Wiadomości Lekarskie
Medical Advances

Official journal of the Polish Medical Association
Wiadomości Lekarskie has been published since 1928

Volume LXXIX, Issue 8, AUGUST 2026 ISSN 0043-5147 E-ISSN 2719-342X

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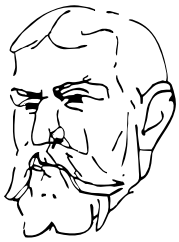
Volume LXXIX, Issue 8, AUGUST 2026



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Publisher:
ALUNA Publishing
29 Przesmyckiego St.,
05-510 Konstancin – Jeziorna, Poland
www.wydawnictwo-aluna.pl
www.wiadomoscilekarskie.pl
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ORIGINAL ARTICLE

Histological features of the remodeling of rat submandibular salivary glands following the administration of a combination of monosodium glutamate, sodium nitrite, and Ponceau 4r

Kostiantyn V. Shevchenko[1], Ihor S. Bieliaiev[1], Alona S. Grygorenko[1], Olena M. Bieliaieva[1], Nataliia M. Sharlai[1], Oksana V. Kokovska[1], Valentyna V. Onipko[2]

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ABSTRACT

Aim: To determine the dynamics of histological changes in the lobules of rat submandibular salivary glands under normal conditions and following the combined administration of the food additives monosodium glutamate, sodium nitrite, and Ponceau 4R.

Materials and Methods: Rats of the experimental group received sodium nitrite at a dose of 0.6 mg/kg, monosodium glutamate at a dose of 20 mg/kg, and Ponceau 4R at a dose of 5 mg/kg dissolved in 0.5 mL of distilled water and administered orally once daily. The animals were euthanized after 1, 4, 12, and 16 weeks of the experiment. Histological examination of the submandibular salivary glands was performed.

Results: Prolonged administration of the combination of food additives, including monosodium glutamate, sodium nitrite, and Ponceau 4R, resulted in stage-dependent morphological alterations. At the early stages, vascular-stromal disturbances and functional stress of the glandular epithelium predominated, accompanied by the development of persistent interstitial edema, hydropic degeneration, and ductal dysfunction. At later stages of the experiment, compensatory activation of a portion of glandular cells was observed in combination with dystrophic changes and microcirculatory imbalance. By the end of the study, these alterations manifested as chronic dystrophic remodeling, mucinous transformation of the secretory end pieces, desquamation of the ductal epithelium, and disruption of the structural integrity of the ductal system.

Conclusions: Administration of the combination of food additives leads to destructive and dystrophic changes in the structural components of the submandibular salivary glands and is accompanied by remodeling of the extracellular matrix components.

KEY WORDS: food additives, salivary glands, secretory end pieces, intercalated duct, striated duct, histological examination

Wiad Lek. 2026;79(8):1723-1732. doi: 10.36740/WLek/235896 DOI

INTRODUCTION

Saliva formation and secretion constitute a complex physiological process ensured by the coordinated functioning of all parenchymal components of the salivary glands [1]. The secretory end pieces produce acinar fluid, referred to as primary saliva, which consists of water, ions, and secretory products of acinar cells and originates from the interstitial fluid formed through blood filtration from the surrounding capillaries. This fluid undergoes substantial modification while passing through the ductal system, which plays a crucial role in the processing and maturation of primary saliva [2, 3]. An integral component of the salivary glands is the interstitial compartment, which is filled with the ground substance whose physicochemical properties determine the transport processes occurring within it. Alterations in these properties may result in spatial reorganization of the pathways through which biological fluids are transported.

The functional activity of the salivary glands is influenced by numerous endogenous and exogenous factors. Therefore, the investigation of morphological alterations induced by environmental factors is of considerable scientific and practical importance [4]. Disturbances in saliva formation and secretion affect both the qualitative and quantitative composition of saliva, thereby influencing not only the maintenance of oral homeostasis but also the normal functioning of the digestive system as a whole. Consequently, histological examination, aimed at studying the microscopic architecture of tissues, remains one of the most informative approaches for assessing structural changes in salivary glands [5–7].

In recent years, increasing attention has been paid to the quality composition of industrially manufactured food products. To improve product appearance, extend shelf life, and compensate for the use of lower-quality raw materials, manufacturers increasingly

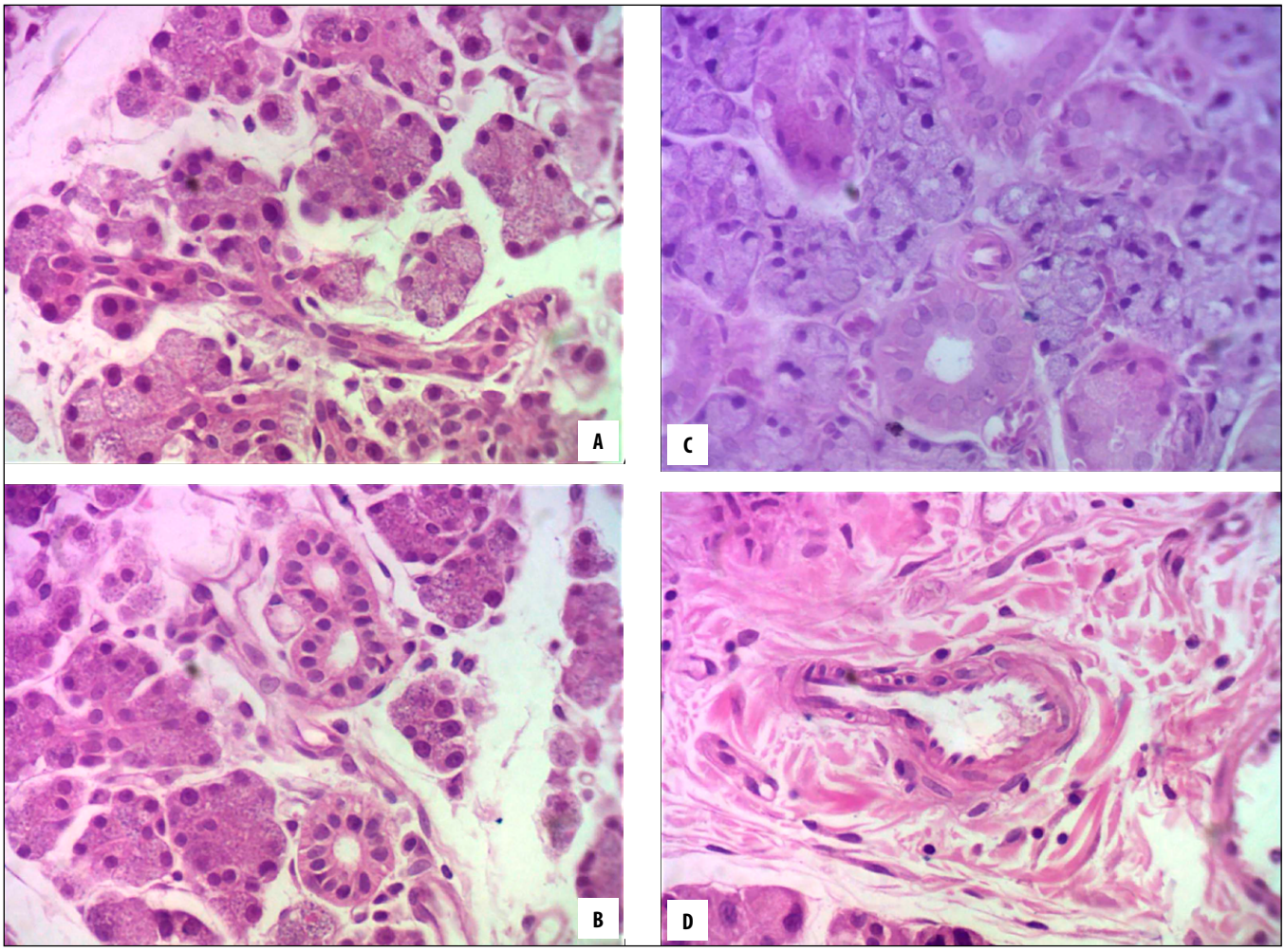

Fig. 1 a). Secretory end pieces and intercalated ducts. B). Striated ducts and the periductal capillary network. C). Vessels of the microcirculatory bed. D). Interlobular interstitial connective tissue of the submandibular salivary glands of rats in the control group. Photomicrograph. Hematoxylin and eosin staining. Magnification ×400
Picture taken by the authors

employ various food additives. Analysis of commercially available food products has demonstrated that monosodium glutamate, sodium nitrite, and Ponceau 4R are among the most commonly used additives. Previous studies have not provided a definitive explanation for the variability in human susceptibility to the effects of these substances, while data concerning their combined action remain limited [8, 9].

Importantly, the combination of the most frequently used food additives includes compounds characterized by different potential mechanisms of tissue injury. Experimental studies have associated monosodium glutamate with oxidative stress and dystrophic alterations in various organs, including the submandibular salivary gland [10, 11]. However, no consensus has yet been reached regarding the safe dosage of monosodium glutamate, and the mechanisms underlying its pathogenic and tissue-damaging effects remain insufficiently understood.

Sodium nitrite has been shown to enhance the generation of reactive oxygen species, disrupt antioxidant homeostasis, and induce histological alterations in salivary glands [12]. Nevertheless, studies investigating its effects on the organs of the digestive system are scarce, and many aspects of its biological action remain inadequately explored [13].

Ponceau 4R, a synthetic azo dye, has demonstrated potential cytotoxic and genotoxic properties in certain experimental models, although its toxicological profile largely depends on dosage, duration of exposure, and the biological system under investigation [14, 15]. The combined exposure to these substances, even at doses below the maximum permissible levels, may impose a cumulative burden on antioxidant defense mechanisms, vascular regulation, epithelial metabolism, and the extracellular matrix.

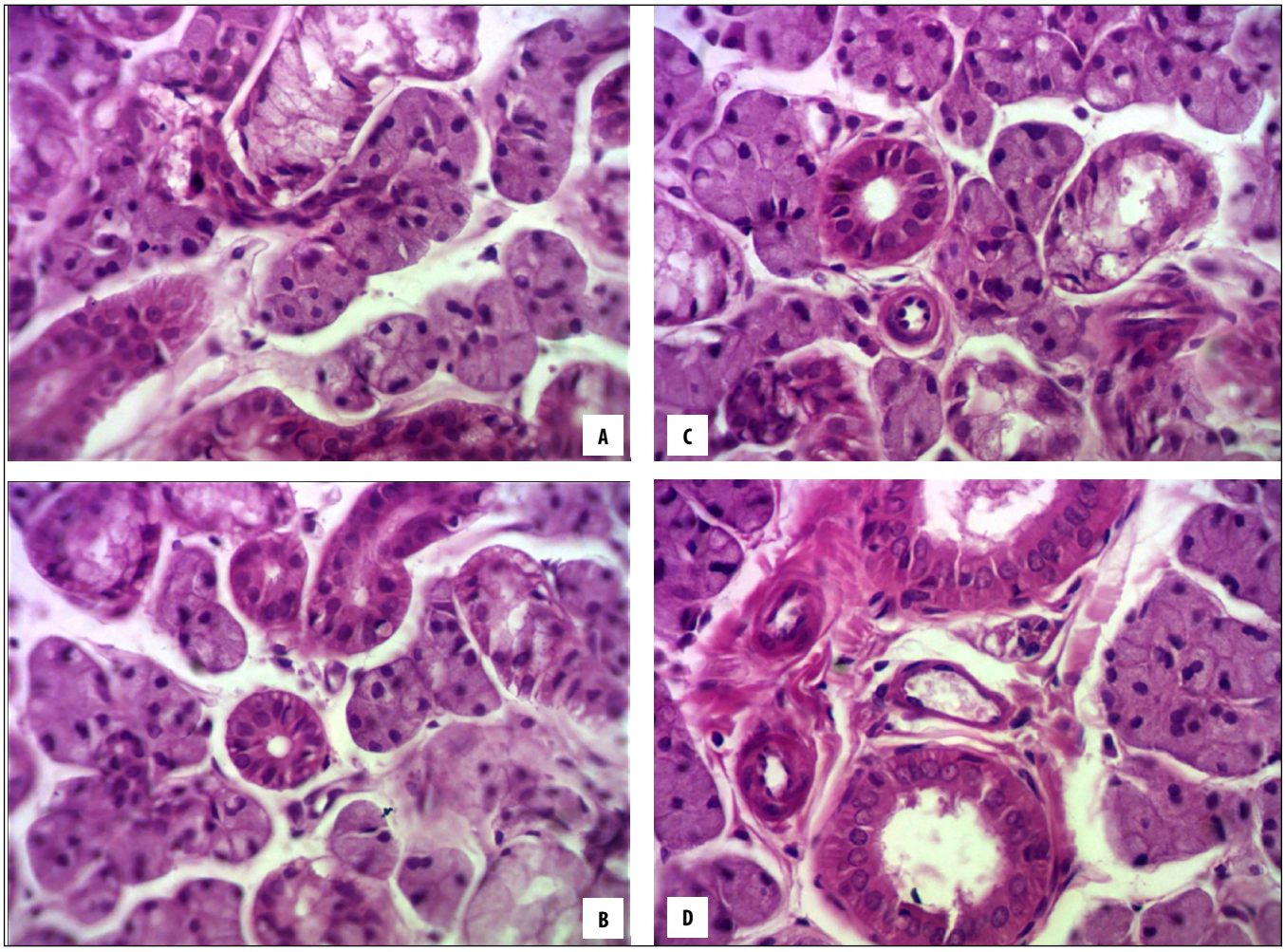

Fig. 2 A). Alterations in the tinctorial properties of the cytoplasm of seromucous cells of the secretory end pieces and reactive changes in the epithelium of the intercalated ducts. B). Initial stages of periductal edema formation around the striated ducts. C). Arteriolar spasm and signs of depletion of the exchange microvascular vessels. D). Expansion of the nodal interstitial compartments of the submandibular salivary glands of rats after 1 week of administration of the combination of monosodium glutamate, sodium nitrite, and Ponceau 4R. Photomicrograph. Hematoxylin and eosin staining. Magnification ×400
Picture taken by the authors

AIM

The aim of the present study was to determine the dynamics of histological changes in the lobules of rat submandibular salivary glands under normal conditions and following combined exposure to the food additives monosodium glutamate, sodium nitrite, and Ponceau 4R.

MATERIALS AND METHODS

The study was conducted on 84 adult male rats. Animals in the control group had free access to drinking water and received physiological saline orally. Rats in the experimental group, under conditions of unrestricted access to water, were administered sodium nitrite at a dose of 0.6 mg/kg, monosodium glutamate at a dose of 20 mg/kg, and Ponceau 4R at a dose of 5 mg/kg dissolved in 0.5 mL of distilled water once daily by oral gavage. The administered doses of the food additives were twofold lower than the maximum permissible levels. The animals were euthanized after 1, 4, 12, and 16 weeks of exposure by overdose of thiopental anesthesia. Following euthanasia, specimens of the submandibular salivary glands were excised and fixed in 10% neutral buffered formalin. Tissue samples were subsequently processed and embedded in paraffin according to standard histological procedures [4, 16]. Histological sections were prepared using an ARM 3600 microtome. After staining with hematoxylin and eosin, the sections were mounted in polystyrene mounting medium and examined under a light microscope. Photomicrographs were obtained using a Levenhuk D740T digital microscope equipped with a digital imaging system and software adapted for morphometric and histological analysis.

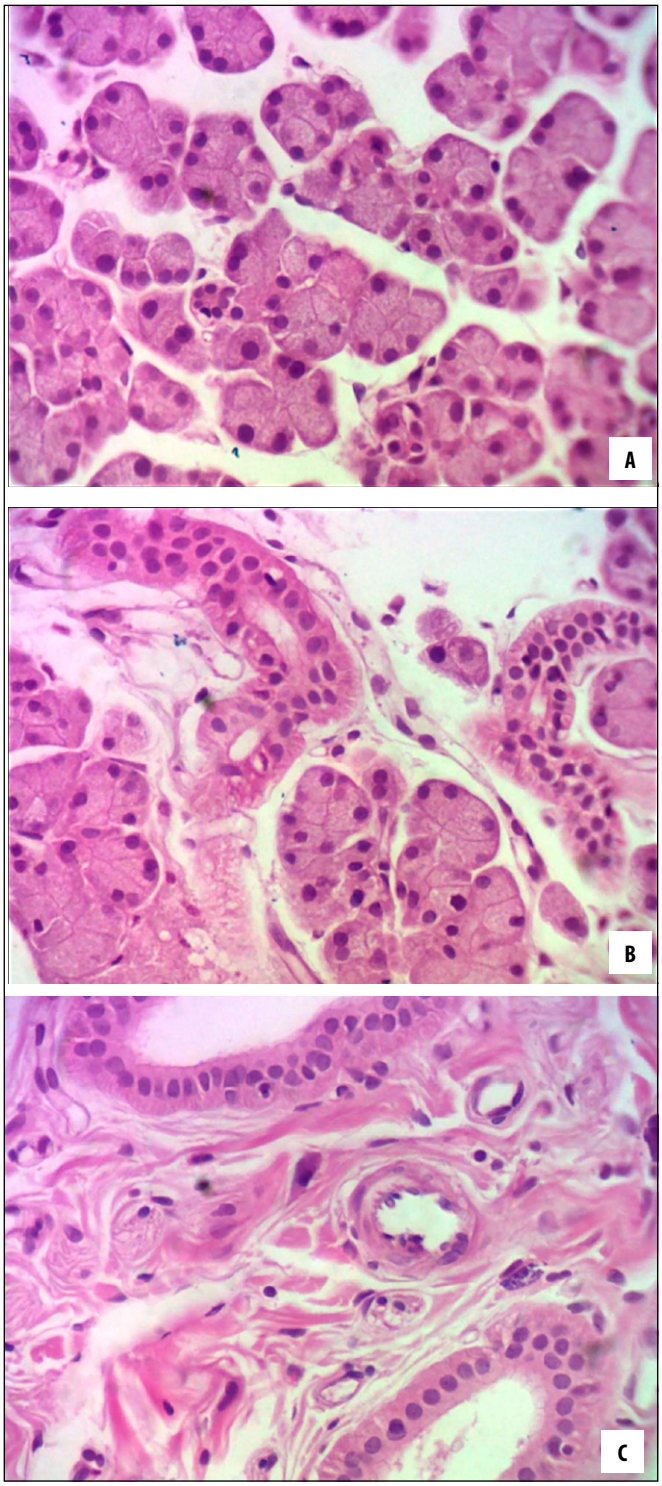

Fig. 3 A). Hydropic degeneration in glandular cells of the secretory end pieces, intercalated duct, and edema of the interstitial tissue. B). Striated ducts and signs of depletion of the exchange microvascular vessels. C). Interstitial tissue at week 4 of administration of the food additive combination. Photomicrograph. Hematoxylin and eosin staining. Magnification ×400
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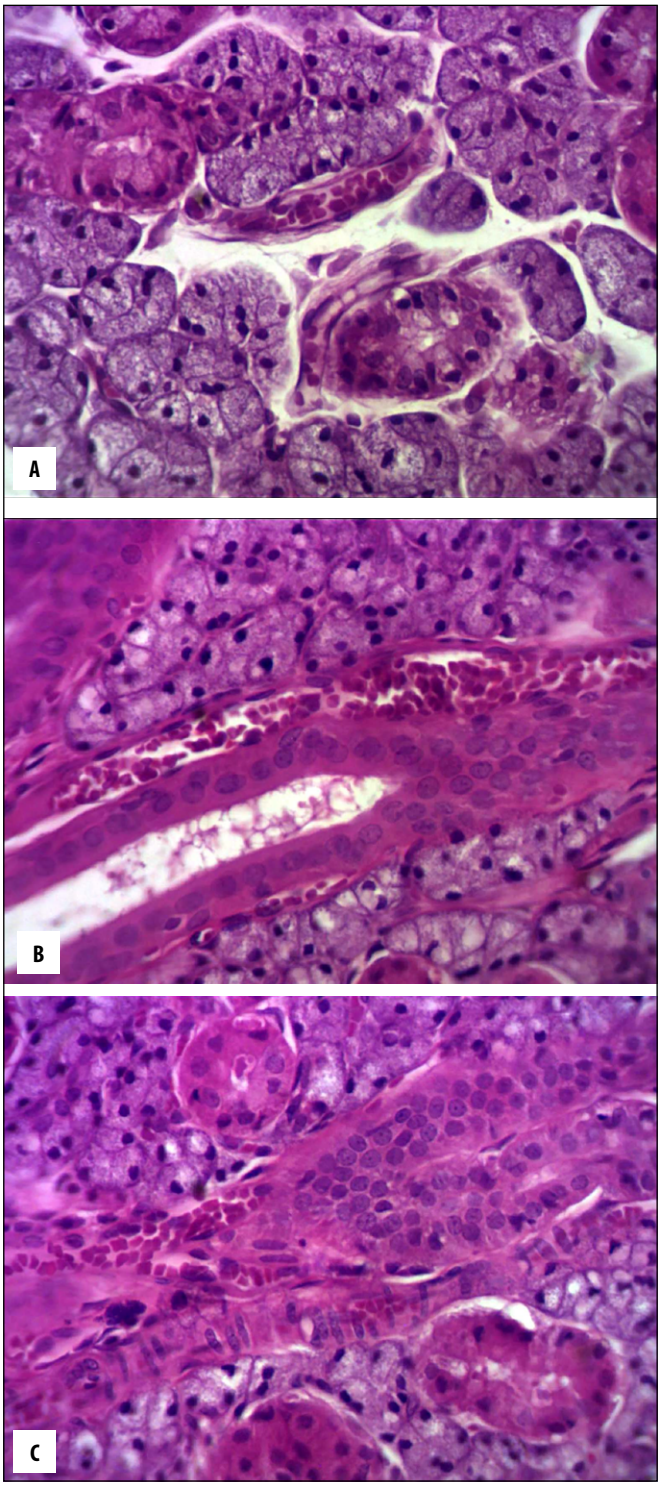

Fig. 4 A). Cytoplasmic vacuolization of the epithelial cells of the striated ducts and increased cytoplasmic basophilia of glandular cells of the secretory end pieces. B). Blood filling of the capacitance vessels. C). Spasm of the resistance vessels and vacuolization of acinar cells at week 12 of administration of the pollutant combination. Photomicrograph. Hematoxylin and eosin staining. Magnification ×400
Picture taken by the authors

All animal experiments were conducted in compliance with the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986), Directive 2010/63/EU of the European Parliament and of the Council on the protection of animals used for scientific

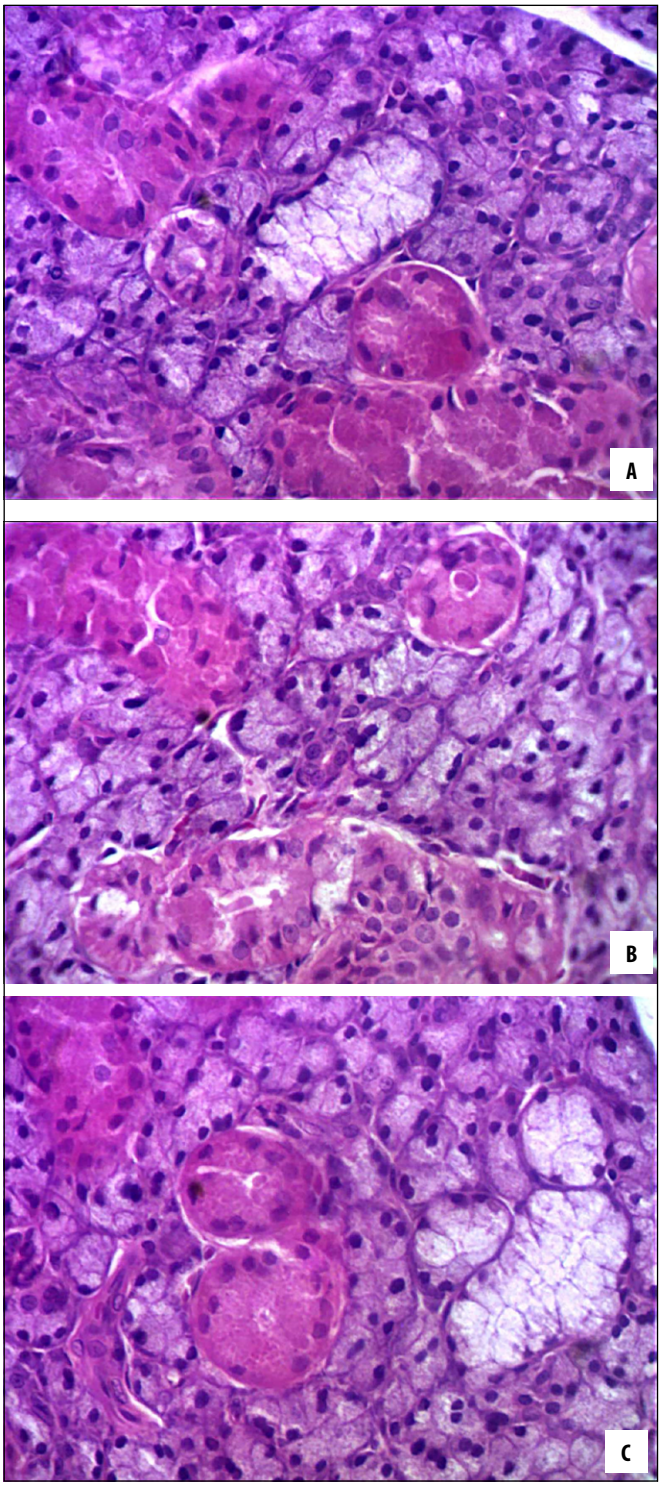

Fig. 5 A). Mucinization of the cells of the secretory end pieces and the appearance of vacuole-like dilatations in the basal portions of the striated ducts. B). Desquamation of the epithelial cells of the striated ducts. C). Degenerative changes in the ductal epithelium of the intercalated ducts of the rat submandibular salivary glands at week 16 of the experiment. Photomicrograph. Hematoxylin and eosin staining. Magnification ×400
Picture taken by the authors

purposes, and Order No. 249 of the Ministry of Education and Science, Youth and Sports of Ukraine dated March 1, 2012, "On Approval of the Procedure for Conducting Experiments and Scientific Studies on Animals by Scientific Institutions." The study also adhered to the recommendations of the First National Congress on Bioethics (2001) and was approved by the Biomedical Ethics Commission of Poltava State Medical University (Minutes No. 220, October 25, 2023).

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

The paper has been written within the research scientific work "Restructuring of the organs of the immune, respiratory and excretory systems under the effect of various exogenous factors (monosodium glutamate, sodium nitrite, Ponceau 4R, ethanol, methacrylate)", State Registration No 0121U108234.

RESULTS

In the control group, the submandibular salivary gland exhibited a typical lobular architecture. The parenchyma consisted of densely arranged secretory end pieces and a well-developed system of intra- and interlobular excretory ducts. The stroma was moderately developed and represented by delicate layers of loose fibrous connective tissue and interlobular septa.

The secretory end pieces were compactly arranged and composed predominantly of pyramidal seromucous cells. The basal portions of the cells exhibited basophilic staining, whereas the apical regions displayed a more eosinophilic and granular appearance. The nuclei of the glandular cells were round, normochromatic, and characterized by distinct contours. Intercellular spaces were not enlarged, and the basement membranes remained intact (Fig. 1a).

The intercalated ducts possessed narrow, well-defined lumina and were lined by simple cuboidal epithelium. Epithelial cells were arranged regularly, and their nuclei were round and predominantly centrally located, indicating preservation of the transport function of the ductal system (Fig. 1a).

The striated ducts were larger in caliber, with wide lumina and tall columnar epithelium. Pronounced eosinophilia of the cytoplasm and preservation of basal striations indicated functional activity and participation in the modification of primary saliva. The surrounding interstitial tissue was moderately developed, and the blood vessels showed no signs of stasis (Fig. 1b).

The microcirculatory bed consisted of arterioles, capillaries, and venules without evidence of vascular stasis

or erythrocyte aggregation (Fig. 1c). The interlobular connective tissue contained orderly arranged collagen fibers, fibroblasts, and fibrocytes, while the parenchyma-to-stroma ratio remained preserved (Fig. 1d).

After one week of administration of the food additive combination, the acinar organization of the gland remained generally preserved; however, the secretory end pieces were arranged less compactly. Optically clear spaces appeared between acini and around ducts and blood vessels, indicating the accumulation of tissue fluid within the interstitium. Some glandular cells exhibited hyperchromatic nuclei, uneven cytoplasmic staining, and occasional vacuolated areas. Acinar lumina varied in size, suggesting disturbances in the secretory cycle and impaired outflow of secretory products.

At this stage, the intercalated ducts displayed a small diameter and narrow slit-like lumina. Clear periductal spaces corresponding to stromal edema were observed and could potentially interfere with the transport of primary saliva (Fig. 2a). In the striated ducts, irregular nuclear distribution, heterogeneous eosinophilia of the cytoplasm, and partial loss of basal striations indicated early functional stress of the ductal epithelium (Fig. 2b).

Alterations in the microcirculatory bed during the first week were predominantly hemodynamic in nature. Arterioles exhibited narrowed or irregular lumina, while endothelial cells protruded into the vascular lumen. Venules were dilated and irregularly shaped (Fig. 2d). Capillaries showed indistinct contours due to edema, and areas of reduced blood filling were observed within their lumina (Fig. 2c). The interstitial tissue was expanded, with fibrous structures separated by accumulated fluid, whereas interlobular ducts demonstrated dilated lumina containing pale secretory material (Fig. 2d).

After four weeks of exposure to the food additive combination, the predominant histological feature was further expansion of the interstitial compartment. Wide optically clear spaces were observed between secretory end pieces, ducts, and blood vessels, indicating edema and disruption of the compact arrangement of the glandular parenchyma. In some secretory cells, the cytoplasm remained moderately eosinophilic, whereas in others it appeared paler, granular, and finely vacuolated, consistent with hydropic degeneration. Acinar lumina were visualized irregularly and varied considerably in size.

The epithelial cells of the intercalated ducts retained their simple epithelial arrangement; however, some nuclei exhibited increased staining intensity. Due to marked expansion of the interstitium, the lumina of certain intercalated ducts were poorly visualized, potentially impairing the drainage of primary saliva (Fig. 3a). In the striated ducts, nuclei appeared intensely basophilic, occasionally clustered, and irregularly distributed. The cytoplasm was heterogeneous, and basal striations were indistinct, indicating impairment of epithelial functional activity.

Capillaries were located within markedly expanded interstitial spaces. Owing to tissue edema, vascular contours appeared indistinct, and erythrocytes were not readily identified within the lumina (Fig. 3b). The interstitial tissue was substantially expanded, with collagen fibers separated by edematous fluid. The presence of fibroblasts, fibrocytes, occasional immunocompetent cells, and mast cells suggested activation of compensatory-reparative processes and progression toward chronic tissue remodeling. Interlobular ducts exhibited wide lumina containing pale secretory masses or amorphous material (Fig. 3c).

At week 12 of prolonged administration of the combination of monosodium glutamate, sodium nitrite, and Ponceau 4R, the condition of the glandular cells was heterogeneous. In some cells, the cytoplasm remained moderately eosinophilic, whereas in others it appeared pale, granular, and vacuolated, consistent with moderate hydropic degeneration. In certain secretory end pieces, increased cytoplasmic basophilia was observed, reflecting compensatory activation of the protein-synthesizing apparatus. The coexistence of enhanced basophilia, cytoplasmic vacuolization, and clearing indicated the simultaneous presence of compensatory and degenerative alterations within the acinar compartment (Fig. 4a–c).

The epithelial cells of the striated ducts at week 12 remained relatively compactly arranged, although their distribution was uneven. Their cytoplasm was eosinophilic, heterogeneous, and vacuolated, while the basal striations were poorly discernible, indicating reduced efficiency of ion transport and secretory modification. The ductal lumina exhibited irregular contours and contained pale secretory material. The apical surface of the epithelium was uneven and demonstrated focal signs of desquamation (Figs. 4a, 4c).

At this stage, the interlobular ducts exhibited relatively wide lumina lined by tall columnar or pseudostratified epithelium characterized by variable cell height and irregular nuclear arrangement. The lumina contained pale amorphous or secretory material, suggesting alterations in the composition of the secretion and partial impairment of its drainage against the background of edematously altered stromal tissue (Fig. 4b).

