that it helps structure thoughts. These findings align with recent research highlighting AI as a facilitator of metacognitive processes in medical training [3, 4].

Psychological interaction is also notable: 57.1% reported turning to AI during periods of stress, and 52.7% experienced social support in interactions with it. However, significant concerns remain (Fig. 2).

Nearly half (48.1%) expressed concern about the rapid pace of development (Fig. 3). Approximately 37.4% believe AI may lead to a loss of human uniqueness, and 34.3% fear professional obsolescence. These attitudes reflect the global duality of techno-optimism and techno-anxiety [5, 6, 9, 13].

Ethical awareness is high: 72.1% believe the education system should ensure ethical AI training (Fig. 4). While 59.2% are aware that use without attribution is plagiarism, only 49.8% consistently acknowledge AI use in their work, suggesting a gap between ethical awareness and practical implementation [10-12]. Regarding social aspects (Fig. 5), AI remains a supportive tool rather than a substitute; 78.4% believe that human empathy will always remain more important than machine intelligence.

The results of the survey on the perceived benefits of AI applications (Fig. 2) indicate an overall positive perception of AI technologies among respondents and their active

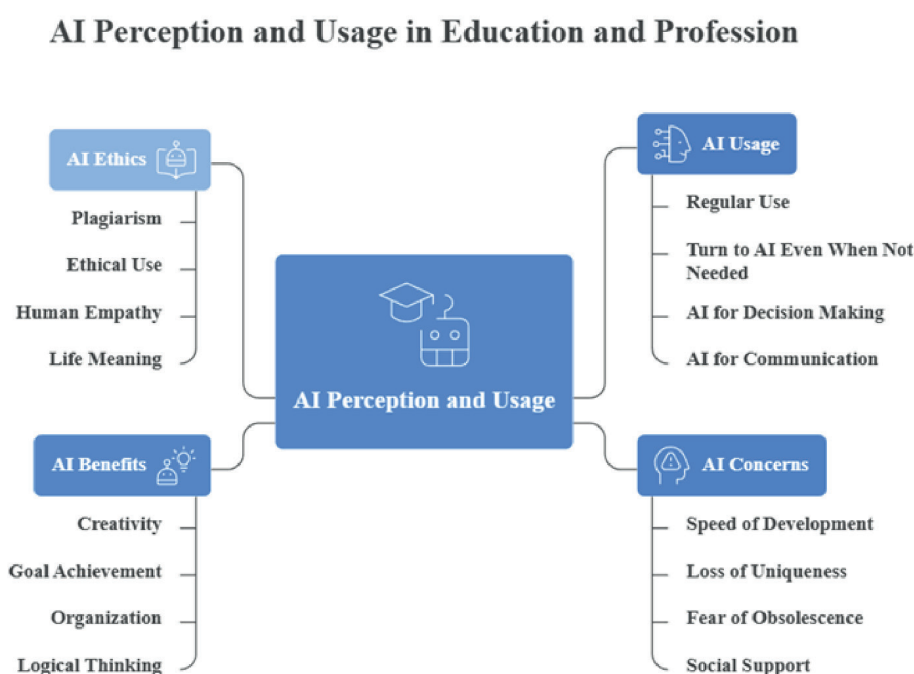


Fig. 1. Mental map of the perception and use of AI in educational and professional contexts

Picture taken by the authors

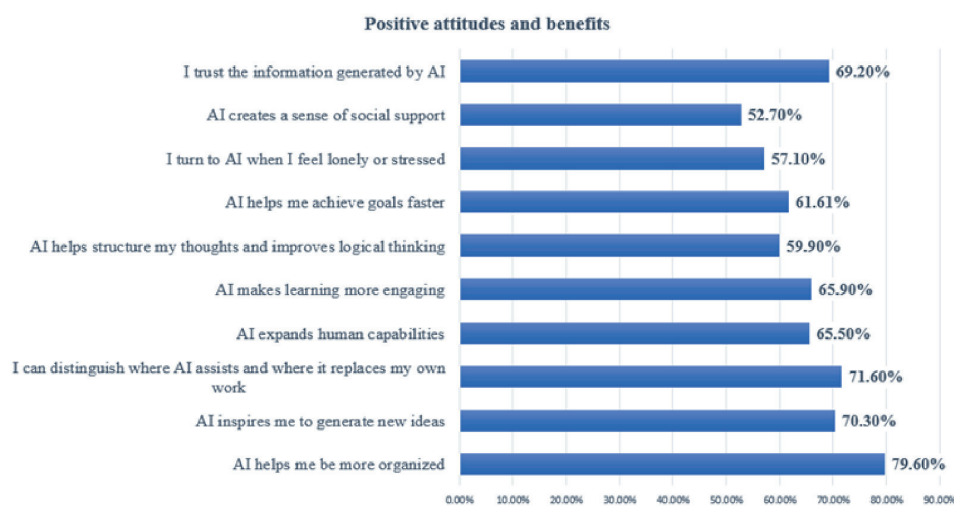


Fig. 2. Distribution of positive responses regarding the perceived benefits of AI use among respondents

Picture taken by the authors

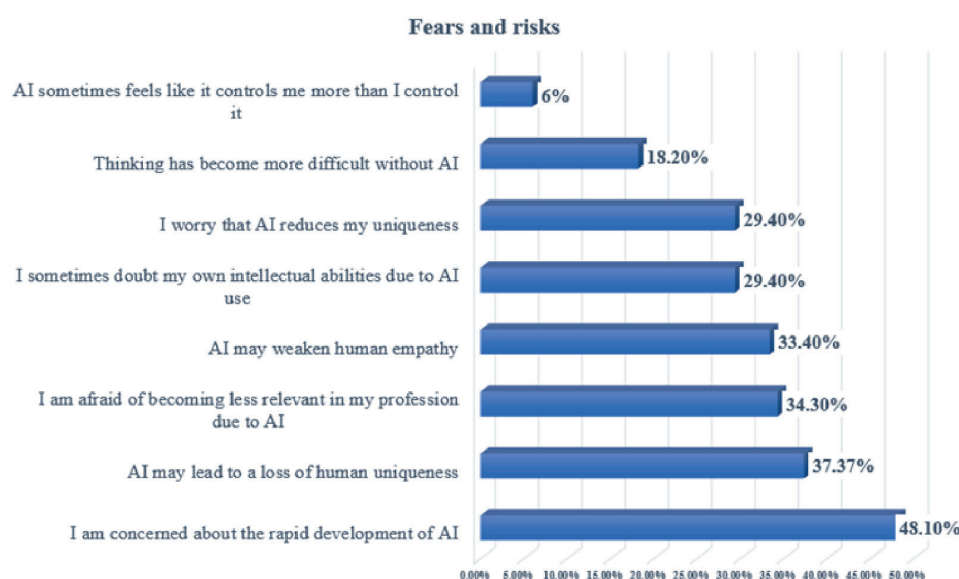


Fig. 3. Affirmative responses of respondents regarding fears and risks associated with the use of AI

Source: compiled by the authors based on [5, 6, 9, 13]

integration into daily activities. In particular, the majority of participants reported that the use of AI contributes to improved organisation (79.6%) and greater efficiency in achieving goals (61.61%), highlighting its role as a tool for optimising performance.

The creative and cognitive potential of AI is also noteworthy: 70.3% of respondents indicated that it inspires the generation of new ideas, while 59.9% reported that it helps structure thoughts and enhances logical thinking. These findings confirm the importance of AI as a tool supporting intellectual activity and cognitive development.

More than half of the respondents (65.5%) perceive AI as a tool that extends human capabilities, and 65.9% believe that its use makes the learning process more engaging. Additionally, 71.6% of participants demonstrated the ability to use AI critically, distinguishing between situations where AI serves as a supportive tool and where it may substitute personal effort.

Particular attention should be paid to the psychological aspects of interaction with AI. Specifically, 57.1% of respondents reported turning to AI during periods of loneliness or stress, while 52.7% experienced a certain level of social support when interacting with it. This suggests the emergence of new forms of emotional interaction between humans and technology.

The level of trust in AI-generated information was also relatively high (69.2%), emphasizing the importance of developing critical thinking skills and the ability to verify information in the context of widespread AI use.

Nearly half of the participants (48.1%) expressed concerns about the rapid pace of AI development, related to awareness of the dynamic nature of technological change and the potential challenges of adapting to it in both societal and professional contexts (Fig. 3).

About one-third of respondents perceive AI as a threat to personal identity, highlighting the need to balance

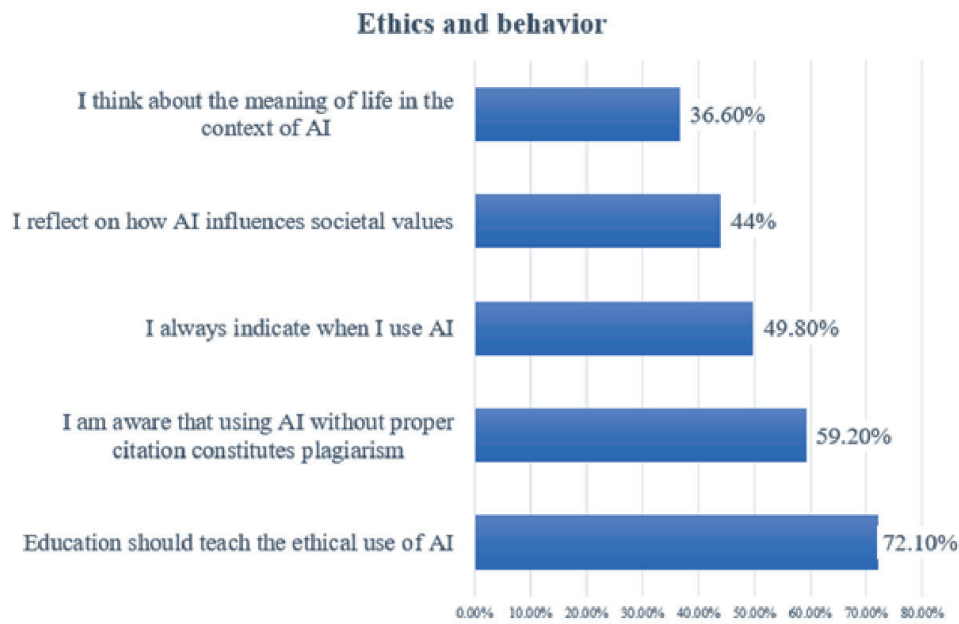


Fig. 4. Responses of respondents regarding the ethical and responsible use of AI

Source: compiled by the authors based on [10-12]

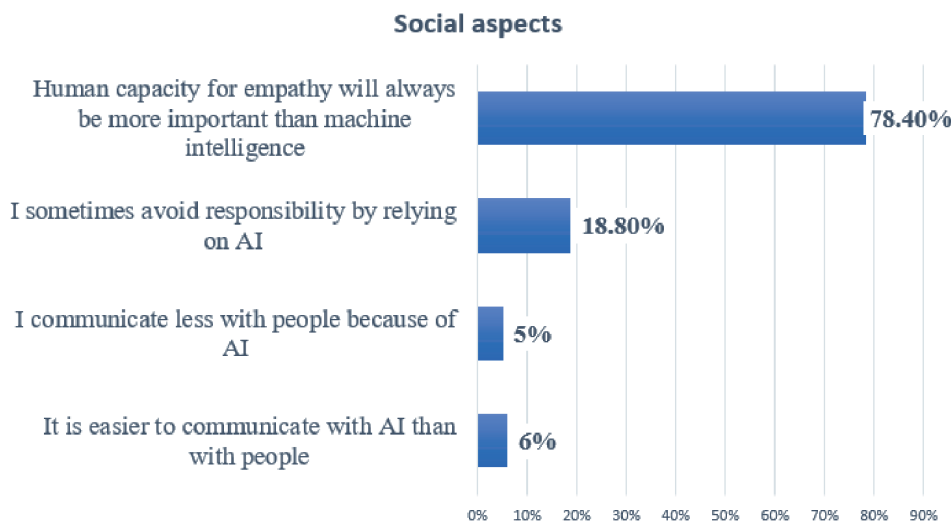


Fig. 5. Responses of respondents regarding the social aspects of AI use

Picture taken by the authors

technological progress with humanistic values (Fig.3.). Concerns also include professional obsolescence (34.3%), reduced empathy (33.4%), and decreased confidence in one's own abilities (29.4%), indicating risks of technological dependence. While 18.2% report difficulty thinking without AI, only 6% feel a loss of personal autonomy.

The results of the survey in the domain of ethics and behavior (Fig. 4) indicate a relatively high level of awareness among respondents regarding the need for responsible use of AI. In particular, the majority of participants (72.1%) believe that the education system should ensure the development of skills for the ethical use of AI, and highlight the importance of integrating such competencies into educational programs.

More than half of the respondents (59.2%) are aware that the use of AI without proper attribution may be considered a form of plagiarism, which is related to academic integrity in the context of digitalization (Fig.4). Only 49.8% consistently acknowledge AI use, indicating a gap between ethical awareness and practice. At the same time, many respondents reflect on AI's broader impact, including societal values (44%) and existential issues (36.6%), showing a deeper understanding of its socio-cultural role.

Regarding the social aspects (Fig. 5), the results indicate that AI is not perceived as a full-fledged alternative to interpersonal interaction. Only a small share of respondents prefer AI over human communication (6%) or report reduced real-life interaction (5%). However, 18.8% admit occasionally

avoiding responsibility by relying on AI, indicating risks to decision-making autonomy. Despite this, most participants (78.4%) emphasize the enduring importance of human empathy over machine intelligence.

DISCUSSION

The high frequency of AI usage among respondents indicates its deep integration into everyday educational activities. Positive aspects, such as improved organisation, increased efficiency, stimulation of new idea generation, and structuring of thoughts, reflect the potential of AI as a catalyst for metacognitive processes and creativity [14]. This aligns with international studies noting that AI tools can allow medical students to devote more time to critical thinking and clinical learning by replacing routine tasks [15, 16].

The study results clearly demonstrate a pronounced psychological duality in attitudes toward AI, reflecting broader global trends of techno-optimism and techno-anxiety [17]. While a significant proportion of participants positively evaluate the impact of AI on creativity and structured thinking, substantial concerns simultaneously arise. Nearly half of the respondents expressed concern about the rapid pace of AI development, which is a common anxiety related to adapting to fast technological changes [18]. The fear of losing human uniqueness and professional obsolescence is a global issue widely discussed in the context of AI's impact on the labour market and the development of professional skills, especially among early-career professionals [19, 20].

Particular attention should be paid to the observed tendency to turn to AI during periods of stress and the perception of social support. These findings resonate with recent studies highlighting the growing popularity of AI companions and chatbots as sources of emotional support

and coping with loneliness [21, 22]. However, this also raises questions about potential risks, including the formation of unrealistic expectations of human relationships and the possible exploitation of emotional needs, particularly among young people [23].

Despite the widespread adoption of AI, the vast majority of respondents remain convinced of the greater importance of human empathy compared to AI. This conclusion emphasises the unique and irreplaceable role of the human element in medical practice, where compassion, interpersonal interaction, and clinical judgement remain essential [24, 25]. It also supports the global consensus that AI should play a complementary rather than a substitutive role in healthcare and education [24, 25].

CONCLUSIONS

The study reveals a complex and ambivalent perception of AI. Respondents recognise AI's potential to enhance creativity, support structured thinking, and accelerate goal achievement, while also expressing concerns about rapid technological development, professional relevance, and the impact on human uniqueness and empathy.

Partial dependence on AI in decision-making and self-evaluation was observed, raising questions about autonomy and critical thinking; yet most participants do not view AI as a substitute for human communication, highlighting its role as an augmentative tool. Ethical considerations are important, with strong support for proper attribution, ethical use, and the inclusion of digital and ethical competencies in education.

Overall, respondents demonstrate a balanced yet cautious engagement with AI, reflecting adaptive integration into cognitive and professional practices. These findings can inform educational strategies for responsible, critical, and effective AI use.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

Dynamics in students' psychosomatic health indicators during their distance learning under martial law

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ABSTRACT

Aim: To investigate the impact of motor activity on the dynamics of students' psychosomatic health indicators during their distance learning under martial law.

Materials and Methods: The research involved 252 female students aged 17-20. Depending on the level of their motor activities, three groups were formed: female students in group a (n=75) engaged in physical exercise 3 or more times a week; female students in group b (n=95) exercised 1-2 times per week; female students in group c (n=82) did not engage in physical exercise. Research methods: theoretical methods, questionnaire, psychodiagnostics methods, statistical methods.

Results: It was found that among female students of group a, psychosomatic health indicators significantly improved ($p < 0.05$). In contrast, group b and group c deteriorated. The most pronounced negative changes in group c were observed in indicators of stress levels, neuropsychological tension, and the emotional state of the female students. At the end of the research, all subgroups of group a exhibited statistically similar indicators of psychosomatic health ($p > 0.05$), regardless of the focus of the physical exercise sessions.

Conclusions: The results demonstrate the effectiveness and appropriateness of incorporating a reasonable amount of physical activity to maintain and improve students' psychosomatic health indicators during distance learning under martial law. At the same time, physical exercise of any type helps reduce stress and neuropsychological tension, strengthen health, improve students' well-being and mood, increase their work capacity, and, consequently, their academic performance during wartime.

KEYWORDS: distance learning, psychosomatic health, motor activities, students, stress, martial law

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INTRODUCTION

Distance (online) learning is a modern form of education in which the instructor and student interact remotely using internet technologies (platforms, video conferencing) while located in different places. This approach provides a flexible schedule, interactive engagement, and the opportunity for independent learning without the need to attend an educational institution [1]. Distance learning became widespread in Ukraine during the COVID-19 pandemic [2]. With the onset of full-scale war, it proved to be a solution that enabled students to continue their studies. This format of learning, first and foremost, creates safe conditions for students who, due to the disasters caused by Russia, cannot physically attend educational institutions [3]. Additionally, the advantages of this form of learning include: accessibility from anywhere in the world, savings in time and money on travel to and from the educational institution, and an individualized approach to the pace of learning [4, 5]. At the same time, distance learning poses significant risks to both the mental and physical health of students, stemming from a lack of face-to-face interaction with peers and instructors, insufficient motor activity, the monotony of the work, and emotional and intellectual overload [6]. Moreover, distance learning is a source of stress and anxiety for students, as it

increases their responsibility for organizing their own study time, self-discipline, and motivation, and is compounded by frequent power outages, which are accompanied by problems with stable internet connectivity and technical support [7]. Additionally, with the introduction of online communication, there is a risk of becoming a victim of cyberbullying, which can hurt students' psychological and emotional well-being [8]. According to many researchers [9, 10], the following factors of distance learning are harmful to students' psychophysical health: an irrational study routine (irregular meals and sleep disturbances due to a flexible but often chaotic study schedule); prolonged use of gadgets (computers, phones, tablets), leading to psychological and emotional strain and deteriorating vision; large volumes of educational information that must be processed independently, leading to intellectual overload, deterioration of cognitive processes (attention, memory, thinking), and emotional exhaustion; prolonged sitting, which leads to monotony, physical inactivity, and is accompanied by deterioration in the functioning of the musculoskeletal, cardiovascular, and respiratory systems. Due to the range of problems and challenges students face during the transition to distance learning, experts are devoting significant attention to developing recommendations to

reduce physical strain and maintain and strengthen their mental and physical health. Among other measures, the most important way to address this problem is to increase daily motor activity [11, 12].

According to researchers [13, 14], motor activity during distance learning is critically important for preventing physical inactivity, reducing stress, and improving students' cognitive abilities. Regular exercise (at least 60 minutes per day) improves blood flow to the brain, attention, and memory, helping offset the effects of prolonged sitting in front of a screen. To maintain health during online learning, experts recommend alternating mental and physical activity, making motor activity a mandatory part of the daily routine [15-17]. Motor activity counteracts a sedentary lifestyle, strengthens the cardiovascular system, muscles, and musculoskeletal system, prevents poor posture and weight gain, reduces irritability and anxiety, and stimulates the release of serotonin, which improves mood, concentration, and cognitive performance [18-20].

AIM

The aim is to investigate the impact of motor activity on the dynamics of students' psychosomatic health indicators during their distance learning under martial law.

Tasks: 1) to investigate the dynamics of psychosomatic health indicators among female students during their distance learning, depending on the weekly volume of motor activity; 2) to investigate the dynamics of psychosomatic health indicators among female students who adhered to a rational regimen of motor activity during their distance learning, depending on the focus of their physical exercise sessions.

MATERIALS AND METHODS

PARTICIPANTS

The research, conducted in 2025-2026 at the Department of Rehabilitation Technology and Sports of the National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" (Kyiv, Ukraine), involved 252 female students aged 17-20 (first-through fourth-year students in the faculties of "Computer Science and Computing" and "Management and Marketing"). Depending on the level of motor activity during 3 months of distance learning (December 2025-February 2026), the female students were divided into 3 groups: group a (n=75) engaged in targeted physical exercise 3 or more times a week for 1.5-2 hours during their distance learning. (subgroup a1 (n=23) – engaged primarily in functional training (HIIT (Tabata protocol), CrossFit, various types of dance aerobics, etc.); subgroup a2 (n=27) – engaged primarily in exercises for posture correction, flexibility development, and joint mobility (stretching, Pilates, yoga); subgroup a3 (n=25) – engaged primarily in endurance-building exercises (running, swimming, cardio machine workouts, etc.); female students in group b (n=95) exercised irregularly 1-2 times per week; students in group c (n=82) did not engage in any targeted physical exercise at all (they used other means to maintain psychosomatic health during their distance learning: regulating diet and sleep

patterns, using hygiene practices and relaxation techniques, maintaining social contacts, routine tasks, and hobbies). Research limitations: We did not account for the female students' levels of daily motor activity.

Inclusion criteria: all female students involved in the research belonged to the general health group (had no health issues or contraindications for motor activity); before distance learning, all female students were informed about their participation in the study for research purposes (those who did not wish to participate had the right to decline). Additionally, all female students were instructed on the importance of motor activity for maintaining psychosomatic health during distance learning under martial law. Each female student had the opportunity to independently choose the type of motor activity according to her own preference, taking into account safety conditions, the availability of infrastructure and material resources, etc. (i. e., there was no special selection of female students for the study groups). The exclusion criterion was a female student's voluntary desire to withdraw from the research at any time. The research was conducted in two phases (Phase 1 (beginning) – before distance learning, Phase 2 (end) – after the completion of distance learning).

RESEARCH METHODS

Theoretical methods, psychodiagnostics methods, questionnaire, statistical methods. The theoretical methods (theoretical analysis and generalization of literary sources) were used to conduct an analytical review of scientific sources on the outlined range of issues (30 sources (2018-2026) from MedLine, Scopus, Web of Science databases were analyzed).

Psycho-diagnostic techniques were used to assess the impact of motor activity on the mental health of female students during their distance learning. Three techniques were used: the "Stress Level Test," the "Assessment of Neuropsychological Stress," and the "Self-Assessment of Emotional State" [21]. The "Stress Level Test" assesses the degree of manifestation of intellectual, behavioral, emotional, and physiological stress symptoms in female students, as well as the overall level of stress. The questionnaire form contains 4 sets of 12 symptoms each. If respondents experienced one of the intellectual or behavioral symptoms, they assigned it 1 point; for emotional symptoms, 1.5 points; and for physiological symptoms, 2 points. The maximum score is 66 points. Stress levels were assessed as follows: 5 points or below – no stress; 6-12 points – moderate stress; 13-24 points – pronounced stress; 25-40 points – severe stress; 41 points or above – excessive stress.

The "Assessment of Neuropsychological Stress" technique includes 30 indicators of this condition, divided into three severity levels (A – low, B – moderate, C – high). By selecting one of the three response options (A, B, C), the female students assessed their current level of neuropsychological stress. Data were processed by summing the scores: 1 point for response A, 2 points for B, and 3 points for C. A score range of 30-50 points indicates a low level of neuropsychological stress; 51-70 points – moderate; 71-90 points – high.

The "Self-Assessment of Psycho-Emotional State" technique is designed to evaluate emotional states on a 10-point scale. The female students selected from each of the proposed sets of statements ("Stability-Anxiety," "Energy-Fatigue," "Elevation-Depression," "Self-Confidence-Helplessness") the one that most accurately reflected their psycho-emotional state at the time of the research. The integrated indicator was calculated using the formula: $PES = (I1 + I2 + I3 + I4) / 4$, where PES is the integrated indicator of psycho-emotional state; I1, I2, I3, and I4 are individual indicators on the respective scales (sets of statements). If the PES falls within the range of 8-10 points, it can be interpreted as very good; 6-7 points – good; 4-5 points – impaired; 1-3 points – poor.

The questionnaire was used to assess the somatic health of female students using V. P. Voitenko's "Self-Assessment of Health" technique [22]. The female students were given a questionnaire containing 27 questions. The first 26 questions had "yes" or "no" answers; the last one ("How would you rate your health?") characterized their health level as "good," "satisfactory," "poor," or "very poor." The first 26 questions were scored as follows: the respondent received 1 point for each "yes" answer and 0 points for a "no" answer. The total score provides a quantitative self-assessment of health. Accordingly, if the answer to the last question was "poor" or "very poor," 1 point was added. The survey results were evaluated as follows: 3 points or below – excellent health; 4-7 points – good; 8-13 points – average; 14-20 points – satisfactory; 21 points or above – unsatisfactory.

STATISTICAL METHODS

Statistical analysis was applied to correctly process the data and identify the difference between the indicators under study. The significance of the difference in the results of the students was determined based on the Student's t-test. The significance for all statistical tests was set at $p \leq 0.05$. All statistical analyses were performed with the SPSS software, version 11.0.

ETHICS

This research followed the regulations of the World Medical Association Declaration of Helsinki and ethical principles for medical research involving human subjects and was approved by the National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" (Protocol No. 5 dated 04.12.2025). Informed consent was received from all students who took part in this research.

FRAMEWORK

This research was carried out according to the research work of National Technical University of Ukraine „Igor Sikorsky Kyiv Polytechnic Institute” for 2024-2027 on the theme of „Information technologies for assessing and correcting the state of health of students in higher educational institutions” (state registration number 0117U006954).

RESULTS

The results of the study on the dynamics of female students' psychosomatic health indicators during distance learning

under martial law, as a function of their level of motor activity, are presented in Table 1.

The study of stress levels indicates that, before distance learning, no significant differences ($p > 0.05$) in stress indicators were found among the three groups of female students. At the same time, the stress level among female students in all three groups (13.8-14.1 points) is pronounced, indicating strain on the body's emotional and physiological systems that arose in response to severe stressors (in particular, the war in Ukraine, anxiety about one's own life and health and those of loved ones, constant air raid alerts, problems with heating and electricity, etc.). During the period of distance learning, the stress level in group a decreased significantly ($p < 0.05$) by 3.1 points, in group b by 0.2 points, and in group c increased by 0.7 points. However, the changes in group b and group c were not statistically significant ($p > 0.05$). At the end of the research, the stress level in group a was assessed as moderate, while in group b and group c, it remained unchanged and was assessed as pronounced. This indicates the effectiveness of rationally organized systematic motor activity in preventing stress among female students during distance learning.

The analysis of neuropsychological stress levels among female students at the beginning of the research indicates homogeneity of indicators across groups a, b, and c: no significant differences were found ($p > 0.05$). Over the research period, the level of neuropsychological stress in group a decreased significantly ($p < 0.05$) by 3.8 points, whereas in group b and group c it did not change significantly ($p > 0.05$). At the end of the research, significantly better indicators were found in group a than in group b and group c by 3.8 and 4.3 points, respectively, confirming our previous conclusions regarding the effectiveness of motor activity during distance learning in strengthening students' mental health. The level of neuropsychological stress among female students in all three groups was assessed as average both at the beginning and at the end of the research.

The assessment of the students' psycho-emotional state indicates that no statistically significant difference was found between the groups at the start of the research ($p > 0.05$). During the period of distance learning, the indicators for group a improved significantly ($p < 0.05$) by 0.9 points, for group b by 0.2 points. Still, the difference was not significant ($p > 0.05$), while group c showed a deterioration of 0.1 points ($p > 0.05$). At the beginning of the research, the psycho-emotional state of the female students was assessed as impaired, and at the end, in group a, it was assessed as good, while in the other groups, it remained unchanged. Furthermore, at the end of the research, the indicators for female students in group a were significantly higher than those in group c by 0.9 points ($p < 0.01$), confirming our previous conclusions.

The analysis of the female students' somatic health levels showed that in group a, there was a statistically significant improvement in health by 1.7 points ($p < 0.01$) during the distance learning period; in group b, the improvement was not statistically significant (by 0.2 points; $p > 0.05$), while in group c, the female students' somatic health

Table 1. Dynamics of female students' psychosomatic health indicators during distance learning under martial law depending on the weekly volume of motor activity (n=252), Mean±m, points

Groups of female students	n	Research stages		Significance of the difference	
		Beginning	End	Difference	t; p
Stress level					
a	75	13.9±0.92	10.8±0.98	3.1	2.31; <0.05
b	95	14.1±0.83	13.9±0.95	0.2	0.16; >0.05
c	82	13.8±0.89	14.5±0.93	0.7	0.54; >0.05
t; p (a-b)		0.16; >0.05	2.27; <0.05		
t; p (b-c)		0.25; >0.05	0.45; >0.05		
t; p (a-c)		0.08; >0.05	2.74; <0.01		
Neuropsychological stress level					
a	75	65.7±1.13	61.9±1.17	3.8	2.34; <0.05
b	95	66.4±1.09	65.7±1.12	0.7	0.45; >0.05
c	82	64.9±1.11	66.2±1.14	1.3	0.82; >0.05
t; p (a-b)		0.45; >0.05	2.35; <0.05		
t; p (b-c)		0.96; >0.05	0.31; >0.05		
t; p (a-c)		0.51; >0.05	2.63; <0.05		
Psycho-emotional state					
a	75	5.3±0.17	6.2±0.16	0.9	3.86; <0.001
b	95	5.6±0.15	5.8±0.16	0.2	0.91; >0.05
c	82	5.5±0.16	5.3±0.17	0.1	0.43; >0.05
t; p (a-b)		1.32; >0.05	1.77; >0.05		
t; p (b-c)		0.46; >0.05	1.71; >0.05		
t; p (a-c)		0.86; >0.05	3.43; <0.01		
Somatic health level					
a	75	14.5±0.42	12.8±0.38	1.7	3.01; <0.01
b	95	14.6±0.37	14.4±0.36	0.2	0.39; >0.05
c	82	14.7±0.39	15.2±0.41	0.5	0.88; >0.05
t; p (a-b)		0.18; >0.05	3.06; <0.01		
t; p (b-c)		0.19; >0.05	1.47; >0.05		
t; p (a-c)		0.35; >0.05	4.29; <0.001		

Notes: Mean – arithmetic mean; m – error of arithmetic mean; n – number of female students; t – Student's test value; p – reliability value

Source: compiled by the authors of this study

deteriorated by 0.5 points ($p>0.05$). At the beginning of the research, the health level in all groups was assessed as satisfactory; at the end, in group a as average, and in the other groups as satisfactory. At the end of the research, the health level of female students in group a was significantly better than in group b and group c by 1.6 and 2.4 points, respectively ($p<0.01$; $p<0.001$). This once again demonstrates the effect of regular, systematic physical exercise in strengthening students' somatic health during their distance learning.

To address the second task of this work, we examined the dynamics of psychosomatic health indicators among female students in group a, depending on the focus of their physical exercise routines (Table 2). Thus, the comparative

analysis of stress levels in the subgroups of female students in group a who adhered to a rational regimen of motor activity during their distance learning indicates that at the beginning of the research, stress levels in all subgroups were significantly similar ($p>0.05$) and were assessed as pronounced. However, following distance learning, a significant decrease in stress levels ($p<0.05$) occurred across all subgroups of female students, regardless of the type of motor activity. At the same time, no significant differences were found between the subgroups at the end of the research ($p>0.05$), indicating the effectiveness of all proposed forms of motor activity during distance learning.

When assessing the level of neuropsychological stress, it was found that across all subgroups of female students in

group a, there were statistically significant decreases of 3.9, 3.8, and 3.7 points, respectively, over the research period ($p < 0.05$). At the same time, both at the beginning and at the end of the research, the level of neuropsychological stress among female students in subgroups a 1, a 2, and a 3 did not differ significantly from one another ($p > 0.05$), which allows us to conclude that any form of motor activity is effective during distance learning.

Based on the results of the study of the psycho-emotional state of female students in the three subgroups of group a, we found no significant differences among subgroups a 1, a 2, and a 3 at either the beginning or the end of the research. At the same time, all three subgroups showed

significant improvements in indicators over the research period ($p < 0.01$), underscoring the benefits of regularly performing physical exercise during distance learning.

It should be noted that, overall, performing physical exercises during distance learning has a positive effect on the somatic health of female students: over the research period, in all three subgroups of group a, health levels improved significantly ($p < 0.05$) by 1.4–1.8 points, respectively. Moreover, no significant differences were found between the subgroups' indicators at the end of the research ($p > 0.05$), indicating a positive impact of targeted, regular engagement across all proposed forms of motor activity on somatic health.

Table 2. Dynamics of female students' psychosomatic health indicators who adhered to a rational regimen of motor activity during their distance learning, depending on the focus of their physical exercise sessions ($n = 252$), Mean $\pm$ m, points

Subgroups of female students	n	Research stages		Significance of the difference	
		Beginning	End	Difference	t; p
Stress level					
a1	23	13.8±1.05	10.7±1.09	3.1	2.05; <0.05
a2	27	14.2±1.11	11.1±1.07	3.1	2.01; <0.05
a3	25	13.9±1.07	10.8±1.10	3.1	2.02; <0.05
t; p (a1-a2)		0.26; >0.05	0.27; >0.05		
t; p (a2-a3)		0.19; >0.05	0.20; >0.05		
t; p (a1-a3)		0.07; >0.05	0.06; >0.05		
Neuropsychological stress level					
a1	23	65.4±1.24	61.5±1.20	3.9	2.26; <0.05
a2	27	65.8±1.21	62.0±1.16	3.8	2.27; <0.05
a3	25	66.0±1.22	62.3±1.18	3.7	2.18; <0.05
t; p (a1-a2)		0.23; >0.05	0.30; >0.05		
t; p (a2-a3)		0.12; >0.05	0.18; >0.05		
t; p (a1-a3)		0.24; >0.05	0.48; >0.05		
Psycho-emotional state					
a1	23	5.5±0.20	6.5±0.19	1.0	3.62; <0.01
a2	27	5.2±0.18	6.0±0.17	0.8	3.23; <0.01
a3	25	5.1±0.19	6.1±0.18	1.0	3.82; <0.01
t; p (a1-a2)		1.11; >0.05	1.96; >0.05		
t; p (a2-a3)		0.38; >0.05	0.40; >0.05		
t; p (a1-a3)		1.45; >0.05	1.53; >0.05		
Somatic health level					
a1	23	14.6±0.55	12.8±0.48	1.8	2.47; <0.05
a2	27	14.3±0.49	12.9±0.45	1.4	2.10; <0.05
a3	25	14.5±0.52	12.7±0.47	1.8	2.57; <0.05
t; p (a1-a2)		1.11; >0.05	1.96; >0.05		
t; p (a2-a3)		0.38; >0.05	0.40; >0.05		
t; p (a1-a3)		1.45; >0.05	1.53; >0.05		

Notes: Mean – arithmetic mean; m – error of arithmetic mean; n – number of female students; t – Student's test value; p – reliability value

Source: compiled by the authors of this study

DISCUSSION

Researchers [23, 24] assert that the quality of the educational process and learning outcomes are directly proportional to students' health. At the same time, a sedentary lifestyle during distance learning prevents students from adequately exercising their heart muscles and blood vessels. This subsequently leads to the development of cardiovascular diseases: narrowing of the smallest blood vessels and capillaries, the onset of vegetative-vascular dystonia, hypotension, hypertension, and underdevelopment of the heart muscle (myocardium) [25]. A student's sedentary lifestyle during distance learning leads to physical inactivity, which negatively impacts the musculoskeletal system and the body's major systems. This leads to a slowing of blood circulation, resulting in a reduced supply of oxygen to all organs and systems; the body cannot keep up with renewal during mental exertion; consequently, the quality of learning new material and the speed of processing it deteriorate [26, 27].

Physical inactivity negatively affects the back muscles and spine; the space between the vertebral discs decreases, and conditions such as osteochondrosis, scoliosis, stooped posture, and muscle spasms develop, resulting in back and neck pain, headaches, and general discomfort [28]. Osteoarthritis of the knee joints may develop, which is a slowly progressive degenerative disease characterized by the gradual deterioration of the articular cartilage. Prolonged sitting weakens vascular tone, causing edema, venous stasis, and heaviness in the legs [29]. Moreover, physical inactivity leads to a significant increase in body weight and even signs of obesity, which, in turn, negatively affects endurance, strength, and other motor abilities, as well as the functional state of the body's vital systems [30].

Scientists [8] also note that constant learning using computer technology contributes to vision deterioration. Eye strain arises from prolonged periods of intense focus, constant reading and writing, and extended use of computers and tablets, leading to noticeable vision impairment, dryness, and redness of the eyes. Prolonged strain on the eye muscles leads to fatigue, irritation, and, over time, chronic headaches, insomnia, and eye diseases [8]. Changes in the central nervous system and the onset of asthenic syndrome are also possible, manifesting as emotional instability and rapid fatigue, a slowing of metabolic processes, hormonal imbalance, and more [4].

As noted by scientists in their studies [5], the shift from in-person to distance learning has increased the risk of mental and physical health strain among students. After all, in the distance learning format, relationships with teachers and students have completely changed in nature; they have shifted from face-to-face to online communication via social media, video calls, email, and other internet resources, which has significantly reduced the effectiveness of information exchange and, consequently, the effectiveness of learning. Constant stress caused by a heavy information load and intellectual strain leads to rapid fatigue, irritability, emotional instability, impaired attention and memory, headaches, and a decline in overall well-being. The large

volume of online information and its processing, the need for analysis and memorization, the monotony of information reception, and the limited feedback cause tension, reduced concentration, and, as a result, intellectual burnout, which lowers the quality of student learning and the retention of acquired knowledge [1].

The scientific literature [9] presents several practical recommendations to improve students' psychophysical health during distance learning. Thus, according to the recommendations of the World Health Organization, students are advised to: engage in moderate- to high-intensity physical activity for at least 60 minutes a day throughout the week, primarily involving aerobic exercise; engage in high-intensity aerobic physical activity at least 3 times a week, as well as activities that strengthen the musculoskeletal system; limit time spent sitting, especially in front of a screen for entertainment purposes [12].

According to researchers [14], reducing the amount of time spent at the computer (screen time), strictly adhering to guidelines for working at a screen (proper organization of work hours), getting sufficient and restful sleep, increasing motor activity (morning exercises, walks in the fresh air, workouts, active recreation), mandatory eye breaks, a balanced diet, the ability to plan one's day, and a proper and comfortable workspace setup – these are the essential conditions that will help mitigate the negative impact of distance learning and the key measures that virtually eliminate the risk of harm to students' health.

In our research, we examined the dynamics of female students' psychosomatic health indicators during their distance learning depending on the weekly volume of motor activity and the focus of exercise sessions. We found that regular exercise during distance learning helps maintain students' psychosomatic health. At the same time, all forms of motor activity studied (of various types) proved to be effective. The results of our research complement and expand upon the recommendations of many researchers [2, 3, 10, 13, 14, 17, 25, 30] regarding the improvement of students' psychosomatic health during their distance learning in wartime conditions.

CONCLUSIONS

It was found that among female students who adhered to a rational regimen of motor activity during their distance learning (group a), psychosomatic health indicators significantly improved ($p < 0.05$). In contrast, group b and group c deteriorated. Furthermore, upon returning from distance learning, female students in group a demonstrated significantly better indicators ($p < 0.05$ – 0.001) than those in group b and group c. The most pronounced negative changes in group c were observed in indicators of stress levels, neuropsychological tension, and the emotional state of the female students. The vast majority of students in group b and group c complained of headaches, sleep problems, digestive disorders, increased fatigue, decreased physical and mental performance, low mood, anxiety, and irritability. At the end of the research, all subgroups of group a exhibited statistically similar indicators of psychosomatic

health ($p>0.05$), regardless of the focus of the physical exercise sessions.

The results demonstrate the effectiveness and appropriateness of incorporating a reasonable amount of physical activity to maintain and improve students' psychosomatic health indicators during distance learning under martial law. At the same time, physical exercise of any type helps reduce stress and neuropsychological

tension, strengthen health, improve students' well-being and mood, increase their work capacity, and, consequently, their academic performance during wartime.

PROSPECTS FOR FURTHER RESEARCH

It is planned to investigate the relationship between students' psychosomatic health indicators and their academic performance during distance learning.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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The impact of controlled physical loads on the level of resilience of cadets

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ABSTRACT

Aim: To investigate the impact of controlled physical loads on the level of resilience of cadets.

Materials and Methods: The study lasted for one academic year (September 2024–June 2025) and had a longitudinal design. It involved 127 cadets divided into an experimental group (EG, N=65) and a control groups (CG, N=62). Cadets of the EG, during sports and mass work (SMW), engaged according to the developed programme, whereas cadets of the CG followed the current programme of SMW. The programme of controlled physical loads included breathing exercises, progressive muscle relaxation, exercises for developing psychophysiological endurance, as well as exercises for maintaining the balance of the neuromuscular system. The resilience of the cadets was assessed using the Connor-Davidson Resilience Scale (CD-RISC-10).

Results: The results of the study of the impact of controlled physical loads on the level of resilience of cadets demonstrated statistically significant differences between the EG and CG at the end of the study ($|t|=3.63>1.96$; $p<0.001$), which confirmed the effectiveness of the proposed programme. In the EG, there was a substantial increase in the number of cadets with a high level of resilience (from 27% to 45%), whereas in the CG this indicator remained unchanged.

Conclusions: The practical significance of the obtained results lies in the possibility of integrating the programme of controlled physical loads into cadet training curricula as a means of purposefully developing their psychological readiness to act under extreme conditions.

KEYWORDS: resilience, controlled physical loads, physical activity, stress resistance, cadets, psychophysiological adaptation

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INTRODUCTION

The Russian armed aggression has significantly transformed all spheres of peaceful life of the population of Ukraine, destroying the basic sense of security and causing profound psychological distress, the consequences of which are dangerous for both children and the adult population. The war has become an extreme, and in some cases hyper-extreme, factor for certain social groups, as the internal psycho-emotional loads it generates often exceed the limits of human adaptive capacities [1, 2].

Armed aggression has led to substantial psychological consequences, in particular a decrease in stress resistance among higher education students and an increase in the intensity and frequency of experiencing stress-related conditions [3, 4]. According to research findings [5, 6], more than half of cadets affected by the war experience manifestations of stress, and about two thirds of them report difficulties in coping with it.

Cadets of higher education institutions are, on the one hand, active students and, on the other, future military personnel.

Thus, in the course of their studies, cadets encounter a multidimensional spectrum of stressors that require targeted intervention in order to optimise the emotional-volitional sphere, reduce the level of psychophysiological tension, and prevent destructive manifestations of stress [7, 8]. The multidimensionality of stress loads is determined by the complex system of social and professional roles combined within the cadet. They simultaneously act as a student mastering an educational programme under conditions of high academic intensity; as a citizen of a state under armed aggression; and as a future officer entrusted with responsibility for fulfilling military duty and readiness to participate in combat operations. Such a combination of roles creates a specific psychological burden that requires targeted psychological support and systematic preparation for overcoming stress [9, 10].

According to scholars [11–14], one of the methods of preventing stress conditions and coping with stress is the use of controlled physical loads. From a practical perspective on the training of future officers, the greatest interest

lies not in the direct struggle against stress, but in the possibility of teaching cadets to counteract the negative effects of stress and to strengthen their resistance to its consequences. Therefore, the main objective of this study is to investigate the impact of controlled physical loads on the resilience of cadets. Resilience, or psychological stability, in contemporary scholarship is defined as the ability of an individual to restore effectiveness after exposure to stressors while maintaining cognitive and emotional balance [15, 16]. For future officers, the development of resilience is critically important, as it determines not only professional reliability but also the ability to maintain viability under combat conditions [17-19].

According to studies [20, 21], physical activity acts as a powerful regulator of emotional states, levels of anxiety, and biochemical indicators of stress. In this context, physical exercise may be considered not only as a means of physical training, but also as an instrument of preventive psychophysiological stabilisation that shapes adaptive behaviour in extreme situations.

AIM

The aim is to investigate the impact of controlled physical loads on the level of resilience of cadets.

MATERIALS AND METHODS

The study involved 127 second-year cadets enrolled in various faculties of the Kruty Heroes Military Institute of Telecommunications and Information Technology (Kyiv, Ukraine). The participants were divided into control groups (CG1, N=32; CG2, N=30) and experimental groups (EG1, N=33; EG2, N=32). In total, the groups comprised 110 males and 17 females. Within the framework of the study, the cadet was considered as a future combat unit; therefore, gender specificity was not analysed. Differences by sex influenced only the selection of exercises during physical training in accordance with the current regulatory documents.

To confirm the homogeneity of the groups at the ascertaining stage, a comparative analysis of the physical fitness and resilience levels of the cadets was conducted. The results of cadets' performance in physical exercises were examined (for males: 100 m sprint, combined strength exercise on the horizontal bar, 3 km run, shuttle run 6 × 100 m; for females: 100 m sprint, trunk flexion and extension, 3 km run, agility exercise), and the level of resilience was assessed using the Connor–Davidson methodology (CD-RISC-10).

The level of physical fitness of the cadets was assessed using a 12-point scale (rating system – RS) and interpreted as follows: 11-12 points – high level, 8-10 – sufficient, 5-7 – satisfactory, <5 – unsatisfactory). Resilience was measured according to the standard scale of the Connor–Davidson methodology (CD-RISC-10): low; below average; average; above average; high [22, 23].

The study of the level of development of physical qualities of cadets in different groups at the ascertaining stage showed that none of the cadets had a low level of physical fitness. The differences between the achievements of cadets in

the respective groups (CG1 vs CG2 and EG1 vs EG2) were not statistically significant. Thus, the mean RS score for CG1 was 8.99 compared to approximately 8.44 in CG2. The difference between the mean scores was $|8.99-8.44|=0.47$ points. The calculation of Student's t-test ($df=60$) showed $|t|=1.005722 < 1.96$ ($\alpha=0.05$). Similarly, the calculation of Student's t-test for the experimental groups showed $|t|=0.963 < 1.96$ ($\alpha=0.05$). Thus, no statistically significant differences were found between the experimental groups or between the control groups, which allowed us, at the ascertaining stage of the experiment, to combine both control groups into a single sample CG (N=62), and to consider the experimental groups as a single group EG (N=65). A comparison between EG and CG using Student's t-test also showed that the differences between them were not statistically significant $|t|=0.763 < 1.96$ ($\alpha=0.05$).

The generalised results of the physical fitness of cadets in the CG and EG are presented in Table 1. The results indicate that 59.2% of cadets in the EG and 59.3% of cadets in the CG were at sufficient and high levels, which confirms the statistical homogeneity of the groups at the initial stage of the study.

STUDY OF THE LEVEL OF RESILIENCE AT THE ASCERTAINING STAGE

The initial measurement of resilience using the CD-RISC-10 scale also confirmed the similarity of the groups. In the CG (N=62) and EG (N=65), the distribution of cadets across categories was similar, with a predominance of the 'average' and 'above average' levels. The mean values made it possible to test the hypothesis of equality of means: $df=123$, $|t|=1.52 < 1.96$ ($\alpha=0.05$), which also confirms the statistical homogeneity of the groups prior to the experimental intervention.

Thus, at the ascertaining stage, the two groups did not differ in terms of the level of physical fitness and resilience, which is a necessary condition for further comparative analysis of the results of the experimental programme.

Both groups performed physical exercises in accordance with the approved physical training programmes and regulatory documents of the Ministry of Defence of Ukraine. The results were conditionally assessed according to four levels: low, satisfactory, sufficient, and high, corresponding to the rating scale (RSO 1-4, 5-7, 8-10, 11-12).

The level of resilience was assessed using the short version of the Connor–Davidson Resilience Scale (CD-RISC-10). This version comprises 10 of the most informative items from the original CD-RISC-25, selected on the basis of factor analysis to ensure validity and reliability [24]. The purpose of applying this instrument was to determine the individual level of stress resistance and the capacity for adaptation under stress, which is essential for preparing cadets to perform combat tasks.

The experimental programme of controlled physical loads included three stages:

Adaptive-toning stage (first 2 months): breathing regulation exercises, stretching, static body holds, and post-tension relaxation.

Table 1. Generalized results of the physical fitness of cadets in the CG and EG, %

Exercise	Level of Physical Fitness					
	Satisfactory		Sufficient		High	
	CG	EG	CG	EG	CG	EG
100 m run	11.3	12.3	11.3	15.4	77.4	72.3
Combined strength exercise (sit-ups)	37.1	33.8	4.8	9.3	58.1	56.9
3 km run	27.4	27.7	12.9	13.8	59.7	58.5
Shuttle run 6×100 m	32.3	33.8	67.7	66.2	0.0	0.0
Agility exercise	30.6	30.8	21.0	21.5	48.4	47.7
Integral assessment	27.74	27.68	23.54	25.24	48.72	47.08

Source: compiled by the authors of this study

Regulatory-dynamic stage (from the 3rd to the 6th months): a combination of aerobic (running, swimming, loaded marches) and moderate-intensity strength exercises with heart rate monitoring (HR=60-70% of the maximum value).

Stabilisation–resilience stage (months 7-9): stress-modelling exercises (training under conditions of noise, time constraints, and temperature variation), short sessions of body-based meditation and self-mobilisation.

The duration of each session was 90 minutes, with a frequency of three times per week. The programme was structured as a controlled intervention: physiological parameters (heart rate, blood pressure, and level of tension) were monitored using portable biomonitors, and the load was adjusted individually.

The main exercises included a 100 m sprint, a combined strength exercise on the horizontal bar, trunk flexion and extension, a 6 × 100 m shuttle run with a rifle and magazine pouch, as well as a complex agility exercise.

Relaxation and psychophysiological stability exercises. The process of practising relaxation techniques involved performing a set of specially selected exercises aimed at the gradual relaxation of the muscles of the arms, legs, trunk, neck, and face. Each exercise was performed sequentially in order to develop the ability to consciously alternate between muscle tension and relaxation, which constitutes a fundamental condition for achieving psycho-emotional balance and maintaining optimal combat readiness.

- The progressive muscle relaxation complex included:
- relaxation of the arm muscles – tension from the shoulders to the hands followed by relaxation and concentration on sensations of warmth and vibration;
 - relaxation of the leg muscles – tension in both legs with simulated pressure of the feet against a surface, followed by complete relaxation and awareness of changes in sensation;
 - relaxation of the trunk muscles – tension of the abdominal and back muscles followed by gradual release of tension;
 - relaxation of the neck muscles – drawing the head into the shoulders to create tension followed by relaxation;

- relaxation of the facial muscles – sequential tension and relaxation of individual muscle groups (forehead, eyes, lips, jaw, tongue) to reduce emotional tension.

Additional exercises were aimed at detailed work with the hands, forearms, shoulders, lower legs, and thighs, performed according to a scheme of short-term (4-5 s) tension followed by rapid relaxation, which contributes to the development of conscious control of bodily states and enhances psychophysiological resilience.

The study was conducted from September 2024 to May 2025. The level of resilience was assessed twice: at the beginning and after completion of the experimental programme. The CD-RISC-10 scale was used to evaluate the dynamics of the results, along with rating systems for assessing the physical performance of cadets.

The procedure for organizing the study and the topic of the article were previously agreed with the Committee on compliance with Academic Integrity and Ethics of the Heroes Military Institute of Telecommunications and Information Technology. Also this study followed the regulations of the World Medical Association Declaration of Helsinki. Informed consent was received from all cadets who took part in this study.

FRAMEWORK

The study was conducted within the framework of the Scientific Research Plan of the Department of Physical Culture and Sports of the National University of Life and Environmental Sciences of Ukraine for 2023-2026 within the framework of the scientific research work «Theoretical and methodological foundations of educational work in environmental and agricultural higher educational institutions». State registration number 0115U003561.

RESULTS

The study of cadets’ resilience levels at the end of the research period demonstrated a pronounced positive dynamic in the experimental group (EG), whereas in the control group (CG) the indicators remained almost unchanged (Table 2).

Table 2. Results of the study of resilience levels in cadets of the EG and CG at the end of the research period, %

Level of Resilience	CG (N = 62)	EG (N = 65)
Low (0-15)	0	0
Below Average (16-20)	6.2	1.3
Average (21-25)	29.0	20.4
Above Average (26-30)	36.6	32.9
High (31-40)	28.3	45.4

Source: compiled by the authors of this study

The calculation of the significance of differences using Student's t-test showed that its value substantially exceeds the critical threshold: $|t|=3.63 > 1.96$. Thus, the obtained t-value is statistically significant at the level of $p < 0.001$. This indicates that the level of resilience in the experimental group (EG) after the implementation of the exercise complex is significantly higher than in the control group (CG) following the experimental programme. The differences exceed the threshold of statistical significance ($\alpha=0.05$), confirming the effectiveness of the proposed intervention.

To assess the stability of changes and the internal consistency of the data, a Pearson correlation analysis was conducted between the mean resilience scores at the baseline and formative stages within each group (assuming normal distribution of the data, as confirmed by the Shapiro-Wilk test at the sample level).

CG: M1const=21.62 points, M1form=28.12 points;

EG: M2const=22.78 points, M2form=30.34 points.

Let us consider the increase in resilience:

$\Delta CG = 28.12 - 21.62 = 6.50$ points;

$\Delta EG = 30.34 - 22.78 = 7.56$ points.

The difference in increase: $7.56 - 6.50 = 1.06$, which constitutes approximately a 16% relative excess of the increase in the EG compared to the CG. This further confirms the effectiveness of the experimental intervention.

Thus, at the beginning of the study, the differences between the results of the CG and EG were not statistically significant; however, after the formative stage, a statistically significant increase in the level of resilience was recorded in the EG.

DISCUSSION

The findings of the study are consistent with the conclusions of scholars [19, 25, 26], who demonstrate that regular physical activity stimulates hormonal regulation of the stress system, particularly through the normalisation of cortisol levels. In the context of military education, the obtained data indicate that systematic physical exercises structured according to the principle of controlled load can enhance cadets' adaptability to psycho-emotional overload and contribute to the development of confidence in their own capabilities.

The results show that controlled physical loads have a significant impact on increasing the level of resilience in cadets. Repeated measurement demonstrated that after the implementation of the experimental programme, the mean level of resilience in the EG increased from 22.78 to

30.34 points, whereas in the CG the increase was smaller, from 21.62 to 28.12 points. The absolute increase in the EG was 7.56 points, compared to 6.50 points in the CG; the relative excess of increase in the EG compared to the CG was approximately 16%, indicating the additional effectiveness of the applied exercises.

Statistical analysis confirmed the significance of the differences. The calculation of Student's t-test yielded $|t|=3.63$ with $df=123$, exceeding the critical value of 1.96 for $\alpha=0.05$ ($p < 0.001$). This indicates that the mean level of resilience in the EG after the experimental programme is significantly higher than in the CG. To assess the effect size, Cohen's d was calculated ($d \approx 0.44$). This value corresponds to a 'moderate effect' according to Cohen's classification, underscoring the practical significance of the intervention. The 95% confidence interval for the difference between means was $CI \approx (2.22 \pm 1.16) \rightarrow [1.06; 3.38]$, which confirms the statistical significance and reliability of the results.

The mechanism of the influence of physical loads on psycho-emotional stability can be explained by both physiological and psychological factors. Physical exercise contributes to the normalisation of cortisol levels and other stress-related hormones, as confirmed by numerous studies [27]. At the same time, regular training enhances brain neuroplasticity, promotes the release of endorphins, and stimulates systems responsible for mood regulation and emotional stability [28]. Psychologically structured physical exercises also function as a form of "controlled stress", preparing individuals for rapid adaptation to extreme situations, which is particularly relevant for cadets [29].

It should be noted that controlled physical loads represent one of the most accessible methods of enhancing resilience, though not the only one. The optimal development of psychological stability requires a comprehensive approach that includes psychological training, cognitive self-regulation techniques, and social support [8, 9, 30].

Thus, the obtained results confirm the effectiveness of implementing structured physical exercises in the educational process of cadets to enhance their psycho-emotional stability and resilience, highlighting the need for a comprehensive and systematic approach to the development of psychophysiological readiness for stressful situations.

CONCLUSIONS

It has been demonstrated that the targeted implementation of a system of controlled physical loads in the process of

cadets' physical training significantly increases their level of resilience. In contrast to the existing physical training programme, the specially designed complex, which combines physical exercises with breathing regulation techniques and progressive muscle relaxation, ensures a statistically significant increase in the individual's adaptive potential.

A comparative analysis of the CD-RISC-10 scale indicators after the completion of the longitudinal study (September 2024 – June 2025) revealed statistically significant differences between the experimental and control groups ($|t|=3.63$, $p<0.001$). The calculation of the effect size (Cohen's $d \approx 0.44$) indicates a moderate yet practically significant impact of the proposed intervention on the psycho-emotional state of cadets.

In the experimental group, a substantial increase in the number of cadets with a high level of resilience was recorded (from 27% to 45%), whereas in the control group this indicator remained almost unchanged. This confirms that controlled physical loads contribute not only to the overall improvement of the psycho-emotional state but also to the transition of the individual to a qualitatively

higher level of stress resistance required for functioning in extreme conditions.

It has been established that the positive dynamics are determined the complex impact of the exercises on the neuromuscular system and hormonal balance. The combination of aerobic loads, balance exercises, and relaxation techniques acts as 'controlled stress', training self-regulation mechanisms, reducing anxiety levels, and enhancing the capacity for rapid recovery after psychophysiological strain.

The obtained results substantiate the feasibility of integrating elements of the controlled physical loads programme into cadet training curricula. The proposed programme may be recommended as a means of preventing professional burnout and enhancing cadets' combat readiness under martial law conditions, and may also be adapted for other categories of individuals exposed to chronic stress.

PROSPECTS FOR FURTHER RESEARCH

Prospect for further research is to investigate the impact of controlled physical loads on the level of cadets' somatic and mental health under martial law.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Maxillofacial surgical care transformation during COVID-19 and war in Ukraine: Hospital experience

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ABSTRACT

Aim: To assess the activity of the maxillofacial service during the COVID-19 pandemic and Russia's military aggression in the context of the burden on the medical service and the transformation of the structure of disease entities and categories of surgical interventions.

Materials and Methods: The study was conducted at a supracluster-level healthcare institution – the Communal Non-Commercial Enterprise “Kyiv Regional Clinical Hospital No. 1”. An assessment of the staffing of the team (physicians and auxiliary personnel) was performed, and an evaluation of the maxillofacial surgery department activity was carried out based on qualitative and quantitative indicators for the reporting period during the COVID-19 pandemic and the beginning of the full-scale invasion.

Results: Analysis of the dynamics of hospitalizations in the maxillofacial department in 2019–2024 showed that the average number of hospitalizations was 1,095 patients per year. The lowest rate was registered in 2022 (886 patients), while the highest was in 2024 (1 224 patients). The proportion of emergency admissions ranged from 23.5% to 57.1%. The highest level of emergency hospitalizations was noted in 2021 (57.1%), after which there was a gradual decrease in this indicator to 23.5% in 2024.

Conclusions: Reforming the maxillofacial service and the field of maxillofacial surgery in Ukraine is necessary to ensure high quality, accessibility, and effectiveness of medical care.

KEYWORDS: maxillofacial surgery, medical care, disease entities

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INTRODUCTION

The maxillofacial surgeon belongs to a specific category of healthcare worker, as they inevitably come into contact with the oral cavity, upper airways, and patients' secretions (such as saliva, mucus, and blood) during the diagnostic and treatment process. This places them at high risk of infection and, in turn, of becoming a source of contagion [1]. In different countries, the current healthcare burden from space infections reflects the ongoing neglect of preventive oral health care and delayed patient presentation [2].

The COVID-19 pandemic has significantly disrupted the delivery of healthcare, including oral healthcare services. The restrictions imposed to mitigate the spread of the virus forced dental practitioners to adopt substantial changes in their workflow [3, 4]. The COVID-19 pandemic has had a profound impact on healthcare systems worldwide. In some cases, it led to the overburdening of healthcare facilities due to the increased number of patients infected with COVID-19, resulting in workload overload and resource shortages. This affected both staff and medical equipment [5, 6].

From a social perspective, this situation highlights the need for a scalable organizational model capable of increasing the safety of surgical interventions, reducing the frequency of complications and repeat operations,

shortening treatment duration, and optimizing the use of healthcare resources. The implementation of these findings at the level of the Ministry of Health of Ukraine and specialized professional associations will contribute to updating professional standards, improving clinical protocols, and strengthening the staffing stability of the surgical service. Thus, this work provides a basis for the transformation of the organization of specialized care for patients with maxillofacial pathology and head and neck injuries under conditions of prolonged military burden and the post-war recovery of the healthcare system of Ukraine [6].

AIM

The purpose of this study was to assess the activity of the maxillofacial service during the COVID-19 pandemic and Russia's military aggression in the context of the burden on the medical service and the transformation of the structure of disease entities and categories of surgical interventions.

MATERIALS AND METHODS

The reference institution was designated as a supracluster-level healthcare facility – the Communal Non-Commercial Enterprise “Kyiv Regional Clinical Hospital No. 1”. As of 2019, the structure of the medical institution included

a head and neck pathology center consisting of two departments: the Department of Maxillofacial Surgery and the Department of Otorhinolaryngology. An assessment of staffing (physicians and auxiliary personnel) was performed. An evaluation of the activity indicators of the maxillofacial surgery department was carried out using qualitative and quantitative indicators for the reporting period during the COVID-19 pandemic and the beginning of Russia's full-scale invasion of Ukraine, based on primary medical accounting and statistical documentation approved by the Ministry of Health of Ukraine.

The scope of treatment activities included standard surgical procedures and both elective and emergency surgical interventions using modern methods for the prevention, diagnosis, and treatment of infectious and purulent-inflammatory processes of the maxillofacial region of various origins.

Among the innovative technologies and new areas of activity, it is worth noting arthrocentesis and arthroscopy of the temporomandibular joint (TMJ), stenting of the excretory ducts of major salivary glands and sialoendoscopy in patients after radioiodine therapy, fabrication of external prostheses of the ear and eye, endoprosthesis-obturators in maxillofacial prosthetics, orthognathic surgery, and, in particular, surgically assisted rapid maxillary expansion with the installation of a palatal distractor; TMJ endoprosthesis using individualized titanium implants; surgical treatment of patients with endocrine orbitopathy; facial nerve reconstruction using the sural nerve after total parotidectomy with facial nerve resection; reconstruction of soft tissue defects using free transfer of complex tissue flaps with restoration of their blood supply and hard tissues using individualized titanium implants; as well as the application of computer-aided design/computer-aided manufacturing (CAD/CAM) technologies (reconstruction of the midface region with individualized titanium implants, production of individualized orbital plates from polyether ether ketone (PEEK), resection guides, and osteotomy templates).

Statistical data processing was performed using descriptive statistics, time-series analysis, and structural analysis with MedStat v. 5.2 and EZR v. 1.68 software. Absolute growth, growth rates, and growth increments were calculated.

Poisson regression was used to assess statistical significance in the dynamics of hospitalizations. The level of statistical significance was set at $p < 0.05$.

ETHICS

The study was conducted in accordance with the principles of the Declaration of Helsinki and bioethical standards for conducting sociological surveys in the medical field. The results are presented in summary tables and charts, which makes it impossible to identify specific individuals. The research protocol underwent peer review and received approval from the local Bioethics Committee of the National Medical University.

FRAMEWORK

The article was prepared according to the scientific research issue of Department of Maxillofacial Surgery at the Bogomolets National Medical University «Clinical and experimental justification of new methods of rehabilitation of patients with defects and deformities of the maxillofacial area using digital technologies and patient-specific solutions» (0125U002378)

RESULTS

An analysis of the dynamics of hospitalization in the maxillofacial department in 2019–2024 showed that the average number of hospitalizations was $1095 \pm 102,1$ patients per year. The lowest rate was registered in 2022 (886 patients), while the maximum – in 2024 (1224 patients). The proportion of urgent hospital admissions ranged from 23.5% to 57.1%. The highest level of urgent hospitalizations was noted in 2021 (57.1%), after which there was a tendency to gradually decrease this indicator to 23.5% in 2024 (Table 1).

Formally, there is a very weak upward trend in the total number of hospitalizations. However, Poisson regression analysis demonstrated no significant temporal trend in hospitalization rates over the 6-year period (Incidence Rate Ratio [IRR] ≈ 0.999), indicating a stable incidence over time (Fig. 1).