Arterioles at week 12 were characterized by relatively thick walls and narrowed lumina, consistent with vascular spasm. These changes indicated impaired regulation of vascular tone, restricted blood supply to the glandular parenchyma, and consequently reduced oxygenation

and trophic support of the secretory epithelium. Perivascular edema was observed around the arterioles (Fig. 4c). In contrast, venules exhibited wider lumina and thinner walls, and their lumina were filled with densely packed erythrocytes. Venular congestion indicated impaired venous outflow and localized blood stasis, which, together with arteriolar spasm, reflected microcirculatory imbalance within the gland (Figs. 4b, 4c).

By week 16 of administration of the food additive combination, further alterations in the tinctorial properties of the cytoplasm were observed within the secretory end pieces. A substantial proportion of cells displayed pale, weakly stained, foamy, or vacuolated cytoplasm, indicative of mucinous transformation of the secretory apparatus and accumulation of mucous glycoprotein-rich secretory material. The nuclei were predominantly located in the basal portions of the cells, occasionally displaced toward the periphery, and exhibited intense basophilia or hyperchromasia. Their irregular distribution suggested disruption of acinar cell polarity. Acinar lumina varied considerably in appearance, ranging from barely discernible to markedly dilated and irregularly shaped structures containing pale material, indicating disturbances of the secretory cycle and impaired secretion outflow (Fig. 5a).

Pronounced destructive alterations were observed in the striated ducts at week 16. The lumina of some ducts were mildly dilated or poorly defined, and the epithelial cells were arranged irregularly. While a portion of the epithelial cells remained attached to the basement membrane, individual epithelial cells and cellular fragments were detected within the ductal lumina, indicating epithelial desquamation. The apical surface appeared irregular and focally loosened, whereas the cytoplasm was heterogeneous and contained vacuole-like areas adjacent to the basal surface (Fig. 5a). Basal striations were weakly expressed or indistinct (Fig. 5b).

The intercalated ducts at week 16 exhibited narrow, occasionally slit-like lumina associated with reactive epithelial remodeling, stromal edema, and mechanical compression by altered acinar structures. The epithelial lining appeared less organized, with indistinct intercellular boundaries and intensely basophilic, hyperchromatic nuclei. The cytoplasm was weakly eosinophilic and focally pale, indicating reactive-degenerative alterations. As remodeling of the secretory end pieces progressed, the secretion became more viscous and enriched with carbohydrate-containing components, thereby increasing the functional load on the intercalated ducts and reducing the flow of primary saliva available for subsequent modification within the ductal system (Fig. 5c).

DISCUSSION

The present findings demonstrate that prolonged administration of a combination of food additives, including monosodium glutamate, sodium nitrite, and Ponceau 4R, induces progressive remodeling of the lobular architecture of the rat submandibular salivary gland. This process is characterized by the development of vascular reactions during the early stages of the experiment and persistent degenerative and destructive alterations of both the secretory and ductal epithelium at later stages. These morphological changes appear to reflect impairment of the two principal functional components of salivary gland activity, namely the production of primary saliva by the secretory end pieces and its subsequent modification within the ductal system.

In the control group, the structural organization of the submandibular salivary glands ensured a normal relationship between the parenchyma, ductal system, stroma, and microvasculature. The secretory end pieces were compactly arranged and composed of seromucous glandular cells exhibiting preserved basophilia in the basal cytoplasmic regions and characteristic granularity in the apical portions, indicating adequate protein-synthesizing and secretory activity. The narrow acinar lumina, without evidence of secretory retention, reflected the coordinated balance between saliva production and drainage. The intercalated ducts were lined by simple cuboidal epithelium with well-defined narrow lumina, consistent with their transport function and role in the initial conveyance of secretory products. The striated ducts displayed preserved tall columnar epithelium, eosinophilic cytoplasm, and distinct basal striations. The interstitium was moderately developed and showed no signs of edema, vascular stasis, or inflammatory cell infiltration, while the interlobular ducts maintained normal histological architecture.

After one week of administration of the food additive combination, early reactive and hemodynamic alterations predominated. These changes resulted in the development of initial interstitial edema caused by increased permeability of the microvascular network. Alterations in the glandular cells of the secretory end pieces reflected an early phase of functional stress, during which a proportion of cells retained secretory activity, whereas others exhibited signs of disturbed intracellular water-electrolyte homeostasis. Compression of the intercalated ducts by the edematous stroma, together with initial reactive epithelial changes, likely impaired saliva drainage from the secretory end pieces. Concurrently, the striated ducts demonstrated early disruption of basal striations, structures essential for active ion transport. Expansion of the interstitial tissue, arteriolar spasm, perivascular edema, and reduced

capillary perfusion collectively compromised trophic support to both acinar and ductal epithelium. These alterations may have contributed to tissue hypoxia and the subsequent development of dystrophic changes. Similar observations have been reported in previous studies investigating the effects of exogenous factors on the submandibular salivary glands [16]. Furthermore, monosodium glutamate has been associated with oxidative stress, histopathological alterations of the submandibular gland, and increased apoptotic activity, including enhanced caspase-3 expression in both acinar and ductal cells [10].

After four weeks of exposure, the observed alterations in the secretory end pieces were consistent with the development of hydropic degeneration and disruption of the secretory cycle. Impaired coordination between saliva production and outflow may lead to a reduction in salivary volume, alterations in protein composition, and increased viscosity of saliva. Early reactive changes within the ductal epithelium progressed toward more persistent functional disturbances. The interstitial tissue exhibited features indicative of a transition from isolated edema to stromal remodeling, characterized by increased numbers of fibroblasts, fibrocytes, and immunocompetent cells. The presence of mast cells within the interlobular connective tissue is of particular pathogenetic significance, as their degranulation may enhance vascular permeability, thereby sustaining edema and promoting a nonspecific inflammatory response. These findings are consistent with previous reports demonstrating the pro-inflammatory and oxidative effects of sodium nitrite on the histological structure of the submandibular salivary gland, including elevated malondialdehyde levels and suppression of antioxidant defense mechanisms. Notably, antioxidant administration has been shown to partially mitigate these alterations [12].

At the later stages of the experiment, combined exposure to monosodium glutamate, sodium nitrite, and Ponceau 4R resulted in the coexistence of compensatory and degenerative responses. At week 12, a subset of glandular cells demonstrated activation of the protein-synthesizing apparatus, which may represent a compensatory response to prolonged exposure to food additives. Simultaneously, other cells exhibited cytoplasmic clearing, granularity, and vacuolization, characteristic of hydropic degeneration. These findings indicate heterogeneity in the functional state of the acinar apparatus, reflecting the coexistence of adaptive and decompensatory phases. Such alterations may contribute to changes in the ratio of protein and mucous components of saliva, thereby reducing its protective properties. Changes observed in the striated ducts suggested decreased efficiency of sodium and chloride reabsorption, as well as impaired secretion of potassium and bicarbonate ions, ultimately affecting the electrolyte composition and buffering capacity of saliva. Occasional epithelial desquamation indicated the onset of destructive remodeling within the ductal system. Vascular alterations were consistent with microcirculatory dysfunction and corresponded to findings reported in previous studies [17]. Arteriolar spasm restricted blood supply to the glandular parenchyma, whereas venular congestion reflected impaired venous drainage. Together with perivascular edema, these changes created conditions conducive to chronic hypoxia and impaired trophic support of the secretory epithelium. Therefore, the combined action of the investigated food additives appears to induce vascular spasm, venous stasis, interstitial edema, oxidative stress, and disturbances of tissue metabolism.

By week 16, the observed histological alterations corresponded to chronic dystrophic remodeling of the submandibular salivary gland. Such changes may result in modification of salivary composition, increased viscosity, reduced lubrication of the oral mucosa, and diminished cleansing and antimicrobial functions of saliva. Narrowing of the intercalated ducts, together with reactive-degenerative epithelial alterations, likely reduced the flow of secretory products into subsequent segments of the ductal system. The striated ducts exhibited pronounced destructive changes that may impede secretory transport and diminish the capacity of the ductal epithelium to perform ion-dependent modification of saliva.

CONCLUSIONS

Prolonged administration of a combination of food additives, including monosodium glutamate, sodium nitrite, and Ponceau 4R, induces stage-dependent morphological alterations in the submandibular salivary glands of rats. During the early stages of exposure, vascular-stromal disturbances and functional stress of the epithelial components predominate, resulting in the development of persistent interstitial edema, hydropic degeneration, and ductal dysfunction. At later stages of the experiment, compensatory activation of a subset of glandular cells coexists with progressive degenerative changes and microcirculatory imbalance. By the end of the study, these alterations manifest as chronic dystrophic remodeling, mucinous transformation of the secretory end pieces, desquamation of the ductal epithelium, and disruption of the structural integrity of the ductal system.

The observed morphological alterations indicate that the combined action of the investigated food additives

adversely affects both the secretory function of the gland and the duct-dependent modification of saliva. These changes may contribute to reduced salivary output, alterations in the protein-mucous and electrolyte composition of saliva, increased salivary viscosity, impaired buffering capacity, and diminished protective properties of the oral fluid.

The principal pathogenetic mechanisms underlying the detected tissue remodeling appear to include microcirculatory disturbances, increased vascular permeability, interstitial edema, oxidative tissue injury, and prolonged functional stress of both the secretory and ductal epithelium, ultimately leading to the development of dystrophic and destructive changes. Functionally, these alterations result in decreased secretory activity of the gland, impaired transport and modification of saliva, changes in its electrolyte and protein-mucous composition, increased viscosity of the secretion, and attenuation of the protective functions of oral fluid.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 05.03.2026
ACCEPTED: 27.07.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

The prevalence of ocular dryness associated with systemic isotretinoin in acne patients in Iraq

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ABSTRACT

Aim: This research was conducted to assess the prevalence of ocular dryness during the course of systemic isotretinoin in acne patients in Iraq.

Materials and Methods: 64 acne patients using systemic isotretinoin in doses ranging from 20mg to 60 mg were enrolled in this study. All patients had been checked for ocular dryness by using Schirmer's test before starting therapy and after each month regularly for 6 times.

Results: 64 acne patients were included in this study with a high percentage of the female gender (81.75%) with a mean age of 21.2± 3.4. The mean duration of systemic isotretinoin is 4.3 months while the mean total cumulative dose is 5.8 grams. About 31.25% among the participants have developed ocular dryness, and the most frequent grade is grade III (50%).70% of patients that have ocular dryness use lubricant eye drops. However, no significant correlations were seen between dosage, gender, duration, age, and TCD with ocular dryness.

Conclusions: This research reveals that ocular dryness may occur during the course of systemic isotretinoin. This research contributes to the raise the awareness of the effects of isotretinoin use on the health of the ocular surface. However, no significant correlations were seen between dosage, gender, duration, age, and TCD with ocular dryness.

KEY WORDS: Schirmer's test, ocular, dry eye, systemic isotretinoin

Wiad Lek. 2026;79(8):1733-1740. doi: 10.36740/WLek/225686 DOI

INTRODUCTION

Acne vulgaris is the most common dermatological disease adolescents, mainly occur in persons aged11–30 years [1, 2]. Acne is mainly classified as mild, moderate, and severe. Acne in the face can cause severe inflammatory responses, which may lead to scarring in the face, making the patients look for reasonable management and helping them to overcome the psychosocial impact and psychological burden [3].

Systemic isotretinoin was approved to be utilized in acne, especially in severe, resistant, and nodular types in1982 [4]. Most pathophysiological factors involved in acne are typically targeted by systemic isotretinoin producing a high satisfaction outcome [5, 6].

Isotretinoin therapy is associated with a variety of side effects ranging in consequences and severity. Mucocutaneous effects are more common adverse effect such as xerosis and cheilitis [7].

There are several reports of ocular side effects ranging in severity from less severe effects such as dry eye diseases and corneal surface alterations e.g. ocular irritation, visual field defects and dark adaptation abnormalities to extremely rare and serious adverse effects include optic neuritis, retinal toxicity and corneal opacities, which may lead to permanent damage of ocular tissue if unrecognized [8, 9]. These ocular adverse effects have been reported within days to years of isotretinoin therapy initiation [10]. Ocular side effects are suspected to be dose dependent and become tolerable with a change in dosing and symptomatic management these notes are reported in some cases [11].

However, these ophthalmological side effects, such as dry eye disease, blepharitis, and conjunctivitis [12]. Systemic administration of isotretinoin may cause change in the structure and function of the meibomian gland and suppress the production of lipids, causing rapid tear evaporation [13]. in addition, it alters the epithelium of conjunctiva, influencing the morphology of goblet cells and affecting mucin production [14]. The alteration of the mucin and lipid layers causes instability of the tear film, leading to dry eye by evaporation, increased osmolarity, and dry eye symptoms [15]. It is important

Table 1. Demographic character of the participants

Character		Number	[%]
Total		64	100
Gender	Male	12	18.75
	Female	52	81.25
Age (years)		(21.2± 3.7)	
Weight (kg)		(58.42± 7.8 kg)	

Source: Authors own work

Table 2. Duration and dosage of isotretinoin

Duration and dosage		Number	[%]	TCD(g)	M	SD
Duration of isotretinoin	3 month	14	21.9			
	4 month	28	43.75			
	6 month	24	37.5			
Dosage	20 mg	11	17.18	1.8		
	40 mg	35	54.68	4.8		
	60 mg	18	28.12	10.8		
Months used					4.3	1.52
Total cumulative dose(g)					5.8	4.58

Note: M: mean, SD: Standard Deviation, TCD: Total cumulative dose
Source: Authors own work

for dermatologists to be aware and educate patients about the possible ophthalmologic adverse effects of systemic isotretinoin [16].

AIM

This study was conducted to assess the prevalence of ocular dryness in acne patients in Iraq who were undergoing systemic isotretinoin treatment and raise their awareness about the adverse effect of systemic isotretinoin on ocular dryness.

MATERIALS AND METHODS

64 patients participated in this study having moderate to severe acne with a mean age of 21.2± 3.7 receiving 20-60 mg of systemic isotretinoin with regular follow up for 6 months durations by an ophthalmologist to evaluate their ocular dryness using Schirmer's test (Most commonly applied in clinical tests for dry-eye disease evaluation, treatment, and management. It is thought that inserting a strip of filter paper into the inferior fornix and measuring the length of the wetted portion after 5 minutes provides a direct assessment of tear production rate).

Schirmer's test has four grades to estimate the ocular dryness that begin with normal (Grad 1), mild (Grade 2), moderate (Grade 3) and severe (Grade 4).

All the patients undergo a checkup before the beginning of the treatment and every month during the course.

The patients who had these criteria had been excluded as follows:

1. Patients that had previous eye surgery.
2. Any systemic diseases.
3. Contact lens use.
4. Dry eye disease.

ETHICAL APPROVAL

This study was done in an outpatient clinic of dermatology and ophthalmology in Baghdad city from April 2023 to April 2024. The study was approved by The Institutional Review Board/Ethical Review Board (EAC1452). All patients read and signed the informed consent when they were included in the study.

RESULTS

64 participants were included in this study, female participants represent 81.25%.The mean age of participants was 21.2± 3.7 years and their mean weight was 58.42± 7.8 kg (Table 1, Fig. 1).

Regarding the duration of systemic isotretinoin, 37.5% of the participants used it for 6 months and 43.75% for 4 months while 21.9% used it for 3 months. Concerning the daily dosage of systemic isotretinoin, 54.68% of the patients used 40 mg, which is the commonest dose of isotretinoin while 28.12% used 60 mg and the rest of the participants were using 20 mg among the course 7.18 % (Table 2, Fig 2-3).

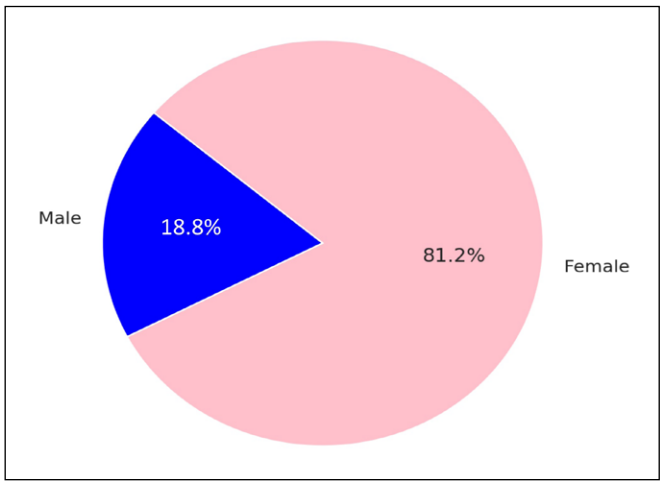

Fig. 1. Gender distribution
Source: Own materials

The total cumulative dose (TCD) of the participants using 20 mg/kg/day was 1.8 g for 3 months, 4.8 gram was for participants that had been using 40 mg/kg/day for 4 months and 10.8 g for participants using 60 mg/kg/day for 6 months (Table 2). Most of the participants that are using systemic isotretinoin had a grad 1 (68.75%), while the other participants had a grad 2, 3, and 4 (31.25).

The number of participants that had a change in the ocular dryness when they were using systemic isotretinoin as a follow-up (a G2 of ocular dryness is 4, 10 had a G3, and 6 of them had a G4) as shown in table 3 and figure 4.

REPEATED-MEASURES ANOVA FOR SCHIRMER'S TEST

A repeated-measures ANOVA was conducted with Time (baseline, Month 1, Month 2, …, Month 6) as the within-subject factor and Isotretinoin Dose (20 mg/day, 40 mg/day, 60 mg/day) as a between-subject factor. Additional covariates included Gender and Age. Mauchly's test of sphericity was satisfied ($p = 0.08$), indicating no violation of sphericity in table 4 and figure 5.

- **Main Effect of Time**: Statistically significant ($p < 0.001$), indicating that tear production changed across the six-month period.
- **Dose**: Did not reach statistical significance ($p = 0.068$) but showed a notable trend.
- **Time × Dose Interaction**: Significant ($p = 0.001$), suggesting that changes in Schirmer's scores over time differed by dose group.

Post-hzoc Pairwise Comparisons (Bonferroni-adjusted) revealed that the largest decreases in Schirmer's scores occurred between baseline and Month 3 (mean difference = 6.2 mm, $p < 0.001$) and that the 60 mg/day group showed significantly lower scores at Month 4 and Month 5 compared to the 20 mg/day group ($p < 0.01$).

Ordinal Logistic Regression for Dryness Grade

An ordinal logistic regression model (proportional odds model) was fitted to dryness grade (1 = Normal, 2 = Mild, 3 = Moderate, 4 = Severe) with Time, Dose, Age, Gender, and Total Cumulative Dose (TCD) as predictors. Dryness grade measurements were taken at each monthly visit, and patient ID was included as a random effect to account for repeated measures (Table 5, Fig 6).

DISCUSSION

The objective of our research was to investigate the prevalence of the eye dryness with the use of systemic isotretinoin, which is measured by Schirmer's test in Iraqi patients.

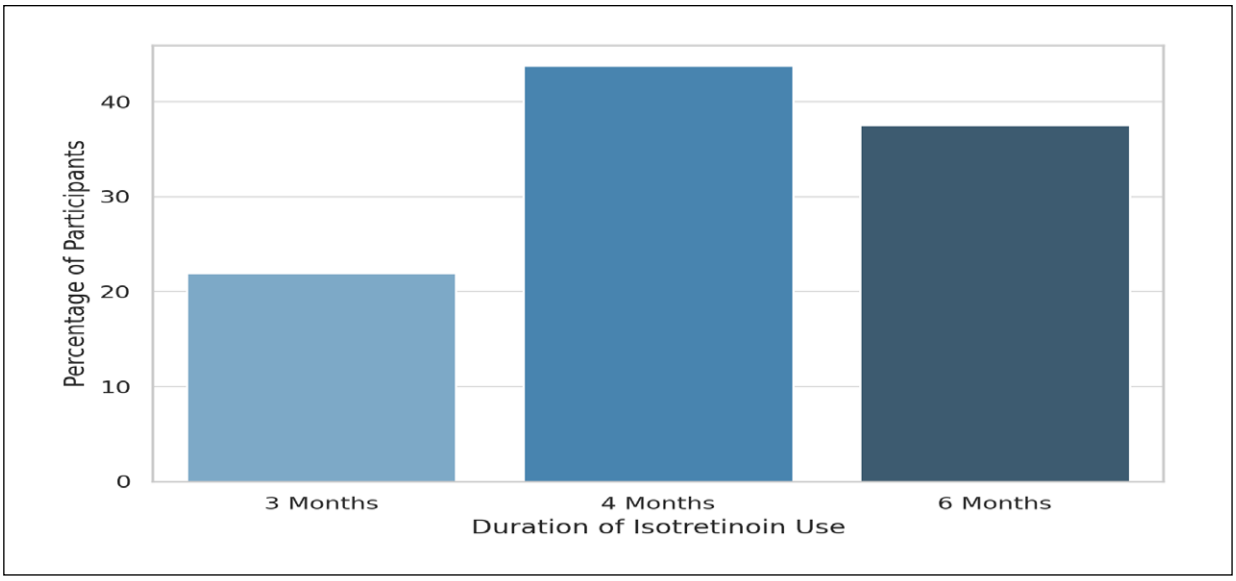

Fig. 2 Duration of isotretinoin use
Source: Own materials

Table 3. Prevalence of ocular dryness in patients using systemic isotretinoin in Iraq

Grade	Number	[%]
1	44	68.75
2	4	6.25
3	10	15.62
4	6	9.37

Source: Authors own work

Table 4. Repeated-measures ANOVA results for Schirmer's test

Source	SS	Df	MS	F	p-value	Partial η^2
Time	3,620.1	5	724.0	11.57	< 0.001	0.21
Dose	920.4	2	460.2	2.78	0.068	0.08
Gender	380.2	1	380.2	2.31	0.135	0.04
Time × Dose	2,040.6	10	204.1	3.84	0.001	0.15
Error	12,100.3	186	65.05	—	—	—

Source: Authors own work

Table 5. Ordinal logistic regression for dryness grade

Predictor	Coefficient (β)	Standard Error	p-value	Odds Ratio (95% CI)
Time (per month)	0.32	0.09	0.001	1.37 (1.14–1.64)
Dose (Ref = 20 mg)				
40 mg	0.28	0.12	0.025	1.32 (1.03–1.70)
60 mg	0.51	0.15	0.001	1.67 (1.24–2.23)
TCD (per gram)	0.04	0.03	0.145	1.04 (0.98–1.12)
Age (years)	–0.01	0.02	0.572	0.99 (0.96–1.02)
Gender (Ref = Male)	0.19	0.14	0.178	1.21 (0.91–1.62)

Source: Authors own work

Before the treatment course began, all the participants didn't experience any eye symptoms. With respect to the duration and dosage of isotretinoin usage, the majority of participants utilize systemic isotretinoin for 4-6 months (81.25%). The most frequently prescribed daily dosage was 40 mg (54.68%).

Our study had tested effect of systemic isotretinoin on ocular dryness in acne patients in Iraq, depending on the duration of isotretinoin use and TCD. The results showed that most of the participants were using 40 mg/kg/day with TCD of 4.8 gram (54.68%), and the highest TCD that was used by the participants is 10.8 gram (28.12%).

About the cease of isotretinoin use, all of the participants hadn't quit using it. This implies that the majority of people in our study kept their isotretinoin intake during the course of the research.

It emphasizes the potential ocular side effects of isotretinoin and the development of symptoms. It assures the importance of addressing and monitoring ocular dryness during systemic isotretinoin treatment to ensure the visual health and well-being of the patients. This provides evidence of the findings of Jarab et al. (2022) [17].

Basheikh et al. (2020), they observed a comparable pattern of lubricant eye drop usage during isotretinoin treatment [18]. As in our study, during the treatment of systemic isotretinoin, about 31.25% of participants had ocular dryness (grades 2, 3, 4) and they needed the lubricant eye drops, about 50% used eye drop lubricant when they needed it and 20% used eye drop lubricant most of the time. Grade 2 (30%) did not use lubricant eye drops at all.

A significant proportion of participants used lubricant eye drops; this indicates the necessity of proactive management of ocular symptoms to assure patient comfort and reduce the risk of ocular side effects during isotretinoin treatment.

The most frequent doses that cause ocular dryness among participants are 40 mg in a 4 month duration, which might be due to a known side effect of systemic isotretinoin on mucosal body membranes or unrevealed causes that need to be investigated more. Most of the participants that developed an ocular dryness had occurred during the third month due to the effect of isotretinoin on mucosal membrane with great individual variation.

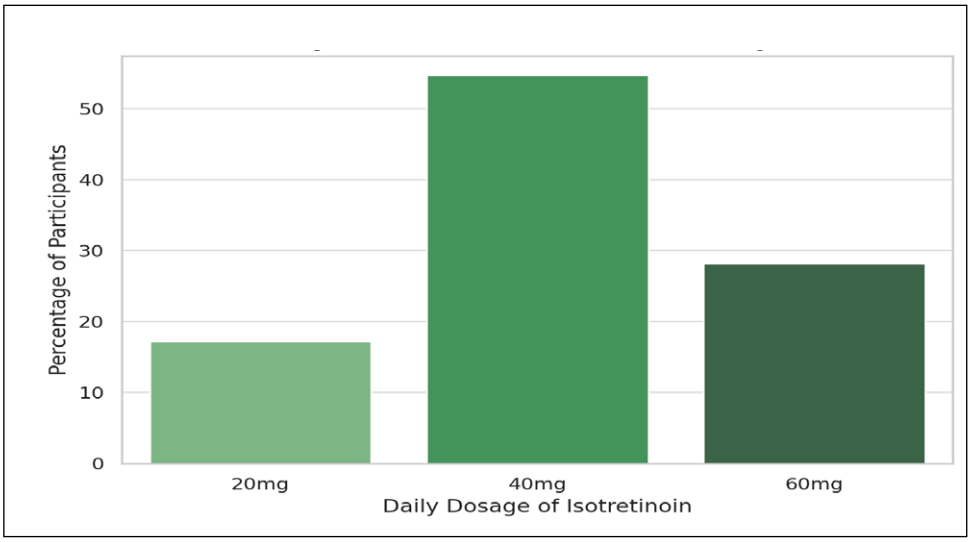

Fig. 3. Dosage distribution of isotretinoin
Source: Own materials

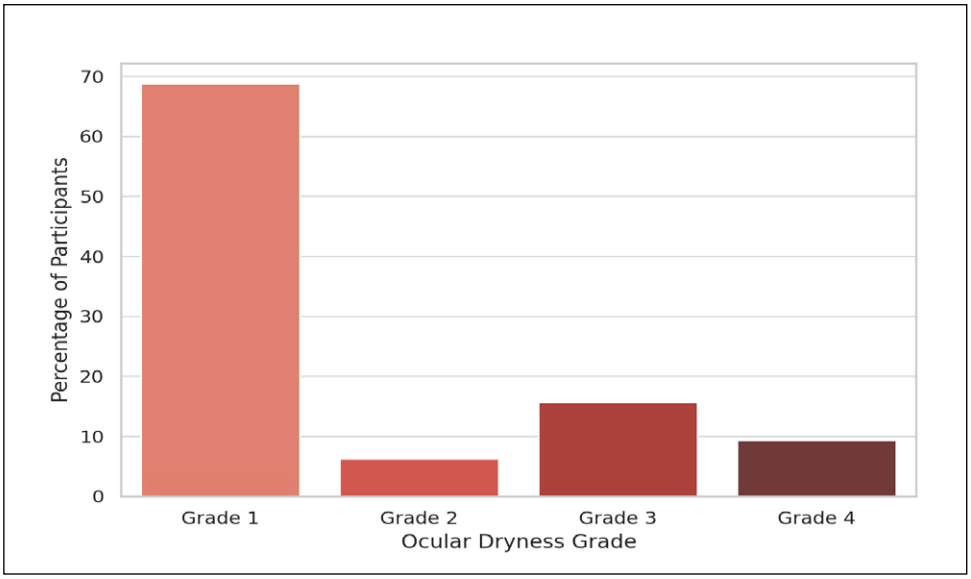

Fig. 4. Prevalence of ocular dryness
Source: Own materials

During the course of the systemic isotretinoin, we did not observe a correlation between TCD of systemic isotretinoin and ocular dryness among the participants. This could be related to the small sample size, the younger age group of the participants, and excluding the patients that already have an ocular dry eye disease.

Table 4 presents the results of the repeated-measures ANOVA on Schirmer's test scores, indicating a significant main effect with time and a significant Time × Dose interaction. The finding indicates that tear production varied significantly throughout the six months of treatment, with this variation being affected by the daily dose of isotretinoin. Especially, patients who were given higher doses experienced a more significant decrease in Schirmer's scores beginning approximately the third month, which is the time when isotretinoin's known mucocutaneous side effects spread to the ocular surface. Although the dose effect per se did not attain conventional statistical significance, the interaction term refers to the way the importance of dosage becomes greater with the passage of time. The results of this study corroborate the clinical observation that the manifestation of increased dryness frequently arises during the advanced stages of isotretinoin treatment and can potentially be alleviated through the implementation of proactive management approaches, including the earlier application of lubricating eye drops.

The lack of a significant influence of gender or age in the ANOVA analysis is consistent with previous research indicating that ocular dryness associated with isotretinoin is predominantly influenced by pharmacological factors rather than demographic variables. Despite this, the descriptive statistics showed a quantitatively greater reduction in tear production in female subjects, suggesting that although not statistically significant, female patients can somehow perceive or experience dryness differently. These findings underscore the necessity for ongoing ocular evaluation independent of patient demographics, particularly when high daily doses of isotretinoin are prescribed.

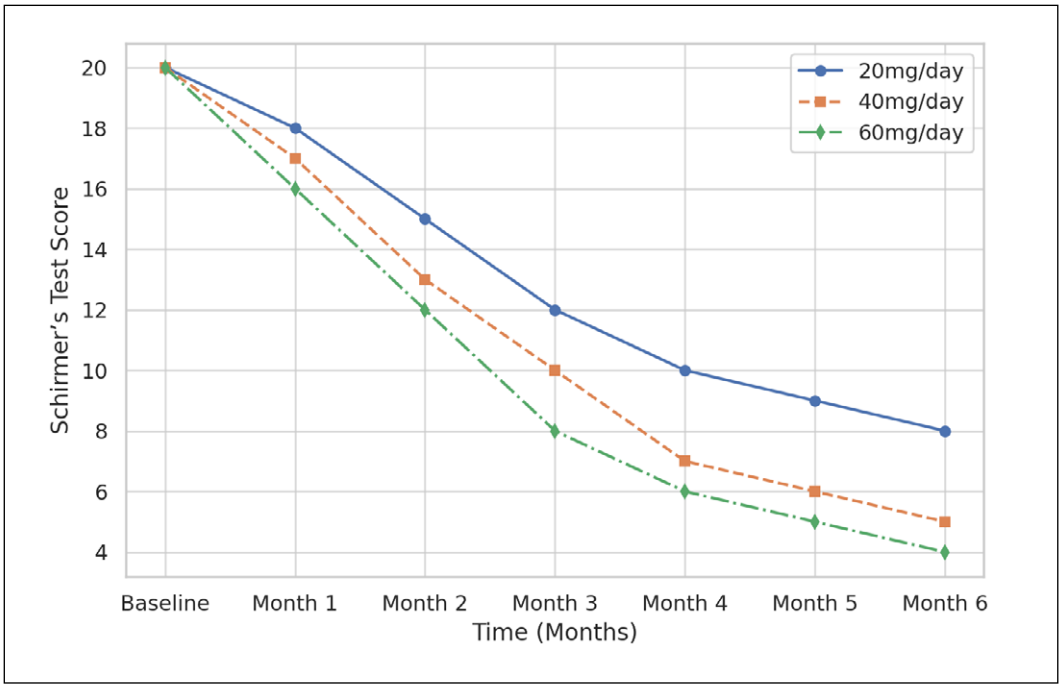

Fig. 5. Schirmer's test scores over time by dose group
Source: Own materials

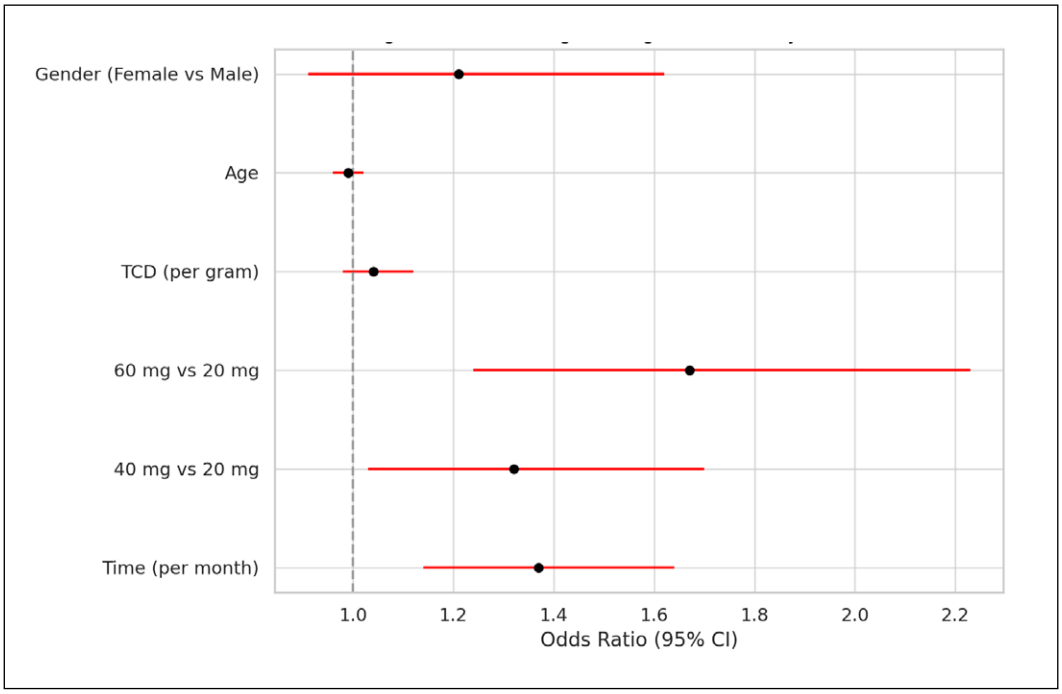

Fig. 6. Ordinal logistic regression for dryness grade
Source: Own materials

Table 5 presents the ordinal logistic regression, which models dryness grade (ranging from mild to severe) as the dependent variable. The positive coefficient sign for time shows that with every month increase in therapy duration, patients were more likely to move to a higher dryness severity grade. Furthermore, the dose-response effect was more pronounced in this model than in repeated-measures ANOVA: both 40 mg and 60 mg daily doses were associated with a significantly higher probability of allocation to a more dryness category than the 20 mg daily dose. From a clinical standpoint, this assists in informing that increased isotretinoin doses heighten the risk of more severe ocular dryness, substantiating individualized dosing schedules and frequent monitoring.

Importantly, total cumulative dose (TCD) was not statistically significantly associated with dryness grade. While TCD is a significant variable for the majority of side effects, there is a chance that regimens with shorter duration and greater dose are more effective on the ocular surface compared to the sum of isotretinoin over time absorbed. Similarly, the lack of a major effect of gender and age in this model suggests that dryness severity is mainly driven by the dosage-time interaction, and not by demographic characteristics alone. This finding also supports the need for clinicians to prioritize ocular

health assessments and patient counseling, especially when prescribing isotretinoin in moderate-to-high doses for extended durations.

CONCLUSIONS

In our study, we found that the prevalence of among the participants that had ocular dryness during the course of systemic isotretinoin is about 30% in Iraqi patients. These findings highlight the significance of evaluating and tracking the condition of the eye surface during isotretinoin treatment on an individual basis. This research contributes to being aware of the effects of isotretinoin use on the health of the ocular surface. However, no significant correlations were seen between gender, dosage, duration, TCD, and age with ocular dryness. Although we exclude those patients that have ocular eye disease, it's important to discover the effect of isotretinoin on their ocular health. Additional research is required to verify and expand upon those findings, with an emphasis on diverse populations and larger sample sizes.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 25.12.2025
ACCEPTED: 10.07.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

The presence of bacteria on long, artificial or polished native nails and risk of surgical site infection in patients who wore these nails

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ABSTRACT

Aim: To determine the bacterial flora present on- and under long, artificial or polished native nails of patients who undergo elective surgery due to common hand diseases and if this poses the risk of surgical site infection.

Materials and Methods: Forty-six female patients having long, artificial or polished native nails were operated on. In 10 of these patients, a swab was taken from the surface of the nails and from under the nails prior to- and after the operation. It was assessed whether there were infections of the operated site in any of the patients.

Results: Before hand preparation cultures were positive in all 10 patients and the most common organisms were coagulase-negative *Staphylococci*. Post-preparation cultures were positive also in all 10 patients with the same organism being the most common. However, the number of organisms in post-preparation samples was significantly lower, than in pre-preparation. No one case of surgical site infection was noted in 46 patients in the study at 1 month assessment.

Conclusions: The bacterial flora present on and under long, artificial or polished native nails is mostly composed of natural skin microbiota. Presence of bacteria on and under nails does not increase the risk of surgical site infection.

KEY WORDS: surgical site infection, artificial fingernails (tips), nails contamination, hand preparation, bacteria culturing

Wiad Lek. 2026;79(8):1741-1745. doi: 10.36740/WLek/222502 DOI

INTRODUCTION

The use of artificial nails (so-called tips) and polished, native nails has become a popular trend among women, including those working in health care - nurses and doctors (Fig. 1, Fig.2). It is unclear whether wearing tips puts patients at increased risk of infection. The results of some studies indicate that the number of bacterial colonies on- and under artificial nails is higher than on- and under natural ones. The same is true of long and polished native nails [1-5]. In addition, they have been shown to worsen the quality of hand disinfection and cause more frequent tearing of the gloves when put on [5, 6]. However, results of some studies do not acknowledge this risk [7]. Infectious bacteria can be of self-origin (found on and under the nail plate) or be transmitted from one patient to another through the nails of the medical staff. However, there is no information in the literature about the risk of surgical site infection (SSI) in a patients operated on due to hand disease or injury, who wear tips or long, polished native nails.

AIM

The aim of the study was to determine the bacterial flora present on- and under long, artificial or polished native nails, as well as to assess the risk of surgical site infection in patients wearing these nails, who undergo elective surgery due to common hand diseases.

MATERIALS AND METHODS

In 2025, 988 patients were operated on in the author's institution due to common hand diseases such as carpal canal syndrome, trigger finger, benign hand tumour, wrist or finger ganglion, Dupuytren's disease and de Quervain's disease. All surgeries were performed in an out-patient setting (one-day care), in the procedure room at the surgical ward, under WALANT or local anaesthesia. Forty-six female patients (4,6%) were identified who wore tips (n=17) or had their own long, polished nails (n=29) that met the criteria for inclusion in the study. Twenty-six pa-

Fig. 1. Artificial nails (tips)
Picture taken by the authors

Fig. 2. Polished, native nails
Picture taken by the authors

tients (56%) were operated on due to carpal tunnel syndrome, 10 due to trigger digits (22%), five due to benign finger tumours (11%) and remaining five (11%) due to Dupuytren's disease, wrist ganglions or de Quervain's disease. In 10 of these patients, a swab was taken from the surface of the nails and from under the nails. The swab was taken twice, before hand disinfection for surgery and after surgery. The biological material was then tested in a microbiology lab for the type of bacterial flora and its abundance (few colonies or numerous colonies) in each of the samples. All patients enrolled in the study were then evaluated at 1 month post-surgery for possible surgical site infection. The results obtained in these stages of the study are the basis for this assessment.

ETHICS

This work complies with the principles of the Declaration of Helsinki.

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

Types and abundance of organisms found in swab samples (Table 1).

Before hand preparation (disinfection) cultures were positive in all 10 patients. The most common bacteria cultured from pre-preparation samples were coagulase-negative *Staphylococci*, followed by, *Rothia* and *Bacillus* species. Post-preparation cultures were positive also in all 10 patients. The most common bacteria culture post-preparation were also coagulase-negative *Staphylococci*. The number of organisms in post-preparation samples was significantly lower, than in pre-preparation (Table 1), but there was no case of total bacteria eradication from the nails or under the nails following disinfection. Among the 10 patients who were sampled for bacteriological examination, one case of the pathogen - *Staphylococcus aureus* - was found in the study in pre-preparation sample. This organism was not present in a post-preparation sample (it has been eradicated).

Surgical site infections after 1 month. No one case of SSI was recorded in 46 patients in the study at 1 month assessment.

Table 1. Types of organisms found in swab samples in 10 patients in the study. Markings: (+) few colonies, (+++) numerous colonies

Name of the organism	Number of positive samples	Colonies of organisms volume in the sample	
		Pre hand disinfection	After hand disinfection
Staphylococcus epidermidis	8	6 (+++) 2 (+)	6 (+)
Staphylococcus pasteuri	7	2 (+++) 5 (+)	1 (+++) 4 (+)
Staphylococcus warneri	9	3 (+++) 6 (+)	1 (+++) 5 (+)
Staphylococcus haemolyticus	8	1 (+++) 7 (+)	1 (+++) 3 (+)
Staphylococcus aureus MSSA	1	1 (+)	(-)
Rothia kristinae	6	1 (+++) 5 (+)	4 (+)
Rothia amarae	5	2 (+++) 3 (+)	1 (+)
Bacillus species	5	2 (+++) 3 (+)	3 (+) 1 (+++)

Source: compiled by the authors of this study

DISCUSSION

There is no information in the literature whether wearing tips or long, polished native nails poses a risk of SSI after operations for hand diseases and injuries. About 10-15 years ago, it was recommended that patients cut long nails, wash off varnish and remove tips before hand surgery [8]. Later, no such requirements were imposed, but this change has not been preceded by official recommendations or scientific studies, but has occurred gradually and spontaneously. While there is a lot of information in the literature about the risk of transmission of bacteria on tips and long nails worn by healthcare workers, particularly nurses and doctors, there is practically no knowledge about it in patients. Therefore, the results of this study are in the first scientific evidence on this issue. Our results show that wearing tips and long, polished nails by patients who undergo surgery due to common hand diseases does not pose a risk of SSI, although bacteriological testing has shown the presence of various organisms on- and under the nails/tips. However, the vast majority of these organisms are physiological flora present on the hands, and only in one case has the pathogen been found - *Staphylococcus aureus*. The results of our study also indicate that standard hand preparation before surgery reduces, but does not eliminate bacteria colonies from nails and tips, but this does not affect the risk of SSI.

The authors did not find any single article in the literature presenting the results of research similar to those presented in this work. The next paragraph is a review of the current literature on the presence of pathogens on nails and tips among healthcare professionals and the associated risks to patients.

Pottinger et al. (1989) reported results of the study comparing the effect of handwashing on presence of organisms on fingertips in women wearing tips vs native nails. Cultures were obtained before and after handwashing from the fingertips of 56 nurses wearing tips nails and 56 nurses with native nails. Results of the study showed that there was statistically significantly more colonies of gram-negative rods cultured from the fingertips with artificial nails than from natural nails, both before and after handwashing. However, washing resulted in significant reduction of number of bacterial colonies present on fingertips. There were no significant differences in carriage of gram-positive cocci or normal flora. The authors conclude that health care workers who wear tips should consider the potential risk of increased carriage of gram-negative rods [1].

Hedderwick et al. (2000), reported results of the study comparing the presence and quantity of potential pathogenic organisms on artificial vs native nails in healthcare workers. Nail and subungual surfaces were swabbed. Thirty persons who wore permanent acrylic artificial nails were compared with 12 controls who had native nails. Organisms such as *Staphylococcus aureus*, gram-negative *bacilli*, *enterococci,* and *yeasts* were considered to be potential pathogens. Results of the study showed that tips were more likely to retain pathogens, especially gram-negative *bacilli* and *yeasts,* than native nails. Colonization of the tips increased over time: the longer they were worn, the more likely that a pathogen was isolated. The authors conclude that current recommendations restricting wearing of artificial fingernails by healthcare workers appear justified [2].

McNeil et al. (2001) reported results of the study undertaken to determine differences in microflora on the nails of health care workers wearing tips compared with control workers with native nails and to assess the effect on these microflora of hand cleansing with antimicrobial soap or alcohol-based gel. Cultures were obtained from 21 persons wearing artificial nails and 20 control persons before and after using antimicrobial soap or alcohol-based gel. Results of this study showed that statistically significantly greater number of healthcare workers with artificial nails had a pathogen (gram-negative *bacilli, Staphylococcus aureus,* or *yeasts*) isolated before cleansing, compared with controls. Similarly, statistically significantly more persons with tips than controls had pathogens remaining after hand cleansing with soap or gel. Of persons wearing tips, only 11% cleared pathogens with soap compared with 38% with gel. Of persons with native nails only 14% cleared with soap compared with 80% with gel. The authors conclude that artificial acrylic fingernails could contribute to the transmission of pathogens, and their use by healthcare workers should be discouraged [5].

In contrast, Arreba et al. (2025) in their recent study showed that compared with native and not polished nails, gel polished nails were not associated with a higher bacterial burden within 3 weeks of application, and even had a significantly lower bacterial burden before hand washing on day 21 [7]. However, this study is the only one among the vast majority emphasising the risk of transmission of bacteria through the long nails and tips of medical personnel [9, 10].

LIMITATIONS

The first is the small number of patients whose samples were taken for bacteriological examination. More reliable results would require testing about 30 subjects, so our results should be considered a preliminary report. A larger number of studies would likely reveal a greater spectrum of bacteria found under the nails. However, lack of SSI in the whole group of 46 patients suggests that the risk of transmission of bacteria from under the nails to the operated site is minimal.

Another problem may be the issue of liability in the event of SSI in a patient with long nails or wearing tips. Lack of evidence in the literature of a higher risk of infection in these cases and the lack of official recommendations on how to proceed in such cases seems to indicate that the risk of the court finding that the infection was the fault of the surgeon is unlikely.

CONCLUSIONS

The bacterial flora present on and under long, artificial or polished native nails is mostly composed of natural skin microbiota. Presence of pathogens is incidental. Presence of bacteria on and under long, artificial or polished native nails does not increase the risk of SSI after elective hand operations. Further studies based on a larger group of patients are required to make conclusions about the risk of SSI in patients wearing long nails an tips more reliable.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 12.03.2026
ACCEPTED: 26.05.2026

CREATIVE COMMONS 4.0

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ORIGINAL ARTICLE

Wound infection in modern war

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ABSTRACT

Aim: To draw the medical community's attention to and outline the main causes of the rapid increase in antibiotic resistance among microorganisms in modern war.

Materials and Methods: Based on the microbiological examination of 2,288 samples from combat wounds, multidrug-resistant Gram-negative pathogens were found to predominate, particularly Klebsiella pneumoniae, Acinetobacter spp., and Pseudomonas aeruginosa, which were resistant to most antibiotics. The microbial load in all wounded patients exceeded 10^5 CFU/g.

Results: The main factors contributing to the development of wound infection are the nature of injuries caused by modern weapons and the characteristics of the wound tract, tissue ischemia, impairment of local and systemic anti-infective defenses, and delayed medical care. In addition to clinical signs, the diagnosis of wound infection requires microbiological identification of the causative pathogens, assessment of laboratory markers, and imaging methods. The leading role of surgical debridement in the treatment of infected wounds and the importance of appropriate antibiotic therapy guided by antimicrobial susceptibility are emphasized. The effectiveness of negative-pressure wound therapy and local antibiotic administration is reviewed. The biological, medical, and social causes of antibiotic resistance are identified, and promising alternative treatment approaches, including bacteriophages and probiotics, are outlined.

Conclusion: The management of wound infection requires a comprehensive approach combining surgical methods, appropriate antibiotic therapy, and innovative technologies, which is essential for improving treatment outcomes in wounded patients.

KEY WORDS: wounds, wound infection, multidrug-resistant microorganisms, antibiotic therapy, bacteriophages, probiotics

Wiad Lek. 2026;79(8):1746-1751. doi: 10.36740/WLek/235899 DOI

INTRODUCTION

Throughout human history, infection and trauma have remained two major problems causing suffering, claiming thousands of lives, but during wars they have often reached catastrophic «Black Death» - like proportions. Today, the life of a wounded person is threatened not only by weapons but also by an invisible enemy – bacteria that cause wound infection with severe consequences. In 2022, Petfield JL et al. published the results of the Trauma Infectious Disease Outcomes Study (TIDOS), which included 826 patients who sustained extremity injuries during the wars in Iraq and Afghanistan. Wound infection was diagnosed in 29% of these patients, and 28% of them experienced recurrent infectious complications [1]. Risk factors for infectious complications included injury severity, a blast mechanism of injury, and extensive soft-tissue damage. Mende K et al. (2022) emphasized that the treatment of wound infections after combat trauma is complicated by polymicrobial wound flora with antimicrobial resistance [2].

In the current war in Ukraine, suppurative and septic complications of gunshot wounds occur in 50-75% of cases [3].

The 2025 WHO report stated that between 2018 and 2023, bacterial resistance to antibiotics increased by more than 40%, and approximately one in six laboratory-confirmed bacterial infections was resistant to available antibiotics [4].

AIM

To draw the medical community's attention to and outline the main causes of the rapid increase in antibiotic resistance among microorganisms in modern war.

MATERIALS AND METHODS

Microbiological examination of swabs from infected combat wounds in patients treated at a military field hospital and the Military Medical Clinical Center of

the Western Region revealed polymicrobial flora consisting predominantly of staphylococci, streptococci, and Escherichia coli that were susceptible to many antibiotics. However, administration of these antibiotics did not improve the clinical course of the wounds. Therefore, microbiological examination of biopsy specimens from infected wounds was performed and revealed other predominant pathogens. Among 2,288 biopsy specimens obtained from infected combat wounds in patients who had remained at previous levels of medical care for more than 48 hours before admission to the Military Medical Clinical Center of the Western Region, multidrug-resistant microorganisms were isolated from 88.9% of the wounded patients. The predominant isolates were Klebsiella pneumoniae (34.9%), Acinetobacter spp. (27.8%), and Pseudomonas aeruginosa (12.8%). These microorganisms were resistant to most antibiotics but remained susceptible to colistin and tigecycline in 95% of cases. Other isolates recovered from infected wounds included Enterococcus faecalis in 9.4%, Staphylococcus aureus in 8.7%, and Escherichia coli in 4.5% of cases. The microbial load in all wounded patients exceeded 10^5 CFU/g. Shrapnel wounds were present in 75% of patients, bullet wounds in 14.3%, and mine-blast injuries in 10.7%. Shrapnel wounds were multiple and involved the extremities and trunk. After specimens had been collected for bacteriological examination, all wounded patients with purulent wound complications underwent secondary surgical debridement.

ETHICAL APPROVAL

Protocol No. 9, dated December 19, 2022, and Protocol No. 11, were approved by the Committee on Bioethics of Scientific Research, Experimental Development and Scientific Works of LNMU

RESULTS AND DISCUSSION

Objective factors contributing to purulent complications of combat wounds include the nature of injuries caused by modern weapons and the specific morphology of the wound tract in gunshot, shrapnel, and mine-blast injuries. A gunshot wound is always initially contaminated by microorganisms that enter the wound with the rarefied air which, according to the laws of aerodynamics, follows the bullet or shell fragment. The zone of primary traumatic necrosis and the subsequently formed zone of secondary traumatic necrosis provide favorable environments for the development of wound infection.

Injuries caused by modern high-energy weapons produce extensive defects of the skin and underlying tissues, with foreign bodies, blood clots, and devitalized tissues within the wound, while prolonged tourniquet application and hypotension cause ischemia of the tissues surrounding the wound. These factors weaken the local anti-infective defenses and promote the proliferation of microorganisms that have entered the wound and the development of inflammation. In addition, blood loss, traumatic shock, and exhaustion reduce nonspecific resistance and immune reactivity, thereby impairing the body's systemic defenses against infection. Diseases associated with low serum protein levels and combined combat injuries, such as a gunshot wound accompanied by thermal injury to the skin, also contribute to the development and spread of wound infection.

A major factor in the development of wound infection is delayed provision of specialized medical care because the wounded person cannot be evacuated in a timely manner due to an unfavorable operational and tactical situation at the front.

Some causes of wound infection in wounded patients are potentially preventable. These include failure to apply an initial dressing after injury, limb ischemia caused by tourniquet application without appropriate indications, inadequate primary surgical debridement, primary closure of a gunshot wound, uncorrected blood loss, and inappropriate antibacterial therapy. The objective, organizational-tactical, and avoidable causes of infectious complications of combat wounds in modern warfare were described in our previous publication [5].

Clinical signs allow the diagnosis of infectious complications of the wound-healing process, while ultrasonography can visualize the spread of inflammation within the tissues, heterogeneous fluid collections, and cavities containing purulent collections extending along tissue planes. Microbiological identification, histological examination, and assessment of laboratory markers of infection are required for the qualitative and quantitative characterization of wound infection and for monitoring its course.

For reliable microbiological identification of the pathogens causing wound infection, researchers recommend obtaining at least five biopsy specimens from different areas of the wound using separate sterile instruments. If the same pathogen is identified in two specimens, the reliability of the result is >68%; if it is identified in three specimens, the reliability is >84% [6].

The main laboratory markers of infection are C-reactive protein (<1.0 mg/L indicates the absence of

infection, whereas >8 mg/L indicates significant infection), the absolute lymphocyte count (<1,500/μL indicates immune deficiency and a risk of infection), hemoglobin (a level >10 g/dL is required for wound healing), and serum albumin (3.5 g/dL or lower indicates a reduced ability of the wound to clear purulent exudate).

Radiographic signs of deep wound infection also have diagnostic value. These include increased volume and density of the tissues in the affected area, visualized as widening of the soft-tissue shadows, loss of clear boundaries between individual muscles and other structures, bone lysis at the fracture site, and sequestration.

Surgical debridement remains the main component of contemporary treatment of soft-tissue and bone wound infections. Because this procedure is performed for complications of the wound-healing process, that is, for secondary indications, it should be considered secondary surgical debridement. Its objectives are the excision of purulent and necrotic tissues, opening of purulent wound pockets, and creation of conditions for external drainage of wound contents. When wounded patients were admitted to our institution, biopsy specimens were obtained from the wound for microbiological examination before debridement; the surgical procedure was then performed, and the wound was thoroughly and repeatedly irrigated with an antiseptic solution. A single operation frequently failed to eliminate the purulent and necrotic process; therefore, serial surgical debridements were performed. The number of such procedures for an individual wounded patient depended on the course of the wound-healing process and ranged from 2 to 10 in our patients. Their timing and frequency depended on the changes in the wound. It should be emphasized that when sequestra and bone necrosis were present, these areas were removed, while circumferential bone involvement required segmental resection. The microbial spectrum of infectious complications of combat wounds in our patients was consistent with the results of studies conducted at the National Military Medical Clinical Center and Danylo Halytsky Lviv National Medical University. According to published data, Gram-negative microorganisms caused infectious complications in 79-80% of gunshot wounds; Klebsiella pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa accounted for 71% of isolates and were resistant to most antibacterial agents [7].

Negative-pressure wound therapy, which was used in 91.1% of our patients, helped clear purulent exudate from the wound. This method has proven effective and has become widely used in clinical practice. The vacuum dressing was changed every 2-3 days. Negative-pressure wound therapy shortened the time to wound clearance in our patients by 15-17 days. However, if no improvement in the wound condition was observed after two vacuum dressing changes, further negative-pressure wound therapy was discontinued. This occurred in wounded patients with adherent purulent and necrotic masses, which were removed by daily serial surgical debridement.

Systemic antibiotic therapy depends on the specific clinical situation and should be administered according to the antimicrobial susceptibility of the microorganisms. The severity of the infectious complication, the patient's general condition and immune status, and the presence of implanted devices must also be considered. According to the recommendations of the international consensus group on fracture-related infection, antibiotic therapy should last 1-2 weeks for superficial infection, 4-6 weeks for deep infection, and 12 weeks in the presence of internal fixation implants [8]. After microbiological results have been obtained, the authors recommend switching to oral antibiotics on days 7-10 because no difference in clinical effectiveness has been established between parenteral and oral antibiotic administration. The multicenter randomized controlled VANCO trial statistically demonstrated that local antibiotic therapy has advantages over systemic therapy for infection at the fracture site [9]. This is explained by the high antibiotic concentration achieved at the infected fracture site, minimal systemic toxicity, independence from local blood flow, and protection of the implant and devascularized bone against biofilm formation. Other researchers have also reported the effectiveness of local antibiotic therapy for soft-tissue and bone wound infections [10, 11]. The authors consider the combination of systemic and local antibiotic administration to be most effective because systemically administered antibiotics reduce the number of pathogens entering the body but do not provide effective protection against colonization due to their limited ability to penetrate bone.

Antibiotic-loaded cement spacers have been widely introduced into practice to provide prolonged local antibiotic delivery and are implanted into the wound tract after surgical debridement. In infected wounds with bone defects, the two-stage Masquelet technique is effective. During the first stage, after wound debridement, the fracture is stabilized with an external fixation device, and the bone defect is filled with an antibiotic-loaded cement spac-

er. Given the multidrug resistance of the flora in wounded patients with combat-related extremity trauma we used, as recommend researchers, adding 2 g of vancomycin per batch of bone cement for Gram-positive flora and 5 million units of colistin plus 2 g of meropenem per batch of bone cement for Gram-negative flora. Systemic intravenous antibiotic therapy is administered according to antimicrobial susceptibility for 10 days, followed by oral therapy for 30 days [12, 13].

Analysis of the causal relationships underlying complications of the wound-healing process caused by multidrug-resistant infection allowed us to identify three main causes of microbial resistance to antibiotics: the biological properties of bacteria, medical factors, and social factors.

Modern microbial pathogens are characterized by biofilm formation in the wound within 48 hours, creating a mechanical barrier to antimicrobial agents. In addition, microorganisms possess enzymes capable of degrading antibiotics.

Medical factors include over-the-counter sale of antibacterial agents, their inappropriate use and short courses of antibiotic therapy, as well as breaches of aseptic and antiseptic practices under combat conditions.

Social causes of microbial resistance to antibiotics include insufficient public education regarding antibiotic treatment and wartime population movements and the concomitant spread of resistant bacteria. In addition, microbial mutations are influenced by medications, including diuretics, proton-pump inhibitors, ibuprofen, and statins.

Because of the rapid global increase in microbial resistance to antibiotics, alternative technologies for controlling wound infection are being investigated. Bacteriophages – viruses that infect bacteria – have been known for more than 90 years. They spread within biofilms and destroy bacteria. Their pharmacokinetics remain insufficiently studied; however, published data and our observations indicate that they are effective when combined with antibiotic therapy. No contraindications or adverse reactions to phage therapy have been identified [14, 15].

One novel approach to protecting wounds from colonization by pathogenic microorganisms is the use of probiotics, which the International Scientific Association for Probiotics and Prebiotics defines as «live microorganisms that, when administered in adequate amounts, confer a health benefit on the host» [16, 17]. In particular, probiotic Bacillus bacteria disrupt and prevent the formation of pathogenic microbial biofilms. According to published data, they are nonpathogenic to humans and are not antagonistic to the normal human microbiota; they restore the intestinal microbiome and form a probiotic film that protects the wound surface from pathogenic microorganisms. Bacillus bacteria produce bioactive substances with antibacterial activity lasting 48 hours. Combining topical and oral administration of Bacillus with antibiotic therapy increases the effectiveness of managing purulent infection and prevents antibiotic resistance and intestinal dysbiosis [18, 19].

Our experience with the use of bacteriophages and Bacillus bacteria for the treatment of wound infection in wounded patients will be reported in our subsequent publications.

CONCLUSIONS

Injuries caused by modern high-energy weapons are complicated by wound infection due to multidrug-resistant microorganisms, representing a major challenge for the entire medical community.

Surgical wound debridement remains the principal method for preventing and controlling wound infection.

Replacement of lost blood, adequate oxygenation of injured tissues, and appropriate nutritional support for the wounded patient are essential for improving the body's systemic resistance to infection.

Antibiotic therapy should be appropriate, include both local and systemic administration, be guided by the antimicrobial susceptibility of the microorganisms, and be continued for a sufficiently prolonged course.

Combining antibiotic therapy with alternative methods for controlling multidrug-resistant infection may improve treatment outcomes in this complex category of patients.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 12.03.2026
ACCEPTED: 26.05.2026

CREATIVE COMMONS 4.0

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ORIGINAL ARTICLE

A comparative study of low-level laser therapy combined with drugs versus drug therapy alone in the management of myogenic TMJ pain

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ABSTRACT

Aim: To compare the effect of low-level laser therapy combined with pharmacotherapy (naproxen + orphenadrine with paracetamol (myogesic)) and pharmacotherapy alone in treating myofascial pain related to temporomandibular joint.

Materials and Methods: Twenty-four participants with myofascial pain related to TMJ diagnosed according to diagnostic criteria DC/TMJ are randomly divided into two groups (n=12); Group1 received naproxen 500mg twice a day and myogesic three times a day for 21 days, Group 2 received Low-Level Laser Therapy for nine sessions three sessions a week with a diode laser with dual-wavelength with the same drugs as group1. Measures of myofascial pain during the function were evaluated at baseline, after 10 days, at the end of treatment, and 3 months after the end of treatments using the visual analog scale VAS, which has scores from zero (no pain) to ten (sever pain) also maximum mouth opening was measured in each session.

Results: VAS scores decreased in both groups but significantly more in Low-Level Laser Therapy with pharmacotherapy group at 10 days, 21 days, and 3 months ($p < 0.05$). Maximum mouth opening highly improved in Group 2 with significantly more significant gains in Low-Level Laser Therapy group at all follow-up points except baseline ($p < 0.05$).

Conclusions: These results indicate that Low-Level Laser Therapy with pharmacotherapy was more effective than pharmacological therapy in decreasing pain and improving jaw function in patients with TMJ-related myogenic pain.

KEY WORDS: temporomandibular joint, naproxen, Low-Level laser therapy, myogesic, myogenic pain

Wiad Lek. 2026;79(8):1752-1759. doi: 10.36740/WLek/225695 DOI

ABBREVIATIONS

TMD: Temporomandibular Disorders
TMJD: Temporomandibular Joint Disorder
LLLT: Low-Level Laser Therapy
TMJ: Temporomandibular Joint
DC: Diagnostic Criteria
DC/TMD: Diagnostic Criteria for Temporomandibular Disorders
MMO: Maximum Mouth Opening
VAS: Visual Analog Scale
MMD: Masticatory Musculature Disorder

INTRODUCTION

Temporomandibular disorders (TMDs) are an umbrella term encompassing disorders of both the temporomandibular joint disorder (TMJD) and masticatory musculature disorder (MMD) [1], TMDs include both painful and painless disorders that involve masticatory muscle and TMJ and its surrounding structures with prevalence to masticatory disorders, given that the temporomandibular joint TMJ is used approximately 1500-2000 times a day, the discomfort caused by symptomatic TMDs can significantly impair daily activities [2]. Temporomandibular pain commonly manifests in the preauricular region, masticatory muscles, or temporomandibular joint (TMJ). Patients frequently describe symptoms besides localized discomfort, such as facial pain, headaches, and cervical discomfort. Jaw dysfunction often accompanies these complaints, including restricted mouth opening capacity, mechanical locking in either the open/closed position, or joint noises like clicking, popping, or crepitus during movement [3]. The difficulty of treating TMD arises from a poor understanding of the aetiology and pathogenesis of this condition. Understanding the aetiology of TMDs is very important in identifying and avoiding potential pathologic factors [4]. Diagnosing TMD has become more accurate with modern tools like the Diagnostic Criteria for TMD (DC/TMD). These guidelines are trusted for identifying the

most common TMD types and help doctors, dentists, and therapists work together effectively. The system groups TMD into two main categories:

Pain-related issues: Muscle pain (myalgia), joint pain (arthralgia), and headaches linked to TMD

Non-painful problems: Jaw disc misalignment, joint wear (degenerative disease), and unstable jaw movement (subluxation) [5], (DC/TMD) was created to standardize diagnoses based on epidemiological studies from multiple centers [6]. Because the causes and mechanisms of TMD are complex, many different treatment approaches have been used to manage it. These include acupuncture, bite splints, physical exercises for the jaw, physical therapy, posture correction, psychological support, medication, TENS (transcutaneous electrical nerve stimulation), and behavioral therapies [7]. Given the complex causes of TMD, current research supports starting with non-invasive, team-based care combining self-care, behavioral techniques, physical therapy, and medication [5]. Among these approaches, LLLT is sometimes used to ease symptoms and improve jaw function. LLLT uses a gentle laser with minimal energy output that does not raise skin temperature. Its effects come from light absorption, typically wavelengths between 630–1300 nanometers. Though the exact mechanism is not fully understood, LLLT is thought to reduce pain and inflammation by stimulating tissues [8]. Specialized lasers (like diode lasers at 630–670 nm, 800–830 nm, or 900–940 nm) deliver red or near-infrared light at safe energy levels (up to 500 mW). These tools promote healing and reduce swelling through biostimulation (using 2–4 Joules/cm^2) or pain relief (using 10–12 Joules/cm^2) [9]. LLLT used for many purposes. For example, it helps faster healing after tooth extraction by reducing the chance of infection, lowering pain, and decreasing problems that may happen after the procedure [10]. LLLT also speeds up tooth movement during orthodontic treatment [11], supports better healing of episiotomy wounds [12], and helps treat long-lasting wounds, especially in patients who cannot have surgery due to health issues like epilepsy or chronic hepatitis [13]. Another treatment option is using medications. Several types of drugs can help manage temporomandibular disorders (TMD). These medicines are usually not used alone but are often combined with other treatments, such as mouth splints or physical therapy [14]. Medication is often the first step in treatment and is commonly used alongside non-surgical methods. Different drugs can be used for TMD, including anti-inflammatory medicines (NSAIDs), muscle relaxants, and steroids. These drugs often work better when used together, helping reduce symptoms and stop the condition from worsening. Naproxen is one of the most used NSAIDs for TMD. It has been shown to lessen pain and improve jaw movement [15]. Muscle relaxants are also used often in TMD treatment, as they help reduce the extra activity in the chewing and neck muscles. According to Shaffer et al., "physical therapy is the preferred conservative approach for treating TMD" [16], while pharmacological therapy remains a first-line treatment for myogenic TMJ disorders, its efficacy may be limited when used in isolation. Low-level laser therapy has shown promise in enhancing tissue healing and reducing pain. However, there is still a lack of high-quality comparative studies evaluating the combined use of LLLT and drugs versus drug therapy alone. This study seeks to address this gap by investigating the potential synergistic effects of these two approaches in the management of myogenic TMJ pain.