There was a tendency toward a decrease in the number of emergency hospitalizations of approximately 29.6 cases per year; however, given the available number of observations,

Table 1. Dynamics of operational processes related to bed fund and patient route

Year	Number of consultations in the department	Total number of hospitalized patients (N)	Proportion of urgent patients (n)	Average length of stay of the patient on the bed (days)	Overall lethality *
2019	-	1134	388	5.6	0.1
2020	-	1107	373	4.3	0.2
2021	-	1104	630	3.5	0.6
2022	2197	886	306	5.1	0.6
2023	3073	1117	302	4.8	0.8
2024	-	1224	288	-	-

Note: * – it was calculated as the ratio of the number of dead and the total number of discharged and deceased over a certain period of time

Source: compiled by the authors of this study

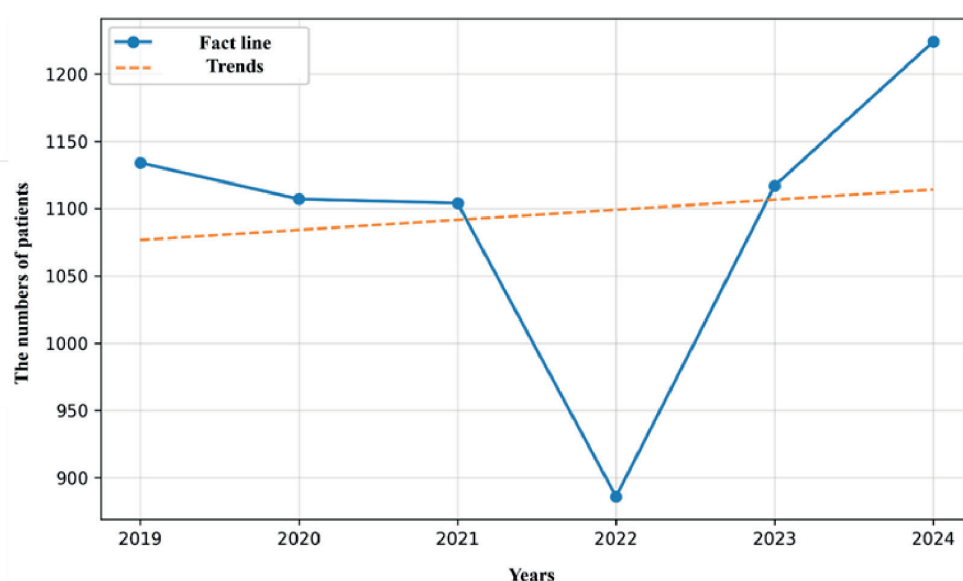


Fig. 1. Dynamics of general hospitalization in the maxillofacial department (2019-2024)

Picture taken by the authors

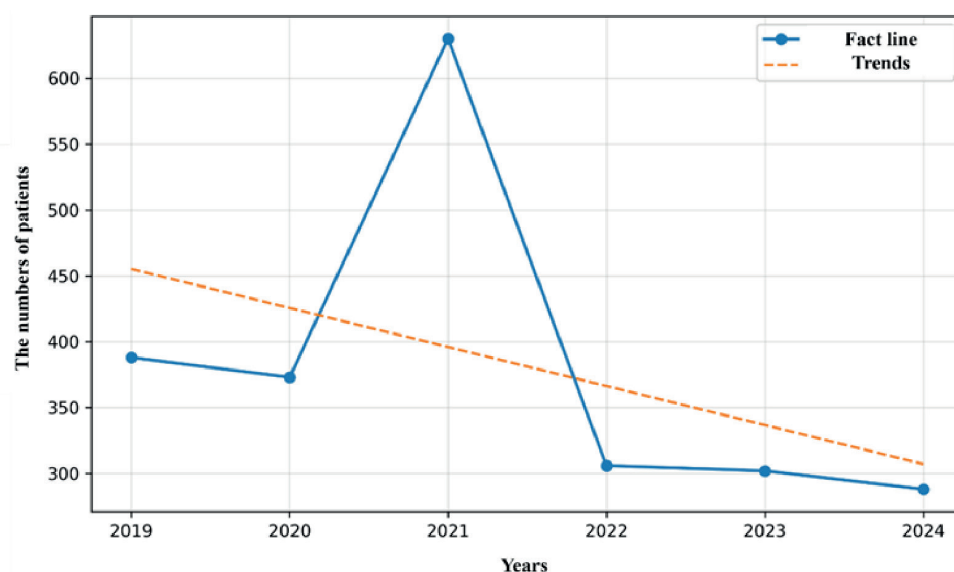


Fig. 2. Urgent share of hospitalization in the structure of the maxillofacial department (2019-2024)

Picture taken by the authors

this trend was not statistically confirmed. Poisson regression analysis also showed a non-significant decreasing trend in hospitalization rates over time (IRR=0.963, 95% CI: 0.917-1.011, $p=0.13$) (Fig. 2).

It is important to note that during the COVID-19 pandemic, a special algorithm for testing primary patients was introduced. The activities of the unit were focused exclusively on emergency conditions and urgent specialized medical care, as shown in Fig. 2. Hospitalization was carried out through the reception department. An important aspect was the requirement of a recent SARS-CoV-2 test (valid for 3 days), or alternatively, the test could be performed on site using a rapid test, followed by PCR confirmation.

The subsequent algorithm was standard. Prior to obtaining PCR test results, the patient was placed in an isolation box

(single occupancy room). If a specific viral pathogen was detected, physicians, nurses, and other support staff provided care using appropriate personal protective equipment in the patient's room. After providing specialized care, such as abscess/phlegmon drainage or osteosynthesis of facial bone fractures, and once patients no longer required special supervision, they were transferred to a designated department within the healthcare facility.

A qualitative analysis of the structure of hospitalizations in terms of disease entities and performed surgical interventions revealed a heterogeneous pattern (Table 2). The main profile of the department included purulent-inflammatory processes, traumatic injuries, and neoplasms. It is noteworthy that in 2020-2022 there was a temporary decrease in surgical activity, followed by a subsequent recovery and

Table 2. Dynamics of changes in the structure of disease entities and types of surgical interventions of the maxillofacial department in 2019–2024

The types of surgery and diagnostic entities	2019	2020	2021	2022	2023	2024	Totally (N/%)
Traumatic damage to the bones of the facial skull	308	190	162	150	136	94	1040 (16 %)
Purulent-inflammatory processes of the soft tissues of the maxillofacial area	285	259	240	285	236	222	1527 (23.6%)
Inflammatory processes of the maxillary sinus of odontogenic origin	111	87	55	52	55	43	403 (6.2%)
Neoplasms of the maxillofacial area	200	151	147	143	188	177	1006 (15.5%)
Post-traumatic osteomyelitis. osteonecrosis	42	33	27	19	49	63	233 (3.6%)
Difficulty erupting teeth (retention. dystopia)	78	74	87	63	110	164	576 (8.9%)
Reconstructive surgery	24	22	35	31	81	93	286 (4.4%)
bone autotransplantation and bone augmentation	17	5	7	12	10	37	88 (1.36%)
Soft tissue plastic surgery	18	11	15	13	43	71	171 (2.6%)
Primary surgical treatment of wounds	11	21	32	25	31	46	166 (2.5%)
Biopsy	29	56	77	1	0	25	188 (2.9%)
Microvascular tissue transplantation	0	0	0	5	7	11	23 (0.35%)
Other types of operative diagnostic procedures (arthroscopy, arthrocentesis, incomplete tooth extraction, blepharoplasty, fat pad tissue removing, etc.)	104	107	86	134	165	178	774 (12%)
All disease and procedure entities	1227	1016	969	933	1111	1244	6500 (100%)

growth trend. A significant expansion of reconstructive and aesthetic surgery was also observed. In 2024, the indicator almost reached the baseline level of 2019 (1,224 vs 1,227 cases). Since 2022–2024, the introduction of high-tech methods (including microvascular transplantation) has been observed, which is likely related to the evolving clinical needs, complex high-energy maxillofacial trauma, and the necessity to implement new approaches for the treatment of gunshot injuries of the facial region.

The high proportion of treatment for purulent-inflammatory processes of the maxillofacial tissues (23.6%) indicates a significant prevalence of odontogenic infections, the need for emergency surgical care, and the predominance of urgent pathology in the structure of hospitalizations.

At the same time, there was a pronounced decreasing trend in the number of injuries, from 308 cases in 2019 to 94 cases in 2024. The overall reduction amounted to 69.5%. This may be due to changes in patient routing, concentration of trauma care in specialized centers, as well as changes in the structure of hospitalizations.

The dynamics of cancer incidence and surgical interventions for maxillofacial neoplasms were characterized by relative stability, with a tendency toward an increase in 2023–2024. This may indicate improved oncological awareness, increased availability of specialized care, and an expansion of surgical activity in oncological practice.

The analysis of elective surgical care showed that the proportion of dental impactions and dystopias (8.9%) and odontogenic sinusitis (6.2%) together accounted for more than 15% of all surgical interventions, which reflects the

significant role of planned dental surgery in the structure of departmental activity. At the same time, the number of operations for impacted teeth increased more than twofold during the study period. This reflects integration with the orthodontic rehabilitation pathway for complex patients.

DISCUSSION

In conditions of martial law, the provision of effective and high-quality medical care in maxillofacial surgery requires a comprehensive approach that includes planning and preparedness, resource provision, psychological support, increased accessibility of services, and continuous quality monitoring. The implementation of these measures may reduce the risk of complications, improve treatment outcomes, and ensure adequate support for medical personnel in emergency situations [8, 9].

Similar to global experience, maxillofacial surgical services during the COVID-19 pandemic were significantly reduced and reorganized, with prioritization of emergency care, implementation of strict infection control protocols, and suspension of elective procedures [10, 11].

Similar findings have been reported in Ukrainian clinical and national studies, where maxillofacial surgical services experienced a significant shift toward high-energy ballistic trauma and resource-limited reconstructive care during the war and COVID-19 period [12].

A survey [13] of respondents (maxillofacial surgeons from different regions of Ukraine) demonstrated the following results. In response to the question “Has full-scale invasion affected the quality of urgent surgical treatment of patients

not associated with mine-explosive and firearm injuries in your clinic?”, 94.8% of respondents reported that the quality had not changed, while 5.2% noted a decrease in quality. In response to the question “Which group of urgent patients not related to mine-explosive and gunshot trauma was most affected by the full-scale invasion?”, 48.2% of respondents identified traumatic injuries of the facial skeleton, 22.9% indicated purulent-inflammatory processes, while the remainder stated that it was difficult to provide a precise and unambiguous answer.

In general, the shift in emphasis in the treatment of certain pathologies within maxillofacial departments is caused by both general factors (war, shortage of personnel, administrative and managerial decisions of the Ministry of Health, etc.) and local factors (changes in referral pathways, bed capacity, and internal restructuring of hospitals).

We consider it necessary to identify the following factors that qualitatively influence the structure of hospitalizations in healthcare institutions, including maxillofacial units.

1. Demographic changes.

Martial law affects the demographic structure of the population, which, in turn, affects the contingent of patients who seek specialized medical care. Hostilities cause mass displacement of people. In the regions where refugees are concentrated, there is an increase in the number of visits to medical institutions. For example, in the western regions of Ukraine, the number of patients doubled, which created a significant burden on local medical institutions [5]. In areas of active hostilities, the population is decreasing due to evacuation, which reduces the number of initial visits to local hospitals. This may lead to a decrease in the number of planned operations and consultations, as a result of mass internal migration of the population.

2. Changes in the structure of injuries and diseases.

Martial law significantly changes the nature of injuries and diseases with which patients turn to maxillofacial surgeons.

The number of patients with injuries of the maxillofacial area caused by explosions, shooting and other combat operations is increasing. Stress and psychosomatic disorders: Psychological stress caused by war can cause an increase in cases of disorders such as bruxism (tooth grinding), psychosomatic jaw pain, etc.

3. Availability and functioning of medical institutions

Hostilities affect the ability of health facilities to provide care. Damage or destruction of hospitals and clinics limits the possibility of providing qualified medical care. In wartime conditions, it is difficult to ensure uninterrupted supply of medicines and medical equipment, which affects the quality and timeliness of medical care. This is particularly true in remote or blocked areas.

PROSPECTS FOR FURTHER RESEARCH

It is worth noting that the analysis of the structure of the activity of the maxillofacial departments requires global, national scaling in order to identify incorrect patient routes, overload the resource base and identify «weak points» in the provision of highly specialized medical care to the population.

CONCLUSIONS

Reforming the maxillofacial service and the field of maxillofacial surgery in Ukraine is necessary to ensure high quality, accessibility, and effectiveness of medical care. The main directions of reform should include the modernization of infrastructure, improvement of medical personnel qualifications, the introduction of modern technologies, and the enhancement of financing and organization of healthcare institutions. The development of new models for organizing the work of the maxillofacial service should optimize the use of human resources and improve the quality of medical care. The implementation of these measures will contribute to improving population health and increasing patient satisfaction.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Monitoring system for practical skills of the future gnathologist: Criteria and descriptors

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ABSTRACT

Aim: Theoretical substantiation, development, and validation of a system of criteria and descriptors for monitoring the formation of professional practical skills of future gnathologists.

Materials and Methods: Theoretical and empirical methods were applied: a comprehensive analysis of scientific literature; comparative and generalisation methods for theoretical substantiation of systematic quality monitoring approaches; interviews with academic staff for criteria and descriptor elicitation; and a survey of gnathology specialists for problem identification and expert validation of the proposed system. We assessed the relative importance of each criterion on a 5-point scale using the following indicators: the expert competence coefficient, the generalised opinion score, the degree of consensus of opinions, and the statistical significance of the expert consensus coefficient.

Results: Four principal interdisciplinary integration domains relevant to gnathological training have been identified: anatomical-morphological, kinematic-dynamic, system-functional, and clinical-diagnostic. A five-criterion monitoring system with four-level descriptors (basic, intermediate, advanced, and high) has been developed for each criterion: cognitive-analytical, diagnostic-interpretive, biomechanical-design, practical-operational, and prognostic-reflective. Expert evaluation confirmed the high validity of, and consensus on, the proposed system. Expert competence was assessed using the Kk coefficient ($Kk=0.87$). The degree of consensus was quantified via Kendall's concordance coefficient ($W=0.8$), with statistical significance verified by the Pearson chi-square test ($\chi^2_p=28.97 > \chi^2_i=9.5$; $\alpha=0.05$).

Conclusions: The developed system of criteria and descriptors constitutes a methodological framework for comprehensive monitoring of the formation of practical skills in future gnathologists. The high level of expert consensus confirms the validity and practical applicability of the proposed system for improving dental education curricula.

KEYWORDS: gnathology, biomechanics, orthodontics, monitoring, practical skills

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INTRODUCTION

Contemporary dental medicine increasingly encounters challenges that require a comprehensive understanding of the multifunctional interrelationships among the elements and tissues of the dentofacial system, systemic knowledge of the biomechanics of the musculoskeletal and dentofacial apparatus, and the ability to apply this knowledge in reconstructive dentistry, diagnostics, and prevention of dental diseases. In Ukraine, these challenges have become particularly acute in the context of military aggression – there is a growing incidence of injuries and stress-related conditions, along with patients neglecting minor functional disturbances of the masticatory system and neuromuscular coordination. Consequently, the demand for qualified gnathology specialists is rising.

Professional activity as a dental gnathologist requires the systematic integration of knowledge from anatomy, orthodontics, biomechanics, and functional diagnostics. Some issues have already been raised in scientific sources, for example, the integration of knowledge from mechanics and biomechanics in professional training [1], and the application of blended learning technology in orthodontics

for dental students [2]. Article [3] also substantiates the concepts for designing the content of elective courses aimed at developing competitive orthodontic specialists, particularly in the field of gnathology. The authors of article [4] present the theoretical and applied aspects of organizing simulation-based training and the assessment of practical skills, particularly for dental students. However, expert surveys and content analysis of academic curricula and scientific literature indicate insufficient attention to this problem in the training of higher medical education graduates.

AIM

Theoretical substantiation, development, and validation of a system of criteria and descriptors for monitoring the formation of professional practical skills of future gnathologists.

MATERIALS AND METHODS

To accomplish the tasks set, the following theoretical and empirical methods of scientific research were applied: comprehensive analysis of scientific literature; comparison

and generalisation for the theoretical substantiation of approaches to systematic quality monitoring of practical skills of future gnathologists; interviews with academic staff for the elicitation of criteria and descriptors; and a survey of gnathology specialists for problem identification and expert evaluation of the developed system of criteria and descriptors.

We assessed the relative importance of each criterion on a 5-point scale using the following indicators: the expert competence coefficient, the generalised opinion score, the degree of consensus of opinions, and the statistical significance of the expert consensus coefficient.

The expert competence coefficient was determined using a composite method [5]:

$$K_k = \frac{K_z + K_a}{n + 1}$$

where K_z – the degree of a specialist's suitability for the expert assessment; K_a – self-assessment competence coefficient; n – the number of self-assessment methods used.

The generalised opinion score was defined as the arithmetic mean of the rating assigned to a given requirement [6, 7]:

$$M_j = \frac{1}{m_j} * \sum_{i=1}^m C_{ij}$$

where m_j – the number of experts who rated requirement j ; m – the total number of experts; C_{ij} – the rating of the relative importance of requirement j assigned by expert i .

The sum of ranks assigned by experts to direction j of requirements was determined by the formula [6, 7]:

$$S_j = \sum_{i=1}^m R_{ij}$$

where R_{ij} – the rank rating assigned by expert i to requirement j .

To assess the overall degree of consensus across all directions (requirements), the concordance coefficient was used [6, 7]:

$$W = \frac{\sum_{j=1}^n d_j^2}{\frac{1}{12} [m^2(n^3 - n) - m \sum_{i=1}^m T_i]}$$

where d_j – deviation of the rank from the mean rank sum; n – number of criteria; T_i – recurrence of tied ranks for expert i .

The statistical significance of the expert consensus coefficient was verified using the Pearson chi-square criterion [6, 7]:

$$\chi_p^2 = \frac{\sum_{j=1}^n d_j^2}{\frac{1}{12} [mn(n+1) - \frac{1}{n-1} \sum_{i=1}^m T_i]}$$

ETHICS

The study was conducted in accordance with the Declaration of Helsinki and the Convention on Human Rights and Biomedicine [8, 9]. The data were collected from adult participants using a structured questionnaire. Participation was voluntary, and informed consent was obtained from all participants prior to questionnaire completion.

FRAMEWORK

The study was conducted as a fragment of the scientific project «Ensuring the quality of computer science and physics and mathematics training of future healthcare professionals in the classroom and distance learning environment» (2024-2026, state registration № 0124U000724).

RESULTS

To develop the system of criteria and descriptors for monitoring the formation of professional skills of future master's students in dentistry, we drew on the analysis of interdisciplinary integration domains between academic disciplines carried out in references [10, 11], studies focusing on the design of elective academic disciplines for dental students [3], their motivation and readiness for professional activity [12], contemporary clinical principles of gnathology [13], and approaches to interdisciplinary integration [1]. At the first stage, based on the analysis of content intersections between disciplines, we identified the principal interdisciplinary domains relevant to the training of gnathology specialists, namely:

The anatomical-morphological domain is an integration zone within which the structural characteristics of the dentofacial system (DFS) are analysed through the correspondence between the morphology of DFS components and the required functional load. This domain integrates anatomy, morphology, histology, and load physics. Examples of content intersection between two disciplines include: the anatomical-histological structure of DFS components (teeth, periodontium, jaws, masticatory muscles, temporomandibular joints); occlusal determinants (occlusal plane, anatomical form of occlusal surfaces, Spee's curve, Wilson's curve, incisal guidance, condylar guidance, Bennett movement); occlusal interferences (undesirable contacts between teeth that impede harmonious mandibular movements) and their consequences.

The kinematic-dynamic domain is an integration zone for reconciling motion parameters (trajectory, velocity, rotation) with force parameters (magnitude, direction, moment), ensuring a predictable morphofunctional tissue response. The content intersection zone between two disciplines includes: laws of mechanics (statics, dynamics); system of forces and moments; centre of resistance of the tooth; displacement vectors.

The system-functional domain is an integration zone in which the components of the DFS are regarded as a coherent biomechanical system, where functional equilibrium ensures its harmonious operation. The content intersection zone between two disciplines includes: coordination of muscular activity and the position of the mandible relative to the maxilla at rest and during movement; physiological mandibular movements in three mutually perpendicular planes; adaptation mechanisms and compensatory responses of the dentofacial system to changes in occlusion; the process of formation of pathological changes in DFS structures.

The clinical-diagnostic domain is an integration zone in which the understanding of biomechanical interactions among DFS components is directly translated into a

diagnostic protocol and clinical decisions. The content intersection zone between two disciplines includes: clinical diagnostics (assessment of occlusal contacts, evaluation of mandibular movement trajectories); visualisation of anatomical structures (computed tomography, magnetic resonance imaging); functional diagnostics (axiography, analysis of models in an articulator, electromyography); differential diagnostics (determination of the type of temporomandibular joint dysfunction); digital modelling (CAD/CAM, 3D analysis).

This integration facilitates the development of DFS analysis skills with the assessment of its functional dynamics, ensuring stable biomechanical and clinical equilibrium.

Based on approaches to defining the competency structure of future master's students in dentistry outlined in references [1, 2], we present the criteria, levels, and descriptors we have identified for assessing the formation of professional practical skills of future dental master's students:

The cognitive-analytical criterion presupposes the formation of a system of conscious knowledge in the biomechanics of the maxillofacial apparatus and gnathology. In the context of integrating the disciplines «Gnathology in orthodontics» and «Biomechanics of the dentofacial apparatus. Physical foundations of gnathology», the cognitive component acquires an analytical character, since it implies not merely the reproduction of knowledge, but its interpretation, systematisation, and application in clinical reasoning. Measurable manifestations of the criterion (indicators) are: understanding of physical laws underlying gnathology; interpretation of biomechanical processes; and integration of fundamental knowledge into clinical reasoning.

By differentiating descriptors across four levels, the following skills and competencies of higher education students can be identified: basic – reproduces individual physical concepts without clinical interpretation; intermediate – explains the interrelationship between forces and occlusion; advanced – analyses clinical situations from a biomechanical perspective; high – integrates physical models into clinical prognostication.

Monitoring methods for the formation of professional practical skills for this criterion: situational tasks, clinical cases, computer modelling.

The diagnostic-interpretive criterion is central to the transition from knowledge of biomechanical patterns to clinical decision-making. In the context of integrating**, this criterion reflects** the student's ability not only to collect data, but also to interpret it within the context of the functional biomechanics of the DFS. Indicators of this criterion are: assessment of the functional state of DFS components; application of clinical, functional, and supplementary diagnostic methods; and interpretation of diagnostic data and formulation of a diagnosis.

Descriptors: basic – differentiates between normal and pathological DFS states; intermediate – performs gnathological analysis according to protocol; advanced – independently interprets data from supplementary diagnostic methods; high – formulates an integrated functional-biomechanical conclusion.

Monitoring methods: OSCE stations [4], analysis of digital models, analysis of diagnostic protocols.

The biomechanical-design criterion presupposes the formation of professional practical skills in dental master's students, specifically: modelling the functional system of the DFS from the perspectives of rigid body mechanics, material resistance, kinematics, and mandibular dynamics; forecasting the biomechanical consequences of orthodontic or gnathological interventions; and designing clinical solutions accounting for load distribution, force moments, displacement vectors, and the functional state of the temporomandibular joint. Indicators of this criterion are: designing treatment stages with consideration of gnathological parameters; selection of constructions in accordance with biomechanical principles and the clinical situation; and modelling of expected gnathological treatment outcomes based on baseline data.

Descriptors: basic – possesses fundamental biomechanical principles of DFS modelling; intermediate – calculates the force system according to the clinical situation; advanced – selects the appliance design with regard to the clinical situation and provides biomechanical justification; high – optimises the biomechanical scheme with a stability prognosis.

Monitoring methods: calculation tasks, simulation tools, virtual models.

The practical-operational criterion characterises the ability to implement a biomechanically and gnathologically justified clinical treatment plan through specific actions. The transition occurs from the theoretical understanding of the physical foundations of gnathology to the practical realisation of orthodontic and gnathological intervention. Indicators of this criterion are: clinical implementation of biomechanical principles; interdisciplinary collaboration with related dental and general clinical fields regarding comprehensive treatment; monitoring of occlusal stability.

Descriptors: basic – performs manipulations with minor errors; intermediate – performs manipulations without errors under supervision; advanced – performs manipulations without errors independently; high – performs manipulations ensuring stability and minimising complications.

Monitoring methods: skills checklists, portfolio of clinical cases, physical simulation tools of varying levels of realism.

The prognostic-reflective criterion presupposes the possession of skills for predicting the biomechanical and gnathological consequences of interventions; assessing the stability of outcomes; modelling relapse risks; conducting professional clinical reflection; and adjusting the treatment plan based on obtained data. The emphasis shifts from algorithm execution to clinical foresight and self-correction. Indicators of this criterion are: evaluation of long-term treatment outcomes; analysis of sources of error; clinical decision-making based on biomechanical prognosis.

Descriptors: basic – analyses treatment outcomes without assessing long-term consequences; intermediate – partially predicts treatment results and consequences; advanced – evaluates and substantiates the stability of treatment; high – analyses long-term outcomes and adjusts the treatment strategy.

Table 1. Determination of the generalized opinion score, mean rank sum, and squared deviations of rank sums from the mean rank sum

Criteria	Arithmetic mean (M_i)	The sum of ranks (S_i)	Deviation of the rank from the mean rank sum (d_i)
Cognitive-Analytical	4.6	35.5	2.5
Diagnostic-Interpretive	4.1	20.5	-12.5
Biomechanical-Design	5.0	45.5	12.5
Practical-Operational	5.0	45.5	12.5
Prognostic-Reflective	4.0	18	-15.0

Source: compiled by the authors of this study

Monitoring methods: analysis of completed cases, use of digital prognostication tools (3D modelling).

To determine the significance of the requirements for the developed system of criteria and corresponding descriptors, an expert survey of gnathology specialists ($n=11$) was conducted using the methodology described in reference [6]. The high reliability of the expert assessments is evidenced by the expert competence coefficient $K_k=0.87$, which permits their use for further statistical analysis (in particular, calculation of the Kendall concordance coefficient).

The degree of expert consensus is at the level of $W=0.8$; intermediate calculations are presented in Table 1. The concordance coefficient ranges from 0 to 1. The higher the value of the concordance coefficient, the greater the degree of expert consensus. The calculated value $\chi^2_p=28.97$ was compared with the tabulated value $\chi^2_i=9.5$ for $n-1$ degrees of freedom and a significance level of $\alpha=0.05$. In our case, $\chi^2_p > \chi^2_i$; consequently, the concordance coefficient is statistically significant. This allows us to assert the correctness of the level of expert consensus.

DISCUSSION

The obtained results are consistent with the contemporary concept of gnathology development presented in reference [13], where the authors substantiate the importance of a deep understanding of the biomechanical interrelationships among the components of the dentofacial apparatus for a gnathological clinician. The four interdisciplinary domains identified in our study correspond to this integrated approach and create a structured foundation for the formation of clinical reasoning in future specialists.

The results of our study are consistent with the conclusions of contemporary research on the role of interdisciplinary

training in the preparation of gnathology specialists, which is considered an interdisciplinary field integrating classical occlusal concepts with advances in rehabilitation medicine, functional diagnostics, and digital technologies [13]. Studies [14, 15] have demonstrated that interdisciplinary training enhances the readiness of future dentists for professional activity, develops clinical reasoning, and improves confidence in oral health assessment.

The authors of reference [16] emphasise the importance of visualisation through digital models and simulations of mandibular movements, occlusal interactions, and force systems for understanding the biomechanical principles of gnathological interventions. The importance of the biomechanical approach to the analysis of the functional state of the dentofacial system is further supported by the results of clinico-physiological studies devoted to the treatment of occlusal disorders [17].

The high level of expert consensus obtained in our study confirms the validity of the proposed system of criteria and descriptors, and indicates that the defined criteria adequately reflect the structure of professional competencies required for gnathological practice. The proposed system may serve as a methodological framework for improving dental education curriculums in the areas of functional occlusion, orthodontics, and diagnostics of temporomandibular joint disorders.

CONCLUSIONS

The developed system of criteria and descriptors constitutes a methodological framework for comprehensive monitoring of the formation of practical skills in future gnathologists. The high level of expert consensus confirms the validity and practical applicability of the proposed system for improving dental education curricula.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Study of the environment and conditions for implementing the project to develop telemedicine networks at the regional level

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ABSTRACT

Aim: To investigate the professional environment and initial conditions for implementing telemedicine networks in Ukraine (the Chernihiv, Rivne and Odesa regions), and to develop measures facilitating the successful deployment of telemedicine in these regions.

Materials and Methods: A cross-sectional questionnaire survey of 842 healthcare workers across three Ukrainian regions was conducted. The analysis covers five socio-demographic and professional characteristics: age, gender, specialism, length of service and type of healthcare facility.

Results: Average scores exceeded 7.4 across all scales, with 70–75% of respondents giving high ratings (7–10). The desire to learn ($M=7.84\pm2.57$) exceeds readiness to implement ($M=7.45\pm2.61$), suggesting organisational and technical barriers. Gender significantly affects telemedicine scales (women are more motivated), length of service affects overall digital affinity (declining after 10 years), and age correlates weakly only with overall digitalisation. Cluster healthcare facilities (up to 24% sceptics), specialist doctors and male professionals were identified as risk groups. Paediatricians and general practitioners demonstrate the highest motivation and can serve as role models for implementation.

Conclusions: High acceptance of digital and telemedicine technologies ($M>7.4$) provides a strong foundation for large-scale implementation. Priority support should target cluster healthcare facilities, specialist doctors, male professionals and long-serving employees. Paediatricians and general practitioners should serve as role models. Organisational and technical barriers must be addressed to bridge the gap between learning motivation and practical application.

KEYWORDS: digitalisation, telemedicine, adherence, network, barriers, technologies

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INTRODUCTION

The deep integration of digital technologies into healthcare is a defining feature of the twenty-first century, characterised by the comprehensive application of digital technologies across all sectors of human activity [1]. Most healthcare systems face crises due to limited financial and human resources, changing approaches to disease management, an ageing population, and increasing demand for medical services [2–5]. The transition from paper-based medical records to structured electronic health records represents a fundamental shift in healthcare information processing [6, 7]. Over the last decade, the COVID-19 pandemic has acted as a catalyst for the adoption of digital tools and telemedicine technologies [8–10]. Numerous challenges remain in the implementation of these technologies [11, 12]; however, the development of digital technologies and telemedicine is considered a key approach to overcoming obstacles that have accumulated over decades of healthcare practice.

The World Health Organization places key importance on the implementation of digital technologies, including telemedicine, as confirmed by a series of strategic documents [13]. Following the launch of systemic healthcare reform in Ukraine in 2017, a national eHealth system has been developed as a key component of the eHealth ecosystem

and as a reform instrument, with its importance enshrined in legislation [14, 15]. The Ukrainian government has defined a strategy for the development of telemedicine [16], creating favourable conditions for its implementation, particularly in the context of martial law, limited resources, and security risks. The government actively promotes the integration of telemedicine technologies into the daily practice of healthcare professionals.

AIM

To investigate the professional environment and baseline conditions for implementing telemedicine networks in Ukraine (Chernihiv, Rivne, and Odesa regions), to examine healthcare professionals' readiness and acceptance, and to identify barriers to the implementation of telemedicine technologies at the regional level.

MATERIALS AND METHODS

The study was conducted in three regions of Ukraine: Chernihiv (21 August–20 September 2025), Rivne (15 October–15 November 2025), and Odesa (1 December 2025–30 January 2026). The study was based on a cross-sectional questionnaire survey of 842 healthcare workers representing all levels of medical and rehabilitation care provision (primary and specialist care). Respondents were

drawn from 93 healthcare facilities. The analysis covered five socio-demographic and professional characteristics: age, gender, specialty, length of service, and type of healthcare facility.

Respondents were asked three interrelated questions, assessed using a 10-point Likert-type scale (1=lowest, 10=highest): (1) willingness to use digital technologies in professional practice; (2) readiness to implement telemedicine in professional practice; and (3) willingness to learn telemedicine technologies. Data were collected via an online Google Forms questionnaire without collecting respondents' personal data. Respondents indicated their type of healthcare facility in accordance with the Resolution of the Cabinet of Ministers of Ukraine No. 174 of 28 February 2023 [17].