AIM

To compare the effect of low-level laser therapy combined with pharmacotherapy (naproxen + orphenadrine with paracetamol (myogesic)) and pharmacotherapy alone in treating myofascial pain related to temporomandibular joint.

MATERIALS AND METHODS

STUDY DESIGN

The present research was undertaken as a clinical trial to compare the effectiveness of different modalities in managing myofascial pain associated with TMJ.

PARTICIPANTS

The study recruited twenty-four myogenic patients referred for management of TMJ pain according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) in the age group 20-40.

INCLUSION CRITERIA

Patients with a history of pain in the TMJ of more than four weeks duration, a TMD diagnosis of myofascial pain as defined in the DC/TMD.

EXCLUSION CRITERIA INCLUDED

Patients younger than 18 or older than 40, patients with OPG showed joint degeneration, TMJ arthroscopy in the last four months, autoimmune disease, contraindications to drugs included in the study, or with trauma to TMJ area, and pregnant women are excluded.

Fig. 1. Quick Lase Soft Tissue Diode Laser device used in the LLLT sessions
Picture taken by the authors

Fig. 2. A patient undergoing low-level laser therapy targeting TMJ-related tender points
Picture taken by the authors

BASELINE ASSESSMENT

Pain was measured using a Visual Analog Scale (VAS), where zero was defined as the absence of pain and 10 was described as the severity of pain that can be imagined. Pain levels were documented at the baseline prior to treatment while MMO was measured by the interincisal distance were40 mm and more count for normal mouth opening without restriction.

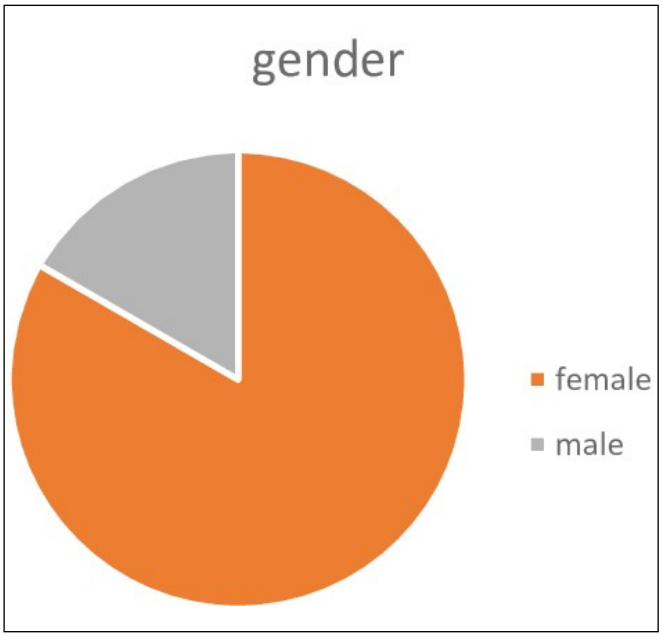

Fig. 3. Gender Distribution
Picture taken by the authors

TREATMENT PROTOCOL

The clinical diagnosis was made using the DC/TMD criteria, based on the patient's history and examination findings. Panoramic X-rays were taken to rule out major bone changes in the jaw joints and to exclude any dental conditions that could be causing the symptoms. However, the radiographs were not used for diagnosing TMD, as the DC/TMD system was followed for that purpose. Patients were advised not to take any painkillers, anti-inflammatory drugs, muscle relaxants, or medications affecting the nervous system during the treatment and evaluation period. They were asked to follow this instruction carefully. In addition, patients in both groups were encouraged to follow simple self-care practices like consuming soft foods and refraining from chewing gum and supporting the jaw when yawning.

LOW LEVEL LASER THERAPY

In this regard, LLLT was accomplished utilizing a Diode laser from Quick Lase Soft Tissue Diode Laser model QWLASER6D-12D (810+980nm) using the dual-wavelength which consider a 4th generation laser using the biostimulation handpiece, Fig. 1. The Quick Lase Soft Tissue Diode Laser device used in the LLLT sessions, the power is 0.4 w for each wavelength, during each session

the laser was directed towards previously demarcated tender spots around the TMJ. Within the muscles, Fig. 2. A patient undergoing low-level laser therapy targeting TMJ-related tender points, sessions were conducted three times per week for nine sessions.

PHARMACOLOGICAL TREATMENT

Naproxen 500 mg was prescribed twice daily to manage inflammation and pain.

Myogesic (a muscle relaxant) was administered three times daily to reduce muscle spasms and continued for 21 days

OUTCOME MEASURES

The outcome measure was a reduction in pain intensity and an increase in mouth opening.

ASSESSMENTS

The pain intensity is measured according to VAS four times the baseline record, after 10 days, at the end of treatment and after three months. MMO was measured in each time points

STATISTICAL ANALYSIS

All statistical analyses were performed using IBM SPSS Statistics software (30). Descriptive statistics were calculated for all relevant variables, including means, standard deviations, and medians. For inferential analysis, the normality of data distribution was assessed using the Shapiro-Wilk test. Between-group comparisons were conducted using the independent samples t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Statistical significance was determined at a p-value threshold of < 0.05, and 95% confidence intervals were reported where appropriate.

ETHICS

The project was carried out after obtaining consent from the Laser Institute for Postgraduate Studies, University of Baghdad, on January 22, 2025 (approval number103). The research was performed in accordance with Helsinki Declaration of the World Association of Physicians and the principles of Correct Clinical Trial Guidance (Guidelines for Good Clinical Practice). Participation in the project was voluntary. Patients had obtained comprehensive information about the nature, scope of clinical activities and the course of the proceedings. At each stage, the respondents had the right to refuse to participate in the study, without any corresponding consequences. Participation in the study was preceded by the patient's written informed consent.

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

A total of 24 patients were included in this comparative analysis, divided equally into two groups: Drug group (n=12) and Combination group (Low-Level Laser Therapy combined with drugs; n=12).

AGE DISTRIBUTION

The mean age of participants in the drug group was 28.92 years (SD = 5.53), while the combination group had a slightly higher mean age of 29.33 years (SD = 5.07). An independent samples t-test was conducted to compare the age between the two groups. Levene's test indicated homogeneity of variances ($F = 0.442$, $p = 0.513$), Table 1, allowing for the assumption of equal variances. The t-test revealed no statistically significant difference in age between the drug and combination groups, $t(22) = -0.192$, $p = 0.849$ (two-tailed), with a mean difference of -0.417 years (95% CI: -4.91 to 4.08). Effect size estimates were also calculated, Cohen's *d* was -0.079, Hedges' *g* was -0.076, and Glass's delta was -0.082, all indicating a negligible effect size. These results suggest that the two groups were comparable in terms of age, and age is unlikely to have confounded the primary outcome comparisons in this study.

GENDER DISTRIBUTION

Out of 24 participants, 20 were female 83.3% and 4 were male 16.7%. In the Drug group, 9 participants were female and 3 were male, while in the Combination group, 11 participants were female and only 1 was male, Table 2. A chi-square test of independence showed no statistically significant difference in gender distribution between the two groups ($\chi^2 = 1.200$, df = 1, $p = 0.273$). Fisher's Exact Test further confirmed the lack of significant association $p=0.590$. These findings suggest that gender distribution was statistically comparable between the Drug and Combination groups, allowing unbiased assessment of treatment effects across groups, Fig.3.

Table 1. Age Distribution by Group

	N	Mean Age (years)	Standard Deviation	p-value
Drug	12	28.92	5.53	0.849
Combination	12	29.33	5.07	

Source: compiled by the authors of this study

Table 2. Gender distribution in the drug and combination therapy

Group	Female (n)	Male (n)
Drug	9	3
Combination therapy	11	1

Source: compiled by the authors of this study

Table 3. Mann-Whitney U Test Results for VAS Scores (Drug vs. Combination)

Time Point	Mann-Whitney U	Z Score	p-value	Interpretation
Baseline	58.000	-0.914	0.361	No significant difference
10 Days	0.000	-4.231	< 0.001	Highly significant difference
21 Days	0.000	-4.320	< 0.001	Highly significant difference
3 Months	0.000	-4.246	< 0.001	Highly significant difference

Source: compiled by the authors of this study

Table 4. Median MMO and IQR values for Drug and LLLT groups with corresponding test results

Time Point	Drug Group (Median, IQR)	Combination therapy Group (Median, IQR)	Test Used	p-value
Baseline	38.5 (1)	39.0 (2)	Mann-Whitney U	0.759
10 Days	39.5 (3)	41.50 (3)	Mann-Whitney U	0.007
21 Days	40.5 (2)	44.50 (3)	Mann-Whitney U	<.001
3 Months	39.5 (2)	45.00 (3)	Mann-Whitney U	<.001

Source: compiled by the authors of this study

VAS SCORES

The normality of the data was assessed using the Shapiro-Wilk test. The results showed that the pain scores (VAS) were not normally distributed in either the drug or LLLT groups at most time points ($p < 0.05$).

Due to this violation of normality and the relatively small sample size, non-parametric tests were used. Specifically, The Mann-Whitney U test was used to compare VAS scores between the two groups at each time point.

VAS SCORES OVER TIME

The Visual Analogue Scale (VAS) was used to assess pain levels at four time points: baseline, 10 days, 21 days, and 3 months after treatment. The Mann-Whitney U test was applied to evaluate differences between the Drug and Combination groups, Table 3.

The results indicate that although baseline pain scores were comparable, patients receiving the combination therapy (LLLT + pharmacotherapy) showed significantly greater reductions in VAS scores at all follow-up periods. These findings suggest superior and sustained pain relief in the combination group compared to drug therapy alone.

MMO SCORES

The normality of MMO data was assessed using the Shapiro-Wilk test. The results indicated that MMO values in the drug and LLLT groups were not normally distributed at several time points ($p < 0.05$). Therefore, the non-parametric Mann-Whitney U test was used for group comparisons. Descriptive statistics are reported using the median and interquartile range (IQR), which are more appropriate for skewed data.

MMO SCORES OVER TIME (MEDIAN AND IQR)

At baseline, there was no significant difference between the drug group (Median = 38.5 mm, IQR = 1) and combination therapy group (Median = 39.0 mm, IQR = 2) with a p-value of 0.759. By day 10, the combination therapy group showed more significant improvement (Median = 41.50 mm, IQR = 3) than the drug group (Median = 39.5 mm, IQR = 3), $p = 0.007$. At 21 days,

the combination therapy group continued to improve (Median = 44.50 mm, IQR = 3) versus the drug group (Median = 40.5 mm, IQR = 2), p = <.001. At 3 months, the combination therapy group maintained better outcomes (Median = 45.0 mm, IQR = 3) than the drug group (Median = 39.5 mm, IQR = 2), p = <.001, Table 4.

These findings demonstrate that the Combination therapy group experienced significantly greater improvements in MMO across all post-treatment time points compared to Drug therapy alone, supporting the effectiveness of combining Low-Level Laser Therapy with pharmacological treatment in managing myogenic TMJ pain.

DISCUSSION

The participants in this study were between 20 and 40 years old. According to epidemiological data, TMDs are most commonly seen in individuals aged 18 to 44 [5], with a noticeably higher occurrence in this age group compared to older adults. [17]; the gender prevalence was female over male with 71% female participant as found by Reny de Leeuw [18], the analysis revealed no significant differences in baseline demographic variables, including age and gender, confirming homogeneity between the LLLT and drug groups. The present study compared the effectiveness of combining Low-Level Laser Therapy (LLLT) with pharmacologic therapy against pharmacotherapy alone in treating myogenic pain related to temporomandibular joint disorders (TMD). Pain intensity was assessed using the Visual Analog Scale (VAS), while mandibular mobility was evaluated through maximum mouth opening (MMO) measurements. The combination therapy group demonstrated a significantly greater and sustained reduction in pain scores across all post-treatment intervals (10 days, 21 days, and 3 months), while both groups had similar baseline VAS scores, which aligns with a systematic review by Melis et al. reported higher efficacy of LLLT in alleviating temporomandibular joint [19]. Similarly, a study by Emshoff et al. found that LLLT significantly reduced pain intensity in TMD patients combination therapy resulted in a more significant and faster reduction in VAS pain scores than pharmacologic treatment at all follow-up intervals, a finding that corroborates several recent randomised controlled trials. like Shobha et al. found significant within-group pain reductions following diode laser treatment in TMD patients, the body of evidence favours LLLT for its analgesic and anti-inflammatory effects, which are thought to occur via photobiomodulation, mitochondrial activation, and modulation of proinflammatory cytokines [20]. These mechanisms may underlie the sustained reduction in myofascial pain observed in the present study. A meta-analysis found that wavelengths of 780 nm and 830 nm—which were also used in our present study—were most effective, producing moderate to large effect sizes (up to −1.72) in reducing pain. These wavelengths are thought to penetrate deeply into soft tissue (1–5 cm), making them particularly suited for treating deep joint or masticatory muscle pain [21]; in addition to pain relief, the current results showed that combination therapy significantly improved maximum mouth opening. The study results agree with the findings of Ahmad et al. (2021), whose systematic review noted functional improvements, including increased MMO, in several randomised trials utilising LLLT for TMJ-related pain [22]. Patients treated with drugs showed an improvement in pain and mandibular function during the treatment, but this result collapsed after treatment terminated. The early but moderate pain reduction observed in the drug group is consistent with previous literature demonstrating the effectiveness of NSAIDs in managing acute TMD-related pain [23]. However, the limited long-term improvement aligns with the known limitations of NSAIDs in chronic or myogenic TMD cases, as their anti-inflammatory action may not address more profound muscular dysfunction. Therefore, combining both modalities offers significantly superior outcomes compared to drug therapy alone in the management of myogenic (TMJ) pain. Patients in the combination group experienced greater and more sustained reductions in pain, along with notable improvements in mandibular mobility, as reflected by Visual Analogue Scale (VAS) and Maximum Mouth Opening (MMO) scores. These findings support the integration of LLLT as an effective, non-invasive adjunct to conventional pharmacological management, particularly for patients with limited response to medication alone. By addressing both inflammatory and neuromuscular mechanisms, combination therapy provides a more comprehensive treatment strategy for TMJ disorders. Future studies with larger sample sizes and long-term follow-up are warranted to validate these results and establish standardized treatment protocols involving LLLT in routine clinical practice

CONCLUSIONS

These results indicate that Low-Level Laser Therapy with pharmacotherapy was more effective than pharmacological therapy in decreasing pain and improving jaw function in patients with TMJ-related myogenic pain. These findings suggest that LLLT may be considered a useful, non-invasive adjunct to conventional pharmacological management of myogenic TMJ pain. Further studies with larger sample sizes and longer follow-up are recommended to confirm these findings and support routine clinical use.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 07.12.2025
ACCEPTED: 10.07.2026

CREATIVE COMMONS 4.0

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ORIGINAL ARTICLE

Somatotypological prerequisites for physical fitness in primary school students

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ABSTRACT

Aim: To experimentally investigate the relationship between somatotype and physical fitness level in primary school students (aged 7-10) during ball-handling exercises.

Materials and Methods: The research, conducted during the 2024-2025 school year, involved 238 students (boys – n = 118, girls – n = 120) aged 7-10. To determine the students' body-build type (somatotype) and their somatometric assessment, the weight-height coefficient and somatoscopy were used. Pedagogical testing was employed to evaluate the results of ball-handling exercises. To determine the relationship between somatotype and indicators of students' physical fitness during ball-handling exercises, Pearson's linear correlation analysis was applied.

Results: It was found that in the distance throwing, the best results were achieved by boys with a higher weight-height coefficient aged 9 and 10 (r = 0.48 and r = 0.43), the best results in the vertical jump were recorded among students with a lower weight-height coefficient aged 8 and 10 (r = -0.64 and r = -0.4). Dribbling speed is higher among 10-year-old girls with a lower weight-height coefficient (r = 0.30), while the best results in the vertical jump are achieved by girls with a lower weight-height coefficient aged 8 and 9 (r = -0.34 and r = -0.3).

Conclusions: It has been established that the somatotype of students aged 7-10 influences only their performance in ball-handling exercises requiring speed and strength. In contrast, coordination skills are closely linked to other motor abilities and mental functions, which may serve as a basis for predicting their motor aptitude in various types of sports games.

KEY WORDS: primary school students, ball-handling exercises, somatotype, physical fitness, physical education, elements of sports games

Wiad Lek. 2026;79(8):1760-1767. doi: 10.36740/WLek/235880 DOI

INTRODUCTION

Physical education, as an integral part of school education, is aimed at fostering students' physical, social, and spiritual well-being and preparing them for an active, long-lasting life. The current trend toward a decline in students' physical condition, a decrease in their motivation to engage in physical exercise, and a decline in the status of physical education classes in schools creates an urgent need to optimize the school's physical education system, particularly by seeking new approaches to teaching the subject referred to as "Physical Education [1, 2].

Primary school age (7-10 years) is an active stage of growth and development of the child's body, the most optimal period for the development of motor skills and the initiation of motor skill training. In primary school, the foundation is laid for schoolchildren's further physical development, based on acquired knowledge, motor experience, and motor readiness [3].

Physical education for primary school students has its own specific characteristics, determined by their age-related anatomical, physiological, and psychological developmental features, as well as their adaptation to new learning conditions, which are characterized by a sharp increase in mental activity against the backdrop of severely limited motor activity. In this regard, properly organized physical education during the primary school years is not only a necessary condition for the comprehensive and harmonious development of students but also the foundation for their continued physical development [4, 5].

Children aged 7-10 have a particular need for movement and play, so active and sports games are a universal tool for the physical education of primary school

students, as they spark interest and have significant educational, health-promoting, and awareness-raising value [6].

It is known that one of the modern trends in improving physical education for schoolchildren is the differentiation of its forms, means, and methods. However, the traditional system of school physical education takes into account only gender- and age-related patterns of development, that is, it is designed for the "average" student, although it has been proven that individual characteristics of their physical development, including somatotype, influence the quality and speed of learning physical exercises and the development of motor skills in students, particularly in primary school [7, 8]. Taking into account the physical characteristics of primary school students when teaching game-oriented physical exercises allows each student to perform at an optimal intensity and increases learning effectiveness.

AIM

The aim is to experimentally investigate the relationship between somatotype and physical fitness level in primary school students (aged 7-10) during ball-handling exercises.

MATERIALS AND METHODS

The research involved 238 students (boys – n = 118, girls – n = 120) aged 7-10 from Lyceum No. 35, Lyceum No. 17 "Kyrylivskyi," Lyceum No. 183 "Fortuna," Lyceum No. 205, and Lyceum "Dominanta" in Kyiv (Ukraine) (7 years old – 54 students: boys – n = 28, girls – n = 26; 8 years old – 58 students: boys – n = 23, girls – n = 35; 9 years old – 59 students: boys – n = 33, girls – n = 26; 10 years old – 67 students: boys – n = 34, girls – n = 33). The research was conducted during physical education classes taught by a qualified physical education teacher. Classes were held three times a week, lasting 35 minutes for first-grade students (7-year-olds) and 40 minutes for grades 2-4 (8-10-year-olds), which helped maintain their physical performance. Physical education classes for children aged 7-10 were primarily game-oriented; their content included elements of sports games and gymnastics, which helped maintain the children's interest, reduce psychological and mental strain, and promote the natural development of coordination, speed, and strength. All schoolchildren involved in the research had no health issues. The research was open in nature; the children's parents were informed and gave consent for their participation. The pedagogical testing was conducted in the gym in November-December 2024 by physical education teachers in the presence of the school physician. The school physician took anthropometric measurements, and the physical education teacher visually determined the somatotype to confirm the results of the metric assessment.

To determine the students' somatotype, the weight-height coefficient was used, in which the body weight (kg) is divided by the body height (m) raised to the third power (a coefficient proposed by Professor T. Yu. Krutsevych [9]). To determine body-build type during the research, somatometric measurements were taken using traditional medical instruments: a height rod and a set of scales. The coefficient obtained from the calculation was compared with tabulated data (Table 1) to determine the somatotype.

In addition, somatoscopy was used to refine the somatometric assessment of body-build type; that is, students' somatotypes were visually assessed based on somatoscopic indicators of physical development (chest shape, leg shape, etc.).

Since physical education classes were predominantly game-oriented, i.e., included elements of sports games, this research aimed to assess students' constitutional type based on their level of physical fitness in ball-handling and jumping exercises. Therefore, using pedagogical testing, the results of the following ball-handling exercises were examined: throwing a small ball over the head at a target from a distance of 8 meters (number of successful throws out of 5 attempts); passing a basketball by bouncing it off the floor (number of successful passes out of 10 attempts); stopping a rolling soccer ball with the sole of the foot (number of successful stops out of 5 attempts); kicking a soccer ball for accuracy from a distance of 6 meters (number of successful kicks out of 5 attempts); throwing a small ball over the head for distance (in meters, best of 3 attempts); dribbling a basketball with the right or left hand in a straight line for 20 meters (time in seconds); catching a volleyball flying toward you (in points based on the number of successful attempts); juggling a balloon (number of times in the best of 2 attempts); throwing a basketball over the head from a sitting position (in meters, best of 3 attempts); throwing a volleyball against a wall for 30 seconds from a distance of 1 meter (number of times); standing vertical jump (in centimeters). Students performed the motor tests after a standard warm-up, which included various types of running and walking, as well as general physical exercises in motion and on the spot without equipment.

The research was conducted during November-December of the 2024-2025 academic year, during which data were collected on body-build type and physical fitness levels in ball-handling exercises for the specified group of students; for the convenience and objectivity

Table 1. Weight-height coefficient in schoolchildren aged 7-10 years of different body-build types (somatotypes)

Age, years	Somatotype			
	Digestive	Muscular	Thoracic	Asthenic
Boys				
7	13.8	12.6	11.8	9.6
8	13.7	12.6	11.4	9.4
9	13.5	12.3	11.1	9.1
10	13.2	12.1	11.1	8.7
Girls				
7	13.5	12.7	11.5	9.2
8	13.2	12.4	11.4	8.8
9	13	12.3	11	8.6
10	13	11.9	11.7	8.3

Source: compiled by the authors of this study

of the data, measurements were taken two months after the summer break following a series of physical education classes incorporating elements of sports games. The data were analyzed at the Department of Theory and Methods of Physical Education at Dragomanov Ukrainian State University (Kyiv, Ukraine).

To determine the relationship between somatotype and the level of physical fitness of 7- to 10-year-old students in ball-handling exercises, Pearson's linear correlation analysis was used. The existence of a relationship and the difference between individual values were considered significant at a 95 % significance level ($p \leq 0.05$).

The participants and their parents were informed about the research objectives and voluntarily agreed to participate. The research results were reviewed and approved by the Academic Integrity Committee of the Dragomanov Ukrainian State University (No. 34 dated May 14, 2025).

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

This study was carried according to the research plan of the Faculty of Physical Education, Sports and Health of the Dragomanov Ukrainian State University in 2023-2027 in accordance with the theme "Monitoring, control and evaluation of learning results in physical culture, the basics of healthy lifestyle" (state registration number 0113U009185).

RESULTS

To confirm differences in the physical development of schoolchildren of the same age and to justify the importance of taking somatotype into account in the physical education of primary schoolchildren, anthropometric measurements were taken from primary school students. Thus, during the pedagogical experiment, the percentage of children in the same age and gender group with different somatotypes was determined (Table 2).

Thus, the average height of 7-year-old boys is 127.7 ± 4.6 cm, and that of girls is 125.6 ± 4.3 cm; the average body weight of 7-year-old boys is 27.0 ± 4.2 kg, and that of girls of the same age is 24.5 ± 3.1 kg. The weight-height coefficient indicators, calculated using the formula for the somatotype of 7-year-old boys (28 individuals in total), indicate that more than one-third of 7-year-olds belong to the asthenic somatotype, specifically 28.6 %, the thoracic somatotype accounts for 14.3 %, the muscular type accounts for over 35 %, and the digestive type 21.4 %. A similar examination of 7-year-old girls (26 individuals) revealed that girls of the muscular and thoracic somatotypes were distributed equally – 19.2 % each, nearly half – 46.2 % – had the asthenic somatotype, and 15.4 % had the digestive somatotype. The results of the empirical somatotype determination coincided with the visual assessment of 7-year-old girls.

Measurements of 8-year-old children revealed that the average height of boys (23 individuals) was 131.0 ± 6.4 cm, and of girls (35 individuals) was 131.1 ± 5.4 cm; body weight was 28.3 ± 5.0 kg and 26.7 ± 4.1 kg for boys and girls, respectively. In terms of the weight-height coefficient, 8-year-old boys with asthenic and digestive somatotypes were distributed almost equally – 34.8 % and 30.4 %, respectively – and the same result was observed for representatives of the muscular and thoracic body-build types – 17.4 % each. Among 8-year-old girls, about half – 51.4 % – had the asthenic somatotype, more than a third – 22.9 % – had the

Table 2. Characteristics of the somatotypological status of the research participants aged 7-10 years, %

Somatotype	Age, years							
	7		8		9		10	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
Asthenic	28.6	46.2	34.8	51.4	12.2	19.2	17.6	33.3
Thoracic	14.3	19.2	17.4	22.9	15.1	30.8	23.5	24.3
Muscular	35.7	19.2	17.4	14.3	15.1	38.5	26.5	21.2
Digestive	21.4	15.4	30.4	11.4	57.6	11.5	32.4	21.2

Source: compiled by the authors of this study

Table 3. The relationship between the physical fitness levels of students aged 7-10 and their somatotype

Weight-height coefficient	Throwing a small ball for distance, m	Vertical jump from a standing position, s	Dribbling a basketball for speed, m
Boys, aged 8	0.01	-0.64	0.03
Girls, aged 8	0.14	-0.34	0.11
Boys, aged 9	0.48	0.02	0.22
Girls, aged 9	0.21	-0.30	0.14
Boys, aged 10	0.43	-0.40	0.01
Girls, aged 10	0.002	-0.13	0.30

Source: compiled by the authors of this study

thoracic somatotype, 14.3 % had the muscular type, and 11.4 % had the digestive type. The results of the empirical somatotype determination confirmed the accuracy of the visual assessment of girls in this age group.

Diagnostic assessment of 9-year-old students revealed the following: the average height of boys (33 individuals) was 139.3 ± 6.1 cm, and of girls (26 individuals) was 137.1 ± 6.3 cm; body weight was 37.5 ± 5.9 kg and 31.5 ± 4.1 kg, respectively. Based on the weight-height coefficient, it was determined that among boys of this age group (a total of 33 examined), children of the digestive somatotype significantly predominated – 57.6%, with equal numbers of representatives of the muscular and thoracic body-build types at 15.1% and 12.2%, and of the asthenic type at 12.2%. The 9-year-old girls were unevenly distributed across somatic body-build types. We found that 38.5% of the girls had a muscular somatotype, 30.8% had a thoracic somatotype, and 19.2% and 11.5% had asthenic and digestive somatotypes, respectively. The results obtained were consistent with the visual assessment of the girls' body types.

The average height of 10-year-old boys (34 individuals) is 146.1 ± 9.1 cm, and their body weight is 37.9 ± 8.8 kg. The average measurements for girls of this age group (33 individuals) are 140.7 ± 6.1 cm and 33.4 ± 5.6 kg for height and weight, respectively. Regarding the somatometry of 10-year-old boys, the results of the empirical determination of somatotype revealed 32.4% of the digestive type, 26.5% and 23.5% of the muscular and thoracic types, respectively, and only 17.6% of the asthenic type. All types of somatic body constitution are represented in nearly equal proportions among 10-year-old girls: asthenic – 33.3%, thoracic – 24.3%, and muscular and digestive – 21.2% each. The findings corresponded with the visual assessment of somatotypes in girls of this age group.

The correlation analysis was conducted to examine the influence of somatotype on the level of physical fitness among 7-10-year-old students, revealing correlations that vary by students' age and gender (Table 3).

Table 3 presents statistically significant correlations between the weight-height coefficient and the results of motor tests administered to students aged 7-10. The data show that for 9- and 10-year-old boys, the results of the small-ball throwing for distance, which demonstrates speed and strength capabilities, have a moderate correlation with the weight-height coefficient ($r = 0.48$ and $r = 0.43$, respectively, at $p \leq 0.05$). In boys aged 8 and 10, correlation relationships were found between vertical jump results and the weight-height coefficient ($r = -0.64$ and $r = -0.40$, respectively, at $p \leq 0.05$). In girls aged 8 and 9, a significant relationship was found between vertical jump performance and the weight-height coefficient ($r = -0.34$ and $r = -0.30$ at $p \leq 0.05$). In 10-year-old girls, a significant correlation relationship was found between basketball dribbling speed and the weight-height coefficient ($r = 0.30$ at $p \leq 0.05$). No other significant relationships were found between the results of the remaining motor tests and the constitutional characteristics of the younger schoolchildren's physical development.

The data obtained from the correlation analysis confirm that the performance level of various ball-handling

exercises depends on the weight-height coefficient. The success of performing strength, speed, and speed-strength exercises in boys aged 7-10 years, as well as speed and speed-strength exercises in girls of this age group, depends on the value of the weight-height coefficient. No significant correlation was found between the success of performing exercises of a different nature and the value of the weight-height coefficient, which confirmed the results of pedagogical observations: representatives of different somatotypes perform similar exercises with equal success.

Based on the results obtained, it can be concluded that children's somatotype affects only the performance of speed- and strength-based exercises. In contrast, the performance of coordination exercises is not closely linked to children's constitutional characteristics. These relationships arise because, in motor activity, coordination of movements is a psychomotor process in which its various components – intellectual, psychophysiological, sensorimotor, and motor – are combined.

It has been established that the influence of anthropometric data of primary school-aged children on the level of physical fitness in exercises with elements of sports games is indirect. Thus, their influence has been documented in specific gender-age groups of primary school students, and the significance of children's somatotype has been clarified only in speed- and strength-based exercises (jumping, throwing, and running). The data obtained can serve as a basis for differentiating teaching methods for elements of sports games for students aged 7-10. The research confirms differences in body constitution types among students of the same age and gender, which, in turn, implies varying potential for physical development and success in learning physical exercises. The above justifies taking into account the somatotypological characteristics of schoolchildren in primary school physical education classes, not only in the teaching of physical exercises but also in the objective assessment of their motor performance.

DISCUSSION

The period of a child's life from ages 6-7 to 9-10 is referred to as early school age. When defining its boundaries, consideration is given to the characteristics of children's mental and physical development, as well as their transition to academic activities, which become their primary focus [10]. Throughout early school age, the child's body continues to grow and develop, and body proportions change, particularly the ratio of head size to body length. However, the growth rate of children of both sexes slows down, while weight gain accelerates. On these indicators, boys outpace girls. However, in terms of chest growth, girls catch up with boys by age 9 and surpass them by age 10 [11, 12].

Physical education for primary school students has specific characteristics determined by their anatomical, physiological, and psychological features. In this regard, rationally organized physical education in early school age, taking into account individual differences in growth and physical development, is a priority area for improving school physical education [13].

Somatotype (body-build type, constitution) largely determines children's genetic predisposition to certain motor activities and their performance in various physical exercises. The existence of a correlation relationship between somatotype indicators and indicators of motor abilities in primary school students is explained by their common basis – the body's natural metabolism, which, on the one hand, influences the characteristics of body structure, and on the other, the body's reactivity and the level of functioning of its systems [14, 15].

It has been established that in early school age, the development of speed qualities varies with somatotype and age. Thus, at 6-7 years of age, speed qualities develop best in individuals of the digestive type; from 7 to 8 years of age, in the muscular type; and from 9 to 10 years of age, in the muscular and asthenic somatotypes. Significant differences were also found in the development of physical qualities such as explosive strength, coordination in distance throws, and in cyclic locomotion. It was also shown that absolute muscle strength was greatest in girls with the thoracic and muscular somatotypes [16].

Among boys aged 7 to 10 years with an asthenic body-build type, the greatest improvement was observed in coordination during distance throws with the non-dominant hand; for the thoracic type – explosive strength of the upper limb muscles (distance throws); for the muscular type – explosive strength of the lower limb muscles (jumping) and mobility in the shoulder joints; and for the digestive type – general endurance and coordination in cyclic locomotion. At the same time, in boys aged 7 to 8 years with an asthenic body-build type, there is a sharp improvement in coordination of throws with the dominant hand, cyclic locomotion, explosive strength of the lower-limb muscles, and absolute muscle strength. During this age range, changes in individuals with a thoracic somatic body type occur only in shoulder joint mobility; in the muscular type – in indicators of absolute strength, speed endurance, and speed of individual movements; and in the digestive type – in explosive strength of the lower limb muscles and coordination. Between the ages of 8 and 10, boys show significant improvement in the development of the following physical qualities: in individuals with an asthenic body-build

type – explosive strength of the upper limb muscles, speed of individual movements; in the thoracic type – coordination in throws with the non-dominant hand, speed endurance; and in the muscular type – explosive strength of the upper limb muscles [17].

It has been confirmed that, in the lower grades, the highest level of motor activity throughout the day is observed among children of the muscular type, and the lowest among girls and boys of the digestive type. Girls of the asthenic type show lower results in exercises related to endurance, strength, balance, flexibility, and speed. Other indicators of motor abilities in individuals of the asthenic-thoracic type are high in speed-strength abilities, endurance, and relative strength; average in the development of balance and flexibility; and low in the strength of the hand's flexor muscles [18]. Thus, one of the indicators of individual development in early school-age children is body-build type (body structure or somatotype), which is associated with the rate of ontogenesis and the level of functional indicators of the cardiovascular, respiratory, and motor systems.

At the present stage, a system of physical education has been established that is based primarily on the principles of age and gender differentiation among students, as well as their health and physical fitness, yet the intensity of biological maturation, characteristics of physical development (body height and weight), the development of psychological traits, and body-build type are scarcely taken into account. Thus, age and gender are generally accepted factors in the development of physical education curricula. However, it has been proven that one of the dominant factors influencing changes in students' physical fitness indicators is body-build type, as well as body length, circumference measurements, and body weight [19].

Therefore, anthropometric indicators and constitutional characteristics of students' body structure should form the basis for differentiated instruction in ball-handling physical exercises in primary school as criteria that determine the selection of means and methods for developing motor skills and shape the content of instructional material during ball-handling exercises in physical education classes for students aged 7-10. During primary school, body length and weight have varying effects on students' motor abilities. The specific relationship between anthropometric indicators in various motor actions was identified: in throws and tosses, body weight has the dominant influence; in vertical jumps, taller and relatively lighter students have a noticeable advantage. Taking children's somatotypes into account during physical education classes can enhance the effectiveness of motor training and serve as a basis for predicting children's motor aptitude across various physical exercises. At the same time, the issue of differentiating physical exercises across types, particularly ball-handling exercises, in physical education classes for younger students of different somatotypes remains under-researched.

Traditional criteria for assessing schoolchildren's physical fitness are differentiated by gender and age and do not account for the somatotypological characteristics of children's physical development [20]. To provide a more informative assessment of students' motor abilities, it is necessary to develop educational standards and physical fitness norms based on students' body-build type classifications (their somatotypes). Such criteria will not only allow for an objective assessment of children's motor performance. Still, they will also enable the identification of students' motor aptitude in various types of physical exercises, in this case, in sports games.

CONCLUSIONS

It has been established that the influence of the weight-height coefficient on the success of mastering ball-handling exercises increases with age and is observed only in speed- and strength-based exercises (jumping and throwing) ($p \leq 0.05$). Establishing the relationship between the level of mastery of ball-handling exercises and the physical build of primary school students can form the basis for a differentiated teaching methodology for ball-handling exercises, as well as in the development of criteria for assessing the academic achievements of primary school students in ball-handling exercises during physical education classes based on the level of development of specific motor skills for students in each grade, taking into account gender and somatotype. The results obtained can serve as a basis for developing a methodology to predict the motor aptitude of children aged 7-10 across various sports games.

PROSPECTS FOR FURTHER RESEARCH

Prospects for further research will focus on developing a differentiated methodology to predict motor aptitude in children aged 7-10 across various sports.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 10.03.2026
ACCEPTED: 25.07.2026

CREATIVE COMMONS 4.0

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ORIGINAL ARTICLE

Motivational factors influencing the effectiveness of law enforcement officers' work depending on their years of service

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ABSTRACT

Aim: To examine the motivational factors influencing the effectiveness of modern law enforcement officers' work with varying levels of their professional experience.

Materials and Methods: The research involved 127 law enforcement officers with varying lengths of service: up to 5 years – 28 individuals (Group 1), 5-10 years – 38 individuals (Group 2), 10-15 years – 35 individuals (Group 3), over 15 years – 26 individuals (Group 4). Research methods: theoretical analysis and generalization of literature sources, questionnaire, psycho-diagnostic methods, statistical methods.

Results: The most pronounced manifestation of socio-psychological motivational factors was found among law enforcement officers with up to 5 years of experience, professional-psychological factors – among those with 5-10 years of experience, and individual-professional factors – among those with 10-15 and over 15 years of experience. It was found that 50.0 % of law enforcement officers with up to 5 years of experience and 52.6 % with 5-10 years of experience demonstrate a high level of job satisfaction.

Conclusions: The research shows that as law enforcement officers gain practical experience, they become more motivated to succeed in their service activities. Yet, they increasingly try to avoid failures and mistakes. Job satisfaction becomes more pronounced when the underlying motivation for their service activities aligns with their own expectations (social relationships, working conditions, resources, and career advancement). A lack of adequate motivation and adaptive qualities among law enforcement officers to the specific conditions of their service activities can be a source of negative consequences for their mental and physical health.

KEY WORDS: motivation, law enforcement officers, experience, service activities, psychophysical health

Wiad Lek. 2026;79(8):1768-1775. doi: 10.36740/WLek/235884 DOI

INTRODUCTION

Researchers' interest in studying motivation stems from the fact that gaining insight into the nature of motivational phenomena, the patterns of their formation, and their variability enables prediction and enhancement of the effectiveness of human activities across various spheres [1, 2]. The service activities of law enforcement officers are no exception; their primary tasks include ensuring the proper protection of human rights and freedoms, combating crime, and maintaining public order and public safety, which take on specific significance in conditions of war and active hostilities [3]. These extremely complex tasks require not only a high level of professionalism but also, for law enforcement officers, a deep understanding of and adherence to established legal and moral norms, rapid information processing, and timely and effective decision-making in their professional activities [4]. At the same time, given the ongoing changes in the nature and rhythm of work during wartime, as well as the increased stress and risks to life, the issue of maintaining the motivation of law enforcement officers in their professional activities has become increasingly relevant [5]. The motivation of these specialists is of great importance not only for the effective performance of their service duties but also for the effectiveness of the law enforcement system as a whole, upon which the safety of people and society at large depends [6, 7].

Researchers [8] assert that a decline in a law enforcement officer's professional motivation can lead to a

loss of human capital. Another discouraging fact is that, as research findings [9, 10] indicate, the number of young police officers resigning voluntarily has nearly doubled in recent years, posing a threat to police organizations' staffing levels. At the same time, stressful and unfavorable working conditions can increase team conflict, reduce work efficiency, and negatively affect staff health [11]. Therefore, a lack of proper motivation and adaptive qualities among law enforcement officers to the specific conditions of their professional service can typically lead to negative consequences for both mental and physical health [12, 13].

AIM

The aim is to examine the motivational factors influencing the effectiveness of modern law enforcement officers' work with varying levels of their professional experience.

MATERIALS AND METHODS

PARTICIPANTS

The research involved 127 law enforcement officers (aged up to 45) who served in the National Police in various non-managerial officer positions. Empirical data were collected at Lviv State University of Internal Affairs (LSUIA, Lviv, Ukraine), where respondents attended advanced training courses. The data were processed at the Department of Theoretical Psychology of LSUIA. The research was conducted in 2024-2025. The criteria for including participants in the experiment were defined as follows: holding officer-level positions in the police, relevant professional experience (up to 5 years – 28 individuals (Group 1), 5-10 years – 38 individuals (Group 2), 10-15 years – 35 individuals (Group 3), over 15 years – 26 individuals (Group 4). The exclusion criterion was the participant's voluntary desire to withdraw from the research at any time. Research limitations: the age of law enforcement officers, their physical and mental health status, marital status, education, and salary level were not inclusion criteria and were not taken into account during the research.

RESEARCH METHODS

theoretical analysis and generalization of literature sources, questionnaire, psycho-diagnostic methods, statistical methods. The method of theoretical analysis and generalization of literary sources was used to conduct an analytical review of scientific sources on the outlined range of issues (24 sources (2016-2025) from MedLine, Scopus, Web of Science databases were analyzed).

The survey was conducted to identify the key motivational factors that either encourage or, conversely, hinder the effective performance of law enforcement officers. The survey was conducted using the author's questionnaire, consisting of two sections of questions (1 – incentives for effective work; 2 – job satisfaction), each of which identified the corresponding motivational factors. Specifically, the first section considered the following factors: socio-psychological (team-building recreational activities; support from colleagues and management; the opportunity to express one's opinion and have it taken into account by the team); individual-professional (vacation; additional days off; career growth; monetary bonuses for achieved results); professional-psychological (favorable working conditions; adherence to the work schedule; improvement of relationships within the team). The section of questions regarding job satisfaction (Section 2) established the corresponding level: low (depression and apathy toward work; pessimism regarding career prospects); average or neutral (work proceeding as usual); high (satisfaction with working conditions; positive attitude of supervisors toward work; improved team relationships). Each question in both sections had four response options (a – "never"; b – "sometimes"; c – "often"; d – "always"). All respondents had the opportunity to select one of the response options.

The following psycho-diagnostic methods were used in the research: D. McClelland's "What Drives You?" to identify the sources of motivation, as well as "Measuring the Motivation to Succeed" and "Diagnostics of Motivation to Avoid Failure" by T. Ehlers [7, 14]. D. McClelland's "What Drives You?" method consists of 15 statements designed to identify a law enforcement officer's attitude toward work, satisfaction with it, and relationships within the team and with management. The respondents were asked to rate their agreement with each statement on a five-point scale ranging from 1 – strongly disagree to 5 – strongly agree. Based on the method's results, the law enforcement officer's level of motivation was assessed across three dimensions: desire to succeed, desire for power, and desire to be part of the organization. The "Measuring the Motivation to Succeed" method by T. Ehlers method of 41 questions to which respondents were asked to answer "yes" or "no." Scores were calculated according to the test key. Based on the results, the following indicators of the level of motivation for success were determined: high level – over 21 points; average level – 11–20 points; the respondent does not always clearly define the motives behind their actions but demonstrates persistence in

Table 1. The distribution of motivational factors for effective performance among law enforcement officers with varying levels of professional experience (n = 127), %

Motivational factors	Frequency of occurrence	Law enforcement officers' groups			
		Group 1 (n = 28)	Group 2 (n = 38)	Group 3 (n = 35)	Group 4 (n = 26)
Socio-psychological factors	a	3.5	7.9	14.3	19.2
	b	28.6	39.5	42.9	46.2
	c	50.0	36.8	31.4	23.1
	d	17.9	15.8	11.4	11.5
Individual-professional factors	a	17.9	13.2	5.7	7.9
	b	35.7	34.2	27.1	30.6
	c	32.1	36.8	48.6	42.3
	d	14.3	15.8	18.6	19.2
Professional-psychological factors	a	7.1	7.4	11.4	15.4
	b	42.9	34.7	42.9	42.3
	c	32.1	39.5	28.6	26.9
	d	17.9	18.4	17.1	15.4

Legend: a – never; b – sometimes; c – often; d – always
Source: compiled by the authors of this study

achieving goals; low level – the respondent exhibits a low level of motivation for success (1 to 10 points). The "Diagnostics of Motivation to Avoid Failure" method consists of 30 rows of three words, from which one must be selected in each row. Points are awarded according to the test key. The result determines the level of motivation to avoid failure, with a higher score indicating a higher level of motivation to avoid failure: 2-10 points – low level; 11-16 points – average level; 17-20 points – high level; over 20 points – very high level of motivation to avoid failure.

STATISTICAL METHODS

The statistical method was used to process the experimental data obtained. The reliability of the difference between the indicators presented in percentages was determined using Pearson's Chi-square (χ^2) criterion. The significance of the difference was set at $p<0.05$. All statistical analyses were performed using SPSS version 10.0 software 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 LSUIA. Also this study followed the regulations of the World Medical Association Declaration of Helsinki. Informed consent was received from all participants who took part in this study.

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

This scientific article was carried out according to the plan of the research work of the Lviv State University of Internal Affairs for 2021-2027 «Psychology of the personality of a specialist in wartime and post-war rehabilitation» (state registration number 0122U002532).

RESULTS

The analysis of the motivational factors influencing law enforcement officers' performance revealed an uneven distribution of these factors. Specifically, regarding the incentive category, a trend is observed whereby law enforcement officers with more years of service experience are increasingly losing interest in socio-psychological motivational factors (from 50.0 % for employees with up to 5 years of experience to 23.1 % for those with over 15 years of service experience (in the "often" category) (Table 1). This refers to support from colleagues and management; the opportunity to express one's own opinion and have it taken into account by the team; time off with colleagues; and so on. This can be explained by the fact that a focus on social relationships within the work team is a priority primarily for young law enforcement officers (with up to 5 years of experience), who are in the stage of socio-psy-

Table 2. Levels of motivation among law enforcement officers, taking into account their professional experience and priority factors (n = 127), %

Priority motivating factor / Significance of the difference	Law enforcement officers' groups and their motivation levels											
	Group 1 (n = 28)			Group 2 (n = 38)			Group 3 (n = 35)			Group 4 (n = 26)		
	L	I	H	L	I	H	L	I	H	L	I	H
Desire to achieve success in general	25.0	42.9	32.1	10.5	34.2	55.3	14.3	34.3	51.4	15.4	34.6	50.0
χ^2, p	1-2: 13.062; <0.001			2-3: 0.725; >0.05			3-4: 0.061; >0.05			1-4: 7.072; <0.001		
Desire for power	46.4	35.7	17.9	23.7	31.6	44.7	8.6	34.3	57.1	11.6	34.6	53.8
χ^2, p	1-2: 19.074; <0.001			2-3: 8.680; <0.001			3-4: 0.545; >0.05			1-4: 38.872; <0.001		
Belonging to an organization or leader	21.4	21.5	57.1	21.1	36.8	42.1	31.4	37.2	31.4	42.3	30.8	26.9
χ^2, p	1-2: 6.285; <0.001			2-3: 3.580; <0.01			3-4: 2.561; <0.05			1-4: 19.368; <0.001		

Legend: L – low level; I – intermediate level; H – high level.; χ2- Pearson's Chi-square criterion value; p – probability value
Source: compiled by the authors of this study

Table 3. Manifestations of motivation among law enforcement officers based on their service experience (n = 127), %

Types of motivation / Significance of the difference	Law enforcement officers' groups and levels of motivation											
	Group 1 (n = 28)			Group 2 (n = 38)			Group 3 (n = 35)			Group 4 (n = 26)		
	L	I	H	L	I	H	L	I	H	L	I	H
Motivation to success	21.5	46.4	32.1	13.1	34.3	52.6	8.6	40.0	51.4	11.7	34.5	53.8
χ^2, p	1-2: 8.815; <0.001			2-3: 1.384; >0.05			3-4: 0.934; >0.05			1-4: 10.125; <0.001		
Motivation to avoid failure	28.6	50.0	21.4	21.1	31.6	47.3	11.4	34.3	54.3	7.8	34.5	57.7
χ^2, p	1-2: 15.045; <0.001			2-3: 3.488; <0.01			3-4: 0.778; >0.05			1-4: 31.387; <0.001		

Legend: L – low level; I – intermediate level; H – high level.; χ2- Pearson's Chi-square criterion value; p – probability value
Source: compiled by the authors of this study

chological adaptation (50.0 % in the "often" category and 17.9 % in the "always" category). At the same time, professional-psychological motivational factors that stimulate their work are becoming increasingly relevant (favorable working conditions; adherence to the work schedule; improved relationships within the team, etc.) (the highest percentage among the groups of respondents was found among law enforcement officers with 5-10 years of service experience – 39.5 % in the "often" category and 18.4 % in the "always" category). For them, it is important to have a certain stability in their work routine, as this category of respondents is in the active phase of their professional careers, where acquired competencies are combined with the capacity for further development. Regarding individual-professional motivational factors for effective law enforcement work (career advancement; monetary bonuses for achieved results, etc.), these factors predominate among respondents with greater professional experience (10-15 and over 15 years of service in law enforcement agencies: 48.6 % and 42.3 % in the "often" category, as well as 18.6 % and 19.2 % in the "always" category). This suggests that utilitarian motivation predominates, as perceptions of the law enforcement profession and one's place within it are shifting at this stage.

To confirm or refute the findings presented above, we used D. McClelland's "What Drives You?" method to examine the role of certain motivational factors in the professional activities of law enforcement officers, as these factors potentially influence the effectiveness of their work. Using this method, we identified the frequency distribution of law enforcement officers' motivation levels for effective service activities (Table 2).

Thus, as demonstrated by the diagnostic assessment conducted using D. McClelland's "What Drives You?" method, law enforcement officers with up to five years of service experience exhibit a predominance of the motivational factor of belonging to an organization

Table 4. Comparison of job satisfaction levels among law enforcement officers with varying lengths of service (n = 127), %

Job satisfaction levels	Frequency of occurrence	Law enforcement officers' groups			
		Group 1 (n = 28)	Group 2 (n = 38)	Group 3 (n = 35)	Group 4 (n = 26)
Low	a	21.4	7.9	20.0	19.2
	b	42.9	42.1	48.6	38.5
	c	21.4	36.8	20.0	26.9
	d	14.3	13.2	11.4	15.4
Avarage	a	10.7	14.7	3.4	3.3
	b	28.6	31.6	22.3	14.3
	c	46.4	47.4	54.3	53.8
	d	14.3	15.8	20.0	28.6
High	a	10.7	6.3	11.4	7.7
	b	21.4	23.7	34.3	42.3
	c	50.0	52.6	42.9	30.8
	d	17.9	18.4	11.4	19.2

Legend: a – never; b – sometimes; c – often; d – always
Source: compiled by the authors of this study

or leader (the high level in Group 1 is 57.1 %), which indicates a fairly high level of team orientation; in other words, the socio-psychological manifestations of their professional motivation become increasingly significant. As they gain experience in law enforcement (5-10 years), the respondents increasingly demonstrate a desire to achieve success in general (the high level in Group 2 is 55.3 %), which characterizes them as sufficiently motivated employees focused on success in their service activities. This indicator remains largely unchanged in groups of respondents with more work experience (10-15 years and over 15 years) – the high levels stand at 51.4% and 50.0%, respectively – though it is further influenced by another motivational factor: the desire for power. In Group 3 and Group 4, it is quite pronounced: high levels of 57.1 % and 53.8 %, respectively. The data obtained are corroborated by statistically significant differences among law enforcement officers with varying levels of service experience ($p < 0.01$-0.001). This position can be explained by the fact that, as they gain practical experience, law enforcement officers consider assuming managerial positions, primarily at the middle management level, and are thus capable of leading law enforcement organizations and taking on responsibility.

At the same time, the application of the methods referred to as "Measuring the Motivation to Succeed" and "Diagnostics of Motivation to Avoid Failure" by T. Ehlers confirmed the finding that, as they gain practical experience, law enforcement officers, on the one hand, maintain their motivation to achieve success – as we observed using the previous method – and, on the other hand, strive to avoid failures and mistakes. This trend is particularly evident among respondents with 10-15 years of service (high level: 54.3 %) and over 15 years (57.7 %) (Table 3). Hence, more experienced respondents are characterized by greater moderation, caution, a moderate degree of risk-taking, and an understanding of the specifics of police work. In general, the tendency to avoid failure serves a protective function of the psyche and is prioritized according to situational factors. It is believed that professionals whose primary motivation is to avoid failure tend to avoid competitive situations. This is also due to the realism of participants' perceptions, as the drive for success is a function of three variables: the motivation to succeed, the perceived probability of success, and the subjective appeal of success in a specific life or professional situation. The statistical analysis corroborated the obtained data: for both types of motivation, significant differences were found between the indicators of Group 1 and Group 4 ($p < 0.001$).

Using the second section of the author's questionnaire, we analyzed law enforcement officers' job satisfaction by years of service. It was found that in the early stages of professional development (up to 5 years) and as they gain more experience (5-10 years), law enforcement officers demonstrate sufficiently high levels of job satisfaction (50.0 % and 52.6 % in the "often" category) (Table 4).

This indicates relative satisfaction with working conditions, a positive attitude among managers and staff, and good team dynamics, among other things. Meanwhile, among those with more work experience (10-15

years and over 15 years), an average (neutral) level of satisfaction becomes more pronounced – work in a routine mode (the average-level indicator in the "often" category is 54.3 % and 53.8 %, respectively).

DISCUSSION

Under martial law, law enforcement officers' professional tasks have become significantly more complex [3]. Every day, they must carry out a large volume of diverse tasks under conditions of time and information shortages, uncertainty, active counter-offending, and the decision of people's fates. Against a backdrop of extreme conditions, danger, tension, and heightened responsibility, they must also maintain a positive professional image and public trust. All of this creates risks of neuropsychological overload and occupational stress among law enforcement officers [15, 16]. The strong negative impact of the nature of their work on a law enforcement officer's personality can lead to gradual disillusionment with the profession, loss of professional motivation, the emergence of psychosomatic illnesses, and so on. This has prompted research into motivational factors for effective performance and job satisfaction among law enforcement officers, as these factors determine the future application of appropriate psychoprophylactic measures.

As some researchers note [14, 17], the individual's motivational sphere is central to their orientation, including their professional orientation. This is also confirmed by our research, as the system of primary motivational factors can determine the effectiveness of service activities and overall job satisfaction. It is also worth noting that in the course of performing duties, motives – which are dynamic constructs – can transform; therefore, the professional activities of law enforcement officers can be characterized not only by primary but also by transformed motivation.

A motive is an integral way of organizing human activity, any of its impulses, the determinants of which are both internal and external causes [18]. According to researchers [19, 20], the connection between professional success and motivation is evident: for any employee, the motives for achieving success or avoiding failure become priorities. In our research, this connection and the relevance of the aforementioned motivation were also taken into account; however, they were further combined with such an indicator as the experience of law enforcement officers in their service activities. It can be argued that the motivational sphere of law enforcement officers directly depends on a combination of factors, at the core of which lies the satisfaction of basic needs through working conditions, which determines overall job satisfaction.

Researchers [5, 21] note that the performance of service duties by law enforcement officers requires a high level of psychological support, which necessarily includes stimulating motivation for their professional activities. According to our findings, the incentives for effective work among modern law enforcement officers may vary, including due to service experience, ranging from socio-psychological motivational factors (support from colleagues and management; recognition of one's own affiliation with the law enforcement structure) to the dominance of purely utilitarian motivation (career advancement; monetary bonuses for achieved results, etc.). At the same time, the overwhelming majority of modern law enforcement officers, being in the active phase of professional development, demonstrate the capacity for further growth.

Some researchers argue [22-24] that key factors in boosting police officers' motivation within the framework of psychological support for their work include the development of self-regulation and stress resilience skills, the organization of work processes and rest periods, the maintenance of social connections, and teamwork. The results of our research complement the information mentioned above, demonstrating that modern law enforcement officers systematically pay attention to these factors. At the same time, they feel engaged in the organization's activities, indicating sufficient satisfaction with their professional needs and interest in their work. Moreover, the more the underlying motivation for their service activities aligns with their own expectations, the more pronounced their job satisfaction becomes. Conversely, as the sense of disappointment with work in law enforcement agencies intensifies (indicated by average or even low levels of job satisfaction), the motivation driven by the desire to avoid failure increases. According to our data, this pattern is demonstrated by law enforcement officers with over 15 years of experience. This highlights the need to identify effective means of motivating law enforcement personnel, particularly in wartime conditions, as well as strategies to prevent the development of negative phenomena that hinder success and to cultivate interest in service duties.

CONCLUSIONS

A lack of proper motivation and adaptive qualities among law enforcement officers to the specific conditions of their service activities can be a source of negative consequences for mental and physical health. Service experience can determine the factors that motivate effective performance: among law enforcement officers with little work experience (Group 1), socio-psychological factors dominate;

(50.0 % in the "often" category and 17.9 % in the "always" category); professional-psychological motivational factors predominate in Group 2 (39.5 % in the "often" category and 18.4 % in the "always" category); individual-professional factors are more clearly evident in Group 3 and Group 4 (48.6 % and 42.3 % in the "often" category, as well as 18.6 % and 19.2 % in the "always" category). This trend is also evident across the motivation levels of law enforcement officers with varying levels of service experience: Group 1 exhibits a fairly high level of focus on the team and the organization (57.1 %), while Group 2 demonstrates a drive to achieve success in general (55.3 %); Group 3 and Group 4 also demonstrate a desire to achieve success in their work, though this is further influenced by a motivational factor such as the desire for power (57.1 % and 53.8 %, respectively). As they gain practical experience, law enforcement officers, on the one hand, maintain their motivation to succeed (primarily in Groups 2-4), and, on the other hand, try to avoid failures and mistakes (most frequently observed in Group 4).

It was found that the more the basic motivation for their service activities aligns with their own expectations, the more pronounced their job satisfaction becomes. With greater service experience, a sense of disappointment with work in law enforcement agencies gradually intensifies, resulting in an average or even low level of job satisfaction.

The research indicates the need to identify and implement effective measures to incentivize law enforcement officers and to systematically carry out activities aimed at preventing negative phenomena, as such practices can significantly contribute to success and foster interest in service activities.

PROSPECTS FOR FURTHER RESEARCH

It is planned to investigate the dynamics of motivational factors in the service activities of law enforcement officers before and after performing service and combat tasks during wartime.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 09.03.2026
ACCEPTED: 10.07.2026

CREATIVE COMMONS 4.0

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ORIGINAL ARTICLE

Molecular characterization of periodontal bacteria by 16S rRNA Sequencing in periodontitis patients

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ABSTRACT

Aim: To identify periodontopathogenic bacteria in periodontal pockets and subgingival plaque of patients with periodontitis in Karbala, Iraq, using 16S rRNA gene sequencing, the gold standard for molecular identification of microorganisms.

Materials and Methods: Molecular techniques based on 16S rRNA gene analysis provide reliable identification of bacterial species associated with periodontal infections. A crosssectional study was conducted with 26 patients, ranging in age from 20 to 50 years. The patients were excluded of the study if they had been on systemic antibiotics or periodontal therapy within the past three months. Every sample was aseptically collected with informed consent. The sterile paper points were used to take sample of the subgingival plaque, and they were inserted in the deepest periodontal pockets with a duration of 20 30 seconds. The samples were instantly frozen in sterile microtubes with transport buffer and frozen at -20 o C until further molecular analysis.

Results: The study population consisted of 65.38% females and 34.62% males. The most frequent clinical findings were gingival bleeding (55%) and inflammation (33%), with no significant differences observed between sexes. Molecular analysis revealed a high prevalence of *Porphyromonas gingivalis* (20/26) and *Tannerella forsythia* (18/26). *Veillonella parvula* was detected in 12 patients, while *Treponema denticola* was identified in 11 patients. *Actinobacillus actinomycetemcomitans* and *Fusobacterium nucleatum* were detected at lower frequencies, in 3 and 2 patients, respectively. Successful amplification of the 16S rRNA gene was confirmed by the presence of a ~1500 bp band in all samples.

Conclusions: Sequencing PCR is a powerful tool for the diagnosis of the subgingival microbiota in periodontitis, showing that Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola are the most frequently encountered pathogens in the sampled population. Moreover, the strong link between Treponema denticola and diabetes mellitus highlights the need to take into account systemic health factors when analysing microbiological data.

KEY WORDS: periodontal diseases, 16S rRNA, *Porphyromonas gingivalis*

Wiad Lek. 2026;79(8):1776-1782. doi: 10.36740/WLek/222501 DOI

INTRODUCTION

Periodontitis is a long term inflammatory disease of tissues supporting the teeth, which is triggered by certain pathogenic microorganisms. It causes gradual degeneration of periodontal ligament and alveolar bone causing periodontal pocket formation, gingival recession, or both [1].

Metagenomics has made it possible to generate projects unimaginable to humanity in past decades, such as the Human Microbiome Project, which will allow us to analyze and understand the complex communities and interactions of the microorganisms in the oral cavity. Genomic techniques will also allow us to understand how the host's immune system interacts with the oral microbiota and explain its relationship to oral health or disease [2], This knowledge will lead dentists to make the oral microbiome a routine clinical tool for assessing their patients' susceptibility to certain oral diseases.

The mouth cavity has a set of surfaces, and each of them is covered with dense and heterogeneous populations of bacteria that create structured biofilms. Some of the members of these microbial populations are related to oral diseases such as dental caries and periodontitis that are among the most common bacterial infections, in humans [3].

There is mounting evidence that the oral microbiota happens to be at the centre stage in the pathogenesis of the two most common human oral diseases--dental caries and periodontal disease. These circumstances have been identified as some of the significant risk

factors of various systemic health conditions such as malignancies, diabetes mellitus, cardiovascular diseases, bacteremia, premature birth, and low birth weight. It is generally thought that oral microorganisms cause disease upon synergistic and cooperative interaction, the relationships between oral microbial species are of critical determinence concerning pathogenicity [4].

Understanding the oral microbiome is a complex task due to the wide variety of habitats within the oral cavity, which depends on oxygen concentrations, nutrient availability, temperature, exposure to immunological factors, and anatomical characteristics, the species of the genus (*Streptococcus*) are found in high proportions in soft tissues, saliva, and on the tongue. Species of the genus (*Actinomyces*) are found supragingivally and infragingivally, and in lingual fissures. Other bacteria, such as (*Veillonella parvula*) and (*Neisseria*), can be isolated from all oral habitats. Intracellular colonization can also occur in oral epithelial cells by bacterial complexes composed of *Aggregatibacteractinomycetemcomitans*, *Porphyromonas gingivalis*, and *Tannerella forsythia* [5]. Recent studies have shown that most oral microorganisms are cultivable; that the oral microbiome is much more diverse than previously thought; and that oral infections are polymicrobial in nature [6].

The human mouth cavity acts as a significant entry point to the environment and its viruses and bacteria and thus among the most highly colonized microbial habitats in the human body. It carries around six billion bacteria and possibly as many as 35 times the amount of viruses. It is due to the large population of bacteriophage communities in the oral cavity that the molecular diversity among bacterial populations is encouraged, and both the phages and their hosts continuously mutate in order to gain some evolutionary benefits [7]

Due to the peculiarities of primary oral ecosystems, and especially to the variability, heterogeneity, and quantity of the microbiota, there are numerous challenges in accurately determining its microbial composition. Up to 200 different species have been isolated in a single oral cavity over time; most of these appear to be transient, leaving only about 20 as resident species [8].

The role of the oral fungal microbiota has not been well established despite the comprehensive nature of the characterisation of the bacterial constituent of the oral microbiome. Fungus and bacteria are becoming increasingly considered to be significant results of interactions in oral health, with the synergistic relationship between *Candida albicans* and oral *streptococci* being an example of a fungus-bacteria interaction. Future research needs to combine research with pertinent disease models to mechanistically substantiate relationships in human research and determine fungal-bacterial interactions that could be used to prevent and treat oral diseases [9].

AIM

The aim of the study was to identify periodontopathogenic bacteria in periodontal pockets and subgingival plaque of patients with periodontitis in Karbala, Iraq, using 16S rRNA gene sequencing, the gold standard for molecular identification of microorganisms.