Descriptive statistics were used to analyse the numerical response scales (1-10), including arithmetic mean (M), median (Me), and standard deviation (SD). The mean is presented as $M \pm SD$. Statistical analysis was performed using non-parametric methods due to the non-normal distribution of the dependent variables (Shapiro-Wilk test: $p < 0.001$). Descriptive statistics included mean, median, mode, standard deviation, and summary indices. For intergroup comparisons, the Kruskal-Wallis test and the Mann-Whitney U test with Bonferroni correction were applied. Paired comparisons between scales were performed using the Wilcoxon signed-rank test. Correlations were assessed using Spearman's coefficient (r_s), and categorical distributions using Pearson's χ^2 test. Effect size was calculated as $r = |z|/\sqrt{N}$ and Cramér's V. The significance level was set at $\alpha = 0.05$.

ETHICS

The study was conducted in accordance with the Declaration of Helsinki and bioethical standards for sociological surveys in the medical field. All participants (N=842) provided voluntary informed consent. Participation was anonymous, ensuring the protection of personal data and professional reputation. The results are presented in aggregated form, making individual identification impossible. The study protocol was approved by the local Bioethics Committee of Bogomolets National Medical University.

FRAMEWORK

The study was conducted within the framework of a research project of the Bogomolets National Medical University

2023-2025: «Digitalization and digital transformation in healthcare» (state registration number 0121U107784).

RESULTS

The largest age group is 31-40 years ($n=222$; 26.37%), forming the modal class. The 41-50 ($n=206$; 24.47%) and 51-60 ($n=183$; 21.73%) groups together account for 46.20% of the sample. Those over 60 account for 16.86% ($n=142$), whilst the youngest cohort (under 30) represents only 10.57% ($n=89$). The proportion aged over 50 totals 38.60%, indicating workforce maturity and a potential shortage of young specialists. The low proportion under 30 reflects the general trend of slow replenishment of the medical workforce. The sample reveals marked feminisation: women account for 86.70% ($n=730$), men for 13.18% ($n=111$), with a ratio of 6.6:1, typical for primary and secondary healthcare in Ukraine. One respondent identified their gender as non-binary (0.12%). Gender composition varies significantly by age group ($\chi^2=28.05$; $p=0.0005$; $V=0.129$), though the association is weak, indicating relative uniformity of feminization across all cohorts (Table 1).

The sample covers 47 medical specialists. The largest groups among them were nurses (33.85%); four doctors' specialties, which together accounted for 42.28% of the study cohort; and 42 other specialties (23.87%). All five leading specialisms account for three-quarters of the sample (76.13%) (Table 2):

An important characteristic of the study cohort was the level of healthcare provision according to the type of healthcare facility. It is also important to compare this distribution across medical specialties. The study cohort was categorised according to employment status, as shown in Table 3.

The majority (51.43%) represent primary healthcare, reflecting the study's focus on the patient's initial contact with the healthcare system. Specialised inpatient care (cluster and supra-cluster levels) accounts for 16.4% ($n=138$). The association between specialism and institution type is significant and moderately strong ($\chi^2=364.31$; $p < 0.001$; $V=0.380$): general practitioners are predominantly employed in primary healthcare centres (85.9%), specialist doctors in general (50.0%) and cluster (34.2%) facilities, and rehabilitation specialists in general (71.4%) and cluster (21.4%) facilities.

Table 1. Distribution of respondents by gender and age group ($n=842$)

Age group	Female		Male		Other		Total
	n	%	n	%	n	%	n
Under 30	72	80.90	17	19.10	0	0.00	89
31-40	192	86.49	30	13.51	0	0.00	222
41-50	189	91.75	17	8.25	0	0.00	206
51-60	168	91.80	14	7.65	1	0.55	183
Over 60	109	76.76	33	23.24	0	0.00	142
Total	730	86.70	111	13.18	1	0.12	842

Source: compiled by the authors of this study

Table 2. Leading specialisms by frequency (n≥45)

Field of study	n	%
Nursing	285	33.85
General practice – family medicine	163	19.36
Therapy	79	9.38
Pediatrics	69	8.19
Obstetrics and Gynaecology	45	5.34
The other 42 specialisms	201*	23.87

Note: * – this group comprises 42 different specialisms, with between 1 and 18 representatives in each

Source: compiled by the authors of this study

Table 3. Breakdown by type of healthcare facility (N=842)

Type of healthcare facility	n	%
Primary healthcare centres (PHC centres)	433	51.43
General healthcare facility	271	32.19
Cluster-based healthcare facility	104	12.35
Super-cluster (regional) healthcare facility	34	4.04

Source: compiled by the authors of this study

Table 4. Descriptive statistics for the three assessment scales (N=842)

Grading scale	M	Me	Mo	SD	1-4 (%)	7-10 (%)
A passion for digital technology	7.44	8	10	2.41	10.5	70.8
Readiness to implement telemedicine	7.45	8	10	2.61	13.2	70.3
Desire to learn telemedicine technologies	7.84	9	10	2.57	10.9	74.7

Note: M – mean; Me – median; Mo – mode; SD – standard deviation; 1–4 (%) – low-score index; 7–10 (%) – high-score index

Source: compiled by the authors of this study

Table 4 presents the results of the questionnaire-based assessment of the study cohort. All three assessment scales demonstrated a pronounced negative skew, with responses concentrated in the high-score range. The highest level was recorded for willingness to learn about telemedicine ($M=7.84\pm2.57$; $Me=9$), whilst digital affinity and readiness to implement telemedicine had virtually identical scores ($M=7.44\pm2.41$ and 7.45 ± 2.61 respectively; $Me=8$ for both).

Between 70.3% and 74.7% of respondents fall within the high-score range (7–10), whilst sceptics (scores 1–4) do not exceed 13.2%. The mode for all distributions is 10 – the maximum value on the scale. These data indicate a generally favourable attitude among healthcare professionals towards digitalisation and telemedicine. The mean score for desire to learn telemedicine ($M=7.84\pm2.57$) is significantly higher than that for readiness to implement ($M=7.45\pm2.61$); Wilcoxon signed-rank test: ($Z=-8.877$; $p<0.001$; $r=0.306$) with a medium effect size. Among those whose scores differed, 76.3% rated their willingness to learn higher than their readiness to implement. This gap may indicate the presence of organisational, technical or institutional barriers between motivation and actual implementation.

Gender is the only factor with a significant effect on two telemedicine scales simultaneously. Women score higher on implementation and learning (Table 5).

Women demonstrate significantly higher scores on both telemedicine-related scales (implementation and learning), whereas gender differences are not statistically significant for general digital affinity ($M=7.46$ vs 7.33). The proportion of sceptical respondents among men is approximately twice that among women. This contrast indicates that gender differences are specific to telemedicine rather than digitalisation in general.

The data in Table 6 show that age does not significantly affect attitudes towards telemedicine but demonstrates a weak negative relationship with overall digital affinity at the individual level.

Age has no significant effect on either telemedicine scale ($p=0.858$; $p=0.925$; $p\approx0$). For digital affinity, the intergroup difference is borderline ($H=7.854$; $p=0.097$), but Spearman's correlation at the individual level is significant ($r_s=-0.092$; $p=0.008$), confirming a monotonically decreasing trend.

Table 7 shows the impact of length of service on digital commitment. Length of service is the only variable with

Table 5. Mean scores by gender

Scale	M (women)	M (men)	p-value	Effect size (r)
Digital affinity	7.46	7.33	0.651	0.016
Readiness to implement telemedicine	7.56	6.75	0.004	0.097
Desire to learn telemedicine	7.95	7.09	0.003	0.098

Source: compiled by the authors of this study

Table 6. Age-related trends in digital affinity

Age group	M (digital affinity)	High scores (7–10), %	Note
Under 30	7.78	75.3	-
31–40 years	7.78	78.8	Highest mean
41–50 years	7.30	67.0	-
51–60 years	7.20	66.1	Lowest mean
Over 60 years	7.22	66.9	-

Source: compiled by the authors of this study

Table 7. Digital affinity by length of service

Experience group	M (digital affinity)	High scores (7–10), %	Significance
≤5 years	7.78	73.0	–
6–10 years	8.05	84.8	p=0.002 vs >30 yrs
11–20 years	7.60	74.0	–
21–30 years	7.30	68.2	–
Over 30 years	7.13	65.2	Lowest

Source: compiled by the authors of this study

Table 8. Mean scores by specialism

Specialism	M (implementation telemedicine)	M (learn telemedicine)	M (digital affinity)	High %	Sceptics, %
Paediatricians	8.04	8.48	7.78	81.2	8.7
General practitioners	7.77	8.09	7.56	76.1	9.2
Specialists	7.01	7.50	7.50	63.4	21.8

Source: compiled by the authors of this study

a significant overall impact on digital affinity. The peak is at 6–10 years of service.

Length of service is the only variable with a significant overall effect on digital affinity ($H=12.592$; $p=0.014$; $rs=-0.113$; $p=0.001$). The only significant pairwise difference after Bonferroni correction: 6–10 years vs >30 years ($p=0.002$). For telemedicine scales, experience has no significant effect.

Table 8 shows the mean scores across specialties. Paediatricians and family physicians consistently outperformed specialists in pairwise comparisons, although the overall test did not reach significance.

The overall Kruskal-Wallis test did not reach statistical significance for any of the scales. However, pairwise

comparisons revealed a significant advantage of paediatricians over specialist physicians in implementation ($p=0.037$) and learning ($p=0.042$). General practitioners also significantly outperformed specialists in implementation ($p=0.043$). Specialists demonstrated the highest proportion of sceptical respondents (10.9–21.8%).

Table 9 demonstrates the impact of facility type on survey scores. Cluster-based facilities consistently show lower scores across all scales, likely due to their predominantly inpatient orientation.

The overall Kruskal-Wallis test does not reach significance on any scale ($p=0.069$ for implementation; $p=0.679$ for digital affinity). However, pairwise comparisons consistently

Table 9. Summary of healthcare facility type effects

Facility type	M (imp. TM*)	M (learn TM**)	M (digital affinity)	Low, %	High, %	Pairwise p
PHC centres	7.68	8.03	7.44	9.0	73.2	ref.
General healthcare facility	7.28	7.71	7.48	15.5	67.9	-
Cluster-based facilities	6.80	7.29	7.22	24	60.6	0.014 / 0.026
Supra-cluster (regional) facilities	7.82	8.15	7.91	14.7	82.4	-

Notes: * – implementation telemedicine; ** – learn telemedicine

Source: compiled by the authors of this study

reveal lower scores for cluster-based facilities. PHC centres significantly outperform cluster facilities for implementation ($p=0.014$; $r=0.104$) and learning ($p=0.026$).

DISCUSSION

A comparative analysis reveals several key patterns. First, the overall level of positive attitudes is high and consistent. Across all three scales, the mean score exceeds 7.4 out of 10, and the proportion of respondents giving high ratings (7–10) ranges from 70% to 75%. This pattern is consistent across all socio-demographic and professional subgroups without exception: even in the least motivated categories, the proportion of high scores does not fall below 60%. The mode of all distributions is 10. This pattern is supported by studies on the use of telemedicine during the COVID-19 pandemic [18].

Second, influencing factors vary depending on the scale. Gender is a significant predictor for both telemedicine-related scales, but not for overall digital engagement. Similar findings were reported by Haluza D and Wernhart A (2019) at the Medical University of Vienna [19]. Conversely, years of experience are significant for digital affinity but not for telemedicine. Age correlates with a decrease in overall digital readiness but does not influence attitudes towards telemedicine. This asymmetry indicates that general digital readiness and attitudes towards telemedicine are not identical constructs and require differentiated managerial approaches.

Third, there are consistent “at-risk” groups. Regardless of the scale used, cluster healthcare facilities and specialists in narrow fields consistently receive the lowest ratings. Male healthcare professionals constitute a “risk group” specifically in the context of telemedicine, whereas staff with long service (over 20 years) represent a risk group in the context of general digitalisation. Similar observations

were reported in a literature review on telemedicine in primary care, where primary care physicians demonstrated more favourable attitudes towards telemedicine [20].

Fourthly, the desire to learn exceeds the readiness to implement. The mean score for willingness to learn ($M=7.84\pm 2.57$) is statistically higher than that for readiness to implement ($M=7.45\pm 2.61$). This may indicate the presence of barriers between motivation and actual implementation – whether organisational, technical or institutional. This observation is also systematic in nature and has been confirmed by other studies [21].

CONCLUSIONS

High overall acceptance ($M > 7.4$ across all scales) creates a favorable environment for the large-scale implementation of digital and telemedicine technologies. Priority support should target:

Cluster healthcare facilities, where scepticism is most concentrated (up to 24%), requiring demonstration of the practical relevance of telemedicine in inpatient settings.

Specialised training for medical specialists who consistently demonstrate the lowest level of preparedness, focusing on specific teleconsultation scenarios.

Gender-sensitive motivational interventions for male healthcare professionals in relation to telemedicine, as their motivation is significantly lower.

Support programmes for long-serving employees (20+ years) in the context of digital transformation, given the identified downward trend in engagement.

Engagement of paediatricians and general practitioners as role models, leveraging their consistently highest motivation across all scales.

Removal of organisational and technical barriers to bridge the gap between learning motivation and practical application of digital skills.

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Structural changes in the testes during ethanol intoxication following modulation of testicular blood flow

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ABSTRACT

Aim: To examine the structural changes in the testes during various stages of alcohol intoxication and after alcohol cessation; to assess the potential for regenerative processes following surgically improved testicular blood supply.

Materials and Methods: The experiment was conducted on 60 adult male outbred albino rats, allocated into three experimental groups, the intact group, and the control group. The effects of alcohol were studied at the light-microscopic and ultrastructural levels, followed by statistical analysis. Alcohol was administered for one, two, three, or four weeks. Tissue samples were collected immediately after each exposure period, as well as 30 days after one-, two-, three-, and four-week exposure durations. In addition, in animals exposed to alcohol for four weeks, tissue samples were collected on postoperative days 14 and 30 following ligation of the caudal epigastric arteries above the origin of the cremasteric arteries.

Results: Chronic alcohol intoxication adversely affected the testes of outbred albino rats, inducing destructive changes in the arterial system, the microvasculature, the blood-testis barrier, and the spermatogenic epithelium. The severity of morphological changes in the testes of rats exposed to chronic alcohol intake correlated with the duration of exposure to the damaging agent. Spermatocytes, i.e., cells at more advanced stages of differentiation, were most sensitive to alcohol-induced damage. Recovery processes in the testes of rats exposed to chronic alcohol intake occurred after short-term intoxication (one to two weeks) but were absent following four weeks of alcohol exposure. Targeted enhancement of testicular blood supply by ligation of the caudal epigastric arteries above the origin of the cremasteric arteries promoted more intensive reparative processes and restoration of the testicular morphological structure.

Conclusions: Alcohol intoxication induces significant hemodynamic changes, which underlie the maladaptive responses and degenerative processes in the testes. After cessation of alcohol exposure, regenerative and adaptive processes proceed slowly. Enhancing testicular blood flow surgically via collateral vessels improves microcirculation and stimulates regenerative processes within the testicular parenchyma.

KEYWORDS: testis, ethanol, blood vessels, modulation of blood supply, experimental animals

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INTRODUCTION

In contemporary medicine, considerable attention is devoted to elucidating the pathogenesis of male reproductive system diseases that affect fertility. Infertility represents a major medical and social concern, given its close association with family stability, birth rates, mental health, and the functional capacity of affected individuals. Researchers consistently report the negative impact of alcohol on male reproductive health. Alcohol consumption impairs sperm maturation and damages DNA more frequently than cigarette smoking [1]. The extent of these effects, including reduced testosterone levels and impaired semen quality, varies depending on the frequency, duration, and intensity of alcohol consumption and is further influenced by diet, stress, and physical activity [2]. Disorders associated with chronic alcohol intoxication play a significant role, reflecting the sensitivity of the blood-testis barrier and germ cells to alcohol and its metabolites [3]. Vascular factors play a critical role in the pathogenesis of alcohol-

induced hypogonadism, underscoring the importance of searching for strategies to improve blood supply and restore spermatogenic and endocrine functions. Nevertheless, many aspects of this issue remain insufficiently explored in the scientific literature.

AIM

This experimental study aims to examine the morphological changes in the testes of adult outbred albino rats induced by chronic alcohol intoxication; to identify the spermatogenic cells most sensitive to ethanol; to assess the effects of alcohol on Leydig cells and supporting epithelial cells; and to investigate the regenerative processes in the testes following alcohol exposure of varying durations and after restoration of testicular blood supply.

MATERIALS AND METHODS

Sixty adult male outbred albino rats weighing 180-200 g were used in the experiment. All procedures were carried

out in strict adherence to the Guide for the Care and Use of Laboratory Animals. Rats were intragastrically administered a 40% ethanol solution at a dose of 4.0 g of pure ethanol per kg of body weight. Testicular blood flow modulation was performed surgically under ether anesthesia, following strict aseptic and antiseptic procedures. After disinfecting the skin with a 5% iodine solution, a longitudinal incision was made to open the abdominal cavity. On the inner surface of the abdominal wall, on both sides of the linea alba, the caudal epigastric artery was identified and ligated. The wound was then closed in layers. Group 1 (n=20): alcohol exposure for one, two, three, and four weeks; Group 2 (n=20): tissue collection 30 days after the last alcohol administration which lasted one, two, three, and four weeks, respectively; Group 3 (n=10): alcohol exposure for four weeks, followed by caudal epigastric artery ligation, with tissue collected on postoperative days 14 and 30. Five animals were allocated to both the intact and control groups, with the latter undergoing sham surgeries without arterial ligation. Morphological (light-microscopic and ultrastructural) and morphometric analyses were conducted, followed by statistical data processing [4].

RESULTS

At the early time points (one to two weeks), a drastic vascular response to alcohol intoxication was observed, characterized by arterial lumen dilation and blood stasis. Focal desquamation of endothelial cells and fragmentation of the internal elastic lamina were detected. Capillary lumens were reduced due to endothelial swelling. Postcapillary venules were dilated and engorged with blood, with cell proliferation in the adventitial layer (Fig. 1A). At the later stages of chronic alcohol intoxication (three to four weeks), the previously observed changes in the arterial circulation and microvasculature became more pronounced, including diffuse hyperemia, thickening of submucosal arterial walls, marked endothelial cell swelling, and increased density of peripheral microvessels (Fig. 1B). Cytological analysis demonstrated a proportional increase in the number

of seminiferous tubules exhibiting varying degrees of damage to the spermatogenic cell population with longer durations of chronic alcohol intoxication. After one week of alcohol intoxication, only 4.4% of seminiferous tubules displayed mild damage. In contrast, following four weeks of intoxication, 36.1% of tubules exhibited severe damage, with the majority of cells exfoliated into the lumen, undergoing degeneration, or the tubules appearing empty. The tunica propria of the seminiferous tubules was thickened due to the proliferation of connective tissue elements. In structurally preserved tubules, the population of spermatogenic epithelial cells was reduced. The interstitium exhibited proliferative inflammation, while small blood vessels showed stasis and perivascular hemorrhages.

In Group 2 animals, 30 days after one week of alcohol exposure, the histological architecture of the testicular vasculature and parenchyma was comparable to that of intact animals. In contrast, in animals exposed to alcohol for two weeks, a one-month recovery period was associated with structural changes in individual vessels, including wall thickening, poorly defined vascular wall components, endothelial cell swelling, and blood stasis. Mild damage to the spermatogenic epithelium, with focal disorganization of its layers, was observed in 14.1% of seminiferous tubules. Severe damage was detected in 3.5% of tubules. Capillary lumens were narrowed, and endothelial nuclei were irregularly shaped. Osmophilic cytoplasmic organelles exhibited degenerative changes and were reduced in number. The capillary basement membrane was unevenly thickened. Myoid cell nuclei in the tunica propria of the seminiferous tubules were deformed and exhibited increased electron density. Mitochondrial cristae were reduced, and the mitochondrial matrix appeared vacuolated. Lipids were accumulated in the cytoplasm of supporting epithelial cells. Mitochondria with sparse cristae were reduced in size, while Golgi cisternae and endoplasmic reticulum tubules were dilated. The structure of specialized intercellular junctions was disrupted. Spermatogenic cells exhibited disorganization of cytoplasmic organelles in spermatocytes and spermatids,

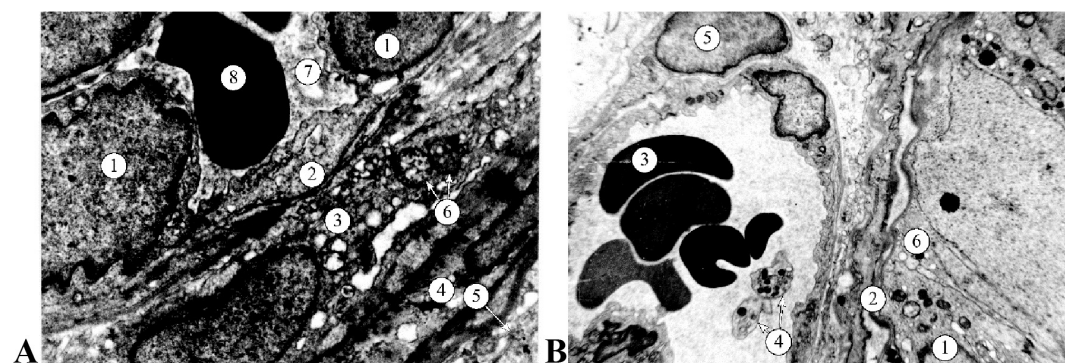


Fig. 1. Structural changes in the testes in alcohol intoxication (Group 1). A. Testicular structure after one week of the experiment: 1 – nucleus; 2 – endothelial cell; 3 – fibroblast; 4 – myoid cell; 5 – supporting epithelial cell; 6 – mitochondria; 7 – capillary lumen; 8 – erythrocyte. B. Testicular structure after three weeks of the experiment: 1 – nucleus; 2 – basement membrane; 3 – erythrocytes; 4 – platelets; 5 – pericyte; 6 – supporting epithelial cell. A, B – electron micrographs; magnification: A, B $\times 4,000$.

Picture taken by the authors

while Leydig cells showed reduced nuclear volume, indicating reduced functional activity. Pathological changes in the testis at the early stages of chronic alcohol intoxication progressed with increasing exposure duration. Thus, 30 days after the final alcohol administration, marked destructive alterations were observed in the microvasculature of rats exposed to alcohol for four weeks, including pronounced desquamation of endothelial cells into the vascular lumen, homogenization of the arterial tunica media, focal thinning and disruption of the internal elastic lamina, along with focal spermatogenesis in the seminiferous tubules. Of the seminiferous tubules, 10.2% exhibited normal morphology, 15.4% showed mild cellular damage, and 42.1% displayed destructive changes in spermatocytes and spermatids, ranging up to necrosis and disintegration. Depletion was observed in 32.3% of tubules, accompanied by a significant reduction in diameter ($161.31 \pm 4.27 \mu\text{m}$, $p < 0.001$). The greatest sensitivity to alcohol was observed in cells at more advanced stages of differentiation, specifically spermatids and pachytene spermatocytes. In some areas, connective tissue proliferation caused deformation of the seminiferous tubules. Testicular capillary walls were unevenly thickened due to swelling of the endothelial cell cytoplasm and the basement membrane. Endoplasmic reticulum cisternae were dilated and degranulated, mitochondrial cristae appeared fragmented, and the number of pinocytotic vesicles increased. Endothelial nuclei were irregular with peripheral chromatin condensation, and endothelial junctions were disrupted. The acellular layers of the tunica propria were unevenly expanded, accompanied by increased collagen fiber deposition. Myoid cell nuclei were deformed and exhibited reduced cytoplasmic electron density. Mitochondrial cristae were fragmented, the matrix appeared vacuolated, and endoplasmic reticulum cisternae and Golgi elements were swollen. The cytoplasmic matrix of supporting epithelial cells exhibited increased electron density and contained numerous vesicles. Mitochondria were small, with a dense matrix and damaged cristae, while elements of the endoplasmic reticulum and Golgi apparatus were reduced, accompanied by abundant lipid

inclusions and ribosomes. Specialized intercellular junctions exhibited plasmalemmal separation and microfilament reduction. The nucleoplasm of Leydig cell nuclei was unevenly condensed, while the cytoplasm showed dilated endoplasmic reticulum cisternae with degranulation and mitochondrial destruction.

In Group 3 animals, 14 days after the start of the experiment, the organ exhibited a range of destructive changes, including perivascular and interstitial edema, slight spiralization of the internal elastic lamina in certain arteries, and endothelial cell swelling. Normal morphology was observed in 45.4% of tubules; mild impairment of spermatogenesis in 27.2%; and severe damage to the spermatogenic epithelium in 15.1%. Despite this, spermatogenesis was more active than in controls, with increased numbers of developing germ cells. The mean tubule diameter was $179.42 \pm 2.59 \mu\text{m}$. Ultrastructurally, endothelial cells showed cytoplasmic vacuolization with reduced electron density, and nuclei with numerous invaginations. Mitochondria exhibited a lucent matrix and fewer cristae. Endoplasmic reticulum and Golgi tubules were dilated. The capillary basement membrane was thickened, with disruption of its trilaminar organization. Structural changes in the tunica propria of the seminiferous tubules included uneven thickening of acellular basement membranes and disruption of individual myoid cell plasma membranes, with nuclei exhibiting finely granular peripheral chromatin and irregular nuclear envelope contours. Endoplasmic reticulum cisternae and Golgi elements were dilated, while mitochondria showed a lucent matrix and disorganized cristae. The nucleoplasm of supporting epithelial cells was electron-lucent, vacuolated, and of reduced electron density. Mitochondria displayed a vacuolated matrix with fewer cristae. Some tubules showed disruption of specialized junctions between supporting epithelial cells. Leydig cells exhibited pronounced nuclear envelope folding, an electron-lucent cytoplasmic matrix, increased vesicles, and fragmented mitochondrial cristae (Fig. 2A, B).

In Group 3 animals, 30 days after surgery, testicular histology showed further normalization, with most arteries displaying

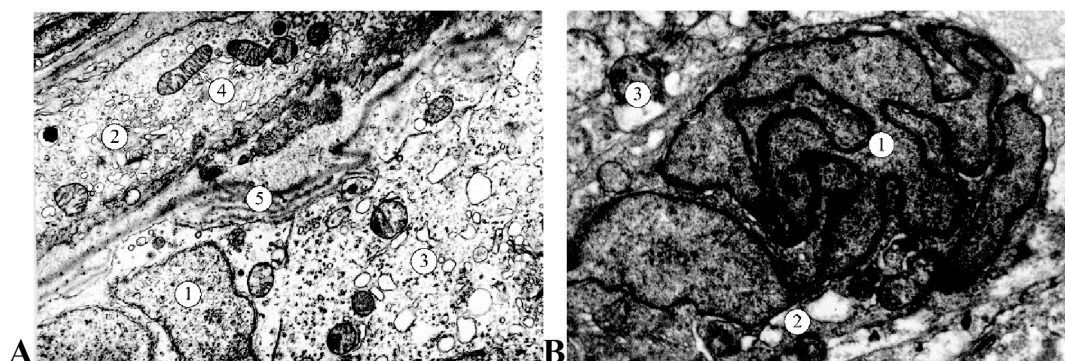


Fig. 2. Testicular ultrastructure in Group 3 animals, day 14 of the experiment. A. Spermatogenic epithelium: 1 – nucleus, 2 – myoid cell, 3 – supporting epithelial cell, 4 – mitochondria, 5 – basement membrane. B. Leydig cell: 1 – nucleus, 2 – vacuoles, 3 – mitochondria.

A, B – electron micrographs; magnification $\times 9,600$.

Picture taken by the authors

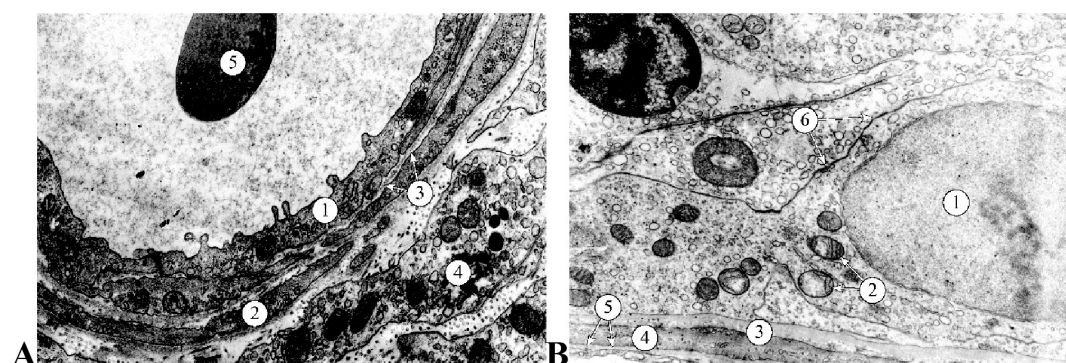


Fig. 3. Testicular ultrastructure in Group 3 animals, day 30 of the experiment. A. Testicular vein: 1 – endothelial cell, 2 – myocyte, 3 – basement membrane, 4 – fibroblast, 5 – erythrocytes. B. Spermatogonium: 1 – nucleus, 2 – mitochondria, 3 – basement membrane, 4 – myoid cell, 5 – fibroblast, 6 – intercellular junctions.

A, B – electron micrographs; magnification: A, B $\times 8,000$.

Picture taken by the authors

wall architecture comparable to that of intact and control animals. The proportion of seminiferous tubules exhibiting normal spermatogenesis increased to 67.1%, with mild damage observed in 21.4% and depletion in only 3.1%. The number of germ cells at various stages of spermatogenesis increased markedly. Electron microscopy revealed slight cytoplasmic vacuolization and active micropinocytosis in endothelial cells. Endoplasmic reticulum tubules and Golgi elements were dilated. Mitochondria retained their shape, with partial cristae damage. Endothelial cell junctions remained intact. The acellular layers of the tunica propria of the seminiferous tubules appeared thickened. Basement membranes retained their linear morphology. Myoid cell nuclei were elongated with normal electron-dense nucleoplasm. The cytoplasm was electron-lucent. Endoplasmic reticulum tubules were slightly dilated and contained electron-lucent material. Cytoplasmic microfilaments were reduced, and some mitochondria exhibited fewer cristae. The nucleoplasm of supporting epithelial cells was electron-lucent, with diffusely distributed chromatin. The nuclear envelope exhibited multiple invaginations, with a poorly defined perinuclear space. The cytoplasm of these cells was electron-lucent, and the cisternae of the rough endoplasmic reticulum and Golgi apparatus were dilated. Some mitochondria exhibited matrix vacuolization and reduced cristae. The intercellular junctions between supporting epithelial cells remained intact. The cytoplasm of spermatogonia contained numerous vesicles, mitochondria with reduced cristae, and dilated cisternae, tubules, and vesicles of the endoplasmic reticulum and Golgi apparatus (Fig. 3A, B).

DISCUSSION

In an experimental study of ethanol-fed mice, the structural integrity of the testes and spermatozoa was preserved; however, sperm count and motility were reduced. The authors attributed these findings to gene set enrichment analysis, which revealed the downregulation of sperm tail structure-related genes, including forkhead box J1 (Foxj1), in the testes of ethanol-exposed mice [5-7]. Alcohol may adversely affect semen parameters through disruption of

the hypothalamic-pituitary-gonadal axis, direct toxicity to Leydig and Sertoli cells, as well as oxidative damage to sperm DNA [8]. A decrease in the nuclear volume of Leydig cells to $67.22 \pm 3.15 \mu\text{m}$ (vs. $83.12 \pm 1.42 \mu\text{m}$ in controls) in the testes of Group 1 animals after four weeks of the experiment indicated reduced functional activity, which might also adversely affect spermatogenesis [9-11]. Overall, the nuclear volume of Leydig cells decreased, reflecting reduced functional activity, a parameter commonly used as an indicator of testicular endocrine function [12, 13]. Chronic alcohol consumption is associated with reduced semen quality, mediated by oxidative stress and the genotoxic effects of alcohol on hormonal regulation and DNA integrity. Ethanol is primarily metabolized in the liver, producing acetaldehyde and acetate, which are toxic and potentially carcinogenic metabolites. In addition, ethanol can interact with lipids, forming fatty acid ethyl esters and phosphatidylethanol, which interfere with physiological cellular pathways [14]. Lipid peroxidation was identified as the primary mechanism mediating ethanol's detrimental effects on the testes and spermatozoa in a study investigating 63-day alcohol exposure in rat gonads. In animals receiving supplemental vitamin C, sperm count, spermatogenesis kinetics, lipid peroxidation levels, and sperm motility were normalized, and histopathological changes in the testes were partially restored [15].

Acute ethanol exposure enhanced autophagy in Sertoli cells of adult rats. Stages VII-VIII of spermatogenesis were found to exhibit high levels of autophagy, which is associated with androgen receptor suppression, mitochondrial damage, lipid accumulation, and phagocytosis of apoptotic cells. This process may play a critical role in preserving Sertoli cell viability and sustaining germ cell function under toxic conditions [16]. Specialized junctions between supporting epithelial cells constitute the most critical and vulnerable component of the blood-testis barrier [17]. The dilation of endoplasmic reticulum elements, reduction in microfilaments, and cytoplasmic clearing and vesiculation observed in these cells indicate disruption of their barrier function [12]. Thus, structural changes in the blood-testis barrier induced

by chronic alcohol intoxication may disrupt homeostasis and contribute significantly to impaired spermatogenesis [13]. The acrosome, a characteristic feature of spermatids and a marker of the spermatogenic epithelial cycle stage, forms a distinct umbrella-like structure at stage VII and is readily identifiable [18].

Numerous studies have demonstrated that the severity of adverse effects on male reproductive health correlates with the frequency, duration, and intensity of alcohol consumption. Chronic alcohol use impairs liver function, disrupts lipid metabolism, and changes glucose homeostasis, thereby contributing to obesity, metabolic syndrome, and related systemic disorders [2]. The multifactorial nature of alcohol's effects is further amplified by individual variability and its interaction with other contributing factors. Specifically, iodine deficiency, particularly when combined with goitrogen intake, induces edematous and degenerative changes in connective tissue elements, vascular walls, and the epithelial tissue of the prostate gland. Altered thyroid status thus initiates systemic, interconnected changes that reflect the functional relationship between the testis and prostate gland in male reproductive function [19, 20]. Potential determinants of sperm quality include inadequate nutrition, obesity, and exposure to environmental toxins [6].

Ethanol reduces sperm viability, increases cell death, and promotes apoptosis, resulting in long-term reproductive consequences [21]. Comparable apoptotic effects of alcohol have been reported in male Wistar rats [22]. Consistent with our findings on alcohol's effects on the testes, fibrotic changes have been reported by other researchers [23]. Moreover, alterations in testicular protein expression have been implicated in the mechanisms of ethanol-induced male infertility [24].

Based on previous studies [25, 26] and clinical observations [25-27] showing that ligation of the inferior epigastric arteries enhances testicular blood flow in hypogonadism

of various etiologies, we applied this surgical technique to promote reparative processes in the testes of adult outbred albino rats subjected to chronic alcohol intoxication. Our findings suggest that enhancing testicular blood flow via this approach stimulates reparative processes in the testis.

CONCLUSIONS

Short-term (one to two weeks) alcohol exposure induces degenerative changes in the arterial system, the microvasculature, and the spermatogenic epithelium. This is accompanied by moderate desquamation of germ cells into the lumen of the seminiferous tubules and their subsequent death. Prolonged chronic alcohol exposure (four weeks) results in marked destructive changes in the arterial system, the microvasculature, and the blood-testis barrier. Progressive desquamation of the spermatogenic epithelium is observed in 54-70% of seminiferous tubules, resulting in their complete depletion and reduced tubular diameter. Cells of the spermatogenic epithelium at more advanced stages of differentiation are more susceptible to alcohol-induced damage. The numbers of spermatids and pachytene spermatocytes decrease after two, three, and particularly four weeks of chronic alcohol exposure. Alcohol exposure for three and four weeks irreversibly reduces the number of preleptotene spermatocytes. Reparative changes in the testes of rats exposed to chronic alcohol intake are observed only in cases of short-term exposure (one to two weeks). Extension of alcohol exposure to three weeks reduces the intensity of reparative processes in testicular structures, while four weeks of exposure results in an almost complete absence of reparative activity. Ligation of the caudal epigastric arteries above the origin of the cremasteric arteries improves testicular blood supply via the cremasteric arteries and promotes more robust reparative processes, restoring the morphological structure of the damaged organ.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Support for the physical and mental health of Ukrainian youth during the war

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Aim: to highlight the role of health-preserving technologies in supporting the physical and mental health of Ukrainian youth during the war.

Materials and Methods: The study employs a comprehensive set of research methods: theoretical (search-targeted analysis, comparison, and generalization of literature to systematize key concepts; structural-functional analysis of university activities); practical (observation of the psycho-emotional state of young people; a survey of 200 students from Vasyl Stefanyk Carpathian National University (CNU) and I. Horbachevsky Ternopil National Medical University (TNMU) interviewing); and methods of mathematical data processing.

Results: The research results confirm that under conditions of Russian aggression, Ukrainian youth face challenges that affect not only the educational process, but also their psycho-emotional state. The war has caused increased levels of stress, instability, and psychological pressure on young Ukrainians who are forced to study under constant threat. In the fourth year of the war, about 60% of young people report a deterioration in their emotional state; none indicated an improvement. Anxiety has risen (59% of respondents experience it, compared to 52% previously). The number of young people who feel depressed has tripled compared to 2022 (59% now, previously 20%). An even larger share feel sadness (about 60%), whereas earlier this figure was significantly lower – up to 13%. The percentage of young people who express joy and describe their emotional state as positive has increased slightly (up to 8%, compared to 5%). In this context, innovative health-preserving technologies – which help maintain the physical and mental health of Ukrainian youth during wartime – are becoming especially relevant.

Conclusions: Supporting an individual's mental health is one of the priority tasks of state policy. Higher education institutions emphasize innovative health-preserving methods and technologies that allow Ukrainian youth to adapt to wartime conditions, care for their mental health, maintain their well-being, and strengthen their resilience.

KEYWORDS: post-traumatic stress disorders, accessibility, health-preserving technologies, mental health, physical health, mental well-being, psychological support

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INTRODUCTION

The war unleashed by Russia in Ukraine has led to increased levels of stress among Ukrainian youth, who are forced to study under conditions of constant threat and limited resources. Young men and women who live in occupied territories or in frontline areas with daily missile and artillery shelling and bombing, as well as those studying in other regions of Ukraine that are also subjected to attacks, remain in constant stressful situations.

Based on the results of a survey conducted in late March–early April 2025 among students of Vasyl Stefanyk Carpathian National University (CNU) and I. Horbachevsky Ternopil National Medical University (TNMU) (200 respondents) regarding their emotional state in the fourth year of the war and the impact of the war on mental health, as well as the results of a U-Report survey – a UNICEF digital platform – published in early February 2023, which included 4,765

responses out of 24,624 surveyed young people (the sample covered virtually all regions of Ukraine except the temporarily occupied ones), we assert the following: 73% of young people need psychological support after the outbreak of the war; however, only 30% have sought help. Additionally, 56% of respondents sought information on how to improve their mental health during the war, nearly 70% reported a deterioration in their emotional state, and 100% of respondents from the Autonomous Republic of Crimea (AR Crimea) reported a worsening of their emotional state [1] (Fig. 1).

Based on the results of a survey of students from CNU and TNMU (2022–2025), we identify the main challenges faced by young people. These include, first and foremost, emotional strain caused by studying under air raid alerts; a constant sense of danger due to missile strikes and UAV (drone) attacks; stressful situations resulting from power outages;

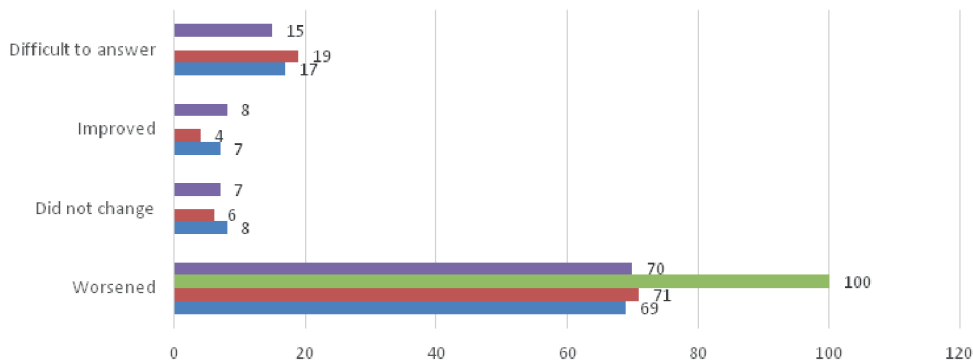


Fig. 1. Results of a survey on the impact of war on the mental health of young people, according to U-report

Source: [1]

the loss of relatives and loved ones in the war; psychological tension caused by combat operations and events at the front; insufficient physical activity due to forced distance learning; low levels of concentration and productivity caused by stress and a lack of quality rest; difficulties adapting to changes in the educational process and in life in general; and the difficult psycho-emotional state of internally displaced young men and women due to the loss of a familiar environment, friends, and their home, among other factors. Vulnerability to psychosocial stress is also experienced by young people who have gone abroad. In particular, young individuals note that the reasons for this include longing for their homeland, job loss, everyday hardships, certain financial difficulties, feelings of social isolation, uncertainty about the future, frequent inability to find employment in their field of training, and anxiety about relatives and loved ones who have remained in frontline areas (or in Ukraine in general), etc. [2]. All of this significantly increases the vulnerability of Ukrainian youth to psychosocial stress and contributes to the emergence of mental disorders (depression, anxiety, post-traumatic stress disorders, etc.) [3, 4].

We believe that innovative health-preserving technologies are intended to address these problems, as they create conditions for supporting the physical and mental health of Ukrainian youth.

As the results of the analysis of the source base of our study have shown, Ukrainian scholars (medical doctors, psychologists, educators, sociologists, philosophers, and others) are examining the impact of crisis situations on people's health. In particular, certain aspects of the problem of mental health under such conditions, including wartime conditions – namely, post-traumatic stress disorder as a medical, psychological, and social problem; collective trauma and group identity; medical and psychological consequences of war-related distress in Ukraine; individual mental health during war; directions of psychological support for Ukrainian students during the war; and emergency psychological assistance to victims in emergency situations: theoretical and applied aspects, among others – have been addressed in the studies of such scholars as O. Lazurenko, N. Tertychna and N. Smila [2], O. Chaban and O. Khaustova [5], V. Chorna, M. Antomonov, N. Pavlenko, S. Khlestova,

V. Kolomiets, M. Syrota [6], and others [7]. However, in Ukrainian scholarly discourse, there are almost no studies that analyze the problem raised in the title of this article.

The war launched by Russia against Ukraine has led to heightened stress levels among Ukrainian youth, who are forced to study under conditions of constant threat and limited resources. Young men and women living in occupied territories or in frontline zones – where daily missile and artillery attacks, as well as airstrikes, are a reality – remain in continuous stressful situations. Likewise, those studying in other regions of Ukraine, which are also subjected to frequent attacks, face ongoing psychological pressure.

According to the results of a survey conducted in late March – early April 2025 among students of CNU and TNMU (200 individuals) concerning their emotional state in the fourth year of the war and the war's impact on mental health, as well as according to the results of the U-Report survey by UNICEF's digital platform, published in early February 2023, based on 4,765 responses out of 24,624 young people surveyed (a sample representing almost all regions of Ukraine except the temporarily occupied territories), we state the following: 73% of young people need psychological support after the outbreak of the war, yet only 30% sought help; 56% of respondents looked for information on how to improve their mental health during the war; nearly 70% reported that their emotional state had worsened; and 100% of respondents from the Autonomous Republic of Crimea (ARC) reported a deterioration in their emotional state [1] (Fig. 1).

Based on the survey results of CNU and TNMU students (2022–2025), we identify the main challenges faced by young people. These include, first and foremost, emotional strain caused by studying under air-raid alarms; a persistent sense of danger due to missile strikes and UAV attacks; stressful situations resulting from power outages; the loss of relatives and loved ones in the war; psychological pressure caused by ongoing fighting and frontline events; insufficient physical activity due to forced remote learning; low levels of concentration and productivity due to stress and lack of adequate rest; difficulties adjusting to changes in the educational process and life in general; and the complex psycho-emotional state of internally displaced young people who have lost their familiar environment, friends, and homes.

Youth who have gone abroad also experience vulnerability to psychosocial stress. Young respondents report that this is caused by homesickness, job loss, difficulties with daily living, certain financial hardships, a sense of social isolation, uncertainty about the future, frequent inability to find employment in their field, and constant worry about relatives who remain in frontline regions (or in Ukraine in general). All these factors significantly increase the vulnerability of Ukrainian youth to psychosocial stress and contribute to the emergence of mental disorders such as depression, anxiety, and post-traumatic stress conditions.

We argue that innovative health-preserving technologies are essential for addressing these problems, as they create conditions for maintaining the physical and mental well-being of Ukrainian youth.

AIM

The aim of the article is to highlight the role of health-preserving technologies in maintaining the physical and mental health of Ukrainian youth during wartime.

MATERIALS AND METHODS

In the process of studying the issue under consideration, a number of scientific research methods were used: theoretical methods (a targeted-search method – analysis, comparison, and generalization of scientific literature on the problem of preserving the physical and mental health of Ukrainian youth during the war, aimed at systematizing and summarizing facts, information, and materials on the researched topic, and at defining the essence of key concepts; a structural-functional method – analysis of the content of activities of universities that use health-preserving technologies to support the physical and mental health of young men and women under conditions of Russian aggression); practical research methods: observation of young people regarding their mental health during the war, its impact on personal development, and their responses to stressful situations; a survey among CNU and TNMU students (200 individuals) concerning their emotional state in the fourth year of the war and the impact of the war on their physical and mental health; interviews with students to clarify survey responses (as a supplement to the questionnaire); as well as methods of mathematical processing of research results, and others.

RESULTS

The full-scale war launched by Russia has significantly increased Ukrainians' need for psychological assistance. It is projected that by the end of the war, nearly 15 million citizens will require psychological support, including 1.8 million service members, 7 million older adults, and 4 million children. According to WHO data, one in five residents of combat zones faces mental health disorders. In 2023, the number of cases of post-traumatic stress disorder (PTSD) increased fourfold compared to 2021, and by early 2024 had nearly equaled the total number recorded throughout 2021.

PTSD is one of the most common consequences of war and develops as a result of experiencing or witnessing a traumatic event (combat actions, terrorist attacks, natural

disasters, accidents, traffic collisions, physical or sexual violence, captivity and torture, threats, psychological abuse, or any event perceived as traumatic) [8].

The risk of developing PTSD increases with the intensity of the traumatic event, lack of social support, stressors experienced after the trauma, and the presence of preexisting mental health disorders. This critical mental health condition further burdens the healthcare system, contributing to increased rates of cardiovascular, oncological, respiratory diseases, and diabetes among individuals with mental disorders.

According to the Electronic Health System (EHS), a significant increase in the number of patients diagnosed with PTSD has been recorded over the past two years.

As of February 2025, nearly 9,000 primary care physicians and 1,800 mental-health specialists in Ukraine are able to provide free psychological services. However, this remains insufficient. The shortage of qualified psychologists and psychiatrists continues to pose a serious challenge [9].

The government has responded to this issue by implementing the National Mental Health Program in 2022. To overcome the ongoing crisis, it is essential to improve specialist training, raise certification standards, and introduce international guidelines in the field of psychological care. Ensuring the availability of competent professionals and strengthening the regulation of psychological services are of critical importance [8].

It is also crucial to adapt best international practices in psychological support and ensure that such services are accessible to everyone who needs them, especially under conditions of Russian aggression. Health-preserving technologies play a significant role in this process. In the Ukrainian context, crisis conditions primarily refer to the war triggered by Russia's full-scale invasion on February 24, 2022. However, the aggressor state began military operations as early as 2014. Thus, more than a decade of living under crisis conditions has profoundly affected the physical and mental health of Ukrainian youth.

Educational institutions first faced the need to adapt the learning process to new realities in 2014, working to provide young people with a safe environment and preserve their well-being. In this context, after the full-scale invasion of February 24, 2022, health-preserving technologies became a key factor in supporting and developing the potential of Ukrainian youth.

Below are selected examples illustrating how health-preserving technologies are used to support the physical and mental health of Ukrainian youth during wartime with the support of the state (Table 1), civil society organizations (Fig. 2), and higher education institutions (Fig. 3, Table 2).

For instance, in June 2022, the creation of the National Mental Health and Psychosocial Support Program was initiated. Its goal is to establish a Ukrainian model of a "mental-health and psychosocial support system that incorporates the best global and domestic practices", and to build an effective system of accessible, high-quality mental-health services available to everyone in need [10].

The establishment of the Interagency Coordinating Council on Mental Health and Psychological Assistance for

Table 1. State support for the use of health-preserving technologies for Ukrainians during the war (2023)

Ministry of Health	Project "Protection of Mental Health within the Structure of Medical Care." It covers all population groups, from whom mental health services are provided at the primary and secondary levels of medical care through a family doctor. If necessary, the doctor (manager) refers the patient to a specialized specialist.
Ministry of Social Policy	Project "Establishment of Resilience Centers in Ukraine". It is aimed at providing psychosocial support to community residents, frontline professionals, and volunteers.
Ministry of Veterans Affairs	Project "Transition from Military Service to Civilian Life (in terms of psychological assistance)". It envisages a digital solution (the creation of a mobile application) to support defenders and female defenders, as well as their families, during their return to peaceful civilian life.
Ministry of Youth and Sports	Project "Youth Centers and Active Parks as Part of the Mental Health Ecosystem". One of its components is the provision of psychological support services for adults, children, and adolescents through the "SpivDiia" platform.
Ministry of Education and Science	Project "Psychosocial Support and Psychological Assistance at All Levels of Education." It provides for the implementation of psychological resilience skills at all levels of education - from preschool to higher education - as well as the transformation of psychological services within the education system.
Ministry of Defense	Project "Creation of a System for Psychological Recovery of the Personnel of the Armed Forces of Ukraine (RECOVERY)". It is aimed at the psychological recovery of servicemen and servicewomen and their family members after discharge from service, in particular through the establishment of specialized centers.
Ministry of Internal Affairs	Ministry of Internal Affairs of Ukraine - Psychological Assistance Routing Algorithm. In crisis and emergency situations, after providing emergency psychological assistance at the scene of the incident, the victim should have a clear pathway for further referral within the chain of psychosocial support.

Persons Affected by the Armed Aggression of the Russian Federation is an important step toward implementing this national program and advancing the development of a comprehensive mental-health and psychosocial support system in Ukraine [10].

Several civil society initiatives also effectively employ innovative health-preserving technologies, which have

a positive impact on supporting the mental health of Ukrainian youth (Fig. 2).

Therefore, civil society initiatives that support physical and mental health are of great importance for preserving the health of Ukrainians in war conditions: National Psychological Association (NPA), Stress Resilience Center in Kyiv, "RAZOM with You" Psychological Support Center (opened in Bucha), "Step Toward You" Rehabilitation Center, providing free psychological assistance, National Suicide Prevention and Mental Health Support Line "Lifeline Ukraine", Online program "Being the Parent of an Angel", "Razom" Psychological Support Group, "Resilience Hub", "Zaporuzhka", "24/7 Psychological Support Services", "Telegram channels: 'Psychological Support', 'Peremcha' (the latter intended for individuals aged 3–22)", "Open Doors" Psychological Counseling Center, online platform "Tell Me".

**Fig. 2.** Selected civil society initiatives supporting the physical and mental health of Ukrainian youth (2023)

Source: [1]

(opened in Bucha), "Step Toward You" Rehabilitation Center, providing free psychological assistance, National Suicide Prevention and Mental Health Support Line "Lifeline Ukraine", Online program "Being the Parent of an Angel". "RAZOM" Psychological Support Group, 24/7 Psychological Support Services: "Zaporuka", "Resilience Hub", Telegram channels: "Psychological Support", "Peremoha" (the latter intended for individuals aged 8-22), "Open Doors" Psychological Counseling Center, online platform "Tell Me".

A common feature of initiatives undertaken by the state and civil society organizations is their emphasis on health-preserving technologies, which we understand as a system of organizational methods, tools, and forms aimed at maintaining and strengthening an individual's health – physical, mental, social, and spiritual.

Health-preserving technologies include:

- health-promoting content,
- guiding principles,
- psychological and pedagogical conditions ensuring effective implementation,
- an interdisciplinary and person-centered approach, and more.

These technologies contribute not only to the formation of healthy-lifestyle skills among young people but also to the development of a responsible attitude toward their own well-being. In other words, they foster health-preserving behavior.

Health-preserving technologies (in our case, as will be shown below, coaching technologies) are a key factor in developing the potential of Ukrainian youth during wartime. They ensure not only the preservation of physical and mental health but also foster an individual's capacity for adaptation, resilience, and self-development.

As demonstrated by our practical experience in higher education institutions (CNU, TNMU, and others), health coaching is a powerful factor in youth development, especially under conditions of social upheaval caused by Russian aggression. Such circumstances significantly affect the psycho-emotional state of students, leading to elevated stress, anxiety, and other disorders. These challenges can be addressed through health-preserving technologies, such as coaching technologies, which support the development of self-regulation skills, stress resilience, and a responsible attitude toward personal health and life [11]. Selected types of coaching technologies aimed at supporting the physical and mental health of Ukrainian youth during wartime: Life Coaching, Health Coaching, Success Coaching, Healthy Lifestyle Coaching, Holistic (Comprehensive) Health Coaching, Art Coaching, Emotional Coaching, Christian Coaching, Christian Coaching.

The types of coaching we identify for health preservation are somewhat conditional. On one hand, the coaching types in this group overlap with other forms of interpersonal relations. On the other hand, health, spiritual, and moral-psychological coaching are distinguished by their specific focus on change, self-organization, and self-improvement of the internal world of students. They aim to organize feelings, emotions, behaviors, life values, and other aspects of personal development.

At the beginning of the 21st century, life coaching (Life Coaching – coaching for personal life, or coaching for individual growth) became one of the fastest-growing and most in-demand areas in the coaching system. According to our analysis, this type of coaching is among the most controversial in professional and academic literature, which is reflected in how it is presented in scholarly sources. A common approach is to "universalize" the tasks and functions of life coaching – for example, it is described as being offered to anyone seeking self-improvement and personal development – and to equate it with the entire coaching movement. In this context, its conceptual foundations and historical development [11] are discussed, a perspective especially prevalent in Latin American discourse.

According to the official documents of the Latin American Society of Coaching, life coaching is conducted to help clients "develop everything necessary on their life path", including health, professional activity, interpersonal relationships, and more. In the vision of this institution, life coaching assists individuals in identifying and realizing their dreams, effectively "building a bridge" for a person to move successfully from point "A" to point "B" as the realization of life plans [12]. We believe that under conditions of war, this type of coaching is particularly important for supporting the physical and mental health of Ukrainian youth and fostering their personal development.

An analysis of the source material allows us to distinguish a conditional "psychophysiological direction" of life coaching, which focuses on:

- Developing cognitive processes, emotional intelligence, and creativity;
- Improving mental functions such as memory and attention;
- Building skills to control emotions and make conscious decisions;
- Maintaining stable mental health and enjoying life.

In this approach, life coaches (coaches for personal growth) are often compared to psychotherapists [13], although they do not work with deep psychological disorders. Instead, they help improve quality of life and make personal behavior more flexible and adaptive.

For example, the Psychological Support Center "Razom z Toboyu" provides free consultations at the Faculty of Psychology, CNU. The project is implemented by the Charitable Foundation "Razom for Ukraine" with support from Direct Relief. The center offers psychological counseling and support for children, adolescents, youth, and adults affected by the war. Its staff implements the concept of post-traumatic growth for those in crisis situations caused by Russian aggression. Their goal is not only to stabilize emotional states and help cope with fear, anxiety, chronic stress, panic attacks, and apathy but also to help individuals find inner resources, feel support, and stimulate personal development [14].

Thus, these are health-preserving technologies, whose objectives include:

- Increasing independence in managing one's own life;
- Promoting self-development;

- Improving social functioning;
- Implementing new projects for the future;
- Restoring motivation for transformation, identity development, and readiness for change.

This is achieved through individual consultations, growth groups, and training for specialized groups such as social workers, educators, and medical personnel. Consultations are conducted online or offline, one-on-one with a psychologist. Group and individual consultations are provided at centers, with outreach services offered at centers for internally displaced persons and hospitals. Appointments for psychological consultations can be made via the following link: https://docs.google.com/forms/d/e/1FAIpQLSeVIlFLBAI3d8bqBgdmSp_GC2bcl4RL3FMeoLI1yBHFopyhTA/viewform

On the Department of Developmental Psychology of Vasyl Stefanyk CNU website, a set of audio exercises is offered, which young people can use to support their physical and mental health, stabilize their emotional state, and promote self-development [14]. These include exercises that help students, pupils, and adults cope with stress (Table 2); exercises aimed at developing mindfulness (teaching how to be less distracted by thoughts or feelings and cope with stress) (7 minutes); Grounding 1 (a technique that helps stay in the present moment and return to reality when experiencing stress) (5 minutes); Grounding 2 (a short, guided exercise teaching how to pause and notice one's thoughts and feelings) (2 minutes); Grounding 3 (a longer guided exercise to maintain presence in the moment) (9 minutes); Focus and Name It (teaches how to use attention-directing and naming techniques to disengage from negative thoughts and feelings) (6 minutes); Getting Off the Hook of Negative Thoughts (teaches how to detach from harmful thoughts about oneself) (4 minutes); Creating Space (teaches how to "create space" for difficult thoughts instead of struggling against them) (5 minutes); Showing Kindness to Yourself (teaches how to treat oneself kindly, especially when there is no supportive friend nearby) (8 minutes).

Other forms of psychological support for youth are also important, especially for girls as future mothers. For example, an online lecture titled "Features of Psychological Support During Pregnancy Considering Age-Related Characteristics" (CNU, January 27, 2025) was organized by the Department of Clinical and Rehabilitation Psychology for students from various universities in Ukraine, including Kryvyi Rih State Pedagogical University and South Ukrainian National Pedagogical University named after K. D. Ushinsky. The lecturer emphasized the need to improve approaches to psychological support during motherhood, particularly considering age factors, crisis conditions, war, and other contemporary challenges, and stressed the importance of providing quality support for future mothers and their families [14]. On the basis of coaching, the Tutoring Academy at PNU ("Academy of Tutoring") provides support for CNU students. A team of six active CNU students developed the Academy of Tutoring project, aimed at enhancing psychological resilience and improving mental health among youth. The project emphasizes the importance of health preservation during war, self-help techniques, and personal development [14].

Similar methods and forms of support for physical and mental health are implemented at the Psychological Counseling Center of TNMU, where a special space has been created for self-exploration, unlocking the potential and resources of young men and women for personal growth, and providing support in difficult life situations. The Center operates according to the Ethical Code of the Psychologist, whose main principles are recognition of each person's uniqueness and value, an individual approach, respect, and confidentiality [15].

The Psychological Counseling Center of Dnipro State Medical University offers youth not only long-term, widely recognized stress management methods (healthy nutrition, sufficient sleep, exercise, relaxation, and changing attitudes toward an imperfect world) but also other effective techniques aimed at urgent support for youth during wartime (Fig. 3).

Table 2. Audio exercises aimed at stabilizing emotional state, supporting physical and mental health, and promoting self-development of individuals under conditions of war

Audio Exercise Name	Purpose	Duration
Mindfulness Development	To teach young people to be less distracted by thoughts or feelings and cope with stress	7 min
Grounding (Grounding 1, 2, 3)	To help young people stay in the present moment and return to reality when experiencing stress	Short-term: 2 min, Medium/Long: 5-9 min
Focus and Name It	To teach young people to use attention-directing and naming techniques to disengage from negative thoughts and feelings	6 min
Getting Off the Hook of Negative Thoughts	To teach young people how to detach from harmful thoughts about themselves	4 min
Creating Space	To teach young people how to "create space" for difficult thoughts instead of struggling against them	5 min
Showing Kindness to Yourself	To teach young people how to treat themselves kindly, especially when no supportive friend is nearby	8 min

Source: [1]

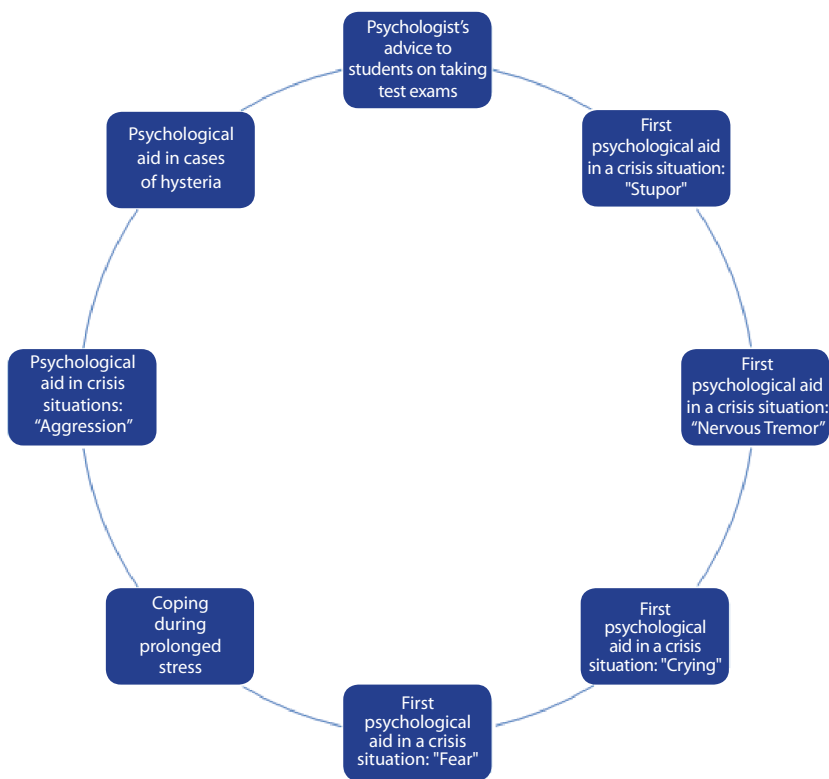


Fig. 3. Types of psychological support for youth at Dnipro State Medical University during the educational process under wartime conditions
Source: [16]

Types of Psychological Support at Dnipro State Medical University during the Educational Process under Martial Law: Psychologist's advice to students on taking test exams, First psychological aid in a crisis situation: "Stupor", First psychological aid in a crisis situation: "Nervous Tremor", First psychological aid in a crisis situation: "Crying", First psychological aid in a crisis situation: "Fear", Coping during prolonged stress, Psychological aid in crisis situations: "Aggression", Psychological aid in cases of hysteria.

As we can see, Dnipro State Medical University, like other universities in Ukraine, provides a wide range of psychological support for youth under wartime conditions, since a stable psychological state is essential for life and learning in crisis situations. To help young people, specialists from the Department of Psychiatry, Narcology, and Medical Psychology offer effective self-help techniques – simple life-coaching methods that help cope with stress and foster personal development.

DISCUSSION

In our view, life coaching should focus not only on improving young people's lives during their studies, but also beyond them. This rejects the approach according to which it is included in the group of professionally oriented coaching. From the perspective we have defined, it is necessary to distinguish life coaching (coaching for personal development) from personal effectiveness coaching, which is objectively connected with professional activity. Life coaching differs from it in terms of its goal (directing a person toward

finding ways of effective mental self-improvement); its philosophical basis (a person's understanding of the value of life and the desire to gain maximal return from using their own potential); and its expected outcomes (increased levels of personal happiness, love, material well-being, life satisfaction, etc.). Such differentiation is also reasonable considering the existence of separate training programs for coaches in life coaching and in personal growth coaching.

The essence of life coaching lies in individual work with young people, aimed at improving various spheres of their personal life – health, spirituality, morality, self-esteem, relationships, etc. – which form the foundation and precondition for achieving life success. In the philosophy of life coaching, every person is unique, possessing natural abilities as well as values, beliefs, aspirations, and needs acquired through socialization [13].

Life coaching can be considered a set of tested tools deemed effective for helping youth in personal and social development, as well as for addressing various life challenges, especially those associated with war.

Youth are a particularly vulnerable social group in terms of emotional well-being during wartime, as evidenced by U-Report data [1] (Table 3).

It is worth noting that by the fourth year of the war, the emotional state of young people had changed. This is confirmed by the results of our survey conducted at the end of March – beginning of April 2025 among students of CNU and TNMU (200 respondents). Our questionnaire included the same questions as the U-Report survey, UNICEF's

Table 3. Survey results on the emotional state of youth after the start of the war, according to U-Report

Emotional State	Number of respondents (2023, U-Report)	Number of respondents (2023, U-Report)
Feel anxious	52	54
Feel depressed	18	19
Feel sad	12	13
Calm	9	6
Show a positive state	5	2
Show joy	1	-
Could not respond	4	5

Source: [1]

Table 4. Survey results of CNU and TNMU students regarding their emotional state in the fourth year of the war

Emotional State	Number of respondents (CNU 2025)	Number of respondents (TNMU 2025)
Feel anxious	59	59
Feel depressed	61	57
Feel sad	60	58
Calm	7	9
Show a positive state	6	8
Show joy	6	5
Could not respond	22	19

digital platform, published in early February 2023, which assessed the emotional state of youth and the impact of the war on their mental health (Table 4).