MATERIALS AND METHODS

PATIENTS AND SAMPLES COLLECTION

Iraqi patients with periodontitis and those that had visited dental clinics in Iraq were used as study subjects and sampled to get periodontal samples. Periodontitis diagnosis was made on clinical periodontal parameters such as probing pocket depth, clinical attachment loss and radiographic indicators of alveolar bone loss. The patients were excluded of the study if they had been on systemic antibiotics or periodontal therapy within the past three months. Every sample was aseptically collected with informed consent. The sterile paper points were used to take sample of the subgingival plaque, and they were inserted in the deepest periodontal pockets with a duration of 20 30 seconds. The samples were instantly frozen in sterile microtubes with transport buffer and frozen at -20 o C until further molecular analysis.

A crosssectional study was conducted with 26 patients, ranging in age from 20 to 50 years. Of these 26 patients, 21 presented with aggressive periodontal disease and 5 with chronic periodontal disease.

Both types of periodontal disease were preceded by a series of symptoms, such as gingivitis, occlusal trauma, halitosis, and inflammation. The pocket depths in subjects with aggressive periodontal disease ranged from a maximum of 6 mm to a minimum of 4 mm. Similarly, in patients with chronic periodontal disease, pocket depths ranged from 8 mm to 2 mm.

The first step consisted of completing the designed periodontal record form. Subsequently, samples were taken for PCR testing, following this procedure.

DNA EXTRACTION

According to the instructions of the manufacturer, bacterial genomic DNA was extracted in the collected periodontal samples with the help of a commercial DNA extraction kit. Spectrophotometric analysis of the concentration and purity of the extracted DNA was measured and the DNA samples stored at -20 C awaiting polymerase chain reaction (PCR) amplification.

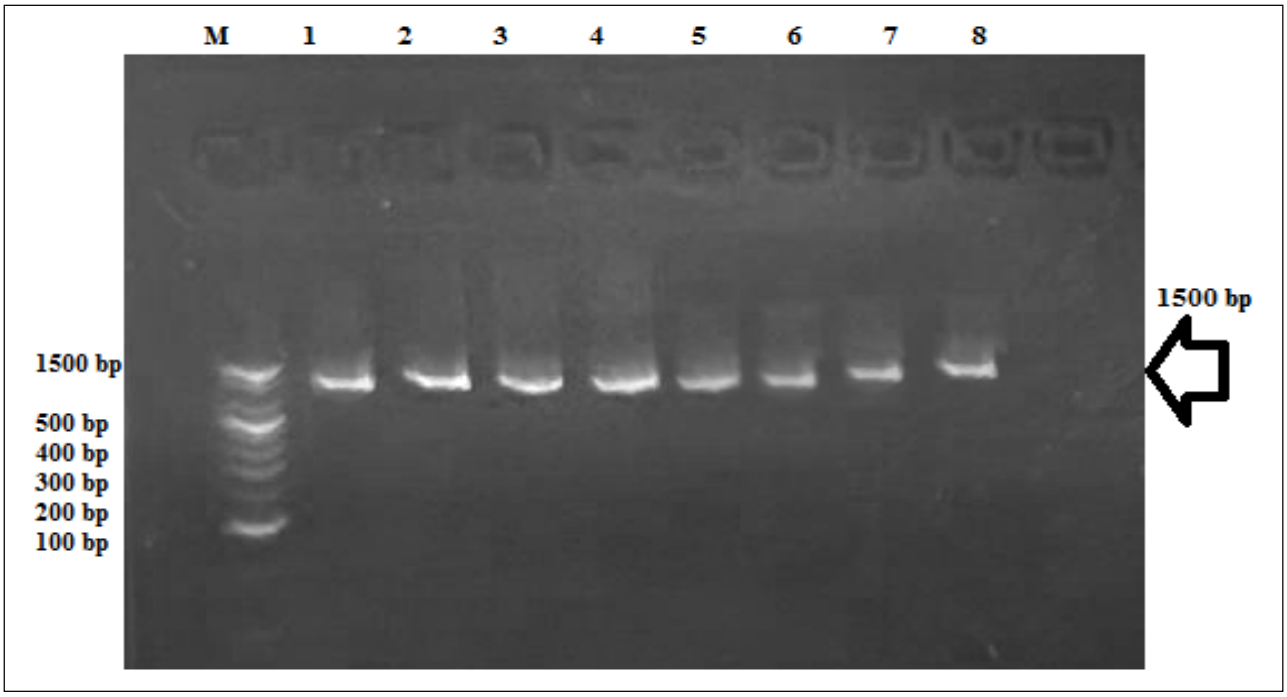

Fig. 1. Agarose gel electrophoresis showing PCR amplification of the bacterial 16S rRNA gene (~1500 bp) from periodontal samples. PCR products were resolved on a 1.5% agarose gel prepared in TBE buffer and run at 70 V for 1 hour. Lane M represents the DNA molecular weight marker, while lanes 1–8 correspond to clinical samples. All samples exhibited a clear band at approximately 1500 bp, indicating successful amplification of the 16S rRNA gene
Picture taken by the authors

PCR AMPLIFICATION OF 16S RRNA GENE SEQUENCING

Universal primers were used to amplify bacterial 16S rRNA gene which targeted about 1500 base pairs of the gene. The bacterial 16S rRNA gene was amplified using universal primers targeting approximately 1500 base pairs. The primer sequences used were as follows: Forward primer (27F): 5'-AGAGTTTGATCMTGGCTCAG-3'

Reverse primer (1492R): 5'-TACGGYTACCTTGTTACGACTT-3'[10]. PCR amplification was performed in a total reaction volume containing template DNA, primers, PCR master mix, and nuclease-free water. The amplification was carried out in a thermal cycler with an initial denaturation step 95C for 3 minutes, followed by 35 cycles of denaturation 95C for 30 second, annealing 56C for 30 second, and extension 72C for 60 second, and a final extension step 72C for 5 minutes.

The PCR products were analyzed by electrophoresis on a 1.0% agarose gel stained with an appropriate nucleic acid dye. A single DNA band of approximately 1500 bp indicated successful amplification. Thermal cycler amplification was performed under standard conditions, that is, initial denaturation, then repeated denaturation, annealing, and extension cycles, and finally a conclusion of the extension cycle. PCR products were separated by gel electrophoresis using agarose gel and the presence of one band with about 1500 bp size was taken to suggest successful amplification.

DNA SEQUENCING

The purified PCR products were sequenced. Pure PCR products were sent back to a certified sequencing laboratory in the Republic of Korea using DHL courier service under controlled conditions. The Sanger sequencing used the same primers that were used in the PCR amplification.

BACTERIAL IDENTIFICATION AND SEQUENCE ANALYSIS

The received nucleotide sequences were revised and put together under the use of relevant bioinformatics software. The agreement sequences were compared to reference sequences in National Center of Biotechnology Information (NCBI) database with the help of BLASTn tool. The identification of bacterial species was done according to the best sequence similarity, and a similarity of 97% and above were deemed to be species level.

ETHICS

This work complies with the principles of the Declaration of Helsinki.

Table 1. Number and percentage of bacterium detection in patient with periodontitis

Bacterium	Female n (%)	Male n (%)
Porphyromonas gingivalis	12 (46.1%)	8 (30.7%)
Tannerella forsythia	11 (42.3%)	7 (26.9%)
Veillonella parvula	9 (34.6%)	3 (11.5%)
Treponema denticola	7 (26.9%)	4 (15.3%)
A. actinomycetemcomitans	2 (7.7%)	1 (3.8%)
Fusobacterium nucleatum	1 (3.8%)	1 (3.8%)

Source: compiled by the authors of this study

Table 2. Distribution of bacterial detection in periodontitis patients with and without diabetes

Bacterium	Diabetic Patients (n = 10) n (%)	Non-Diabetic Patients (n = 16) n (%)	χ^2 Value	p-value
Porphyromonas gingivalis	9 (90.0%)	11 (68.8%)	1.57	0.210
Tannerella forsythia	8 (80.0%)	10 (62.5%)	0.90	0.343
Veillonella parvula	6 (60.0%)	6 (37.5%)	1.27	0.260
Treponema denticola	7 (70.0%)	4 (25.0%)	5.20	0.023*
Aggregatibacteractinomycetemcomitans	1 (10.0%)	2 (12.5%)	0.04	0.848
Fusobacterium nucleatum	0 (0.0%)	2 (12.5%)	1.33	0.248

Source: compiled by the authors of this study

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

The study included 26 patients with periodontitis. Sex distribution indicated that there was a high number of females (65.38%) than males (34.62%). In terms of clinical presentation, the most common results were gingival bleeding (55%), and gingival inflammation (33%). Under the analysis of the clinical findings based on the sex, there was no significant difference between the two sexes as similar clinical features dominated both among the female and the male patients.

Bacterial DNA analysis using PCR showed that some of the periodontopathogen species were present among the research subjects. *Tannerella forsythia* was found in 18 of 26 sample subjects and *Porphyromonas gingivalis* in 20 patients. The *Veillonella parvula* was identified in 12 subjects. Moreover, 11 patients also had *Treponema denticola*. The most common species was actinobacillusactinomycetemcomitans with 3 patients and *Fusobacterium nucleatum* was the least common species which was found in 2 patients only.

Bacterial distribution analysis data were categorized by sex whereby *Veillonella parvula* was most frequently identified in female patients then Tannerella forsythia. *Porphyromonas gingivalis* was found in equal measures in male patients, with *Fusobacterium nucleatum* having the lowest prevalence Table 1.

Agarose gel electrophoresis demonstrated successful PCR amplification of the 16S rRNA gene in all periodontal samples, as evidenced by the presence of a single band at approximately 1500 bp (Fig. 1).

A total of 10 patients (38.5%) in this study were diagnosed with type 2 diabetes mellitus (DM) and 16 patients (61.5%) had no systemic disease. Table 2 shows the detection rates of the bacteria in diabetic and non-diabetic patients.

Using the Chi-square test, we found that the detection of *Treponema denticola* was significantly higher in diabetic patients (70.0%) than in non-diabetic patients (25.0%) ($p = 0.023$). While *Porphyromonas gingivalis* and *Tannerella forsythia* had a higher detection rate in diabetic patients (90.0% and 80.0%, respectively) than non-diabetic patients (68.8% and 62.5%, respectively), it

did not reach a level of statistical significance ($p > 0.05$). *Fusobacterium nucleatum* was only detected in non-diabetic patients (12.5%) and *Aggregatibacter actinomycetemcomitans* had similar detection rates in both groups

DISCUSSION

The current research study examined the bacterial profile of periodontitis in Iraqis through the use of PCR amplification and Sanger sequencing of the 16S rRNA gene. The results showed that periodontopathogenic bacteria have a heterogeneous distribution, which indicates the polymicrobial nature of periodontal disease, the study population was found to be more composed of female participants. This distribution can be showing variation in health seeking behavior and not actual sex differences in prevalence of diseases. The most frequent clinical findings were gingival bleeding and inflammation which are well-known predictors of active periodontal inflammation, as well as, as per the classical clinical presentation of periodontitis [11,12].

Traditional periodontal assessments, including probing pocket depth and radiography of alveolar bone destruction, measure the outcome of the disease, but don't directly address the causative agents or microbial infection, the cause of periodontal disease. This highlights the importance of sensitive and specific microbiological diagnostics to better understand the disease process and inform treatment [13].

In this study, we used sequencing PCR to profile the subgingival microbiota. Our findings on the high presence of "red complex" pathogens (including *P. gingivalis*) are consistent with their role as keystone pathways of disease dysbiosis [14].

Yet, the real power of our diagnostics is not only that it can detect, but it can also quantitate. As pointed out in the literature, qualitative testing has "limited clinical value" for periodontitis . Our quantitative PCR approach provides information on bacterial load, allowing a more sophisticated interpretation based on disease severity; this is an improvement on traditional colony culturing which may not detect important anaerobes [15].

Hundreds of different species have been isolated from the oral cavity, but only a few have been associated with periodontal pathogenic bacteria. Among these are Porphyromonas gingivalis, *Tannerella forsythensis* (*Bacteroides forsythus*), and *Actinobacillus actinomycetemcomitans*, although other *Gram-negative bacteria* also cause chronic and aggressive periodontitis[16].

Several methods exist for enumerating the number of bacteria present in subgingival plaque. These include bacterial culture, which has been the classic method par excellence for detecting and enumerating periodontopathogenic microorganisms [17,18]; immunofluorescence microscopy; and DNA probes. Unfortunately, these methods have certain limitations, such as a lack of specificity and limited sensitivity.

On the other hand, there is PCR, a simple technique that replicates fragments of RNA or DNA and has been developed following recent studies by Astorgia [19] in 2022, and Meurman et al. [20] in 2022. It is a rapid and relatively simple method that can detect bacteria even in low numbers. This method does not require live cells [21]. It offers high sensitivity and specificity in detecting bacteria in biological samples. Between 25 and 100 cells can be detected [22,23].

However, PCR has its limitations, including the possibility of false-positive results due to contamination [24]. The use of microbiological tests for diagnosing the different destructive forms of periodontal disease remains controversial. The limitations of this test, regarding the presence or absence of Pg and Aa, and its purpose of distinguishing subjects with aggressive periodontal disease from those with chronic periodontal disease, were clearly outlined in a review recently published by Mombelli et al. [25] in 2002. When diagnosing aggressive periodontal disease, we can often overlook a clear indicator of this type of periodontal disease, was not detected. For a correct microbiological diagnosis, we need a test with high specificity and sensitivity, such as the PCR test. Even if the presence of this bacterium is low, we must not discriminate, because its mere presence is a clear indicator of aggressive periodontal disease.

The data obtained regarding clinical history show that the most frequent findings were bleeding (55%) and inflammation (33%). However, in the study conducted by [26], which compared two groups-one with aggressive periodontal disease and the other with chronic periodontal disease-they concluded that, based on clinical history, aggressive periodontal disease presents with less inflammation and bleeding, but crevicular fluid is similar to that of chronic periodontal disease.

Regarding the PCR test results, where samples were taken from pockets 4 mm or larger, we found the presence of various bacteria: *Actinobacillus actinomycetemcomitans (Aa), Tannerellaforsythensis (Tf), Prevotella intermedia (Pi), Porphyroma gingivalis (Pg), Treponema denticola (Td), and Fusobacterium nucleatum (Fn)*. In the studies conducted by Herrera et al. [27] in 2023 concluded that Aa is a typical bacterium of aggressive periodontal disease.

While Pg is more typical of chronic periodontal disease, it has been observed in patients with aggressive periodontal disease, as corroborated by studies conducted by Vandesteen et al. [28] in 1984.

Diabetes mellitus is also known to affect the subgingival microbiota; thus, the present study investigated the effect of this comorbidity on the subgingival microbiota. We found that *Treponema denticola* was significantly more common in diabetic patients than in non-diabetic patients ($p = 0.023$). This observation is in agreement with earlier reports that have shown an increased prevalence of spirochetes, such as *T. denticola*, in diabetic patients with periodontitis . This finding

may be explained by changes in host immune responses caused by hyperglycemia, which may provide a suitable niche for certain anaerobic bacteria , while the prevalence of *P. gingivalis* and *T. forsythia* was higher in diabetic patients, these results were not significant [29]. This could be due to the limited number of diabetic patients in our study (n = 10), where smaller effect sizes might be undetected. Larger sample sizes are needed to help clarify the association between diabetes and the microbiome in periodontal disease [30]. In the study conducted by Takeuchi et al. [6], Pg and Td were detected, which, although more typical of chronic periodontal disease, can also appear in aggressive periodontal disease.

CONCLUSIONS

Sequencing PCR is a powerful tool for the diagnosis of the subgingival microbiota in periodontitis, showing that *Porphyromonas gingivalis, Tannerella forsythia*, and *Treponema denticola* are the most frequently encountered pathogens in the sampled population. Moreover, the strong link between *Treponema denticola* and diabetes mellitus highlights the need to take into account systemic health factors when analysing microbiological data, and the inclusion of molecular diagnosis into the planning of individualised periodontal treatment.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 31.01.2026
ACCEPTED: 26.05.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

The influence of chemical irrigants on the condition of the root canal biofilm in case of periodontitis treatment

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ABSTRACT

Aim: To evaluate and compare the antimicrobial efficacy of commonly used endodontic irrigation solutions against bacterial and fungal isolates recovered from infected root canals in patients with apical periodontitis, in order to determine their relative effectiveness against clinically relevant endodontic microorganisms.
Materials and Methods: The strains of opportunistic microorganisms representing the optionally anaerobic transient microflora of the oral cavity were used in the study. 11 chemical solutions used to eliminate microorganisms in the root canal, were applied in the microbiological study. Microbial cultures were isolated from the infected root canal and identified on the basis of morphological, cultural properties and such biochemical microtests as "STAPHYtest 16", "STREPTOtest 16" (Lachema, Czech Republic) and test systems VITEK 2 GP and VITEK 2 YST (biomerieux, France) using VITEK 2 Compact analyzer.
Results: Comparing the effect of irrigation solutions on *S.aureus* MSSA bacteria, such irrigant as *Chlorhexedin* 2% (*Endohex*) provided the most positive result *Hypochlorite* 5.25% (*Cerkamed*) provided a positive effect on *C.ablicans* as well constituting 88.82±1.65 in comparison with Chlorhexedine 2% (29.22±0). Citric acid 40% (Cerkamed) was the best to eliminated S.gordonii (27.28±0.35). However, *Maleic acid* 6% showed the least effect on it (6.55±0.45). *Hypochlorite* 5.25% (*Cerkamed*), *Hypochlorite* 6% *Chloran* showed the best influence on the *Candida* group, while *Citric acid* 40% showed the lowest influence.
Conclusions: The conducted microbiological studies showed a diverse effect of irrigation solutions on groups of different microorganisms causing periodontitis. The obtained results provide an opportunity to select differentially irrigation solutions for the elimination of microorganisms detected in the root canals. A positive result of the elimination of irrigation solutions on microorganisms causing periodontitis is observed.

KEY WORDS: apical periodontitis, irrigation solutions, microbial biofilm

Wiad Lek. 2026;79(8):1783-1790. doi: 10.36740/WLek/222258 DOI

INTRODUCTION

The etiological basis of apical periodontitis is a bacterial infection of the root canal system. Despite significant advances in modern dentistry, this disease remains one of the most prevalent worldwide. Nowadays apical periodontitis is considered to be a inflammatory response of the body to the tooth pulp destruction and the root canal infection [1,2]. According to a systematic review and meta-analysis conducted by C.S. Tiburcio-Machado et al. (2019) [3], the global prevalence of apical periodontitis among the adult population is 52%, increasing to 62% in individuals over the age of 60.

However, mechanical instrumentation alone is insufficient due to the complex anatomy of root canals, which leaves 35–40% of the canal walls untouched. In addition, preparation procedures result in the formation of a smear layer that blocks dentinal tubules and creates a physical barrier, hindering the penetration of antiseptic agents into deeply located biofilms [4].

Therefore, chemical irrigation represents a critically important stage of endodontic treatment. Sodium hypochlorite (NaOCl) remains the "gold standard" due to its ability to dissolve organic tissues and its pronounced antimicrobial activity. At the same time, its cytotoxicity and inability to remove the inorganic component of the smear layer necessitate the use of chelating agents such as EDTA, citric acid, or maleic acid [5].

Chlorhexidine (CHX) is considered a less aggressive alternative due to its high substantivity and long-lasting antimicrobial effect, although it lacks proteolytic activity and the ability to remove the smear layer. Although a wide range of irrigating solutions is available on the modern market, the selection of an optimal protocol is complicated by the lack of high-quality comparative data on their effectiveness against clinically significant pathogens [5].

AIM

The aim of this study was to evaluate and compare the antimicrobial efficacy of commonly used endodontic irrigation solutions against bacterial and fungal isolates

recovered from infected root canals in patients with apical periodontitis, in order to determine their relative effectiveness against clinically relevant endodontic microorganisms.

MATERIALS AND METHODS

The study protocol was approved by the Bioethics Committee of Ivano-Frankivsk National Medical University. Written informed consent was obtained from all patients prior to inclusion in the study. Clinical material for microbiological analysis was collected from infected root canals of 30 patients diagnosed with apical periodontitis or pulpitis. To ensure the accuracy and reliability of microbiological results, patients who had received systemic or local antibiotic therapy within the previous 30 days were excluded.

RESEARCH HYPOTHESIS

It was hypothesized that different chemical irrigation solutions used in endodontic treatment would demonstrate significantly different antimicrobial efficacy against clinically relevant microorganisms isolated from infected root canals in patients with apical periodontitis. In particular, sodium hypochlorite solutions with higher active concentration were expected to exhibit superior broad-spectrum antimicrobial activity due to their pronounced oxidizing and tissue-dissolving properties. At the same time, it was assumed that modified hypochlorite formulations containing surfactants might provide enhanced penetration into dentinal tubules and irregular root canal structures, thereby improving their antifungal effectiveness.

It was further hypothesized that chlorhexidine-based solutions would demonstrate strong antibacterial activity because of their well-known substantivity, but would remain limited as primary irrigants due to the absence of organic tissue dissolution. In contrast, chelating agents and organic acids, including EDTA, citric acid, and maleic acid, were considered primarily adjunctive components of irrigation protocols, contributing mainly to smear layer removal, canal wall conditioning, and facilitation of antimicrobial penetration rather than acting as potent standalone disinfectants.

Thus, the study was based on the assumption that the antimicrobial effectiveness of endodontic irrigation depends not only on the chemical identity of the solution, but also on its concentration, physicochemical modification, and functional role within the overall irrigation protocol.

MICROBIAL STRAINS

The antimicrobial activity of the irrigation solutions was studied against eight bacterial strains: α-hemolytic streptococci of the *mitis* group (*Streptococcus oralis*, *Streptococcus sanguinis*, *Streptococcus gordonii*), β-hemolytic streptococci (*Streptococcus pyogenes*, group A; *Streptococcus dysgalactiae* ssp. *equisimilis*, group G), staphylococci (methicillin-susceptible *Staphylococcus aureus* (MSSA); methicillin-resistant *S. aureus* (MRSA) with associated resistance to fluoroquinolones, macrolides, tetracyclines, and aminoglycosides; methicillin-susceptible *Staphylococcus epidermidis*), as well as five yeast-like strains of *Candida* spp. (*C. albicans*, *C. tropicalis*, *C. lipolytica*, *C. lusitaniae*, and *C. kefyr*).

Microbial cultures were isolated from infected root canals using sterile Teflon brushes, which were placed in tubes containing 1.0 ml of sterile physiological saline and thoroughly suspended for 5 minutes using a Vortex Nest mixer at 3000 rpm. The resulting microbial suspension was plated with a calibrated bacteriological loop (5 мl inoculation dose) using Gold's sectoral streaking method onto nutrient media: blood agar (for isolation and differentiation of streptococci and staphylococci), Endo medium (for enterobacteria), and Sabouraud agar (for yeasts). The cultures were incubated for 24 hours at 37°C under aerobic conditions, with streptococci additionally incubated in a CO_2-enriched atmosphere.

Identification of the isolated pure cultures was performed based on morphological, cultural, and biochemical characteristics using STREPTOtest 16, STAPHYtest 16, and the VITEK 2 GP and VITEK 2 YST test systems (bioMérieux, France) on the VITEK 2 Compact analyzer.

Tested irrigation solutions. Ten irrigation solutions were included in the study and are presented in Table 1 in the same sequence and under the same commercial names as used throughout the manuscript.

EXPERIMENTAL DESIGN

The study was designed as a controlled in vitro comparative microbiological experiment. Each tested irrigation solution was evaluated against all isolated microbial strains under identical laboratory conditions. Sterile isotonic saline solution (0.9% NaCl) served as the negative control. For each microbial strain, all experiments were performed in triplicate to ensure reproducibility, analytical reliability, and statistical validity of the obtained results.

ASSESSMENT OF ANTIMICROBIAL ACTIVITY

Antimicrobial activity of the irrigation solutions was evaluated using the agar-gel diffusion micromethod. Molten agar (30 ml) was poured into Petri dishes placed on a strictly horizontal surface. After solidification, wells with a diameter of 4.0 mm were punched. The agar sur-

Table 1. Antimicrobial activity of irrigation solutions on root canal microorganisms (growth inhibition zone diameters, mm)

Microbial strains	Control Saline solution 0.9%	Sodium hypochlorite 2% Cerkamed (Poland)	Sodium hypochlorite 5.25% Cerkamed (Poland)	Sodium hypochlorite 5.25% Extra + Deterg. Cerkamed (Poland)	Sodium hypochlorite 6% (Ukraine)	Sodium hypochlorite 6% Chemoplus Chloran (Poland)	Chlorhexi dine 2% Cerkamed (Poland)	Chlorhexi dine 2% Endohex (Ukraine)	EDTA 17% + Benzalkonium bromide (0.1%) Endo-Solution (Poland)	Maleic acid 6% (Ukraine)	Citric acid 40% Cerkamed Poland)
S. aureus MSSA	0	22.22±1.50 a	25.63±0.14 a	22.65±0.09 a	19.33±0.26 a	22.22±0.49 a	28.06±0.25 a	30.95±0.51 a	24.17±0.46 a	8.97±0.53 ag	28.88±0.96 af
S. aureus MRSA	0	29.73±1.65 ab	47.45±3.24 a	39.20±1.31 a	24.17±0.69 a	43.80±1.93 a	25.69±0.18 a	28.07±0.24 a	22.26±0.52 ae	8.41±0.87 ag	28.36±0.55 afg
S. epidermidis	0	41.34±1.12 ab	49.94±1.12 a	42.24±1.68 a	28.86±1.47 a	43.16±1.52 a	31.65±0.37 a	36.01±0.44 a	25.91±0.53 ae	9.25±0.87 ag	34.14±0.66 afg
S. pyogenes (β Str A)	0	13.54±0.34 ab	17.13±0.26 a	14.66±1.12 a	11.68±0.69 a	14.89±0.42 a	20.17±0.36 a	23.7±0.35 a	18.27±0.24 a	7.44±0.95 g	25.74±0.43 af
S. dysgalactiae ssp. equisimilis (β Str G)	0	7.76±0.47 ab	15.06±0.28 a	14.09±0.29 a	11.16±0.33 a	8.71±0.30 a	19.38±0.12 a	21.79±0.78 a	16.65±0.28 a	6.32±0.53 g	26.09±0.37 af
S. gordonii	0	12.30±0.21 ab	16.11±0.32 a	11.80±0.49 a	11.91±0.77 a	15.57±0.45 a	20.37±0.95 a	22.94±0.15 a	17.63±0.44 a	6.55±0.45 g	27.28±0.35 af
S. oralis	0	15.92±0.61 ab	14.56±0.70 a	13.59±0.57 a	11.87±1.17 a	15.59±0.45 a	23.72±0.39 a	24.75±0.28 a	21.39±0.36 at	7.13±0.12	26.84±0.61 af
S. sanguinis	0	13.25±1.11 a	14.99±0.73 a	15.29±0.42 a	11.36±0.28 a	14.10±0.16 a	21.42±2.20 a	24.51±0.72 a	22.90±0.76 ae	10.53±0.90 a	20.98±0.23 af
C. albicans	0	55.46±1.12 ab	88.82±1.64 a	74.60±0.63 ac	41.96±0.71 a	79.80±0.51 a	29.22±0.64 ad	30.25±0.97 ad	35.46±0.48 ae	0 g	0 g
C. tropicalis	0	43.77±1.05 a	51.86±1.11 a	40.50±1.29 a	15.88±0.65 ab	48.86±1.19 a	26.73±0.41 ad	25.64±0.62 ad	28.63±0.47 ae	0 g	0 g
C. lipolytica	0	37.84±0.74 a	54.47±1.63 a	35.10±1.06 ac	18.75±0.20 ab	48.46±0.49 a	28.89±0.85 ad	29.21±0.41 ad	39.08±0.50 a	0 g	0 g
C. lusitaniae	0	56.64±1.05 ab	84.76±1.25 a	59.64±1.10 ac	22.4±0.37 ab	59.00±1.41 a	26.59±0.41 ad	29.23±0.32 ad	32.03±0.42 ae	0 g	0 g
C. kefyr	0	36.57±0.68 a	44.99±0.54 a	35.44±0.97 a	14.61±0.20 ab	39.50±0.39 a	27.70±0.71 ad	29.01±0.30 ad	37.48±1.04 a	0 g	6.89±0.63 g

Note. Superscript letters indicate statistically significant differences ($p < 0.05$, Dunn's post hoc test with Holm correction) when compared as follows:
a – any irrigant vs. negative control (saline solution);
b – Sodium hypochlorite 2% vs. Sodium hypochlorite 5.25% (Cerkamed);
c – Sodium hypochlorite 5.25% with detergent vs. Sodium hypochlorite 5.25% without detergent;
d – Chlorhexidine 2% vs. any sodium hypochlorite solution;
e – EDTA 17% + benzalkonium bromide 0.1% (Endo-Solution) vs. Sodium hypochlorite 5.25%;
f – Citric acid 40% (Cerkamed) vs. Maleic acid 6%;
g – Citric acid 40% (Cerkamed) or Maleic acid 6% vs. Sodium hypochlorite 5.25%.
Source: compiled by the authors of this study

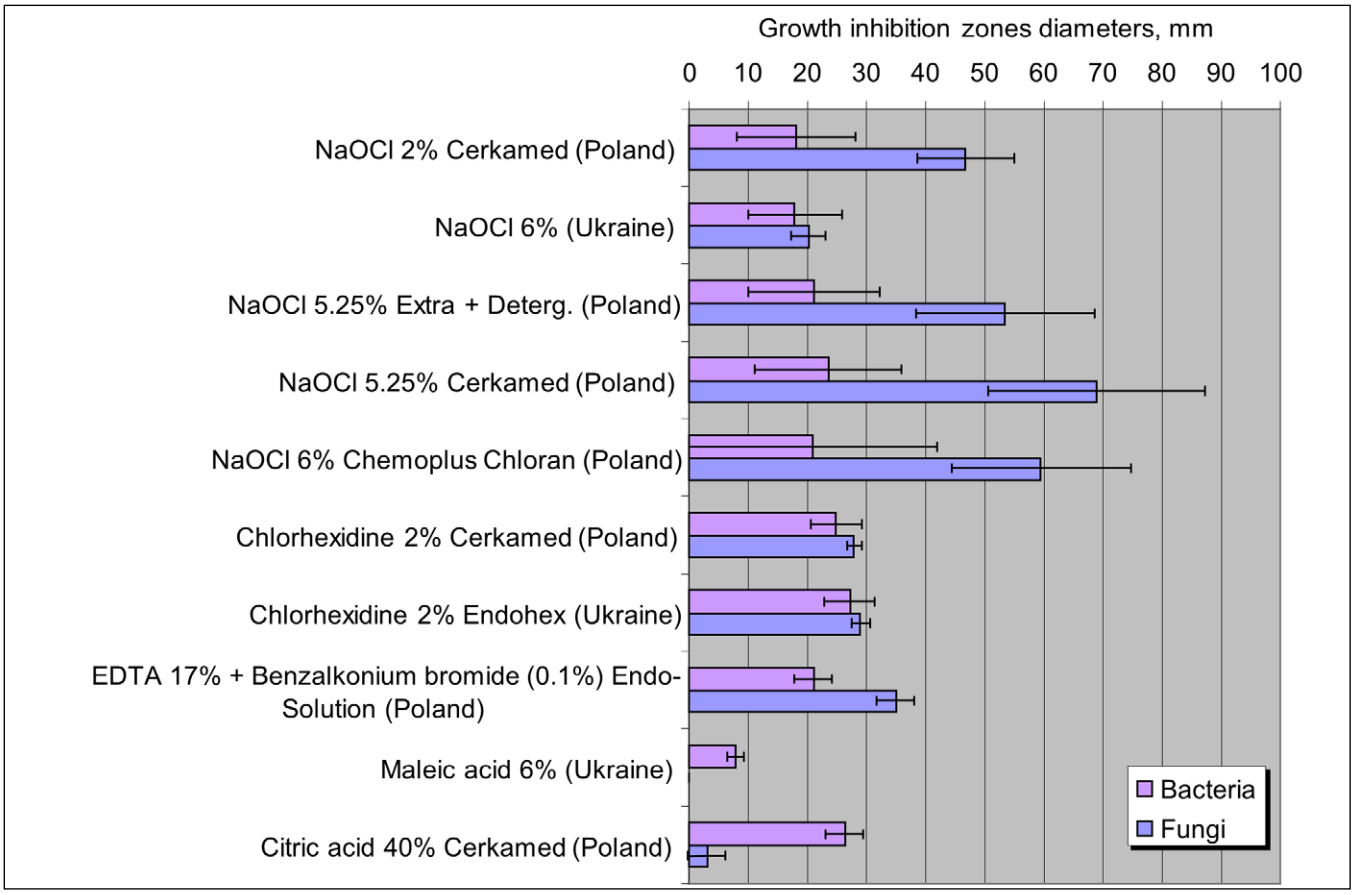

Fig. 1. Average values of growth inhibition zones diameters for each irrigation solution for all strains of bacteria and fungi separately
Picture taken by the authors

face was evenly inoculated with microbial suspensions at a concentration of 1×10^7 CFU/ml. A volume of 20 ml of each tested irrigant and sterile saline (control) was added to the wells. The diameters of the growth inhibition zones were measured after 24 hours of incubation at 37°C for bacteria and after 48 hours for fungi. Digital images of the plates were obtained and analyzed using ImageTool 2.0 software (UTHSCSA ImageTool 2.0, University of Texas Health Science Center at San Antonio, 1995–1996). For each microbial strain, all experiments were performed in triplicate to ensure reproducibility and analytical reliability of the obtained results.

STATISTICAL ANALYSIS

Growth inhibition zones are presented as mean ± standard deviation. Preliminary statistical assessment revealed deviations from normal distribution (Shapiro–Wilk test) and heterogeneity of variances (Levene's and Bartlett's tests). Therefore, two complementary statistical approaches were applied: the non-parametric Kruskal–Wallis test with Dunn's post hoc analysis (Holm correction) and Welch's ANOVA with Tukey's HSD post hoc test. All statistical analyses were performed in R version 4.5.1 using appropriate packages for robust ANOVA and multiple-comparison correction. A significance level of $p < 0.05$ was considered statistically significant.

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

The study included 13 microorganisms capable of causing periodontitis and ten irrigation solutions intended to eliminate pathogenic biofilm within the root canal system. The tested irrigants represented various concentrations of sodium hypochlorite (2%, 5.25%, 5.25% Extra with detergent, and 6%), chlorhexidine 2% (from two manufacturers), EDTA 17% with benzalkonium bromide (0.1%), maleic acid 6%, and citric acid 40%.

Comparison of the efficacy of key irrigation agents: Sodium hypochlorite 5.25% — the clinically recognized standard; Chlorhexidine 2% — an alternative with a broad antimicrobial spectrum; Chlorhexidine 2% Endohex — a commercial CHX modification; comparison

with other hypochlorite solutions, acids, and chelating agents.

Growth inhibition zone diameters for all tested strains (mean ± standard deviation) are presented in Table 1. Pairwise comparisons between irrigation solutions were performed using the Kruskal–Wallis test followed by Dunn's post hoc analysis with Holm correction.

The results demonstrated that sodium hypochlorite 5.25% (Cerkamed) exhibited statistically equivalent antimicrobial activity to sodium hypochlorite 6% and sodium hypochlorite 6% (Chemoplus Chloran) across all tested strains ($p = 0.999$), indicating no significant difference in efficacy between these concentrations or commercial formulations. In contrast, sodium hypochlorite 2% (Cerkamed) showed significantly lower antimicrobial activity compared with 5.25% NaOCl in 11 out of 13 strains, including *Staphylococcus aureus*, *S. epidermidis*, *Streptococcus* spp., and *Candida* spp. ($p = 0.0286$). Only α-hemolytic *Streptococcus sanguinis* did not reach statistical significance ($p = 0.0571$), although a trend toward decreased efficacy was observed.

The detergent-enhanced formulation, sodium hypochlorite 5.25% Extra + Detergent (Cerkamed), demonstrated a significant increase in antifungal activity against *Candida albicans*, *C. lipolytica*, and *C. lusitaniae* ($p = 0.0286$) compared with the corresponding formulation without detergent. These findings suggest that the addition of a detergent to sodium hypochlorite may enhance its antifungal activity, especially against *Candida* species. The trend observed across bacterial strains, while not statistically significant, may warrant further investigation with larger sample sizes to clarify potential synergistic or antagonistic effects. For all other microorganisms tested, including *Staphylococcus aureus*, *Streptococcus* spp., and other *Candida* species, no significant differences were observed ($p = 0.999$), indicating comparable efficacy between the two formulations.

The both tested Chlorhexidine 2% solutions (Cerkamed and Endohex) exhibited statistically equivalent antimicrobial activity to all sodium hypochlorite-based formulations (all $p = 0.999$). Similarly, no significant differences were observed between Chlorhexidine 2% and Chlorhexidine 2% Endohex for any strain. Simultaneously Chlorhexidine 2% demonstrated significantly greater antimicrobial activity compared to Maleic acid 6%, EDTA 17% with benzalkonium bromide (0.1%), and Citric acid 40% for the majority of tested strains. These differences were particularly pronounced for all *Candida* species (p-values were consistently below 0.05).

Maleic acid 6% exhibited significantly lower antimicrobial activity compared to both EDTA 17% and Citric acid 40% across all *Staphylococcus*, *Streptococcus*, and *Candida* strains ($p < 0.0001$). Besides, Maleic acid 6% exhibited significantly lower antimicrobial activity than Sodium hypochlorite 6% in several bacterial strains, including *S. aureus*, *S. epidermidis*, and *Streptococcus spp*. ($p = 0.0286$). These differences were consistent and robust, indicating a clear inferiority of Maleic acid in terms of antimicrobial performance.

In contrast, EDTA 17% with benzalkonium bromide (0.1%) and Citric acid 40% did not differ significantly from each other in any of the tested strains ($p = 0.999$), suggesting comparable antimicrobial efficacy. This equivalence was observed across both Gram-positive bacteria and fungal species, reinforcing the notion that both agents possess similar antimicrobial potential. The both agents demonstrated statistically significant superiority over Sodium hypochlorite 6% in antifungal activity, especially against *Candida albicans*, *C. tropicalis*, *C. lipolytica*, *C. lusitaniae*, and *C. kefyr* ($p = 0.0286$ for all). These findings highlight the potential of chelating agents and organic acids in targeting fungal pathogens, possibly due to their ability to disrupt biofilms or chelate essential ions.

These findings confirm that while EDTA and Citric acid are equally effective and broadly active, Maleic acid 6% is significantly less potent against a wide range of clinically relevant microorganisms. This has important implications for the selection of acidic irrigants in endodontic protocols, particularly when targeting polymicrobial infections

The Kruskal–Wallis test followed by Dunn's post hoc analysis revealed that sodium hypochlorite 5.25% did not differ in antimicrobial activity from 6% NaOCl (both the standard formulation and Chemoplus) but was significantly more effective than 2% NaOCl ($p < 0.05$). Both chlorhexidine 2% solutions (Cerkamed and Endohex) demonstrated antimicrobial activity comparable to NaOCl formulations but markedly exceeded the efficacy of acidic and chelating agents (maleic acid, EDTA, and citric acid) for the majority of tested strains, particularly *Candida* spp. chlorhexidine ($p < 0.0001$). Welch's ANOVA with Tukey's HSD post hoc test confirmed these results, yielding similar conclusions regarding the equivalence of chlorhexidine and NaOCl and their superiority over acidic solutions. All *Candida* spp., as well as most *Staphylococcus* and *Streptococcus* strains, exhibited higher susceptibility to chlorhexidine-based formulations compared with acidic agents.

Figure 1 (Fig.1) summarizes the integral activity of irrigating solutions against bacterial and fungal strains from root canals used in the study. In general, NaOCl- and chlorhexidine-containing irrigation solutions showed comparable antibacterial activity. But sodium hypochlorite solutions 5.25% (Cerkamed) and 6%

(Chemoplus Chloran) both with and without detergent exceed significantly in their antifungal activity. Maleic acid та Citric acid showed almost no activity against root canals *Candida sp*. isolates.

NOVELTY OF THE RESEARCH

The study provides a direct, head-to-head comparison of an extended spectrum of endodontic irrigation solutions (10 formulations) antimicrobial activity under identical *in vitro* conditions against 13 clinical microbial strains associated with the apical periodontitis pathogenesis. The obtained results expand current understanding of the properties, potential advantages, and limitations of commonly used irrigants within the context of root canal infection control.

The findings provide a foundation for further investigations into potential synergistic interactions between individual irrigating agents and may contribute to the refinement of chemomechanical root canal treatment protocols, particularly in clinical situations involving mixed bacterial–fungal infections.

DISCUSSION

The present study demonstrated that sodium hypochlorite-based irrigation protocols exhibited the highest antimicrobial activity against microorganisms isolated from infected root canals of patients with apical periodontitis. The strongest effect was observed in the groups using 5.25% and 6% sodium hypochlorite, whereas the protocol based on 2% sodium hypochlorite showed lower efficacy against several tested strains. These findings are consistent with the results of Vianna et al. [6] and Gomes et al. [7], who reported pronounced antimicrobial activity of sodium hypochlorite against a broad spectrum of endodontic pathogens. Thus, our results confirm the well-established role of NaOCl as one of the most effective chemical irrigants in root canal disinfection. The superior antimicrobial performance of higher-concentration NaOCl observed in the present study can be explained by its stronger oxidative and proteolytic action, which promotes disruption of microbial cells and dissolution of organic tissue remnants. Similar observations have been reported in previous experimental studies, where higher concentrations of sodium hypochlorite showed increased antimicrobial potency, although the difference was not always proportional for all microbial groups [6,7]. At the same time, our findings are in agreement with contemporary reviews emphasizing that antimicrobial efficacy depends not only on concentration, but also on contact time, delivery technique, canal anatomy, and irrigant activation [8,9]. An important result of the present study was the enhanced antifungal activity of the sodium hypochlorite formulation containing surfactants. This finding expands the existing evidence on modified hypochlorite formulations, as most previous studies have primarily focused on antibacterial rather than antifungal effects. The observed improvement may be explained by reduced surface tension and enhanced penetration of the irrigant into dentinal tubules and anatomical irregularities. This is particularly relevant given that Candida spp. have been repeatedly detected in infected and persistent root canal infections, as demonstrated by Rozas and Siqueira [10]. Therefore, our findings not only support previously reported antifungal efficacy of NaOCl [6], but also suggest that surfactant modification may provide an additional clinical advantage in fungal-associated endodontic infections. The antibacterial performance of chlorhexidine observed in the present study is also in line with previously published data. Basrani et al. [11] demonstrated the stability and antimicrobial substantivity of chlorhexidine, while Ballal et al. [12] and Prabhat et al. [13] confirmed its effectiveness against resistant endodontic microorganisms. In our study, CHX Endohex produced the largest inhibition zones against several bacterial strains, which is consistent with these reports. However, in agreement with the literature, chlorhexidine should not be regarded as a full substitute for sodium hypochlorite, because despite its strong antibacterial action, it lacks tissue-dissolving capacity and therefore cannot replace NaOCl as the principal irrigant [11-13].

The findings related to EDTA, citric acid, and maleic acid should also be interpreted in the context of previous studies. Our results showed that these agents demonstrated lower overall antimicrobial efficacy than sodium hypochlorite and chlorhexidine, which supports the concept that their primary role in endodontics is adjunctive rather than disinfectant. This interpretation is consistent with the conclusions of Tonini et al. [9] and Rath et al. [14], who emphasized that chelating and acidic solutions are mainly important for smear layer removal, dentin conditioning, and facilitation of irrigant penetration rather than for direct antimicrobial elimination. Therefore, the present study agrees with existing evidence that these agents should be incorporated into irrigation protocols as complementary components rather than primary antimicrobial solutions. The present findings are also consistent with more recent studies. Hackbarth et al. [15] confirmed the strong antimicrobial efficacy of sodium hypochlorite compared with newer irrigants, reinforcing its position as the gold standard in end-

odontic disinfection. Celikel et al. [16] also showed that NaOCl and chlorhexidine remain highly effective against Enterococcus faecalis, one of the most resistant microorganisms in endodontic infections. Furthermore, the umbrella review by Orozco-Gallego et al. [17] highlighted the clinical value of combining sodium hypochlorite with chelating agents, which supports the multimodal irrigation concept reflected in our findings. Taken together, the results of the present study both confirm and expand the available evidence regarding the antimicrobial performance of commonly used endodontic irrigants. Our data support previously reported superiority of sodium hypochlorite and chlorhexidine over acidic and chelating solutions, while also providing additional comparative information regarding surfactant-modified NaOCl formulations and their enhanced antifungal potential. This may be of particular clinical relevance in cases of persistent or mixed bacterial–fungal root canal infections. The main limitation of this study is its in vitro design and the absence of irrigant activation techniques, which may influence disinfecting performance under clinical conditions. Future research should focus on dynamic activation systems and advanced irrigant formulations, including nanoparticle-based and modified solutions, in order to improve root canal disinfection and enhance the predictability of endodontic treatment outcomes.

CONCLUSIONS

The obtained microbiological findings allow for a differentiated selection of irrigation solutions during endodontic treatment. Chlorhexidine solutions demonstrated superior performance in clinical situations dominated by bacterial flora, whereas sodium hypochlorite remained essential for the effective elimination of fungal biofilms and mixed microbial infections. The comparatively limited antimicrobial potential of acidic and chelating agents confirms their auxiliary role rather than a primary disinfecting function, reinforcing the need for tailoring irrigant selection to the microbial characteristics of each case.

A rational irrigation strategy should integrate the complementary use of chemical agents to achieve broad-spectrum activity against polymicrobial biofilms commonly found in infected root canals. Future research should focus on identifying synergistic irrigant combinations and improving activation techniques to overcome the inherent limitations of in vitro models and enhance the predictability and long-term success of endodontic treatment.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 21.10.2025
ACCEPTED: 20.05.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Improving students' somatic health through aerobic-oriented motor activity

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ABSTRACT

Aim: To investigate the impact of a rationally organized motor activity incorporating aerobic-oriented exercises on the somatic health of university students.

Materials and Methods: The research, conducted in 2025-2026, involved 82 first-year education majors. An experimental group (EG, n = 42) and a control group (CG, n = 40) were formed. The EG students followed the author-developed motor activity program, which incorporated aerobic-oriented exercises, while the CG students followed the traditional physical education program. The students' somatic health was assessed using body mass index (BMI), vital index (VI), strength index (SI), and the Ruffier test.

Results: Positive dynamics in indices were observed in the EG during the research: among male students – BMI by 0.3 kg/m^2, VI by 2.9 ml/kg, SI by 3.5 %, and the Ruffier test by 0.4 c. u.; female students – BMI by 0.5 kg/m^2, VI by 3.1 ml/kg, SI by 1.8 %, the Ruffier test by 0.9 c. u. No significant changes were observed in the CG. The comparative analysis of the studied indicators at the end of the research demonstrated statistically significant ($p \leq 0.05$-0.001) better health indicators in the EG students compared to the CG.

Conclusions: The results of this research demonstrate the effectiveness of a rationally organized motor activity incorporating aerobic-oriented exercises in improving students' somatic health. This will help enhance mental and physical performance, reduce illness incidence, and, consequently, improve students' academic performance during martial law.

KEY WORDS: physical education, motor activity, somatic health, students, aerobic-oriented exercises

Wiad Lek. 2026;79(8):1791-1798. doi: 10.36740/WLek/235893 DOI

INTRODUCTION

Harmonious personal development is supported by adequate motor activity, a key factor in determining the population's health. Adequate motor activity among students is the foundation for proper physical development. Insufficient motor activity leads to declines in students' health and physical fitness and contributes to the onset and progression of various diseases [1, 2].

The ineffective organization of physical education in higher education institutions (HEIs) in Ukraine under current martial law conditions leads to decreased motivation to engage in physical exercise and, as a result, a decline in motor activity among students [3]. According to researchers [4, 5], insufficient motor activity (hypodynamia) significantly affects students' bodies, leading to general weakness, apathy, memory impairment, and a weakened immune system. Prolonged sitting at a desk or computer disrupts metabolism and leads to serious health problems. This can lead to poor posture, scoliosis, osteochondrosis, and muscle atrophy; ligaments become less elastic, increasing the risk of injury. The heart muscle weakens, the volume of blood pumped decreases, tachycardia occurs, and the risk of developing hypertension increases. Due to oxygen deprivation, concentration decreases, mental performance deteriorates, and insomnia, chronic fatigue, anxiety, and de-

pressive states appear. A slowed metabolism can cause weight gain, impair bowel function, and contribute to obesity [6, 7].

The analysis of the literature [8] indicates that most researchers focus on general issues regarding motor activity among young people; however, questions regarding the rational organization of students' motor activity using aerobic-oriented exercises to improve their somatic health remain unresolved. Aerobic exercises are rhythmic activities that engage large muscle groups and use oxygen to produce energy [9]. They train the cardiovascular system, accelerate metabolism, and reduce the risk of developing chronic diseases. Cardio training increases the amount of oxygen supplied to the muscles and improves cardiovascular function. They also help reduce the risk of cardiovascular disease, diabetes, and obesity [10]. Programs incorporating aerobic-oriented exercises consist of cyclic forms of motor activity: walking, running, swimming, cross-country skiing, cycling, aerobics, and cardio machine exercises [11, 12]. Therefore, research on the impact of motor activity involving aerobic-oriented exercises on students' somatic health during martial law is timely and relevant.

AIM

The aim is to investigate the impact of a rationally organized motor activity incorporating aerobic-oriented exercises on the somatic health of university students.

MATERIALS AND METHODS

PARTICIPANTS

The research, conducted in 2025-2026, involved 82 first-year students majoring in education at Dragomanov Ukrainian State University (aged 17-18), including 43 males and 39 females. An experimental group (EG, n = 42 (20 female students and 22 male students)) and a control group (CG, n = 40 (19 female students and 21 male students)) were formed. The students in the EG participated in the author-developed motor activity program incorporating aerobic-oriented exercises (4 training sessions of 1 hour per week under the guidance of health and fitness trainers). In comparison, the CG students followed the traditional physical education program at the HEI (2 training sessions of 2 hours per week under an instructor's guidance). The weekly volume of motor activity (exercise) in the EG and the CG was the same. No special selection of students for the EG and the CG was conducted: the EG included students from the 1st and 2nd academic groups enrolled in 2025 at the Faculty of Pedagogy, and the CG included students from the 1st and 2nd academic groups enrolled in 2025 at the Faculty of Natural Sciences. The exception was students with health impairments, who were assigned to a special medical group and did not attend physical education training sessions. Assessment of baseline somatic health indicators also showed no significant differences between the EG and the CG ($p > 0.05$). The duration of the experiment was 9 months (September 2025 – May 2026). Limitations of the research: during the experiment, we did not account for students' motor activity levels in the EG and the CG during extracurricular hours (such as household and daily activities).

RESEARCH METHODS

Theoretical, medical-biological, and statistical. Theoretical methods enabled us to review the literature on the subject, develop a program for rationally organized motor activity among students, and discuss the results obtained. A total of 20 sources from international scientometric databases were used.

Medical-biological methods were applied to study indicators of students' somatic health. Students' somatic health was assessed using the following morphofunctional indices: body mass index (BMI), vital index (VI), and strength index (SI) (Table 1) [13, 14].

In addition, the Ruffier test was used to assess the functional status of the students' cardiovascular system. After a 5-minute rest in a seated position, the students' heart rate was measured over 15 seconds. Following this, the student performed 30 squats with arms extended forward for 45 seconds. After completing the squats, the HR was measured during the first 15 seconds of the first minute of recovery and during the last 15 seconds of the first minute of recovery. The assessment of the cardiovascular system's functional capacity was determined using a calculation method. The level of the heart's functional reserve and the body's adaptation to physical exertion were determined as follows: less than 3 c. u. – high level; 4-6 c. u. – above average (good); 7-9 c. u. – average; 10-14 c. u. – below average (satisfactory); above 15 c. u. – low level [15].

To determine the students' motor activity at the beginning of the research, we used the Framingham method, according to which each student recorded in a table the number of hours per day spent on activities of varying levels of physical activity. Accordingly, the motor activity index (MAI) was determined. This method describes the day from when students woke up after a night's sleep until they fell asleep, and daily

activity is divided into five levels: baseline, sedentary, low, average, and high [16].

STATISTICAL METHODS

At the beginning of the experiment, the homogeneity of all indicators of the EG and the CG was determined, i.e., the absence of a significant difference in the studied indicators ($p>0.05$), and it was found that the distributions of the EG and the CG are normal, which allowed us to assess the reliability of the results using Student's t-test. The reliability of the difference was set at $p \leq 0.05$. All statistical analyses were performed using SPSS software. The results were presented as Mean ± m, where Mean is the arithmetic mean and m is the standard error of the arithmetic mean.

ETHICAL STANDARDS

The process of research implementation is built following the requirements of scientific ethics. The Academic Ethics Commission of the Dragomanov Ukrainian State University approved the research. The pedagogical experiment was open, and its participants were informed about the aim and tasks of the research, and they voluntarily participated in it.

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

This study was carried according to the research plan of the Faculty of Physical Education, Sports and Health of the Dragomanov Ukrainian State University in 2023-2027 in accordance with the theme "Monitoring, control and evaluation of learning results in physical culture, the basics of healthy lifestyle" (state registration number 0113U009185).

RESULTS

At the beginning of the research (September 2025), we determined the students' motor activity levels using the Framingham method. It was found that at baseline, which included sleep and rest while lying down, the level of motor activity among male students was 8.0 ± 1.9 hours. Traveling by public transport, resting while sitting, and eating – activities that fall under the sedentary level of motor activity – accounted for an average of 4.0 ± 1.4 hours. The analysis of the daily motor activity timings of the students showed that the majority of time is spent at the low level (independent study preparation, personal hygiene, walking, learning sessions at the HEI, excluding physical education) of motor activity, the average duration of which is 9.1 ± 2.6 hours for male students. The indicators for average and high levels of motor activity were the lowest. Thus, the average level of motor activity, which includes household chores, walks, and morning exercises, amounted to 2.6 ± 2.0 hours for male students.

The baseline level, which includes sleep and resting while lying down, accounted for 8.7 ± 1.6 hours of motor activity among female students. Traveling by public transport, resting while sitting, and eating – activities that fall under the sedentary level of motor activity – accounted for an average of 4.2 ± 1.3 hours for female students. The average duration of low motor activity among female students was 10.8 ± 1.8 hours. Thus, the average level of motor activity, which includes household chores, walks, and morning exercises, was 2.6 ± 1.1 hours for female students.

The structure of students' daily motor activity indicates a predominance of sedentary and low levels of motor activity. Thus, on average, female students spend 5.1 hours on studying, and male students – 4.5 hours; approximately 2.5 hours for both female and male students are spent on commuting and eating, while preparation for learning sessions takes 3.0 hours for female students and 1.9 hours for male students. Sitting rest takes about 5.0 hours per day for female students and 3.4 hours for male students.

Thus, the MAI score based on the Framingham method was 25.4 ± 1.5 points for male students and 26.8 ± 2.9 points for female students. Given that the optimal MAI score is 42 points, which corresponds to an eight-hour duration of baseline activity, an eight-hour duration of sedentary activity, a two-hour duration of low physical activity, and a three-hour duration of high physical activity, our research found that no student achieved this score, confirming their low level of motor activity. At the same time, specially organized motor activity among female and male students amounted to 1.1 hours and 0.6 hours, respectively. The results indicate a lack of rationally organized motor activity among students before the start of the experiment.

In light of the above, we designed the author-developed program of rationally organized motor activity that incorporates aerobic-oriented exercises to improve students' somatic health. The program for the EG students was based on systematic, health-improving fitness training sessions led by professional trainers, who took into account the students' gender, level of physical fitness, and individual psychological character-

Table 1. Value of indices for assessing students' somatic health indicators

Indices	Male students					Female students				
	Low	Below average	Average	Above average	High	Low	Below average	Average	Above average	High
BMI, kg/m²	≤18.9	19.0-20.0	20.1-25.0	25.1-28.0	28.1-30.0	≤16.9	17.0-18.6	18.7-23.8	23.9-26.0	26.1-28.0
Points	-2	-1	0	-1	-2	-2	-1	0	-1	-2
VI ml/kg	≤50	51-55	56-60	61-65	≥66	≤40	41-45	46-50	51-56	≥57
Points	-1	0	1	2	3	-1	0	1	2	3
SI, %	≤60	61-65	66-70	71-80	≥81	≤40	41-50	51-55	56-60	≥60
Points	-1	0	1	2	3	-1	1	1	2	3

Source: compiled by the authors of this study

Table 2. Dynamics in somatic health indicators among the EG and the CG students over the course of the research (Mean ± SD)

Indices	Research phase	Study groups		The difference	Significance of the difference	
		EG (n = 42)	CG (n = 40)		t	p
Male students						
BMI, kg/m²	Beginning	22.8±0.27	23.1±0.25	0.3	0.82	>0.05
	End	22.5±0.26	23.4±0.28	0.9	2.36	≤0.05
	t	0.80	0.81			
VI ml/kg	Beginning	53.7±0.85	54.2±0.89	0.5	0.41	>0.05
	End	56.6±0.86	53.8±0.91	2.8	2.24	≤0.05
	t	2.40	0.31			
SI, %	Beginning	63.6±0.75	63.9±0.78	0.3	0.28	>0.05
	End	67.1±0.74	63.7±0.80	3.4	3.12	≤0.01
	t	3.22	0.18			
Ruffier test, c. u.	Beginning	10.3±0.11	10.2±0.12	0.1	0.61	>0.05
	End	9.9±0.11	10.3±0.12	0.4	2.46	≤0.05
	t	2.57	0.59			
Female students						
BMI, kg/m²	Beginning	21.7±0.19	21.5±0.21	0.2	0.71	>0.05
	End	21.2±0.20	21.8±0.22	0.6	2.02	≤0.05
	t	1.81	0.99			
VI ml/kg	Beginning	44.2±0.79	44.6±0.81	0.4	0.35	>0.05
	End	47.3±0.77	44.1±0.83	3.2	2.83	≤0.05
	t	2.81	0.43			
SI, %	Beginning	48.3±0.71	47.7±0.69	0.6	0.61	>0.05
	End	50.1±0.72	47.2±0.70	2.9	2.89	≤0.05
	t	1.78	0.51			
Ruffier test, c. u.	Beginning	10.7±0.12	10.5±0.114	0.2	1.08	>0.05
	End	9.8±0.13	10.6±0.15	0.8	4.65	≤0.001
	t	5.09	0.49			

Legend: t – Student's t-test value, p – statistical significance indicator
Source: compiled by the authors of this study

istics when planning them. Health-improving fitness is a set of carefully selected physical exercises designed to promote health, prevent disease, improve posture, develop flexibility, and correct body alignment. Its main goal is to increase the body's overall tone without harming the heart or joints. Basic aerobics was used for female students, and strength fitness for male students. Basic aerobics is the most common type of aerobics, consisting of a combination of general developmental gymnastic exercises, various types of running, jumps, and hops, performed to music at a tempo of 120-160 beats per minute, using a continuous or series-continuous method. The primary physiological focus of this type of aerobics is the development of endurance and the improvement of the functional capacity of the cardiorespiratory system. High impact is high-intensity basic aerobics that involves active use of jumps and running; it was recommended for students with a high level of physical fitness. Low impact is low-intensity basic aerobics that includes training sessions primarily involving walking, half-squats, and lunges; recommended for students with low physical fitness levels. Step aerobics involves performing exercises on a special platform with an adjustable height ranging from 10 to 30 cm. In step aerobics, two categories were distinguished: students with coordination issues who could not dance during training sessions on the step platform, focusing not on dance movements but on athletic movements with increased physical exertion. Female students with good coordination and dance training performed dance exercises featuring quick transitions, varied movement patterns, and directions. Climbing up and down the steps strengthens the leg muscles and ligaments, while vigorous arm movements strengthen the upper body. Using dumbbells weighing up to 2 kg helped engage the shoulder girdle muscles. Approximately 250 movements were performed on the step platform. To prevent joint overload, the step height should be such that the angle of leg flexion when stepping onto the step is 90 degrees. The load (intensity) was adjusted based on heart rate.

Strength-fitness training sessions for students are aimed to improve cardiovascular function and building strength. Over 50 % of the exercises in the training sessions focused on developing the strength of the shoulder girdle, trunk, and abdominal muscles, as well as the leg and back muscles. Dumbbells, body bars (gymnastic sticks), barbells, medicine balls, and kettlebells were used in the training sessions. Various resistance bands were used to increase the load during strength exercises. Each training session included 6-10 exercises, with 10-12 or more repetitions per set, in 3-6 sets. The load was adjusted by the weight, number of repetitions, sets, exercise pace, and the complexity of coordination.

The results of the study on the effect of a rationally organized, author-developed motor activity program on students' somatic health are presented in Table 2. For all indicators studied in both male and female students, no significant difference was found between the EG and the CG at the beginning of the experiment ($p > 0.05$).

The analysis of BMI showed that during the experiment, the BMI values improved among students in the EG, by 0.3 kg/m^2 among male students ($p > 0.05$) and by 0.5 kg/m^2 among female students ($p > 0.05$). In the CG, conversely, a non-significant deterioration in BMI was observed, by 0.3 kg/m^2 in male students ($p > 0.05$) and by 0.3 kg/m^2 in female students ($p > 0.05$). At the end of the experiment, the BMI values in the EG students were significantly ($p \leq 0.05$) better than in the CG, by 0.9 kg/m^2 in male students and by 0.6 kg/m^2 in female students, respectively. The improvement in BMI among the EG students can be explained by the positive effect of aerobic-oriented exercise on reducing body weight. The BMI values in the EG and the CG correspond to the average level.

Assessment of VI indicates that in the EG, there was a statistically significant ($p \leq 0.05$) improvement in the functional state of the respiratory system among students during the experimental period: by 2.9 ml/kg in male students and by 3.1 ml/kg in female students. In the CG, a negative trend in the VI values was observed ($p > 0.05$): in male students, by 0.4 ml/kg; in female students, by 0.5 ml/kg. At the end of the experiment, the VI values were significantly higher ($p \leq 0.05$) in the EG than in the CG, by 2.8 ml/kg in male students and 3.2 ml/kg in female students. This indicates that aerobic-oriented exercises positively increase vital lung capacity and are quite effective in improving the respiratory system in students. In the CG, the VI at the end of the research was assessed as below average, while in the EG, it was assessed as average.

Assessment of students' muscular system development using the SI values indicates that, in the EG, as with the previous indices, there was an improvement in students' strength, particularly among male students. Thus, over the course of the experiment, the SI values in male students of the EG improved significantly by 3.5 % ($p \leq 0.01$), and in female students by 1.8 % ($p > 0.05$). In the CG, the SI values did not change significantly ($p > 0.05$), although a tendency toward deterioration was observed during training. At the end of the research, the SI values in the EG were significantly higher than in the CG, by 3.4 % in male students ($p \leq 0.01$) and by 2.9 % in female students ($p \leq 0.05$). In the EG, the SI was assessed as average after the experiment, while in the CG, it was assessed as below average.

Assessment of the functional state of the cardiovascular system in students using the Ruffier index indicates that the EG students exhibited positive changes in indicators of cardiac functional reserve and the body's adaptation to physical exertion. Thus, during the experiment, the EG students showed a statistically significant improvement in the Ruffier index values of 0.4 c. u. in male students ($p \leq 0.05$) and 0.9 c. u. in female students ($p \leq 0.001$). No significant changes were observed in the CG ($p > 0.05$). After the experiment concluded, the Ruffier index values in the EG were significantly higher than those in the CG by 0.4 c. u. in male students ($p \leq 0.05$) and by 0.8 c. u. in female students ($p \leq 0.001$). This allows us to conclude that aerobic-oriented exercises positively affect endurance development and the functional capacity of the cardiovascular system in students during their studies. At the same time, the EG exhibited an average level of cardiovascular functional capacity at the end of the experiment, while the CG's level was below average.

The results convincingly demonstrate the greater effectiveness of rationally organized motor activity, based on aerobic-oriented exercises, in strengthening students' somatic health compared to traditional physical education methods in HEIs.

DISCUSSION

Modern living conditions place increased demands on the health and intellectual abilities of young people. Future professionals must possess high professional qualifications and be healthy and physically fit; therefore, students' health is a crucial factor throughout their learning and professional activities [17].

One of the most important factors in improving students' health is active motor activity [18]. This activity is a complex process given the objectively existing contradictions, which include: the contradiction between the large volume of academic and scientific information and the lack of time for motor activity; the contradiction between the desire for autonomy in selecting physical education and health-promoting activities based on personal interests and the rigid framework of the curriculum and academic programs. Furthermore, an extremely significant negative factor currently adversely affecting students' health and motor activity is the war in Ukraine and all its consequences [2, 19].