As we can see (Fig. 1, Table 3-4), the survey results of CNU and TNMU students in 2023 and 2025 regarding their mental health indicate changes in the fourth year of the war. On one hand, 60% of CNU respondents and 58% of TNMU respondents report a deterioration in their emotional state (previously, these figures were higher: 71% and 70%). On the other hand, no young person reported an improvement in their emotional state (previously, these figures were 4% for Ivano-Frankivsk and 8% for Ternopil). Anxiety has increased among youth, now felt by 59% (previously 52%), the number of young people experiencing depression has tripled (now 59%, previously 20%), and more respondents report feeling sad (60% of CNU students and 58% of TNMU students; previously 12% and 13%). Meanwhile, the proportion of young people reporting joy or a positive emotional state is slightly higher: 6% (Ivano-Frankivsk), 8% (Ternopil) compared to previously 2% (Ternopil) and 5% (Ivano-Frankivsk).

Thus, supporting an individual's mental health is one of the priority tasks of an educational institution [2, 5, 6, 7]. In this regard, life coaching (personal development coaching) offers young people various means of self-improvement depending on their understanding of the value of life

and their aspiration to obtain the maximum return from using their potential.

In a broad sense, it is aimed at increasing levels of happiness, love, overall development, and general life satisfaction. In a narrower, more specific dimension, life coaching helps meet personal needs related to: interpersonal relationships; self-love (without egoism or narcissism); discovering one's "true self"; forming positive thinking and self-motivation; setting clear and realistic life goals; reducing stress and feelings of uncertainty; increasing confidence and levels of joy and interest in life; achieving holistic spiritual self-healing [13].

Under wartime conditions, the use of life coaching in the educational process, as well as in extracurricular and out-of-class activities, becomes particularly relevant.

An example can be seen in the work of the University for Gifted Children (UGC) (director – Prof. Halyna Bilavych), a unique volunteer project with no equivalent in similar higher education institutions, which has been operating since 2017 at Vasyl Stefanyk Carpathian National University and is aimed at the comprehensive development of the individual and the preservation of their health. This is a new environment where experienced teacher-coaches as well as student-coaches implement innovative methods and forms of personal development through master classes and various schools. Since 2022, the UGC has begun

actively introducing health-preserving technologies under wartime conditions. For example, in the summer of 2025, within the framework of the project “Interesting Holidays – 2025”, more than 120 sessions were held by the UGC, aimed at the overall development of personality and, in particular, the support of physical and mental health. An intensive personal development program was delivered by more than 100 teacher and student volunteers, who also acted as coaches. The uniqueness of the UGC lies in its commitment to the principles of accessibility, with many activities for children conducted in the university’s green zone, in the park, outdoors, and similar settings. In the context of Russia’s military aggression, the UGC began working with children of internally displaced persons. The Ukrainian youth – UGC volunteers – understand that in the conditions of the Russian–Ukrainian war, children are the most vulnerable group of Ukrainians who need support. It is necessary not only to preserve children’s lives but also to give them a childhood in which they will be protected, healthy, educated, nationally conscious, and holistically developed. Therefore, great attention is paid to forming the physical and mental health of the individual as the foundation of life under wartime conditions. To this end, the following structures operate: the School of the Healthy and Active Child; the School of Accessibility; the Catechetical School; the Coaching School; the School of Making and Entertainment; the “Red Dragon” School; the School of Language Ecologists; the School of Orators; the Eco-School; the IT School; the School of Journalism; the School of Painting; the School of Polyglots; the School of Creative Ideas; the School of Young Entrepreneurs “How to Become a Millionaire”; the School of Interesting Mathematics; the School of Local History; the School of Logic; the Literary Lounge; the School of Noble Ukrainians; Vocal Schools; the Dance School; the “Skillful Hands” School; the School of Volunteering; the UGC Scientific Society, and others [17].

Art therapy tools have great potential for preserving the physical and psychological health of young people. We view it as a factor in achieving certain goals, and four areas of art coaching are distinguished: the psychophysiological (related to the correction of psychosomatic disorders); the psychotherapeutic (connected with influencing the cognitive and emotional spheres of a person’s personality); the social-pedagogical (focused on the development of aesthetic needs, the expansion of general and artistic-aesthetic horizons, and the activation of artistic activity and creativity); and the psychological (intended to promote personal integration). From different perspectives, they all focus on a common goal – revealing a person’s experiences and guiding them toward awareness of their own desires and needs, improving relationships with their environment, and helping to balance their inner psycho-emotional state [18, 19].

Under wartime conditions, the role of a relatively new and least represented type of coaching in the Ukrainian discourse – Christian coaching – is growing. Its fundamental principles were presented in the book “Christian Coaching: Helping Others Turn Potential into Reality” by the well-

known American actor and television host Gary Ennis Collins [19]. Relying on the basic principles of coaching, he substantiated a version of the coaching process whose center is God.

Encompassing broader spheres of human life than mentoring and discipleship, Christian coaching, in Collins’s understanding, is meant to help a person understand what future God has intended for them. Having clarified the “picture of the present” (a person’s essence, life values, and preferences), the author shows how, with God and through God, a person can confidently orient themselves and move into the future according to their calling; how, with His help, one can move forward, overcoming obstacles and achieving goals.

From this perspective, the following types of Christian coaching are identified: coaching for change; transitional coaching; coaching aimed at solving life-balance problems; relationship coaching, and others. Despite its Christian specificity, these types correspond to the main areas of coaching (career, executive, family, life coaching, etc.) [20]. It is difficult to agree with the interpretation of Christian coaching as “a commercialized version of church discipleship”, whose purpose is “to attract people and even make money off of it.” [11]. We consider that Bible-based Christian coaching represents an innovative model, integrating coaching philosophy with new content, supporting personal development, and preserving health.

CONCLUSIONS

The types of support for physical and mental health through coaching discussed above share a number of common characteristics: they function as health-preserving technologies; under the conditions of full-scale war in Ukraine, they influence the development of resilience, self-regulation among young people, and their psycho-emotional state, and they serve as a factor in developing the potential of pupils and students. The foundation of health-preserving coaching technologies is the partnership between the specialist (coach) and the learner, aimed at achieving personal goals in the field of health and well-being and developing personal potential. This includes increasing awareness of one’s physical and mental state, developing self-regulation and stress-management skills, recognizing the necessity of self-development, forming motivation for a healthy lifestyle, supporting the achievement of personal health-related goals, enhancing the resilience and adaptability of Ukrainian youth under the stress and uncertainty caused by war, reducing levels of anxiety and stress through the development of self-regulation skills, increasing self-esteem and confidence in one’s own abilities, forming a positive outlook on life under wartime conditions, nurturing confidence in a peaceful future for Ukraine, and developing effective communication and conflict-resolution skills. For effective support of the physical and mental health of Ukrainian youth, it is necessary, among other things, to prepare specialists to use coaching methods in working with young people during wartime; to develop programs adapted to the age-specific needs of children

and adolescents; to create a safe environment aimed at supporting and developing the potential of young people under conditions of Russian aggression; and to foster resilience, self-regulation, and a positive attitude toward

life. It is also important to adopt the best global practices related to supporting the physical and mental health of youth, especially from countries that have experienced wartime conditions.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Corruption in the healthcare sector during a war: A threat to human rights

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ABSTRACT

Aim: To show the increase of corruption risks in healthcare during the war, their negative impact on the protection of human rights, and to outline legal ways to minimize these risks.

Materials and Methods: The study was conducted in 2025 and is based on international and humanitarian law, Ukrainian legislation and regulations in the areas of human rights, healthcare, and anti-corruption, interviews with medical professionals and wounded combatants, content analysis of media publications, and Ukrainian judicial practice and statistics. A total of 47 documents were analyzed, and interviews were conducted with three medical professionals and five combatants.

The methods used were legal analysis and systemic-structural analysis, interviews, statistical analysis, content analysis of media information, and analytical methods, including induction and deduction. Artificial intelligence was used as an auxiliary tool for information search; Grammarly was used to edit the text.

Conclusions: While international law has not yet established a binding norm defining corruption as a human rights violation, corruption in healthcare systems constitutes a significant threat to the realization of human rights. No derogation from commitments to the rights to life and health is legally permissible during wartime. To minimize corruption risks, the healthcare system, including military medicine, must be adequately prepared in advance. Digitalization serves as a crucial tool for transparent assessment of functional/ADL status, and the management of humanitarian aid requires a more effective oversight system.

KEYWORDS: human rights; corruption; healthcare; war; white-collar crimes; public health, international humanitarian law, criminal law, constitutional law, medical law

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INTRODUCTION

Corruption is a negative social phenomenon that causes significant harm to human rights, society, and the state. It is inherent in countries with both high, middle, and low incomes. According to estimates in the world, “7% of health spending, amounting to more than \$ 500 billion per year, is lost to corruption and fraud. Even in Western European countries, the United States, and Canada, the losses are high, estimated at up to 10% of public health expenditure in Germany, 56 billion euros annually in Europe, and \$75 billion in the United States for Medicare and Medicaid payments alone” [1]. Corruption is always an obstacle to a person’s access to medical care, as well as to its availability and quality. It therefore requires special attention from society, government, and non-governmental organizations.

In extreme situations across the country and around the world, corruption in the healthcare system increases significantly, with a severe negative impact on the realization of the human rights to life and health. Over the past decade, the coronavirus pandemic has contributed to the growth of corruption in this area. As scientists have rightly warned, it is during the pandemic that “corruption risks can increase due

to the need for accelerated rates of resource deployment that may result in the bypassing of standard operating procedures” [2, p. 1]. Scientists also highlight corruption risks in COVID-19 vaccine deployment [3] and an increase in other corruption risks during the pandemic [4, p. 25–28], particularly due to limited resources [2].

The ongoing war presents an even greater challenge for Ukraine [5]. However, the heightened threat to human rights during wartime resulting from corruption in the healthcare sector, as well as strategies to minimize these risks, remain insufficiently analyzed and warrant comprehensive scholarly investigation.

AIM

The article aims to show (using the case of Ukraine) the objective and subjective factors of the corruption risks growth in the healthcare sector during the war, their negative impact on the protection of human rights to life and health, and to outline legal ways to minimize these risks.

MATERIALS AND METHODS

The study was conducted in 2025 and is based on international and humanitarian law, Ukrainian legislation

and regulations in the areas of human rights, healthcare, and anti-corruption, interviews with medical professionals and wounded combatants, content analysis of media publications, and Ukrainian judicial practice and statistics. A total of 47 documents were analyzed, and interviews were conducted with three medical professionals and five combatants.

The methods used were legal analysis and systemic-structural analysis, interviews, statistical analysis, content analysis of media information, and analytical methods, including induction and deduction. Artificial intelligence was used as an auxiliary tool for information search; Grammarly was used to edit the text.

This article adheres to the principles of academic integrity and research ethics. All interviews were conducted exclusively for academic research purposes, with voluntary, informed participation obtained through explicit consent. Respondents received comprehensive information regarding the study's objectives and the intended use of collected data. Confidentiality and anonymity were maintained throughout the interview process. No personal data that could directly or indirectly identify respondents is disclosed. Information obtained from interviews is presented solely in a generalized and analytical manner.

REVIEW AND DISCUSSION

The Council of Europe's Civil Law Convention on Corruption in Art. 2 defines „corruption” as requesting, offering, giving, or accepting, directly or indirectly, a bribe or any other undue advantage or prospect thereof, which distorts the proper performance of any duty or behavior required of the recipient of the bribe, the undue advantage or the prospect thereof [6]. Based on that, corruption in the healthcare sector should be considered, on the one hand, as the use by a person of official powers granted to him or related opportunities in the healthcare sector to obtain an improper benefit for himself or others, and on the other hand, as the instigation of another person to use such powers or opportunities for an improper reward. A narrower understanding of corruption as entrusted power associated with public functions is also proposed, which includes “a) abuse of, b) entrusted power related to public functions, c) done in private or public sector, d) for the purpose of personal (in a broadest sense), e) gain of any kind, f) infringing the rights of others” [7]. Our study is grounded in the Council of Europe's Civil Law Convention on corruption doctrine.

Corruption in the healthcare sector has been the subject of extensive study over the past five years. It was analyzed how corruption and its forms in the healthcare system were described in legal acts of selected healthcare institutions [8]. Recommendations are given to the government regarding the introduction of anti-corruption measures [7], and the need for a uniform interpretation across different European countries is proposed to increase its effectiveness [9]. Tackling and preventing corruption in Ukraine's healthcare sector, especially during wartime, is not just a matter of scientific interest. It is a fundamental element of the country's ongoing existence and growth [5].

INTERNATIONAL LEGAL MECHANISM FOR COMBATING CORRUPTION IN THE HEALTHCARE SECTOR

Given the breadth of the subject matter under examination, this analysis deliberately circumscribes its scope to two discrete but interconnected dimensions of international law: first, the correlation between fundamental human rights, specifically the rights to life, security, and health and corruption; and second, the legal doctrine of derogation from international obligations during states of emergency, including the permissible substantive limits of such derogation. The interrelation between corruption and human rights has evolved significantly over the past decade. Both the United Nations and the European Union, alongside institutions within the Council of Europe framework, increasingly recognize corruption in healthcare systems as incompatible with binding human rights obligations.

Comparative doctrinal analysis of how corruption in healthcare systems is framed as a threat to human rights in United Nations treaty body and special procedure practice and European Union legal frameworks demonstrates convergence around three propositions: (1) corruption in healthcare systems impairs the right to health and related rights; (2) anticorruption obligations are implicit in states' human rights duties; (3) while corruption is not yet formally codified as a standalone human rights violation, systemic healthcare sector corruption increasingly triggers human rights responsibility.

The foundation of the United Nations approach lies in Article 12 of the International Covenant on Economic, Social and Cultural Rights (ICESCR), which guarantees the right to “the highest attainable standard of physical and mental health”. The interpretation of Article 12 is found in General Comment No. 14 of the Committee on Economic, Social and Cultural Rights (CESCR). The Committee identifies four interrelated components of the right to health: availability, accessibility, acceptability, and quality (paras. 12-21, 30-37) [10]. Corruption directly undermines each component: (a) availability: diversion of funds reduces facilities, goods, and trained personnel; (b) accessibility: informal payments undermine economic accessibility and equality; (c) quality: procurement fraud jeopardizes medical safety standards; (d) non-discrimination: corruption disproportionately burdens marginalized groups.

Over the past decade, CESCR concluding observations increasingly refer to corruption as a barrier to the realization of economic and social rights. References to corruption in treaty body documents doubled between 2012 and 2019 compared to earlier periods [11, p. 305].

Although CESCR does not formally define corruption as a human rights violation, it treats corruption in public service delivery, including the health sector, as incompatible with states' obligations of progressive realization and non-discrimination. Corruption is framed as a structural cause of violations rather than as an autonomous violation itself. This distinction is doctrinally important. The United Nations human rights system remains cautious about expanding the category of “violation” to include corruption. Instead,

corruption is conceptualized as an act that violates rights protected under binding treaties.

The mandate of the Special Rapporteur on the right to health has significantly advanced the corruption and health nexus. The report identifies corruption risks in the following practices, which undermine transparency, accountability and equality: pharmaceutical procurement; hospital administration; licensing and accreditation; informal payments to medical personnel [12]. The Rapporteur further notes that corruption in the healthcare sector exacerbates structural inequality, disproportionately affecting women, children, persons with disabilities, and low-income populations (paras. 24-27).

It is strongly argued that the implementation of the United Nations Convention against Corruption (UNCAC) should be strengthened by explicit integration of human rights principles [13]. Although UNCAC itself does not define corruption as a human rights violation, its preventive measures, such as transparency, accountability, and equal participation, mirror human rights obligations.

Within the Council of Europe system, Article 11 of the European Social Charter protects the right to health. Also, other Council of Europe legal documents emphasize that corruption in public services undermines social rights and disproportionately harms vulnerable groups. This aligns with a broader European approach, which conceptualizes corruption as a systemic threat to constitutional rights and freedoms [14-15].

A recent significant doctrinal development concerns proposals to incorporate grand corruption into the European Union Global Human Rights Sanctions Regime. It is said that large-scale corruption enforces structural human rights abuses and should therefore trigger targeted sanctions. [16]. Such a vision represents a normative shift toward treating systemic corruption, including corruption in a public health system, as conduct that engages international human rights obligations.

So, both United Nations and European frameworks converge on three doctrinal points: (1) corruption undermines the availability, accessibility, and quality of health services; (2) corruption disproportionately harms vulnerable populations and groups; (3) anti-corruption measures are necessary to fulfill human rights obligations.

The issue of a legal mechanism of derogation from international human rights commitments, specifically concerning the rights to life, health, and security, is important for our study. This legal instrument is codified in two primary documents: the Convention for the Protection of Human Rights and Fundamental Freedoms (CHRFF, 1950), Article 15 [17], and the 1966 International Covenant on Civil and Political Rights (ICCPR, 1966), Article 4 [18]. These instruments grant participating states significant legal discretion and authority to determine the conditions, grounds, duration, and territorial scope of measures taken to derogate from obligations. Such measures are triggered by a „state of emergency“ and are justified by the necessity of protecting state sovereignty, preserving national unity, and maintaining territorial integrity.

Ukraine has exercised this legal option. On May 21, 2015, the Parliament adopted Resolution No. 462-VIII, „On the Declaration of the Verkhovna Rada of Ukraine on Derogation from Certain Obligations under the International Covenant on Civil and Political Rights and the Convention for the Protection of Human Rights and Fundamental Freedoms.“ [19]

Despite the legal availability of derogation accompanied by caveats regarding its exceptional nature and the need for caution, there is a strong normative argument for abstaining from such measures. On January 24, 2002, the Parliamentary Assembly of the Council of Europe (PACE) adopted Resolution 1271 (2002), stating: „In the fight against terrorism, Council of Europe member states should not derogate from the provisions of the European Convention on Human Rights“ (Paragraph 9) [20]. The document further advises refraining from applying Article 15 (Derogation in Time of Emergency) to limit rights guaranteed under Article 5 (Right to Liberty and Security). Among the cited reasons for this recommended abstention are the risks of abuse of power, violations of the rule of law, and the proliferation of corrupt practices.

Summarizing the legal positions and consolidated jurisprudence of international institutions, it is evident that the right to life, health, and security constitutes an absolute entitlement; no derogation can be executed. Children, persons with disabilities, the elderly, ill and damaged, and other vulnerable groups are entitled to special protective guarantees from both the state and the global community. States of emergency, natural disasters or war, as well as formal derogation from treaty commitments, do not relieve states or the international community of the obligation to uphold these core guarantees. Consequently, when the inevitability of resource scarcity arises in emergency situations, the international community, either on its own initiative or at the request of an affected state, mobilizes humanitarian and other forms of assistance. Since the onset of the full-scale war in February 2022, Ukraine has exemplified this multilateral solidarity support architecture from states, international institutions, organizations, and public and private donors at an unprecedented level.

However, the absorption of assistance of such magnitude, in the form of massive, heterogeneous resources flowing from diverse sources, demands robust accounting, balanced distribution mechanisms, high-quality management, and rigorous control. Like most states confronting similar circumstances, Ukraine found itself institutionally unprepared to meet such demands. Corruption, which accompanied the formation of Ukrainian statehood and remained an integral component of its system at all levels, did not vanish during the war. Regrettably, corruption schemes must be assessed as a significant driver of negative trends, impacting not only the physical and mental well-being of civilians and military personnel but also negatively affecting war outcomes themselves. This is precisely why the Ukrainian wartime case is of exceptional importance for rigorous and comprehensive scholarly analysis.

CORRUPTION RISKS IN UKRAINE'S HEALTHCARE SECTOR DURING THE WAR AND STRATEGIES TO REDUCE THEM

The study allowed us to identify factors that significantly increased corruption risks in the healthcare system during the war, and to outline ways to reduce them.

Aerial shelling with missiles and uncrewed aerial vehicles across Ukraine results daily in a significant number of injured military personnel and civilians requiring emergency medical care. There has been a dramatic increase in hospital overload not only on the front lines but also in rear areas. The number of hospitals is declining due to the destruction of facilities and territorial seizures. As of early June 2025, the Ministry of Health of Ukraine reported damage or destruction to 2,354 facilities, including 769 medical institutions [21].

Another negative factor is the decrease in the number of medical workers in the healthcare system due to mobilization, migration abroad, and their deaths. By February 2024, 194 civilian medics had died during full-scale hostilities [22]. As a result, many patients, especially those requiring hospitalization, cannot receive timely medical care due to limited beds and a shortage of medical staff.

Interviews with the heads of three hospitals providing secondary (specialized) care in Kyiv, Kharkiv, and Poltava revealed that since February 24, 2022, they have been operating under extremely challenging conditions. A high volume of military injured are consistently receiving inpatient treatment. In these circumstances, routine medical care has significantly declined, and patients face long waits for hospitalization.

Interviews with five military individuals also showed that, during their inpatient treatment in military or civilian hospitals, they consistently faced a shortage of doctors in certain specialties. Among them are neurologists, neuropathologists, traumatologists, and surgeons. One of them even reported that, due to a catastrophic shortage of doctors, the head of the department and a doctor at one of the military hospitals continued to work in their positions during the pre-trial criminal investigation concerning their receipt of a bribe.

This situation has resulted in an increase in corrupt payments for access to inpatient treatment and rehabilitation services. Three interviewed military personnel reported that, following injuries, bribes were required to gain access to rehabilitation institutions or to extend inpatient treatment; otherwise, individuals remained on waiting lists for extended periods. Official law enforcement reports corroborate these accounts for both military personnel and civilians. For instance, on 25 October 2024, the Prosecutor General's Office reported suspicions against a senior manager of a military hospital in the Lviv region for extorting and receiving an illegal benefit of 15,000 UAH from a military patient in exchange for continued treatment [23]. The Dnipropetrovsk Regional Prosecutor's Office also announced suspicion of a municipal hospital director for receiving an illegal benefit of 32,000 UAH, combined with extortion, for the unreported admission of a patient to a palliative care facility [24].

To minimize corruption risks associated with overloading the healthcare system during wartime, the state must focus on developing medicine in peacetime, prevent unjustified reductions, and prepare for emergencies. Ukraine's case has shown the negative consequences of reducing the military medical system in peacetime, including the liquidation of military hospitals.

The establishment of the 4th Medical Battalion as a separate entity in Ukraine has played a crucial role in mitigating corruption risks in the healthcare sector, alleviating the burden on civilian medical facilities, and ensuring high-quality care for wounded military personnel [25]. This battalion is responsible for evacuating the wounded, providing comprehensive specialized medical care at stabilization points and advanced surgical groups, and maintaining its own military medical commission [26]. Content analysis of mass media indicates that military personnel exhibit greater trust in these medical professionals, motivated by the belief that they will receive high-quality care and have the opportunity to return to full health.

In addition to the significant decline in medical care during the war, there was a problem of a backlog in the system of assessing the functional/ADL status of a person (known as an individual disability status). This assessment has legal significance for establishing disability and for determining fitness or unfitness for military service on health grounds. The primary factor driving the increased need to establish these legal facts is the huge rise in the number of wounded individuals, neurological and mental illnesses caused by the war, and the worsening of chronic diseases. This special social status opens the legal way for a person to avoid mobilization and to migrate abroad. Many people with poor health and serious chronic illnesses who never applied for such status during peacetime started to do so also due to the mentioned reasons.

In Ukraine, the number of corruption-related criminal offenses in this area severely surpasses other crimes in the healthcare sector. The media reports almost daily on the detection of corruption related to the establishment of disability status by the military medical commission, including the seizure of bribes paid by doctors to these commissions. The case of the former head of the Khmelnytskyi Regional Center for Medical and Social Expertise, who, according to the investigation, illegally enriched herself by about UAH 160 million from 2020 to 2024, has become a widely discussed topic in Ukraine (more than EUR 3 million). The pre-trial investigation has now concluded, and the case has been handed over to the court [27]. All five of our military interviewers also reported cases of bribery by individual medical professionals during the process of determining military service eligibility.

The state responded to the rampant growth of corruption in this area. The old, corrupt system of medical and social expert commissions was abolished. Instead, a new, transparent, and digitalized one is established. To intensify the process of determining whether submitted documents meet formal criteria, it would be appropriate to utilize artificial intelligence (AI) capabilities. However, researchers are justified in their opinion that recognising AI's decision-making ability is

extremely challenging, and current legislation is not ready for it for ethical reasons [28].

According to the Cabinet of Ministers of Ukraine's resolution „Some issues of introducing an assessment of the daily functioning of a person" dated January 1, 2025 [29], expert groups conduct such an assessment, and the process is recorded on video or audio. Based on a content analysis of the media, the reform has already received a positive response from patients, and no corruption cases involving expert group members have been reported yet.

Another source of corruption that has grown in Ukraine since February 24, 2022, is connected to the unpreparedness to account for and rationally distribute humanitarian aid. Healthcare institutions received medical products, food, energy supply systems, clothing, and other items. The heads of healthcare institutions pointed out that even after four years of war, the healthcare system in Ukraine lacks clear regulatory acts governing the proper accounting and use of humanitarian aid, including the possibility of redistributing it, if necessary, among different healthcare bodies.

Thus, in July 2024, the Red Cross Society found a shortage of humanitarian aid worth UAN 3.6 million. The former head of the Pechersk organization was charged with misappropriation of funds [30]. In Zaporizhzhia, law enforcement agencies uncovered a group that, according to the investigation, sold in 2024-2025 humanitarian aid intended for the military, including turnstiles and medicines. The amount was more than UAH 8 million [31].

Minimizing corruption risks in the receipt and distribution of humanitarian aid requires joint action by the state and non-governmental organizations. Clear, transparent mechanisms to address these risks should be developed. Also, donors should promptly report evidence of theft or misuse to law enforcement agencies.

CONCLUSIONS

Despite the fact that neither international law has yet adopted a binding norm defining corruption as a human

rights violation, corruption in health care systems constitutes a profound threat to the realization of human rights. We observed deeper integration of anti-corruption and human rights law, particularly in healthcare systems where corruption may cost lives. Recently, the normative gap between corruption as a governance failure and corruption as a human rights abuse continues to narrow. No derogation from the commitments to the rights to life, health, and security during the war is legally binding; corruption in a healthcare system is a crime and a direct violation of international obligations.

The study identified three primary factors that significantly influenced the growth of corruption risks in the healthcare sector during the war: 1) overloading of the healthcare system; 2) deficiencies and overloading in the system for assessing functional/ADL status; and 3) the absence of an effective mechanism for accounting and distributing humanitarian aid.

Since the healthcare system's overload during wartime is objective, it is necessary to anticipate the risks of emergencies and avoid poor planning. The study shows the danger of downsizing the military medical services during peacetime, also the effectiveness of developing specialized medical units within military corps during wartime.

To reduce corruption risks in assessing functional/ADL status, which is important for determining the relevance for military service, the digitalization of processes is essential, as audio and video recordings improve transparency. During wartime, it is not realistic to fully eliminate corruption risks in this process. Therefore, greater vigilance by law enforcement agencies in detecting corruption offenses is necessary.

The substantial increase in humanitarian aid in the health sector during wartime raises the risk of corruption through theft and misuse. Reducing this risk requires coordination between government and non-governmental organizations to establish an effective system for donors to account for, distribute, and monitor aid.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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Modern technological innovations in the management of Prader-Willi syndrome: From restrictive supervision to digital autonomy

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ABSTRACT

Aim: The study evaluates the effectiveness of wearable biometric devices, geofencing systems, and artificial intelligence algorithms in improving the quality of life and autonomy of individuals with Prader-Willi syndrome. It analyses the impact of digital ecosystems on reducing caregiver burden and personalizing therapy through objective data analysis.

Materials and Methods: A systematic literature review was conducted in PubMed, Web of Science, and the Cochrane Library databases since 2019. Research focused on metabolic monitoring, the use of gamification and virtual reality in rehabilitation, and the implementation of smart home technologies for patients with rare genetic syndromes.

Analysis indicates that data from wearable devices enables the detection of prodromal states, mitigating episodes of hyperphagia and aggression. Geofencing systems provide a safe environment for autonomous physical activity, improving cardiovascular fitness and reducing caregiver anxiety. Artificial intelligence algorithms, by personalizing the energy balance with a precision of 10 kilocalories, significantly optimize weight reduction.

Conclusions: The digital support ecosystem redefines the care paradigm for Prader-Willi syndrome. Replacing human supervision with autonomous algorithmic control promotes behavioural stabilization and allows for greater patient self-determination. This process increases biological safety and significantly reduces the burden on caregivers, forming the basis of modern, individualized therapy.

KEYWORDS: wearables, geofencing, food security, artificial intelligence

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INTRODUCTION

PATHOPHYSIOLOGY OF PRADER-WILLI SYNDROME (PWS)

Prader-Willi syndrome (PWS) is a rare, multisystem congenital genetic disorder. It is caused by a chromosomal aberration involving the loss of expression of paternal genes in the 15q11.2-q13 region [1]. It is the most common genetic cause of syndromic obesity. The clinical picture is characterized by significant inter-individual heterogeneity and undergoes characteristic evolution as the patient ages. A hallmark of PWS is the evolution of the nutritional phenotype – from neonatal feeding difficulties caused by muscular hypotonia to insatiable hyperphagia and rapid weight gain during childhood and adulthood [2].

Although muscular hypotonia is most severe in the neonatal period, it persists throughout the patient's life. Adults exhibit reduced muscle mass, decreased muscle

strength, and faster muscle fatigue [3]. The average life expectancy of treated PWS patients is slightly lower than the population average, ranging from approximately 50-60 years. The hyperphagia characteristic of PWS results from profound hypothalamic dysfunction, primarily affecting the arcuate nucleus (ARC) and the paraventricular nucleus (PVN), damage to satiety pathways, and chronic elevation of ghrelin levels, which is responsible for the biological compulsion to seek food [4].

THE CONCEPT OF FOOD SECURITY

The premise of this concept is the total restriction of access to food and the provision of a fixed daily meal schedule [5]. Individuals with PWS experience intense anxiety when they see an opportunity to obtain food or when they are uncertain about its availability. Traditionally applied food security methods require the constant involvement of family members, who must maintain continuous supervision and

ensure the patient cannot access food (e.g., by locking refrigerators with padlocks). This leads to family conflicts, social isolation, and a perceived lack of self-determination, significantly lowering the Quality of Life (QoL) [5].

MOTOR AND BEHAVIOURAL BARRIERS TO PHYSICAL ACTIVITY

Patients with PWS are characterized by muscular hypotonia, which predisposes them to frequent injuries. A high pain threshold is also a risk factor [6]. Furthermore, engaging in physical activity in open spaces is difficult because the patient focuses on instinctive food-seeking (foraging) rather than improving physical fitness [7]. Consequently, implementing physical exercise protocols remains a significant therapeutic challenge.

DIGITAL SURVEILLANCE ECOSYSTEM AS A TOOL IN PRADER-WILLI SYNDROME (PWS) CARE

The aim of this study is to analyse available digital technologies that can significantly contribute to improving the quality of life for PWS patients and relieve the caregiver's burden of supervision. Modern methods offer the possibility of independent physical activity and improve the patient-caregiver relationship by partially taking over the supervisory function. This article analyses the following technologies: wearable biometric devices (wearables), geofencing systems, and advanced artificial intelligence (AI) algorithms.

AIM

The aim of this study is to evaluate the effectiveness of advanced technological innovations, such as wearable biometric devices (wearables), geofencing systems, and artificial intelligence (AI) algorithms, in optimizing the quality of life and increasing the autonomy of individuals with Prader-Willi syndrome (PWS). The paper analyses the impact of a digital ecosystem on reducing the psychophysical burden on caregivers and improving patient health parameters through therapy personalization based on objective data analysis.

MATERIALS AND METHODS

A systematic literature review was conducted in the PubMed database, including publications and clinical trials since 2019. The selection process focused on meta-analyses regarding metabolic and behavioural monitoring in rare genetic syndromes and studies on the implementation of Smart Home and Wearable technologies in the care of patients with self-regulation deficits.

REVIEW

Wearable biometric devices as tools for objectifying behavioural and metabolic states

Wearables are electronic devices worn directly on the body. Their sensors read biological signals non-invasively and continuously, allowing for patient monitoring in their natural environment [8]. The collected data serve to establish trends (e.g., increasing sympathetic arousal before a hyperphagia attack), enabling the patient to prepare for independent behaviour correction and the caregiver

to perform pre-emptive intervention [4]. This is crucial as PWS patients have an elevated pain threshold and specific communication disorders, complicating the assessment of emotional tension, which correlates with hunger levels [6]. Wearables used in PWS management are categorized into two groups: behavioural and metabolic [4].

BEHAVIOURAL MONITORING

Electronic devices analyse the excitability of the autonomic nervous system, allowing for the estimation of increasing frustration or anxiety, which is critical in populations with communication deficits. In PWS patients, a so-called „prodromal distress profile“ is typical during a hyperphagia attack. It involves the recording of characteristic digital biomarker changes by wearables approximately 15 minutes before the onset of compulsive food-seeking [9]. Analysed biomarkers include Heart Rate Variability (HRV), Electrodermal Activity (EDA), peripheral temperature fluctuations, accelerometry, and Inertial Measurement Units (IMU), as well as geofencing [4].

HEART RATE VARIABILITY (HRV)

HRV is the most important indicator of autonomic nervous system (ANS) activity. A rapid drop in HRV parameters indicates a decrease in vagal tone and activation of the sympathetic nervous system. Wearables analyse two primary markers: RMSSD and SDNN. RMSSD is the root mean square of successive differences between RR intervals (heartbeats), while SDNN is the standard deviation of all intervals. RMSSD is a highly sensitive marker of vagal activity, the decline of which correlates with sympathetic arousal and heralds affective dysregulation. SDNN determines the body's ability to dynamically modify its response to endogenous stressors. Another important biomarker often evaluated is the LF/HF Ratio, calculated as the ratio of power spectral density in two frequency ranges: Low Frequency (0.04-0.15 Hz) and High Frequency (0.15-0.40 Hz). A high ratio indicates sympathetic arousal and may signal a high risk of a hyperphagic incident in the coming minutes [10].

ELECTRODERMAL ACTIVITY (EDA)

Eccrine sweat glands are innervated exclusively by the sympathetic nervous system. Upon activation, sweat secretion increases, leading to changes in the skin's electrical conductance [11]. EDA sensors detect these changes, enabling the identification of hidden distress associated with an impending hyperphagia attack or aggressive outburst [11]. Notably, PWS patients have an elevated basal Skin Conductance Level (SCL) compared to the general population [11], resulting from a state of constant subclinical physiological tension. Another typical feature in PWS is phasic hyper-reactivity (SCR), where even a minor stimulus leads to a sharp spike in electrical conductance.

In PWS patients, ghrelin levels (the hunger hormone) are chronically elevated, 3-4 times higher than population norms, and hyperghrelinemia is not suppressed even by food intake. This contributes to the patient's constant state of tension, manifesting in the EDA recording as numerous sharp spikes (phasic reaction) instead of a flat line [4].

PERIPHERAL TEMPERATURE FLUCTUATIONS

A healthy organism maintains a stable core body temperature (36.6–37.0°C) regardless of environmental conditions. In PWS patients, hypothalamic dysfunction makes the thermoregulation mechanism unstable [4]. Increased emotional tension or hunger triggers sympathetic arousal and peripheral vasoconstriction [4], clinically manifesting as blood vessel constriction in distal parts of the body due to the „fight or flight” response and blood redistribution [4]. Sensors on distal body parts record a sudden drop in skin temperature (by 0.5–1.5°C) preceding an incident. In PWS, a „metabolic paradox” is observed during stress, involving simultaneous peripheral temperature cooling and a slight core temperature rise. Wearables indirectly determine the core body temperature using mathematical modelling and AI [12].

ACCELEROMETRY AND IMU (INERTIAL MEASUREMENT UNIT)

PWS patients suffer from nociceptive disorders, resulting in a very high pain threshold [6]. A patient may sustain a serious fracture without experiencing typical pain. To detect these „silent injuries,” accelerometry and IMU technology are used. Accelerometers measure linear acceleration, while IMUs also measure angular velocity [13]. Changes in gait kinematics captured by AI algorithms serve as alerts for suspected orthopaedic injury [4]. This allows for early-stage treatment, which is critical as PWS patients are often obese and have a physiologically weak ligamentous apparatus [3].

GEOFENCING

Geofencing allows for the development of safe zones free from high-density stimuli that trigger foraging [14]. The mechanism uses geographic coordinates (GNSS/GPS) and Wi-Fi/Bluetooth networks to define „green zones” (safe) and „red zones” (at-risk) [8]. If a patient enters an inappropriate area, such as near a refrigerator, they receive a voice command to leave immediately. If they do not comply, the caregiver receives a notification with the patient’s exact location and biometric data, enabling remote verbal de-escalation. Furthermore, advanced Smart Home systems can automatically lock food cabinet locks (smart cabinets) when the algorithm detects the patient’s presence in the kitchen outside of scheduled mealtimes [15].

Geofencing enables independent physical activity in open spaces, which previously caused caregiver anxiety. This telemonitoring control reduces patient frustration and increases the sense of self-determination. Consequently, the caregiver is no longer perceived as a constant controller, improving the patient-caregiver relationship [5].

METABOLIC MONITORING

Key technologies for metabolic monitoring in PWS include Continuous Glucose Monitoring (CGM), biochemical biosensors, and digital indirect calorimetry. These methods aid in optimizing energy homeostasis and implementing early intervention for critical hormonal or glycaemic fluctuations that occur during hyperphagia attacks.

CONTINUOUS GLUCOSE MONITORING (CGM)

PWS patients exhibit reactive hypoglycaemia – an excessively large insulin release after a meal that causes glucose levels to drop below normal, triggering intense anxiety, aggression, and food-seeking behaviour [4]. CGM systems minimize the risk of metabolic decompensation via a subcutaneous sensor that measures interstitial glucose. Algorithms predict trends 30 minutes in advance. If a rapid drop is detected, the caregiver is notified to provide a low-calorie snack to stabilize glycemia and suppress the hunger centre.

BIOCHEMICAL BIOSENSORS

Modern biochemical biosensors take the form of transdermal patches that non-invasively analyse body fluids for cortisol, lactate, and ions (mainly sodium and potassium). Elevated cortisol in sweat, combined with unstable HRV and EDA, indicates exhausted adaptive reserves and a high risk of an affective incident [16].

Due to hypotonia and fewer type II muscle fibres and mitochondria, PWS patients rely on anaerobic glycolysis even during low-intensity effort, leading to rapid lactate synthesis [3]. Lactate concentration thus serves as a vital performance biomarker, allowing for precise physical intensity optimization to prevent overexertion [17].

DIGITAL SUPPORT FOR PHYSICAL ACTIVATION

– VR AND GAMIFICATION

Individuals with Prader-Willi syndrome exhibit a natural aversion to physical activity, which results from both biological factors, such as sarcopenia and rapid muscle fatigue, and profound motivational deficits. The use of virtual reality (VR) and gamification mechanisms transforms physical exercise into a more attractive challenge, significantly increasing long-term engagement in the rehabilitation process [3].

Motivational deficit is a hallmark of Prader-Willi syndrome (PWS). By utilizing virtual reality, the patient does not perceive that they are engaging in physical activity; previous monotonous exercises are replaced by engaging challenges that activate the reward system, encouraging the patient to participate in this „virtual rehabilitation” [18]. In PWS, specific abnormalities occur within the reward system, characterized by heightened sensitivity to orexigenic (food) stimuli and weakened responses to non-food reinforcement systems. The pathological food fixation in PWS originates from this exact mechanism [4]. VR technology provides powerful stimuli that can compete with those related to food. This leads to the activation of the mesolimbic pathway and dopamine release through the stimulation of the nucleus accumbens. Research indicates that patients engaged in games set within a virtual reality environment experience lower levels of aggression and stress [3].

Virtual environments also offer a unique opportunity for safe desensitization to orexigenic stimuli. Virtual walks allow for controlled exposure to food distractors without the risk of breaching food security barriers [5]. Through such simulations, the patient learns to recognize early signs of distress and test tension-management techniques, while the caregiver can verify the effectiveness of various

de-escalation methods in an environment free from real metabolic threats [19].

BIOMECHANICAL SAFETY IN VIRTUAL REHABILITATION

One of the challenges during VR training is the risk of balance loss, which frequently occurs in individuals with hypotonia and ligamentous laxity. This happens because the user loses visual contact with the actual ground. To prevent this, Augmented Reality (AR) technology is utilized for PWS patients, enabling them to maintain visual contact with their surroundings while ensuring kinematic stability during exercise. The application of AR guarantees biomechanical safety, allowing for the achievement of cardiovascular and motor goals without exposing the patient to orthopaedic injuries [20].

AI ALGORITHMS AND THE „DIGITAL TWIN“ CONCEPT

A key challenge in the care of patients with Prader-Willi Syndrome (PWS) is the immense inter-individual variability and the multisystem nature of the disorder. The solution to this problem is data fusion from all previously described monitoring systems, allowing for the creation of a so-called „Digital twin“ of the patient. This is a dynamic mathematical model that reflects the current metabolic and behavioural state of a specific individual in real-time [21].

Distributed biometric data from wearables are processed and analysed using specialized algorithms, allowing for the full personalization of the therapeutic model - for example, calculating energy requirements in real-time. This is particularly crucial because PWS patients, characterized by reduced muscle mass, face rapid fat accumulation and the progression of syndromic obesity even with a slight caloric surplus [1].

PREDICTION AND CLINICAL SIMULATION

The implementation of advanced machine learning (ML) algorithms allows the system to identify long-term patterns. These algorithms analyse a patient's specific reactions to given stimuli and are capable of rapidly detecting deviations from the norm, signalling an impending decompensation [4].

A major advantage of the „Digital Twin“ is the ability for clinicians to conduct simulations regarding: the effectiveness of new medications, the impact of caloric changes on glycaemic stability and aggression risk, and optimal training loads that reduce body fat without causing a loss of motivation or chronic fatigue [21].

AUTOMATION OF FOOD SECURITY

The application of Smart Home technologies and wearables has allowed for the automation of food security oversight. These digital technologies take over the role of the „controller“, significantly improving the patient-caregiver relationship by reducing daily tensions and conflicts regarding food access [5].

Modern applications can analyse the composition, caloric content, and volume of a meal after a photo is uploaded. The obtained data are then automatically cross-referenced with the daily energy limit calculated by AI algorithms within the Digital Twin model [21].

Another element strengthening the integrity of the food security protocol is the system of smart storage/cabinets. Automatic locking of food cabinets occurs when the algorithm recognizes that the patient has reached their planned caloric intake or when biometric data from wearables (such as changes in HRV or EDA) predict a high risk of a hyperphagic episode [4].

DISCUSSION

ETHICAL ASPECTS OF IMPLEMENTING CONTINUOUS BIOMETRIC SURVEILLANCE SYSTEMS

The implementation of constant biometric and geolocational monitoring updates a crucial ethical dilemma: whether permanent digital surveillance constitutes a form of invasive monitoring, and where the line is drawn between necessary clinical control and the violation of patient autonomy. Another concerning issue is that some PWS patients have profound cognitive deficits, which may make obtaining informed consent for monitoring impossible. Additionally, one must consider whether the data obtained from wearables for the „Digital Twin“ are fully secure and who becomes the owner of the generated information resources in such a sensitive area [21].

The counterargument to these concerns is that continuous biometric telemetry plays a key role in maintaining long-term homeostasis and prolongs the complication-free period of the disease [1]. Patients with PWS experience a constant need to eat and physiologically do not experience satiety [4]. A lack of control over food intake would inevitably lead to severe complications (e.g., morbid obesity) and even life-threatening events, such as gastric rupture [1]. Given these risks, the use of digital surveillance systems is both substantively and ethically justified as a life-saving measure [5].

From the perspective of psychological mechanisms, the traditional model of direct supervision (the caregiver acting as a „shadow“) often causes a drastic deterioration in the relationship between the caregiver and the patient [5]. In the individual being controlled, frustration builds up, often leading to aggressive and oppositional behaviours directed at the caregiver [3]. Replacing direct human supervision with autonomous algorithmic control and geofencing systems is perceived by the patient as less intrusive to their autonomy and contributes to improved interpersonal relationships. Furthermore, automated supervision relieves the caregiver and significantly lowers chronic stress levels, which is vital for the well-being of the entire family [5].

CONCLUSIONS

Recent years have brought a true breakthrough in the care model for individuals with Prader-Willi Syndrome (PWS). Traditional supervision, relying solely on the constant physical presence of a caregiver, is evolving toward a modern, digital support ecosystem. Through the application of artificial intelligence and wearable biometric devices (wearables), patient monitoring has become not only easier but, above all, more effective in preventing metabolic incidents.

Modern biometric tools allow for the capturing of physiological signals from the autonomic nervous system that precede a hyperphagia attack. This enables the implementation of interventions at the optimal moment, which translates into better health status and a significant reduction in dangerous metabolic complications.

The use of geofencing (digital safe zones) opens up previously inaccessible possibilities for autonomy. Patients can move more safely in open spaces, which drastically reduces their sense of isolation and allows for active participation in social life without the caregiver's constant fear of food security breaches.

Furthermore, the use of virtual reality (VR) allows patients to learn how to react to food stimuli under controlled, safe conditions. This represents an invaluable stage of preparation for independent functioning in the real world. Moreover, by shifting activity to the digital world, the patient no longer perceives physical exercise as an unburden; instead, it becomes an attractive form of stimulation for the reward system, neutralizing primary motivational deficits.

In light of the conducted analyses, it is recommended to incorporate digital technologies into the standard of daily care for patients with Prader-Willi syndrome (PWS) as an essential element of modern personalized medicine.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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A sleep that never comes: Prions and their role in fatal familial insomnia – a literature review

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ABSTRACT

Fatal Familial Insomnia (FFI) is a rare genetic prion disease that leads to progressive neurodegeneration and death. It is caused by the D178N mutation in the PRNP (Prion Protein Gene), combined with the presence of methionine at codon 129. The disease primarily affects the thalamus – a brain structure responsible for regulating the sleep-wake cycle.

FFI develops in four stages, starting with initial insomnia and mood disturbances, progressing to a complete loss of the ability to sleep, and ultimately leading to the final stage of dementia and death within approximately 18 months from symptom onset. Prions – infectious proteins with an abnormal conformation – play a key role in the pathogenesis of FFI. The disease is associated with the misfolding of the normal prion protein (PrP^C) into its pathogenic form (PrP^{Sc}), which accumulates in neural tissue, leading to neuronal death.

Due to its rarity and nonspecific early symptoms, diagnosing FFI is challenging. Genetic testing, neuroimaging techniques such as PET and SPECT, which reveal characteristic thalamic hypometabolism and polysomnography, which identifies distinctive sleep architecture disturbances are crucial in the diagnostic process. Advancing noninvasive diagnostic methods and searching for potential therapies are key directions in FFI research. A deeper understanding of prion mechanisms, including how prion proteins misfold and transmit their aberrant conformation to other proteins, may contribute to the development of effective therapeutic strategies for this and other neurodegenerative diseases.

KEYWORDS: fatal familial insomnia, prion diseases, neurodegeneration

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INTRODUCTION

Imagine suffering from a condition that prevents you from falling asleep. If you have ever experienced a sleepless night, you know how significantly it can affect your well-being and cognitive abilities the following day. Now, imagine being unable to sleep for months – the consequences of such persistent insomnia are not only physical but also psychological. This is the reality of a rare and devastating disease that targets the thalamus, depriving patients of sleep entirely. This condition is known as Fatal Familial

Insomnia (FFI), with the earliest documented case dating back to 1765, when an Italian man presented with symptoms now believed to be consistent with this disorder [1, 2]. It was not until 1986 that the etiology, pathophysiology, and potential clinical course of FFI were formally described [3]. To this day, many aspects of Fatal Familial Insomnia remain poorly understood, and no effective treatment is currently available, which makes this disease always fatal [4, 5].

FFI is a severe neurodegenerative sleep disorder characterized by progressive insomnia, dysautonomia,

motor and behavioral abnormalities, and thalamic and olivary nuclei atrophy, which gradually extends to other brain regions as the disease advances [3].

AIM

The aim of this study is to present the current state of knowledge on Fatal Familial Insomnia (FFI), including its etiology, epidemiology, pathophysiology, clinical course, diagnosis, and therapeutic options.

MATERIALS AND METHODS

This article is a review. The information presented in the study is based on available scientific literature, including publications from databases such as PubMed and Scopus. Clinical data, case reports, and current experimental studies related to FFI and the treatment of prion diseases were taken into account.

REVIEW

ETIOLOGY

Genes contain the information necessary for the synthesis of proteins, which perform essential functions in the human body. When a mutation occurs in a gene, the resulting protein may be defective, inefficient, absent, or produced in excessive amounts. Depending on the role of the affected protein, such a mutation can impact various organ systems, including the brain [1, 2].

Fatal Familial Insomnia (FFI) has been identified as an autosomal dominant mutation in codon 178 of the PRNP gene, located on the short (p) arm of chromosome 20 at position p13 (20p13). This gene is responsible for the production of the prion protein PrP^C. Specifically, FFI is genetically caused by the D178N mutation, which is associated with the methionine homozygosity (M129) genotype at codon 129 [3, 4].

Autosomal dominant genetic disorders occur when a single copy of the mutated gene is sufficient to cause disease. This mutation can be inherited from an affected parent or arise spontaneously in the affected individual. In the case of an affected parent, there is a 50% chance of passing the mutated gene to offspring during each pregnancy, regardless of the child's sex [1, 5].

The PRNP gene encodes the cellular prion protein PrP^C, whose physiological function remains incompletely understood [6]. As a result of the mutation, this protein misfolds, adopting an abnormal three-dimensional conformation. The misfolded form, known as PrP^{Sc}, exhibits neurotoxic properties, particularly affecting the central nervous system.

In FFI, the pathological protein accumulates predominantly in the thalamus – a brain structure responsible for regulating sleep, appetite, and body temperature. The progressive accumulation of the aberrant PrP^{Sc} leads to neuronal degeneration, which in turn gives rise to the clinical manifestations of the disease [7].

In some cases, the PRNP mutation responsible for FFI arises *de novo*, without a prior family history of the disease. This is referred to as a „*de novo*” variant. Such mutations

occur during the formation of an egg or sperm cell and are present only in the affected individual – other family members are not carriers. In this context, the disorder is not inherited nor transmitted by the healthy parents. However, an individual with a *de novo* mutation can pass it on to their own children according to the autosomal dominant inheritance pattern [8].

The term „prion” was introduced to describe a „proteinaceous infectious particle” that accounts for the transmissible nature of prion diseases [9, 10]. It is important to emphasize, however, that FFI is not considered infectious in the classical sense, as the only known mode of prion disease transmission involves direct exposure to infected brain tissue – for example, through ingestion or injection. If a prion disease develops in an individual without a genetic predisposition due to exposure to prions from external sources, it is classified as an „acquired” form [11].

EPIDEMIOLOGY

Fatal Familial Insomnia (FFI) is an extremely rare disorder, identified in approximately 70 families worldwide [5]. The geographic distribution of the disease is uneven, and its prevalence varies by region. The majority of reported cases originate from China, although the highest incidence rates relative to population size have been observed in Spain and Germany [7, 12].

Symptoms of the disease typically manifest between the ages of 36 and 62, with a median age of onset at 51 years. However, significantly younger cases have been documented, including individuals as young as 18, although such occurrences are exceedingly rare [5]. The average life expectancy following the onset of symptoms is approximately 18 months [5]. FFI affects males and females equally [7].

PATHOPHYSIOLOGY

Fatal Familial Insomnia (FFI) is a genetic prion disease inherited in an autosomal dominant manner [1, 2].

It is caused by a mutation in the prion protein gene (PRNP), located on the short (p) arm of chromosome 20 [3, 8]. This mutation leads to an amino acid substitution in which aspartic acid (Asp) is replaced by asparagine (Asn) at codon 178 of the prion protein sequence [3].

In addition, the mutated prion protein exhibits a polymorphism at codon 129, where the presence of methionine (Met) differs from valine (Val) – the latter being characteristic of familial Creutzfeldt-Jakob Disease (fCJD) at the same position [4, 7, 10]. This polymorphism influences both disease susceptibility and clinical presentation. Homozygosity for methionine (Met/Met) in the non-mutated allele is associated with a more rapid disease progression and a more aggressive phenotype, whereas the heterozygous Met/Val configuration may moderate the disease course [4, 7, 10].

Neuropathological changes in FFI include neuronal loss and astrocytic gliosis, particularly within the thalamus, a structure critically involved in sensory processing, motor coordination, and sleep regulation [2,5]. Thalamic damage is responsible for the hallmark clinical features of the disease,

including profound sleep disturbances and autonomic dysfunction. Research suggests that the onset of FFI is triggered once a critical threshold of prion protein PrPC conversion to the misfolded, pathogenic form PrPSc is surpassed [2, 5].

Although neuropathological findings in FFI are not entirely uniform, studies indicate that the disease primarily affects thalamic nuclei – including the anterior, ventral, and medial groups – as well as the inferior olivary nuclei [5,6]. Furthermore, in vivo studies using fluorodeoxyglucose positron emission tomography (FDG-PET) have demonstrated that the thalamus is the first brain structure to exhibit pathological changes, even before the clinical symptoms become apparent [6, 11].

DISEASE PROGRESSION

The onset of symptoms in Fatal Familial Insomnia (FFI) most commonly occurs around the age of 51. The disease progresses through four distinct phases, the first of which is non-specific and may lead to misdiagnosis [2, 5]. The initial prodromal phase is characterized by progressively worsening insomnia, sleep disturbances, excessive sweating, chronic fatigue, and symptoms of depression and anxiety [2, 5]. Due to the non-specific nature of these symptoms, FFI may initially be misdiagnosed as REM sleep behavior disorder, Lewy body dementia, or a manifestation of chronic stress [2, 5]. Psychiatric symptoms such as panic attacks, paranoia, and phobias may also develop [2].

Early signs can be subtle, including distractibility, impaired concentration, and difficulties with speech [7]. Some patients may experience diplopia (double vision) or nystagmus [7]. Dysphagia (difficulty swallowing) and dysarthria (slurred speech) may occur [5]. Over time, some individuals may develop ataxia and involuntary movements, such as tremors or myoclonic jerks.

The second phase of the disease, lasting on average five months, is marked by a worsening of the initial symptoms along with the onset of visual hallucinations [2]. Sympathetic nervous system overactivity becomes pronounced, leading to evening fever, hypertension, excessive sweating, tachycardia, and hyperventilation. This period is also often associated with drastic and rapid weight loss.

The third phase, with an average duration of three months, is characterized by complete insomnia and severe disruption of the sleep-wake cycle [2, 5]. The patient gradually loses the ability to restore physiological functions, resulting in significant health deterioration [2, 5].

The final stage involves rapid cognitive decline, progressive dementia, and complete loss of the ability to speak, move, or interact with the environment [2]. Approximately eighteen months after the onset of symptoms, the patient enters a comatose state and ultimately dies, most often due to respiratory or cardiovascular failure [2, 5].

DIAGNOSTIC

The diagnostic process for Fatal Familial Insomnia (FFI) is challenging due to its non-specific symptoms, which resemble those of other neurodegenerative diseases, particularly prion diseases [5]. It is crucial to exclude other

causes of dementia, such as infections, tumors, metabolic disorders, or poisoning. Slower-progressing diseases, such as Alzheimer's, corticobasal degeneration, or frontotemporal dementia, must also be considered before a final diagnosis is made [6].

Diagnostic Tests

Standard tests used in the diagnosis of infectious prions rely on physicochemical differences between the normal and pathological forms of the prion protein (PrP). A key feature distinguishing these forms is their differing susceptibility to protease digestion [7]. When treated with proteinase K, normal prion protein (PrPC) is completely degraded to amino acids, while in the pathogenic form, PrPSc, the enzyme only removes 67 amino acids from the N-terminus of the protein. This process generates a fragment known as PrP27-30, which retains infectious properties. However, its presence is not a sufficient indicator of disease, as PrPC can change structure without losing its susceptibility to proteases [8].

A promising alternative is aptamers – short RNA or DNA sequences that selectively recognize PrPSc without the need for proteases. Their use may enhance the sensitivity and accuracy of diagnostics, making them a potential tool for detecting prion diseases [13].

Polysomnography

Polysomnography is a valuable diagnostic tool in the early stages of FFI, even in the absence of clear symptoms. The disease is characterized by sleep fragmentation, atypical movements, and the gradual loss of sleep spindles and K-complexes, which differentiates it from other neurodegenerative disorders [5]. In advanced stages, there is near-total loss of REM sleep, which exacerbates cognitive and emotional function.

Additionally, EEG findings reveal low-voltage theta and delta activity, indicating progressive neurodegeneration. When combined with PET imaging showing thalamic hypometabolism, polysomnography aids in early diagnosis and monitoring the course of FFI [6].

Imaging Studies

Neuroimaging techniques are crucial in the diagnosis of FFI, particularly positron emission tomography with fluorodeoxyglucose (FDG-PET) and single-photon emission computed tomography (SPECT) [7].

FDG-PET detects early hypometabolism in the thalamus and cingulate cortex, even a year before clinical symptoms appear, and in advanced stages, it reveals further metabolic activity reduction [9]. SPECT, on the other hand, identifies reductions in dopamine and serotonin transporters in the thalamus and hypothalamus, which can aid in predicting the age of onset and assessing therapy.

Unfortunately, MRI is not useful for early diagnosis of FFI, as it only reveals non-specific cortical atrophy and ventricular enlargement in later stages [11].

Cerebrospinal Fluid Analysis

In the diagnostic process for FFI, cerebrospinal fluid (CSF) analysis for biomarkers such as 14-3-3 proteins, S100b, neuron-specific enolase (NSE), and tau protein is employed

to assess neuronal damage. Unfortunately, the sensitivity of these markers is limited, which reduces their diagnostic value in the context of FFI [8].

An alternative with higher sensitivity is the RT-QuIC (real-time quaking-induced conversion) technique, which enables the direct detection of pathological forms of prion protein (PrP^{Sc}) in CSF [10].

DISCUSSION

TREATMENT

Currently, there is no effective treatment for prion diseases, although their molecular mechanisms are well understood [13, 14].

Stanley Prusiner, Nobel Laureate in Physiology or Medicine (1991), stated that the prion replication mechanism is unique [14]. As a result, traditional antimicrobial agents, such as antiviral, antibacterial, antifungal, and antiparasitic drugs, are found to be largely ineffective in treating these diseases [13, 14]. In recent years, researchers have focused on the elimination of PrP protein as a potential therapeutic target [15]. Among the strategies being explored are immunotherapy, gene therapy, the use of small pharmacological molecules, and stem cell therapy [15, 16].

IMMUNOTHERAPIES AGAINST PRION DISEASES

In 2001, Stanley Prusiner hypothesized that the accumulation of abnormal proteins in affected areas of the brain is a key factor in most neurodegenerative diseases [14]. Based on this, the use of pharmacological chaperones, such as monoclonal antibodies, which stabilize the normal form of the PrP^C protein, preventing its conversion to the pathological PrP^{Sc} form, was suggested [13,15,16]. An example of this is the monoclonal antibody ICSM18, which shows high affinity for a specific epitope on the surface of the physiological form of the prion protein, preventing its conversion to the pathological PrP^{Sc} form. The mechanism of action of ICSM18 is based on stabilizing the native conformation of PrP^C and blocking its interaction with PrP^{Sc}, which is crucial for amplifying the prion process [13, 15, 16].

Another promising approach in immunotherapy is the use of DNA vaccines encoding PrP^C, which can induce an immune response without the risk of triggering an autoimmune reaction. Studies conducted on animal models suggest that administering such vaccines prior to exposure to prions can delay disease progression or reduce its severity [16]. Another strategy involves protein vaccines containing recombinant fragments of PrP^C or its modified variants capable of stimulating the immune system without causing pathological changes in the body [17, 18].

Further research has shown that the activation of neuroinflammatory cells, such as microglia and astrocytes, plays a key role in the pathogenesis of neurodegenerative diseases [16-18]. Excessive activation of these cells leads to chronic inflammation in the central nervous system, contributing to disease progression and neuronal damage.

Therefore, modulation of the immune system by blocking immune checkpoints, such as programmed cell death

protein 1 (PD-1), its ligand PD-L1, and the CTLA-4 receptor, has become a promising therapeutic strategy [16, 17]. Immune checkpoints play an important role in regulating the immune response, preventing excessive activation of T lymphocytes and limiting autoimmunization. However, in the context of neurodegenerative diseases, blocking these checkpoints may support the adaptive immune response, enabling more effective removal of toxic prion proteins and inhibiting pathological processes [17].

Monoclonal antibodies targeting PD-1, PD-L1, and CTLA-4, which are widely used in cancer immunotherapy, show potential in the treatment of neurodegenerative diseases [16]. Preliminary studies in animal models suggest that inhibiting these checkpoints may contribute to reducing neuroinflammation and slowing neuronal degeneration [17, 18].

TARGETED GENE THERAPIES

Antisense Oligonucleotides

Antisense oligonucleotides (ASOs) are short DNA molecules that degrade the target mRNA, reducing the levels of harmful proteins [13, 15]. Sonia Vallabh, a researcher and carrier of the PRNP mutation, proposed a preventive therapy for individuals with early detection of the mutation [13]. Since the symptoms of the disease in mutation carriers appear only in adulthood, ASOs may delay or halt the disease's development [15]. Studies have shown that administering ASOs to brain cells in mice limited the accumulation of PrP^{Sc} and prolonged survival, even after symptoms appeared [13, 15] (Fig. 1).

RNA Interference

RNA interference (RNAi) is a gene-silencing mechanism that plays a key role in regulating gene expression and represents a promising approach in gene therapy for neurological diseases, including prion diseases [13, 15]. Small interfering RNA (siRNA) and microRNA (miRNA) act with the RISC complex to degrade mRNA or inhibit translation. Research by Pfeifer and White showed that RNAi therapy using lentiviruses reduced PrP^C levels and inhibited prion replication, extending the survival of infected mice [13, 15, 19]. Although gene therapies using lentiviral vectors show promising results in animal models, extensive clinical trials are necessary to confirm their safety and effectiveness before they can be applied to humans [15, 19] (Fig. 1).

ADVANCED TARGETED PROTEIN DEGRADATION THERAPIES

In recent years, targeted protein degradation (TPD) therapy has gained significant attention, especially in the context of small molecule-based drugs, such as proteolysis-targeting chimeras (PROTACs) and TPD strategies related to lysosomes, such as lysosome-targeted chimeras (LYTACs) and autophagy-targeted chimeras (AUTACs) [13, 15].

These methods can effectively degrade previously treatment-resistant proteins at low concentrations, with a reduced risk of side effects [13, 15]. CHA (chaperone-assisted protein degradation) operates through the lysosomal pathway, with the most commonly studied molecular

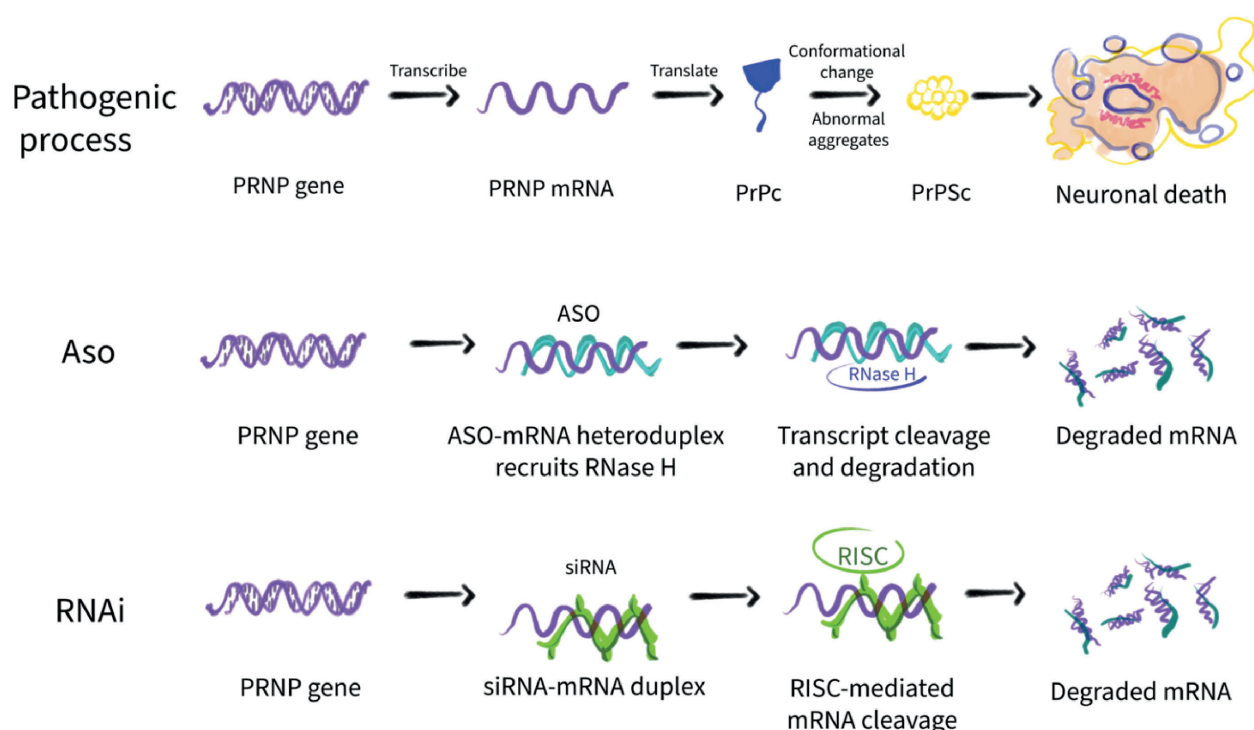


Fig. 1. The illustration presents gene therapy strategies, such as ASO and RNAi, developed to silence the PRNP gene at the RNA level. Antisense oligonucleotides (ASO) are short, synthetic single-stranded RNA sequences that bind to the target mRNA, leading to its degradation by RNase H. Small interfering RNA (siRNA), on the other hand, bind to the RISC complex, which degrades the mRNA, blocking further translation. Both methods effectively reduce the amount of PrP^{Sc} protein in the brain, which may limit the progression of prion diseases [13]. Abbreviations: ASO – antisense oligonucleotides, RNAi – RNA interference, RISC – RNA-induced silencing complex.

chaperone being heat shock protein (HSP), which aids in maintaining normal cellular processes in response to stress [15].

The aforementioned TPD therapies mainly focus on intracellular PrP^{Sc}, while other studies focus on the release of PrP^c on the cell surface [15,20]. A fragment of PrP^c, known as sPrP, plays a neuroprotective role in diseases associated with protein misfolding [13, 15]. Increasing the activity of the metalloproteinase ADAM10, which is responsible for releasing PrP^c, reduces the level of this protein in the brain and may delay the progression of prion diseases [13,15, 20]. TPD represents a promising strategy for treating neurodegenerative diseases; however, there are still many challenges hindering its clinical application [13, 15, 20].

STEM CELLS AS A TOOL FOR REPAIRING DAMAGED NEURONS

Most modern therapeutic strategies focus on eliminating or preventing prion infections, but some researchers are concentrating on cell-based therapies aimed at repairing neurons damaged by pathological prions [16, 21, 22]. Among the most studied cell-based therapies are embryonic stem cells (ESCs), mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), and neuronal stem cells (NSCs) [16, 21, 22].

Research by Relañó-Ginés and his collaborators (2011) showed that transplantation of fetal stem cells into the

brains of prion-infected mice significantly prolonged the incubation period and survival of the animals [16, 14]. New discoveries suggest that cell-based therapies may be the future of treating human neurodegenerative diseases, especially since appropriate neurons can be created in cell cultures [16, 14, 22, 23].

CONCLUSIONS

Fatal Familial Insomnia (FFI) is a rare and still not fully understood neurodegenerative disease, belonging to the group of prion diseases. It serves as an example of how abnormalities in a single protein can lead to fatal consequences.

Currently, diagnosis is based on clinical symptoms, and research aims to develop reliable, non-invasive tests that can detect the disease at an early or even presymptomatic stage. Methods such as polysomnography, imaging studies (PET, SPECT), and cerebrospinal fluid analysis should be refined and widely accepted as standard diagnostic tools.

Despite the lack of effective therapy, promising strategies such as immunotherapy, gene therapy, protein degradation-targeted methods, and stem cell technologies are currently in the in vitro and in vivo research phase. The rarity of the disease and its rapid progression complicate the implementation of clinical studies. However, the growing interest among scientists offers hope for breakthroughs in the treatment and prevention of FFI.

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CASE STUDY

Case report of a 33-year-old patient with a niche in a cesarean section scar

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ABSTRACT

Worldwide, cesarean section procedures are being performed with increasing frequency, which is associated with a growing number of postoperative complications. One of these is the formation of a triangular, anechoic defect of the uterine myometrium at the site of a previous cesarean section scar, referred to as a niche. This condition may lead to abnormal bleeding, pain, fertility problems, and complications in subsequent pregnancies. This paper presents the case of a 33-year-old patient with a history of two cesarean sections, in whom ultrasonographic examination revealed a defect within the scar measuring 4 mm in depth, consistent with a so-called niche. The patient expressed an intention to conceive again; however, the presence of the defect constituted a significant risk factor for complications during pregnancy. The importance of accurate diagnosis and appropriate management of the niche before a planned pregnancy was emphasized to minimize the risk of serious complications, such as uterine scar dehiscence. This case highlights the need for proper management of women with a cesarean section scar who are planning subsequent pregnancies.

KEYWORDS: uterine niche, cesarean scar defect, cesarean section, ultrasonography, case report

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INTRODUCTION

The main indication for performing a cesarean section is the inability to safely complete vaginal delivery due to maternal or fetal complications. This procedure is an important element of modern obstetric care, especially in situations threatening the health or life of the mother or the child. Although cesarean section was originally performed mainly for medical indications, in recent years a marked increase in the frequency of this procedure has been observed [1]. This tendency is also evident in Poland, where in 2024, 116,969 children were born by cesarean section, which constituted 47.9% of all births [2]. This persistent trend means that an increasing number of patients are exposed to complications associated with the procedure. One such complication is the presence of a niche in the uterine scar. A niche is a discontinuity of the uterine muscle at the site of a cesarean section scar, remaining in communication with the uterine cavity or cervical canal, corresponding to the unhealed portion of the scar [3]. The classification of a niche is based on the distinction of three types: simple, simple with a branch, and complex [4]. The etiology of niche formation has not been fully elucidated. However, it is suspected that the most important factor determining its development is the surgical technique used to close the uterine incision

[5]. Other hypotheses suggest the influence of a low uterine incision and stretching of the scar by postoperative adhesions, leading to impaired wound healing [6]. The most important patient-related risk factors promoting the formation of a niche include a high body mass index (BMI), tobacco smoking, and previous multiple cesarean sections [7]. It has been shown that a uterine muscle defect is present in 62% of women after one cesarean section, 68% after two, and 77.8% after three cesarean sections [8]. Transvaginal ultrasonography (TVS) is the most used diagnostic method for assessing the integrity of the uterine wall. In over 50% of women after a cesarean section, a hypoechoic, usually triangular defect at the scar site, corresponding to a niche, can be visualized [3]. The presence of the defect is associated with the risk of long-term complications, such as menstrual disorders, pelvic pain, or difficulties conceiving, which underscores the importance of accurate imaging diagnostics in the prevention and planning of further clinical management.

AIM

The aim of this paper is to present the case of a patient with a history of two cesarean sections, in whom gynecological assessment revealed the presence of an endometrial polyp and a niche in the cesarean section scar.

CASE REPORT

In May 2024, a 33-year-old patient was referred to the gynecological clinic due to heavy, prolonged menstrual bleeding and intermenstrual spotting, which had persisted for approximately three years. Due to iron deficiency anemia of undetermined etiology, the patient was treated with an iron supplement (Sorbifer). In her medical history, the patient had undergone two cesarean sections, in November 2016 and July 2018, with a suspected uterine rupture during the second pregnancy. The patient indicated an intention to pursue another pregnancy. Ultrasonographic examination revealed an endometrial polyp, as well as the presence of a niche in the cesarean section scar. The myometrial thickness over the defect measured 2 mm, and the depth of the defect reached 4 mm. In August 2024, the patient was admitted to the University Oncology Center at the University Clinical Hospital in Białystok for hysteroscopic removal of an endometrial polyp. A hysteroscopic electrosurgical resection of the polyp was performed. The postoperative course was uneventful. Following the procedure, menstrual cycles were restored, spotting resolved, and hematological parameters returned to within reference ranges. In January 2025, the patient was readmitted electively, in good general condition, for the management of a niche in the cesarean section scar. In the preoperative ultrasound examination, the uterus was anteverted and anteflexed, measuring 4.64×4.44 cm, with homogeneous echogenicity. The cesarean section scar was visible. Myometrial thickness over the defect measured 1,6 mm, with a defect depth of 4 mm (Fig. 1).

Laparoscopic surgery was performed, during which the niche was excised, the wound was debrided, and the uterus was re-sutured. Additionally, intraperitoneal adhesions were released with the use of adhesion prophylaxis. On the first postoperative day, the patient reported brief vaginal bleeding and transient pain in the subcostal region, which was resolved with pharmacological treatment. The surgical wound healed appropriately. A control ultrasound examination was performed on the third postoperative day (Fig. 2).



Fig. 1. Preoperative ultrasound examination. A niche was visualized

Picture taken by the authors

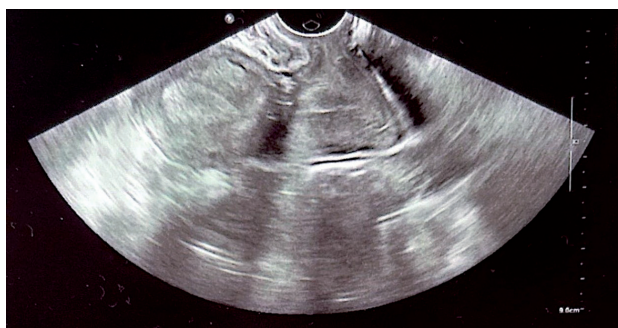


Fig. 2. A control ultrasound examination on the third day after the operation

Picture taken by the authors

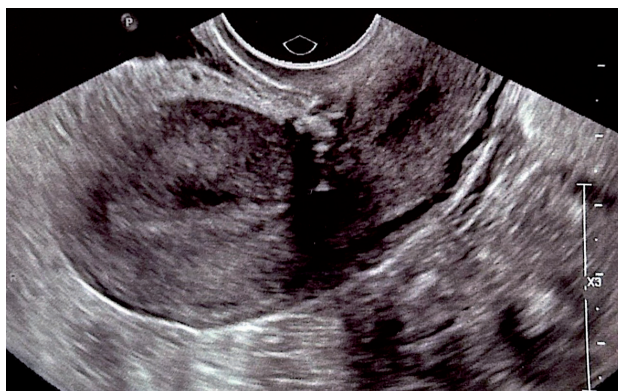


Fig. 3. A control ultrasound examination performed one month after the procedure

Picture taken by the authors

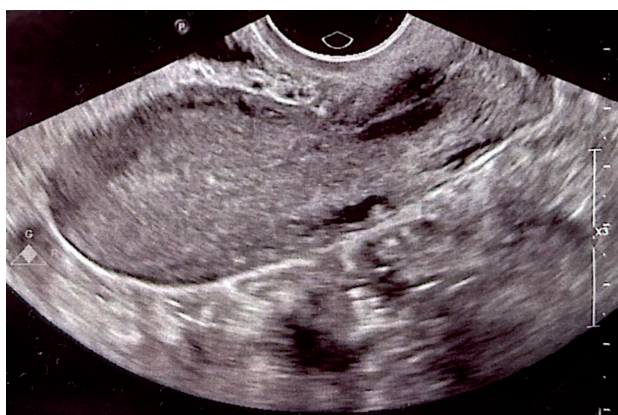


Fig. 4. A control ultrasound examination performed three months after the procedure

Picture taken by the authors

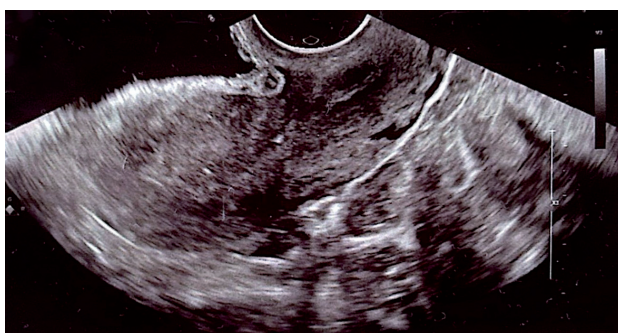


Fig. 5. A control ultrasound examination performed five months after the procedure

Picture taken by the authors

The patient was discharged home in good general condition with a recommendation for assessment in the gynecological clinic. A control ultrasound examination was performed one month (Fig. 3), three months (Fig. 4) and five months (Fig. 5) after the procedure.

As a result of the implemented diagnostic and therapeutic management, proper healing of the cesarean section scar niche was achieved, leading to restoration of uterine wall continuity and consequently allowing the patient to pursue further reproductive plans, including attempts at a subsequent pregnancy.

DISCUSSION

With the significant increase in the number of cesarean sections performed worldwide, cesarean scar niche is an increasingly common complication observed in clinical practice. Although the etiology of the niche formation has not been clearly explained yet, it is believed that its development is the result of the interaction of many factors, including individual factors, factors related to the surgical technique and perinatal factors, including the number of previous cesarean sections [5-8], which was also important in the case of the described patient after two CS procedures.

Among the modifiable factors of niche development, increasing attention is being paid to the importance of the surgical technique used during uterine closure after cesarean section. Reports indicate that the retraction of the endometrium into the suture line promotes the formation of defects in the myometrium. Therefore, precise placement of the needle and suture at the endomyometrial junction is crucial to ensure that the adjacent endometrium remains excluded from the closure of the muscular layer. Additionally, precise approximation of the myometrial layers, minimization of ischemic injury, and reduction of suture tension are important, as they promote proper healing and increase the residual myometrial thickness [9].

While a substantial proportion of women with a cesarean scar niche remain asymptomatic, in some patients the defect within the scar may lead to clinically significant symptoms. The most reported manifestations include prolonged menstrual bleeding and intermenstrual spotting, resulting from the retention of menstrual blood within the niche and its impaired drainage. In addition, patients may report pelvic pain of a chronic nature, which may intensify during menstruation or intercourse. The presence of a niche and chronic retention of menstrual blood may also negatively affect fertility by impairing fertilization or embryo implantation, and in the case of implantation within the scar, increase the risk of uterine rupture [10]. In the presented patient, heavy, prolonged bleeding and intermenstrual spotting could have been a consequence of both - the presence of a uterine polyp and a coexisting niche in the cesarean section scar.

A niche is defined as a defect in the uterine myometrium with a depth of at least 2 mm, most diagnosed using transvaginal ultrasonography (TVS). Clinically relevant parameters for assessing a niche include its length, width, and depth, as well as the residual myometrial thickness (RMT),

the thickness of the myometrium adjacent to the niche (adjacent myometrial thickness, AMT), and the presence and characteristics of any niche branches [4]. The type of niche and its morphological parameters, particularly its depth and residual myometrial thickness, play a crucial role in therapeutic decision-making. Small niches may be managed conservatively, whereas deep niches with low residual myometrial thickness more often require surgical treatment. In patients with an RMT exceeding 2–3 mm, hysteroscopic treatment is considered an appropriate management option, whereas in the case of RMT < 2.5 mm, laparoscopic repair is recommended [11].

Transvaginal ultrasonography of the patient revealed a niche with a depth of 4 mm and a residual myometrial thickness of 1.6 mm, indicating significant weakening of the uterine wall at the site of the scar.

Therapeutic management of a niche should be individualized and guided by clinical presentation as well as the patient's reproductive plans. In symptomatic women who do not plan further pregnancy, conservative treatment, including hormonal therapy, may be considered. Surgical treatment is recommended for reproductive-aged patients planning future pregnancies and includes laparoscopic scar reconstruction or hysteroscopic resection of the defect edges. Hysteroscopic resection may lead to a reduction in symptoms and improvement of implantation conditions, but in patients with low RMT it requires special caution due to the increased risk of complications, including bladder damage. Laparoscopic scar reconstruction, particularly in cases of large niches or a residual myometrial thickness of less than 3 mm, appears to provide better clinical outcomes and greater safety regarding future pregnancies [12].

In the presented case, the presence of a large niche with a depth of 4 mm, the coexistence of clinical symptoms, and the patient's expressed desire for a future pregnancy constituted an indication for surgical intervention. The laparoscopic reconstruction of the scar allowed for the restoration of the continuity of the uterine muscle. The procedure contributed to the alleviation of the patient's symptoms and reduced the risk of obstetric complications in subsequent pregnancy.

The literature shows a growing number of publications addressing niche repair in cesarean section scars, reflecting increasing interest in these procedures in clinical practice. Both hysteroscopic and laparoscopic techniques demonstrate comparable effectiveness in alleviating clinical symptoms and restoring the continuity of the uterine muscle. In patients with smaller niches, the hysteroscopic approach is preferred, as it is a minimally invasive technique offering significant perioperative benefits, such as reduced blood loss, shorter hospital stay, and faster recovery [13]. Studies evaluating the impact of laparoscopic niche repair on short- and long-term outcomes have demonstrated a significant improvement in cesarean scar parameters. On transvaginal ultrasound assessment, the scar thickness increased on average to 6.5 mm, while on hysterosonographic examination it increased to 6.1 mm. Furthermore, a reduction in clinical symptoms was observed, particularly a shortening of postmenstrual

spotting by up to 4 days, as well as alleviation of menstrual pain and a decrease in the duration of menstrual bleeding. Among patients who planned pregnancy after the surgery, a high rate of successful conception was reported [14].

CONCLUSIONS

A cesarean section scar is an increasingly recognized complication, whose clinical significance grows with the increasing number of cesarean sections performed. Although it may remain asymptomatic, the presence of a niche can lead to significant symptoms, including prolonged and intermenstrual bleeding, pelvic pain, and impaired fertility, while in subsequent pregnancies it may increase the risk of serious obstetric complications.

Transvaginal ultrasonography remains the primary and essential diagnostic method for evaluating niche morphology and clinically relevant parameters, particularly the residual

myometrial thickness (RMT). Low RMT values, especially in patients planning a subsequent pregnancy, should prompt consideration of surgical treatment.

Therapeutic management of a niche should always be individualized, considering clinical presentation, imaging findings, and the patient's reproductive plans. In the presented case, the presence of symptoms, the considerable depth of the defect, and the reduced residual myometrial thickness indicated the need for laparoscopic scar reconstruction, which allows for the restoration of uterine wall continuity and may potentially reduce the risk of complications in a future pregnancy.

Appropriate qualification for cesarean section, proper surgical technique and conscious planning of subsequent pregnancies can contribute to reducing the incidence of cesarean section and improving the safety of women in subsequent pregnancies.

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CONFLICT OF INTEREST

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CASE STUDY

Malignant melanoma of small intestine

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ABSTRACT

The purpose of this article is to present a challenging case of recurrent gastrointestinal bleeding caused by malignant melanoma of the small intestine and to discuss the diagnostic approach, highlighting the role of advanced endoscopic techniques. The patient underwent extensive diagnostic evaluation, including repeated gastroscopies, colonoscopies, two double-balloon enteroscopies, scintigraphy with labeled erythrocytes, and capsule endoscopy. Capsule endoscopy provided a decisive contribution to the diagnostic process, guiding further clinical management including segmental small intestine resection with regional lymphadenectomy. Histopathological examination of the resected tissue revealed malignant melanoma of the spindle cell type, infiltrating the mucosa, submucosa, and part of the muscular layer. No primary cutaneous lesion or distant metastases were detected following comprehensive diagnostic evaluation. In patients with suspected lower gastrointestinal bleeding, when standard endoscopic procedures do not allow to identify the source, location in the small intestine should be considered. In such cases, early implementation of advanced diagnostic techniques, such as capsule endoscopy and double-balloon enteroscopy, is recommended. These methods allow identification of lesions in small intestine segments with limited accessibility. A crucial step in the diagnostic process was capsule endoscopy, which enabled identification of an actively bleeding lesion in the distal segment of the small intestine.

KEYWORDS: melanoma, small intestinal neoplasms, gastrointestinal hemorrhage, anemia, iron-deficiency, capsule endoscopy

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INTRODUCTION

Gastrointestinal bleeding is classified according to its location in relation to the ligament of Treitz. The upper gastrointestinal tract, located above the ligament, accounts for approximately 80% of all bleeding cases. The most common causes of upper gastrointestinal bleeding are gastric and duodenal ulcers. The lower gastrointestinal tract, located below the ligament of Treitz, accounts for the remaining 20% of bleeding cases, which most frequently occur secondary to inflammatory, vascular, or neoplastic diseases [1].

In terms of clinical course, bleeding can be acute or chronic. Acute bleeding manifests itself with typical symptoms, such as coffee-ground vomiting in upper gastrointestinal lesions or tarry stools in the case of lesions in the distal parts of the intestine [1].

Diagnostic challenges arise primarily in cases of chronic bleeding, which may remain asymptomatic or present with nonspecific manifestations. The first clinical sign may be iron-deficiency anemia, which can be either subclinical or associated with symptoms such as fatigue and reduced exercise tolerance, depending on its severity. Anemia develops in approximately 61% of patients with chronic gastrointestinal bleeding [2, 3].

Gastrointestinal bleeding located in the small intestine is statistically rare. It accounts for only 5-10% of all gastrointestinal bleeding [4]. Hemorrhages in this area are primarily associated with the presence of neoplastic

lesions, accounting for as much as 80% of all cases in women and 55.9% in men [5]. The most common tumours developing in the small intestine are benign adenomas, adenocarcinomas, carcinoids, gastrointestinal stromal tumours, lymphomas and juvenile polyps [6].

Melanoma arising in the intestine is an exceptionally rare phenomenon. Only a few cases have been reported in the literature [7-10]. The atypical clinical presentation of this tumour significantly complicated the diagnostic process. Nonspecific symptoms, such as weight loss, chronic fatigue, weakness or abdominal pain, are often ignored by patients. Symptoms more typical for tumours of the gastrointestinal tract, such as melena, usually appear at an advanced stage, which notably delays the diagnosis.

Malignant melanoma is a highly aggressive malignant tumour. It originates from melanocytes present in the skin and in certain mucous membranes. It most commonly presents as a cutaneous lesion, whereas it less frequently arises in the uveal tract, oral cavity, rectum, vulva, vagina or within the male genital organs [11].

The incidence worldwide has been steadily increasing. Currently, approximately 150000 new cases of melanoma are diagnosed annually in Europe, whereas the number of deaths caused by this tumour reaches 25000 per year [12].

The high mortality rate is largely associated with delayed diagnosis, particularly in patients with lesions located in anatomically challenging regions. Despite the

development of new treatment modalities the prognosis remains unfavourable and the five year survival rate does not exceed 22% [13].

Intensive exposure to ultraviolet radiation has a significant impact on the risk of melanoma. With the expansion of international travel many individuals visit regions with intense sunlight which results in greater exposure to ultraviolet radiation. According to the medical history the patient travelled regularly and repeatedly experienced such sunburns. After 2 to 5 episodes of sunburn the risk of melanoma increases up to 2.6 fold and each subsequent episode further increases this risk [14].

We present a diagnostically challenging case of recurrent gastrointestinal bleeding caused by malignant melanoma of the small intestine.

CASE REPORT

A 75-year-old man presented to the Gastroenterology Clinic of the Military Hospital in Krakow with chronic fatigue, marked weakness, constipation and reduced appetite. Physical examination revealed pallor of the skin. In addition, the patient reported a weight loss of 6 kg over the previous six months. Laboratory investigations demonstrated severe iron-deficiency anaemia, with a haemoglobin concentration of 7.2 g/dl and serum iron level below 2 µmol/l. In addition, a fecal occult blood test (FOBT) was positive.

The patient was urgently admitted to the Department of Gastroenterology, where intravenous iron therapy was initiated and further diagnostic evaluations were conducted, including gastroscopy and colonoscopy. However, the source of bleeding could not be identified. The patient was discharged from hospital with a recommendation for oral iron supplementation and further outpatient monitoring.

During the following 12 months of observation, no significant clinical improvement was observed. Laboratory monitoring

performed every two weeks consistently showed persistently reduced haemoglobin and iron levels. Over this period, the patient required five re-hospitalisations due to exacerbation of anaemic symptoms. During subsequent hospitalisations, extensive diagnostic evaluations were repeatedly performed, including multiple gastroscopies and colonoscopies, two double-balloon enteroscopies, and scintigraphy with labelled erythrocytes. Despite the diagnostics performed, the bleeding source remained undetected.

Throughout hospitalisations, the patient received intravenous iron preparations (iron(III) hydroxide with dextran and iron(III) derisomaltose) as well as multiple transfusions of red blood cells concentrate to correct the aemia and stabilise the general condition.

A diagnostic breakthrough occurred one year after symptom onset, when capsule endoscopy revealed an actively bleeding ulcerative lesion located in the distal ileum, adjacent to the ileocecal valve (Fig. 1-2).

Two months later, the patient was admitted to the Oncological Surgery Department, where a segmental resection of the small intestine with lymphadenectomy and side-to-side anastomosis was performed. Intraoperatively obtained tissue samples were submitted for histopathological examination, which demonstrated malignant melanoma of the spindle cell type infiltrating the mucosa, submucosa, and part of the muscularis propria. No metastatic involvement of the excised lymph nodes was found.

To determine whether the lesion represented a primary or secondary (metastatic) melanoma, the patient underwent comprehensive imaging and dermatologic assessment, including whole-body videodermatoscopy, PET-CT, and contrast-enhanced CT scans of the head, chest, abdomen, and pelvis. No evidence of distant metastases or another primary tumour was detected. A pigmented lesion excised from the lumbar region was identified histopathologically



Fig. 1. Capsule endoscopy revealing a lesion in the ileocecal valve region

Picture taken by the authors

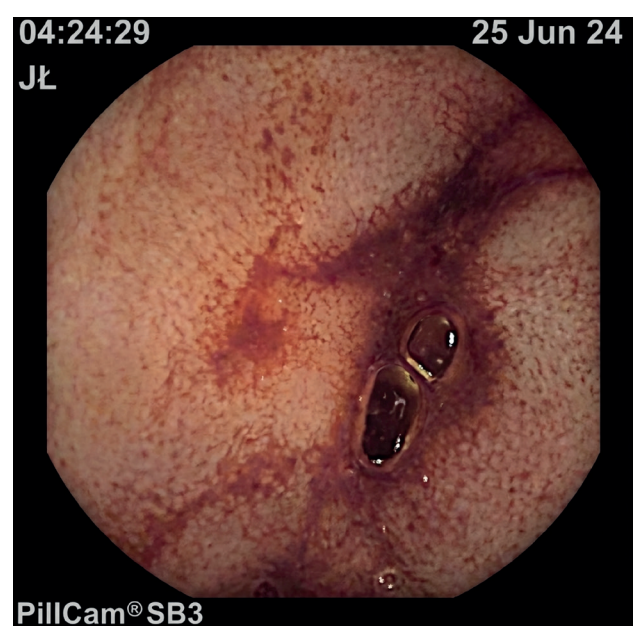


Fig. 2. Capsule endoscopy revealing a lesion in the ileocecal valve region

Picture taken by the authors

as basal cell carcinoma. There was also a scar from a previously removed skin lesion, which was not subjected to histopathological examination.

Genetic testing for the BRAF V600 mutation was performed, which did not reveal the presence of the mutation.

Based on these results, the patient was qualified for adjuvant immunotherapy with Nivolumab at a dose of 480 mg administered every 4 weeks for 12 months (6 cycles). Between treatment cycles, routine laboratory and imaging assessments are conducted to monitor for potential recurrence or metastasis and to ensure therapeutic safety.

DISCUSSION

In the differential diagnosis, both the presence of a primary malignant melanoma and the possibility of metastatic spread to the small intestine must be considered. Notably, melanocytes are not physiologically present in the small intestine. However, isolated cases of primary small-intestinal melanoma have been reported in the literature (7,8,9). Two potential hypotheses have been proposed for this phenomenon. The first involves autoimmune regression of the primary lesion, leading to partial or complete destruction of tumour cells by the immune system [15]. Regression of the primary lesion does not necessarily indicate resolution of the malignancy, as cases of further metastatic spread have also been described [15]. For this reason, the patient should remain under continuous oncological surveillance. An alternative hypothesis is the presence of ectopic melanocytes in the small intestine resulting from abnormal migration of neural crest cells during embryogenesis [8, 11]. The ectopic arrangement of these cells may create conditions for the development of primary small-intestinal melanoma.

According to the published criteria, a primary lesion may be diagnosed only after excluding cutaneous and mucosal melanoma at other locations and confirming mucosal invasion within the small intestine [16]. In light of these criteria, the possibility of a primary lesion should be considered in the presented patient. Furthermore, the lesion is located in an area not typical for metastatic spread, which usually involves the lungs, liver, brain or bones [13]. Moreover, although two years have passed since the onset of symptoms, no metastatic disease has been detected and the patient's condition remains stable. Although melanoma usually progresses rapidly, with metastatic spread occurring within a few years, late metastases have been reported even after 15 years [17].

The diagnostic process in the presented case extended over 12 months. This delay was related to the atypical localisation of the lesion and the difficulty in identifying the bleeding source.

Standard gastroscopy and colonoscopy do not allow complete visualization of the small intestine. When these methods do not provide a diagnosis, capsule endoscopy (CE) is recommended. It is a safe technique with an estimated diagnostic accuracy of 81% [18], but its limitations include high cost, time-consuming image interpretation, and limited availability.

The development of Artificial Intelligence (AI) may partly resolve these limitations by automatically assessing the

Cleanliness Score, which indicates whether the procedure is suitable for diagnostic review [19]. This can save specialists' time and reduce costs by identifying cases that do not require full evaluation. Modern AI models achieve sensitivities and specificities up to 90.27% and 99.78% and can analyze 1013 CE images in 13.5 seconds, demonstrating the potential to accelerate assessment and improve clinical workflow [20].

Double-balloon enteroscopy is an additional method for evaluation of the small intestine. The procedure is more invasive and requires specialised equipment, so it is typically performed after capsule endoscopy. Sequential use of both methods provides a diagnostic effectiveness of about 90% [21].

Insight into the molecular genetics of melanoma enables precise prognostic evaluation and selection of appropriate therapeutic strategies. Highly relevant in the process of melanogenesis are alterations in the Mitogen-Activated Protein Kinase (MAPK) signaling pathway, which regulates cell proliferation, differentiation, and apoptosis. Mutations in genes such as BRAF, NRAS, result in constitutive MAPK pathway activation, leading to uncontrolled cell proliferation. Mucosal and cutaneous melanomas exhibit distinct genetic and molecular profiles [22,23]. Dysregulation of the MAPK signaling pathway is observed in approximately 90% of cutaneous melanomas [22]. The most common mutations involve BRAF (37–60%), followed by NRAS (13–25%), NF1 (12%), MAP2K1 (6–7%), and KIT (2–8%) (christmas 2025). In mucosal melanoma, MAPK pathway alterations are also present but occur considerably less frequently, affecting up to 20% of patients [22]. The most frequently reported mutations include NRAS (14–30%), BRAF (5–16%), NF1 (16%), KIT (5–15%), SF3B1 (12%), TP53 (8.9%), SPRED1 (7%), ATRX (6%), and CHD8 (4%) [24]. Importantly, even when the same genes are affected, the localization and type of mutations differ between melanoma subtypes [23]. For example, BRAF V600 mutations are characteristic of cutaneous melanoma, whereas mucosal melanoma more often harbors atypical variants such as BRAF V600R or BRAF V600N, which has direct implications for treatment selection [23]. Moreover, assessing the molecular background allows for more accurate prognostic evaluation. Melanomas with BRAF mutations are associated with aggressive progression, although their precise impact on prognosis remains unclear [24]. In contrast, NRAS mutation is recognized as an adverse prognostic factor, correlating with worse overall survival (OS) and melanoma-specific survival (MSS) due to an increased risk of visceral and central nervous system metastases [23,24]. Genetic analysis in the reported case was negative for BRAF V600. Although the results did not definitively determine the tumor's origin, the molecular findings enabled an individualized therapeutic approach. In this case, targeted therapy was not indicated, and the patient was managed with surgical resection followed by adjuvant radiotherapy. Further research into MAPK pathway alterations may enable the development of targeted therapies for non-V600 BRAF variants and other mutations, potentially improving prognosis for both cutaneous and mucosal melanoma patients.

CONCLUSIONS

In patients with suspected lower gastrointestinal bleeding, when standard endoscopic procedures do not allow identification of the source, small intestine involvement should be considered. In such cases, early

implementation of advanced diagnostic techniques, such as capsule endoscopy and double-balloon enteroscopy, is recommended. These methods allow identification of lesions in small intestine segments with limited accessibility.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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