Therefore, among the main directions of educational modernization, one key priority is improving the quality of management of students' motor activity, a crucial condition for enhancing their somatic health. This requires developing modern programs that rationally organize motor activity to improve students' somatic health and increase motor activity during physical education [3, 20]. Researchers [9, 10] believe that aerobic-oriented exercises – activities during which oxygen serves as the primary source of energy for muscle activity – are the most effective for improving students' health during their studies under martial law. They are widely used as an effective means of strengthening students' health and enhancing their work capacity. In addition, aerobic activity involves prolonged, intense work of many large muscle groups and has physiological and biomechanical effects. With regular aerobic-oriented exercises, heart and lung function improve, the risk of cardiovascular disease decreases, and so on [8, 11]. Taking into account the findings of numerous studies, we designed the author-developed, rationally organized motor activity program using aerobic-oriented exercises to improve students' somatic health, based on systematic health-oriented fitness sessions during their studies at the HEI. Basic aerobics was used for female students, and strength fitness for male students. The results of the research demonstrated a more pronounced effect of rationally organized motor activity based on aerobic-oriented exercises (health-improving fitness) on strengthening students' somatic health than traditional physical education methods in HEIs.

Thus, rationally organized motor activity, which contributes to increasing the capacity and stability of general adaptation mechanisms by improving the functions of the central nervous system, allows not only for maintaining health but also for ensuring high performance in specific types of student activities. The results of our research confirm the conclusions of many scientists in this field and expand upon them.

CONCLUSIONS

The impact of rationally organized motor activity incorporating aerobic-oriented exercises on somatic health among university students was investigated. Positive dynamics in morphofunctional indices were observed in the EG during the research: among male students – BMI by 0.3 kg/m^2, VI by 2.9 ml/kg, SI by 3.5 %, and the Ruffier test by 0.4 c. u.; female students – BMI by 0.5 kg/m^2, VI by 3.1 ml/kg, SI by 1.8 %, the Ruffier test by 0.9 c. u. No significant changes were observed in the CG. The comparative analysis of the studied indicators at the end of the research demonstrated statistically significant ($p \leq 0.05$-0.001) better health indicators in the EG students compared to the CG, according to the following indices: BMI by 0.9 kg/m^2 in male students and by 0.6 kg/m^2 in female students; VI by 2.8 ml/kg in male students and by 3.2 ml/kg in female students; SI by

3.4 % in male students and by 2.9 % in female students; the Ruffier index by 0.4 c. u. in male students and by 0.8 c. u. in female students.

The results of this research demonstrate the effectiveness of a rationally organized motor activity incorporating aerobic-oriented exercises in improving students' somatic health. This will help enhance mental and physical performance, reduce illness incidence, and, consequently, improve students' academic performance during martial law.

PROSPECTS FOR FURTHER RESEARCH

Future research will focus on determining individual levels of motor activity among students who use information and communication technologies.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 07.03.2026
ACCEPTED: 28.07.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Correction of the trace elements content in the oral liquid of patients with periodontitis influenced by complex non-surgical treatment

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ABSTRACT

Aim: To investigate the mineral homeostasis of oral liquid in patients affected by periodontitis and to analyze the impact of the implemented non-surgical therapy on the content of trace elements in the oral liquid at different observation periods, which depended on the severity of the disease.

Materials and Methods: There were somatically healthy individuals enrolled in this study, among them were 70 patients with periodontitis stage I and II, grade A and B and 17 individuals with intact periodontium. The content of Iron, Zinc, Copper and Manganese in oral liquid was determined by adsorption spectrophotometer before, after and 6 and 12 months following the treatment. Comprehensive non-surgical treatment included exo- and endogenous therapy with the microalgae Spirulina platensis.

Results: Examination of all patients with periodontitis demonstrates the content of biometals in the oral liquid with a probably decrease of Iron, Zinc, Manganese and an increase of Copper ($p<0.001$). Changes in the mineral composition depended on the stage and degree of severity and were intensified in the subgroup I B, and even more so in the subgroup II B. After complex treatment administered the amount of Copper and Manganese was normalized (at all terms, for both stages of the disease) and the content of Iron and Zinc was also regulated (especially 6 months after in the subgroups IA and IIA).

Conclusions: It was established that the method of complex treatment based on administration of the blue-green microalgae Spirulina platensis contributes to the normalization of trace element composition in the oral liquid of patients with periodontitis.

KEY WORDS: periodontitis, Iron, Zinc, Copper, Manganese, oral liquid

Wiad Lek. 2026;79(8):1799-1806. doi: 10.36740/WLek/222256 DOI

INTRODUCTION

According to modern scientific researches, the leading role in the pathogenesis of chronic periodontitis belongs to the complex immune-inflammatory reactions of the macro-organism initiated by the plaque biofilm [1]. There are numerous exogenous and endogenous factors such as host genetic component, smoking and diet that can affect the host's immune-inflammatory response and to contribute to disease progression. The reason for the active alveolar bone resorption are processes accelerated by any inflammatory diseases, immunological damage to cell membranes, the influence of various stress factors on the body, carcinogenesis, lack of vitamins and some trace elements, radiation and aging [2].

The principal role of micro- and macro- elements is crucial for the physiological cell functioning, therefore their alterations in biological fluids can be related to the underlying pathological condition. Data of researchers show that oral liquid is a biological environment with a complex micro- and macro-elemental composition and is a place of constant interaction of the oral cavity organs [3-4].

Deficiency of essential trace elements and accumulation of toxic ones in saliva have a local damaging effect and contribute to the formation of periodontal diseases. Periodontal tissues become susceptible to damaging agents of oxidative stress due to an imbalance of biometals in various biological environments. As a result the reparative activity is inhibited, metabolic and structural changes occur [5].

Natural agents with antimicrobial, antioxidant and anti-inflammatory properties deserve special attention in treatment of periodontal diseases. They act gently, have a regulating and normalizing effect, are easily absorbed and are non-toxic, have few adverse reactions such as the development of drug resistance, hypersensitivity and suppression or imbalance of the normal oral microflora [6].

In view of the above, the study of the biochemical composition in the oral liquid is important in the diag-

nosis of periodontal disorders as well as being helpful for the assessment of the complex treatment used.

AIM

To investigate the mineral homeostasis of oral liquid in patients affected by generalized periodontitis and to analyze the impact of the implemented non-surgical therapy on the content of trace elements at different observation periods, which depended on the severity of periodontitis.

MATERIALS AND METHODS

There were 87 somatically healthy 25-44-year-olds non-smokers enrolled in this study.

Among them, there were 70 patients with periodontitis stages I and II, grades A and B according to Classification of Periodontal and Peri-Implant Diseases and Conditions, 2017 [7], and 17 people with intact periodontium (to compare the indicators of affected patients and healthy individuals before therapy and during the treatment). Patients with periodontitis were further divided into I and II groups according to the stages of the severity, and into A and B subgroups according to the rate of progression. Group I included 26 people - 13 in each subgroups I A (stage I of severity, grade A slow rate of progression) and the subgroup I B (stage I of severity, moderate rate of progression), respectively. 44 persons were included in the group II - 21 in the subgroup II A (moderate stage of severity, moderate rate of progression), 23 in the subgroup II B (moderate stage of severity, moderate rate of progression).

The inclusion criteria for the study were: age 25-44 years; patients with periodontitis of stages I and II, grade of progression A and B, without any general somatic pathology, who were not recorded with any medical registration; also with no contraindications to administered treatment regarding pharmacological agents; non smokers; individuals who followed the doctor's recommendations and strictly adhered to the rules of the controlled study, and provided a signed consent permission.

The exclusion criteria were: patients with somatic pathology who were recorded with medical registration; who express some contraindications to recommended treatment and pharmacological agents; pregnancy and lactation or planning of pregnancy during the study; bad habits, such as: smoking, alcohol and drug addiction; untreated or complicated dental caries; orthodontic pathology; presence of irrational and traumatic orthopedic appliances ; partial adentia (more than three teeth); the oral mucosa pathologies; participation in other clinical studies; violation of the conditions of a clinical controlled study.

Healthy individuals were selected according to the same inclusion and exclusion criteria as patients with periodontitis, but an additional condition was the absence of periodontitis.

The level of Iron (Fe), Zinc (Zn), Copper (Cu) and Manganese (Mn) in the oral fluid was determined four times using a C-115 PC Atomic Adsorption Spectrophotometer: before, after, 6 and 12 months after therapy. Oral liquid of 10 ml was collected before breakfast in the morning between 8:00 a.m. to 10:00 a.m. The data of each patient at each stage of the study was recorded into a special examination card we developed. They became the material for statistical processing.

Complex non-surgical treatment consisted of exo- and endogenous therapy. The patients were prescribed with tablets of the blue-green microalgae Spiruline platentis, to be taken 1-2 g (depending on the severity) twice a day, 20 minutes before meals, for a course of 4 weeks. Local therapy comprised the initial periodontal therapy according to the generally accepted method, which depended on the clinical condition, the stage and degree of the disease. We used our extemporaneous paste, which contained equal parts of powdered blue-green microalgae "Spirulina" and powder of silica enterosorbent "Sylard-P", mixed in a 0.05% solution of Chlorhexidine bigluconate to a gel-like consistency for applications and instillations into periodontal pockets.

"Sylard-P" is a medical sorbent approved for clinical use by the Pharmaceutical Committee of Ukraine (protocol No. 1 dated January 23, 1993). The agent is created on the basis of highly dispersed silicon dioxide. Its specific surface is 300 mg per 1 g of substance. This property is responsible for its high adsorption capacity, 1 g of "Sylard-P" binds up to 300-800 mg per 1 g of protein substances and more than 10^9 microorganisms. The obtained mixture was introduced into periodontal pockets and applied to the gingival mucosa for 20-30 minutes. The course lasted for 6-8 procedures after 1-2 days. The microalgae agent "Spirulina" was prescribed by 1.0-2.0 g to be taken twice a day (or 1.0 g three times a day) for 4 weeks.

Chemical composition of "Spirulina" is: protein 60-70%; carbohydrates 10-20%; lipids- 5%. Vitamins (mg/kg): B-carotene (provitamin A) -1700; B1-55; B_2-35; B_5-11; B_6-3; B_{12}-1.6; B_9-0.5; E-190; C-15; RR-118. Minerals and trace elements (mg / kg): Calcium -1180; Phosphorus - 8280; Iron - 528; Sodium - 344; Magnesium - 1663; Iodine - 3; Selenium - 2, etc.

This particular composition of the paste was chosen based on its multidirectional effect on periodontal tis-

sues such as antimicrobial, anti-inflammatory, sorption, antioxidant, as well as for normalizing microelement metabolism, maintaining the optimal level of redox biometals in periodontal tissues in order to reduce oxidative stress and to activate antioxidant processes in periodontal tissues. This helps to inhibit the destruction of connective tissue and alveolar bone. The action of the paste is also enhanced by the general effect of the spirulina prescribed to be taken orally.

Since the treatment of periodontitis requires staged constant therapy, the control, reassessment and local supportive treatment were conducted 6 months after according to each specific clinical situation, using an exogenous recommended by us treatment. If needed, the local treatment was administered again 12 months after, and for groups II A and II B – endogenous therapy as well.

The clinical study was conducted in accordance with the legislation of Ukraine and the principles of the Helsinki Declaration on Human Rights, without the participation of pharmaceutical companies. This study was approved by the Ethical Committee of Ivano-Frankivsk National Medical University (Protocol No 14/06 from 23/11/06). We followed the ethical standards when working with the examined and obtained the written permission from each participant for collection and investigation of biological materials.

Statistical processing of the gained results was carried out by a personal computer, using the Microsoft Excel spreadsheet program. Statistical management of materials was conducted with the "STATISTICA 6.0" package. Analysis of the distribution of the original data (measurement results of the studied indicators) obtained by the Shapiro-Wilk test showed a distribution close to normal. In view of this, to substantiate the hypothesis of equality (presence of difference) of mean values in unrelated (independent) and related (dependent) samples the paired and unpaired Student's t-tests were employed. The paired criterion was applied for dependent samples, namely: to assess the hypothesis that the mean values in the experimental groups (I and II), in particular in the subgroups (IA, IB, IIA and IIB) before and at different times after treatment, proved to be different. The unpaired Student's criterion, on the other hand, was used to check the hypothesis of a difference in data of independent samples, in particular between healthy individuals and all examined of IA and IB subgroups, as well as between healthy and examined of IIA and IIB subgroups. For correlation analysis, we used Spearman's rank correlation coefficient, which is an indicator of the monotonicity of the relationship between two indicators

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

The study was performed within the framework of the scientific topics "Differentiated approaches to the treatment and prevention of dental diseases in the population of Precarpathia" (state registration number 0121U111146) researched by the Department of Pediatric Dentistry of Ivano-Frankivsk National Medical University.

RESULTS

The study shows that there is an imbalance of biometals in the oral liquid of all examined patients affected by periodontitis. Thus, in subgroup I A the level of Fe was reduced in 1.16 times, and in subgroup I B in 1.23 times ($p1<0.001$) compared to healthy people (Table 1).

Complex treatment contributed to a significant increase of its content in subgroup I A - in 1.18 and in 1.17 times immediately, 6 and 12 months after ($p2<0.001$), with the achieved indicators being higher than in healthy people. Complete normalization of the Fe content in the oral fluid also occurred in subgroup I B ($p2<0.001$).

The level of Cu was also elevated in patients with chronic periodontitis in comparison to individuals with intact periodontium, but in the subgroup I A it was implausible ($p1>0.05$), and in I B - reliable ($p1<0.005$). Analysis demonstrates that after appointed therapy the concentration of Cu in the oral fluid of patients in subgroup I A has sharply decreased in 1.21 times ($p2=0.001$), exceeding the norm in 1.10 times ($p1<0.05$). Subsequently, there was a raise in the level of this trace element, and the difference with the data gained before treatment became insignificant ($p2>0.05$). According to the Cu index in the subgroup I A there was a significant difference ($p3<0.05$) found 6 and 12 months after compared to the data gained immediately after treatment, therefore the achieved result was not maintained in the long-term observation period.

In patients with periodontitis of subgroup IB the Cu content was higher in 1.18 times ($p1<0.005$) before treatment. It lowered immediately after its completion in 1.17 times ($p2<0.005$) and reached the data in healthy people. The amount of Cu fluctuated slightly, but remained at a level close to the normal values even in the long term of observation ($p2<0.05$).

The analysis of the data regarding the amount of Zn in the oral liquid showed that this indicator was reduced

Table 1. Changes of biometals in the oral liquid of patients with periodontitis stage I, grade A and B due the complex treatment (M±m)

Indicators	Healthy n=17	Subgroup I A				Subgroup I B			
		Before treatment, n=13	After treatment, n=13	6 months after, n=12	12 months after n=10	Before treatment, n=13	After tratment, n=12	6 moths after, n=10	12 months after, n=9
Fe, mcg/l	763.00 ± 21.14	658.47± 14.60 p_1<0.001	779.19± 16.63 p_1>0.05 p_2<0.001	774.77± 16.66 p_1>0.05 p_2<0.001 p_3>0.05	769.90± 14.06 p_1>0.05 p_2<0.001 p_3>0.05	619.86± 28.14 p_1<0.001	763.67± 11.72 p_1>0.05 p_2<0.001	770.25± 19.00 p_1>0.05 p_2<0.001 p_3>0.05	755.34± 14.39 p_1>0.05 p_2<0.001 p_3>0.05
Cu, mcg/l	80.25± 2.65	87.72 ±3.11 p_1>0.05	72.48± 2.38 p_1<0.05 p_2=0.001	81.34± 2.77 p_1>0.05 p_2>0.05 p_3<0.05	82.01± 2.58 p_1>0.05 p_2>0.05 p_3<0.05	94.61± 3.26 p_1<0.005	80.62± 2.88 p_1>0.05 p_2<0.005	83.34± 2.48 p_1>0.05 p_2<0.05 p_3>0.05	82.48± 2.82 p_1>0.05 p_2<0.05 p_3>0.05
Zn, mcg/l	521.59± 14.64	454.70 ±18.96 p_1=0.01	534.30± 14.28 p_1>0.05 p_2<0.005	529.99± 13.73 p_1>0.05 p_2<0.005 p_3>0.05	523.13± 12.68 p_1>0.05 p_2<0.01 p_3>0.05	440.06± 16.35 p_1=0.001	522.30± 14.64 p_1>0.05 p_2=0.001	513.98± 11.43 p_1>0.05 p_2=0.001 p_3>0.05	511.30± 12.95 p_1>0.05 p_2<0.005 p_3>0.05
Mn, mcg/l	26.16± 1.38	20.12 ±1.60 p_1<0.01	27.20± 1.32 p_1>0.05 p_2<0.005	26.26± 1.37 p_1>0.05 p_2<0.01 p_3>0.05	26.12± 1.45 p_1>0.05 p_2<0.05 p_3>0.05	16.88± 1.51 p_1<0.001	26.34± 1.22 p_1>0.05 p_2<0.001	26.11± 1.32 p_1>0.05 p_2<0.001 p_3>0.05	25.46± 1.27 p_1>0.05 p_2<0.001 p_3>0.05

Note. Here and in Table 2 is indicated the probability of the difference: p1 - to the value in healthy people; p2 – to the value before treatment; p3 - to the value immediately after treatment

Source: compiled by the authors of this study

in 1.15 times in patients with periodontitis in subgroup I A, and in subgroup I B in 1.19 times (p1=0.01; p1= 0.001). It advanced above the norm in both subgroups immediately after treatment, and the difference with the data before treatment was 1.16 and 1.17 times (p2<0.005; p2=0.001).Six months and a year later, the Zn level remained higher in patients of subgroup I A than in healthy individuals, and in subgroup I B this indicator slightly decreased, but stayed close to the norm (p2=0.001; p2<0.005).

The content of Mn compared to healthy ones was reduced in 1.30 (p1<0.01) and in 1.55 (p1<0.001) times in subgroups I A and I B, respectively. Its level advanced due to complex therapy used and was regulated very similarly to changes of Zn over all observation period (p2<0.05-0.001), which indicates a positive impact of our method on these indicators.

The data given in the Table 2 demonstrates that there are disturbances of mineral composition of oral liquid in patients with periodontitis of the group II, similar to those in the group I, but being more pronounced. In particular, concentration of Fe before treatment in subgroup II A was in 1.36 times lower than the normal value (p1<0.001).

The study suggests that there was a convincing increase of Fe content in the oral liquid, reaching the data of healthy people in the long-term follow-up (p2<0.001) as a result of our comprehensive therapeutic measures in these patients. In subgroup II B, the concentration of Fe before treatment was in 1.47 times lower than in healthy subjects. After treatment, it increased in 1.38, 1.40 and 1.39 times immediately, 6 and 12 months after, respectively (p2<0.001).

The growth of Cu was in 1.26 times higher in subgroup II A compared to healthy individuals (p1<0.001). Complex therapy in these patients induced the results close to the norm (p1>0.05) at all periods of observation (p2<0.001; p2<0.005; p2<0.01). Thus, the elevated in 1.34 times (p1<0.001) content of Cu in the oral liquid, patients from subgroup II B decreased sharply in 1.25 times immediately after treatment, improved for another 6 months and almost did not change 12 months after (p2<0.001; p3 >0.05).

Periodontitis was accompanied by a significant (p1<0.001) decrease of Zn in the oral liquid of patients in both subgroups in 1.30 (II A) and 1.38 (II B) times. Complex therapy contributed to a raise of its content in all patients (p2≤0.001), especially being pronounced 6 and 12 months after in subgroup II A, with almost complete normalization of the indicator (p1>0.05). And in subgroup II B, the level of Zn after treatment advanced in 1.28; 1.30 and 1.27 times (p2<0.001) and also reached a norm (p1>0.05).

Table 2. Changes of biometals in the oral liquid of patients with periodontitis stage II, grade A and B due to the complex treatment (M±m)

Indicators	Healthy n=17	Subgroup II A				Subroup II B			
		before treatment, n=21	after treatment n=21	6 months after, n=19	12 months after, n=16	before treatment, n=23	after treatment n=23	6 months after, n=23	12 months after, n=20
Fe, mcg/l	763.00± 21.14	560.85± 24.24 p_1<0.001	711.59 ±18.05 p_1>0.05 p_2<0.001	750.10± 14.89 p_1>0.05 p_2<0.001 p_3>0.05	729.17± 15.92 p_1>0.05 p_2<0.001 p_3>0.05	518.11 ±26.87 p_1<0.001	713.79± 17.81 p_1>0.05 p_2<0.001	724.81± 16.49 p_1>0.05 p_2<0.001 p_3>0.05	718.77± 15.32 p_1>0.05 p_2<0.001 p_3>0.05
Cu, mcg/l	80.25± 2.65	100.79 ±4.06 p_1<0.01	79.52± 2.71 p_1>0.05 p_2<0.001	81.67± 2.66 p_1>0.05 p_2<0.005 p_3>0.05	83.01± 2.92 p_1>0.05 p_2<0.01 p_3>0.05	107.26 ±4.14 p_1<0.001	86.05± 2.75 p_1>0.05 p_2<0.001	84.42± 2.74 p_1>0.05 p_2<0.001 p_3>0.05	87.27± 2.72 p_1>0.05 p_2<0.001 p_3>0.05
Zn, mcg/l	521.59± 14.64	402.08 ±17.11 p_1<0.001	492.90± 13.95 p_1>0.05 p_2<0.01	513.71± 13.36 p_1>0.05 p_2<0.001 p_3>0.05	513.74± 14.74 p_1>0.05 p_2<0.001 p_3>0.05	378.11 ±15.28 p_1<0.001	483.98± 11.92 p_1>0.05 p_2<0.001	489.37± 13.59 p_1>0.05 p_2<0.001 p_3>0.05	480.65± 13.49 p_1>0.05 p_2<0.001 p_3>0.05
Mn, mcg/l	26.16± 1.38	12.96 ±1.48 p_1<0.001	21.81± 1.33 p_1>0.05 p_2<0.01	21.11± 1.15 p_1>0.05 p_2<0.01 p_3>0.05	21.30± 1.69 p_1>0.05 p_2<0.01 p_3>0.05	13.21 ±1.58 p_1<0.001	24.24± 1.35 p_1>0.05 p_2<0.001	23.14± 1.17 p_1>0.05 p_2<0.001 p_3>0.05	22.32± 1.27 p_1>0.05 p_2<0.001 p_3>0.05

Note. See table 1.

Source: compiled by the authors of this study

According to the data gained from our study, there was the largest deviations from the norm of the trace element Mn observed in patients of the II group: in subgroup II A it was reduced in 2.01 times, and in II B – in 1.98 (p1<0.001). The recommended therapeutic complex proved to be successful: the achieved immediately after the treatment levels of Mn were maintained in all patients of the II group (p2<0.001), especially in the II B subgroup, moreover, over the long-term follow-up the obtained indicators were the closest to the data in healthy individuals (p1>0.05).

Via correlation analysis we established also that there were six strong reliable (p<0.05) correlations between the indicators of biometals in the oral liquid in the patients with periodontitis before treatment. Among them, there were three direct ones: between the content of Fe and Zn (r = 0.99), Fe and Mn (r = 0.98), Zn and Mn (r = 0.98) and three inverse ones: between the level of Cu and Fe (r = -0.98); Cu and Zn (r = -0.98) and Cu and Mn (r=-0.93). There were two strong reliable correlations found after treatment, in particular: between Fe and Zn and Fe and Mn immediately (r=0.94; r=0.94) and after six months (r=0.94; r=0.89). There were three reliable correlations between the contents of Fe and Zn (r=0.89), Fe and Mn (r=0.94), Cu and Zn (r=- 0.83) established after a year.

DISCUSSION

Changes in the macro- and microelement composition of biological fluids, such as blood serum and saliva may indicate pathological changes in periodontal tissue according to modern scientific data [8-9]. After all, mineral components such as Calcium, Magnesium, Iron, Selenium and Zink are responsible for normal processes in periodontal tissues, and their imbalance indicates a violation of osteosynthesis, collagen synthesis as well as alveolar bone destruction.

The role of Fe as an irreplaceable element is not the hemoglobin formation only, but also Fe being an important component of various enzyme systems that ensure tissue respiration and immune responses. The optimal level of Fe maintains alveolar bone homeostasis, cellular metabolism of anaerobic periodontopathogens, and the course of immune-inflammatory reactions of the macroorganism on the whole [10].

Thus, according to some researches, an increased level of free Fe can act as a pro-oxidant and catalyze Fenton's reaction, which leads to the reactive oxygen species (ROS) from neutrophils and macrophages [11]. This, in turn, causes the activation of matrix metalloproteinases and the release of pro-inflammatory cytokines, which participate in the destruction of periodontal tissues and resorption of alveolar bone [12].

The obtained by us results indicate the normalization of Fe in the oral liquid after the recommended treatment, which can be considered as an increase of antioxidant protection and cellular immune reactions. At the same time, some researchers note a growth of Fe in the saliva of patients with generalized aggressive periodontitis compared to individuals with healthy periodontium [8].

Thus, both increased and decreased levels of Fe are harmful to the immune response of the host's organism, susceptibility to infections, alveolar bone remodeling, therefore maintaining its optimal level is an important task in the prevention and treatment of periodontal disorders.

Analyzing the results regarding the increase of Cu in the oral liquid of patients with periodontitis compared to persons with healthy periodontium, it should be noted that this fact is consistent with the data of most researchers as Cu is a part of various enzymes and proteins that regulate Fe metabolism and lipid metabolism, as well as the synthesis of connective tissue [4, 9]. Thus, Cu is also present in the active center of lysyl oxidase, an enzyme that forms cross-links between polypeptide chains of collagen and elastin. Therefore, Cu deficiency can lead to the formation of defective collagen [13]. Furthermore, this trace element is important for the proper functioning of the immune system and for the formation of antioxidant status.

After the comprehensive therapy proposed by us, the concentration of Cu in people with periodontitis significantly decreased compared to the indicators before treatment and remained at the level of healthy people even 12 months after therapy.

The results of our study demonstrate a reduction of the Zn content in the oral fluid of patients with periodontitis compared to people with intact periodontium. This statement is consistent with the conclusions of other researchers [14]. The findings of these researchers declare that levels of redox-active metal ions, including Zn, Cu, Fe, Se, and Mn correlate strongly with SOD in saliva and to a lesser extent to SOD in serum which implies a critical role of these redox-active micronutrients in modulating oxidative stress status in periodontitis. On other hand, some scientific data report about increase Zn in saliva with periodontal disease [8]. This suggests that Zn, which is found in the saliva, plaque, and pellicle in different concentrations, limits acid production in dental plaque and inhibits the colonization of bacterial pathogens.

As a result of appointed therapy, there was a raise in the concentration of Zn in the oral fluid of patients to the level of healthy individuals. Thus, the optimal content of Zn is a necessary condition for the functioning of immune protective mechanisms and periodontal bone tissue regeneration, which will further prevent the progression of periodontitis.

Our research signifies a decline of Mn in the oral liquid of patients with periodontitis compared to healthy individuals and are consistent with the data of other researchers [15]. At the same time, some scientists observed a notable advance of Mn in the oral fluid of patients with periodontitis compared to people with healthy periodontium [8-9]. It is well known that Mn deficiency leads to an overall decrease of antioxidant enzymes, superoxide dismutase (Mn-SOD) in particular, which protects against free radicals. An abate of the antioxidant properties of Mn-SOD increases the destruction of connective tissue and alveolar bone by reactive oxygen. The rise of Mn in the saliva after the treatment proposed by us testifies to its positive effect on the activation of antioxidant processes in periodontal tissues.

To summarize, it should be noted that the use of an agent based on the microalgae Spirulina platensis as a part of complex treatment contributed to the regulation of the detected disorders, especially being successful in subgroups I A, II B and II A. Treatment success was evidenced by a reduction of strong reliable correlations from six before treatment to two immediately and within 6 months, and up to three 12 months later. Such an expressive and long-lasting normalization of Fe, Cu, Zn and Mn in the oral liquid was due to the fact that the agent used is of natural origin based on blue-green microalgae is more easily absorbed by the body, as chelated (combined with amino acids) osteotropic biometals of Spirulina platensis are quickly incorporated into biometals included in the microelement exchange of periodontal bone tissue [16-17]. Such properties of spirulina allowed us to achieve positive outcome over the observation periods and contributed to long-term clinical stabilization. Other researches also demonstrate similar results regarding blood trace element indices in patients with chronic periodontitis [18].

CONCLUSIONS

1. There was a significant imbalance of osteotropic biometals, such as Fe, Cu, Zn and Mn found in the oral liquid of all patients with periodontitis compared to healthy individuals($p1<0.005$-0.001), except for the content of Cu in patients with periodontitis stage I severity and slow rate of progression. Changes in mineral composition depended on the stage of severity and the rate of progression of the disease and were amplified in individuals with periodontitis of stage I severity and moderate rate of progression, and even

more so in patients with periodontitis stage II severity and moderate rate of progression. They demonstrated a notable decreased content of Fe, Zn and Mn and an increased amount of Cu in oral fluid.

2. The administration of the proposed complex non-surgical treatment with pharmacological agent Spirulina platensis and the developed paste on its basis contributed to the steady stabilization of homeostasis of microelements, especially Fe, Zn and Mn (amount of which expressively increased) at all observation periods, both immediately and 6 and 12 months after in patients with periodontitis. The obtained data were close to the indicators of healthy people (p1>0.05).

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 20.01.2025
ACCEPTED: 20.05.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Evaluating the performance of electrocardiography and immunological markers (IL-6, TNF-α, and C-Reactive protein) in the diagnosis of left ventricular hypertrophy using echocardiography as the gold standard

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ABSTRACT

Aim: To evaluate the diagnostic performance of ECG criteria and inflammatory markers—interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP)—in detecting LVH.

Materials and Methods: A total of 241 patients with concentric LVH confirmed by ECHO were included and categorised into ECG-positive and ECG-negative groups. Additionally, 50 age-matched controls without LVH were recruited. The diagnostic performance of Sokolow–Lyon, Cornell voltage, and Peguero–Lo Presti ECG criteria was assessed using sensitivity, specificity, and accuracy. Serum levels of IL-6, TNF-α, and CRP were analysed across different levels of left ventricular mass index (LVMI).

Results: Significant differences were observed between ECG groups in interventricular septal thickness, left ventricular diameter, and LVMI ($p < 0.05$). ECG criteria demonstrated low sensitivity (10.37%–20.75%) but high specificity (up to 100%), with limited overall accuracy. In contrast, IL-6, TNF-α, and CRP levels were significantly elevated in patients with severe LVH ($p < 0.001$).

Conclusions: ECG criteria show high specificity but limited sensitivity in diagnosing LVH. Elevated inflammatory markers correlate strongly with disease severity, suggesting their potential role in improving diagnostic accuracy.

KEY WORDS: IL-6, TNF-α, Echocardiography, Electrocardiography, left ventricular hypertrophy (LVH), and C-Reactive Protein

Wiad Lek. 2026;79(8):1807-1818. doi: 10.36740/WLek/225600 DOI

INTRODUCTION

Left ventricular hypertrophy (LVH) is a cardiac condition characterized by an increase in the size and mass of the left ventricle, often resulting from chronic pressure overload due to hypertension, aortic stenosis or other cardiovascular disease. The presence of LVH is associated with increases risk of adverse cardiovascular outcomes, including heart failure, arrhythmias and sudden cardiac death [1]. Early and accurate diagnosis of LVH is crucial for timely intervention and managing event of the underlying causes, hence diagnosis of LVH has become a vital area of research in the field of cardiology [2]. Electrocardiography (ECG) is a widely used, non-invasive tool for the initial assessment of LVH. Over the years, different criteria have been developed for the identification of LVH on ECG, these include Sokolow-Lyon voltage criteria, the Cornell voltage criteria and the Romhilt-Estes score [3]. Age, sex, and BMI can affect the accuracy of LVH criteria, which vary in sensitivity and specificity [4, 5]. Although ECG is widely used to diagnose LVH, echocardiography (ECHO) remains the gold standard because it directly assesses cardiac structure and function. Therefore, comparing different ECG criteria with ECHO findings is important to improve diagnostic accuracy [6]. The Sokolow–Lyon criteria, based on the S wave in V1 and the R wave in V5 or V6, have been widely studied [7]. In a meta-analysis, You et al. (2020) [8] found that the Sokolow–Lyon criteria have a sensitivity of 50–70% and a specificity of 70–80% for detecting LVH when compared to ECHO. The Cornell criteria including QRS voltage and duration have higher sensitivity but may have lower specificity

in some populations [8]. The Romhilt-Estes score, which includes various ECG findings and clinical factors and may improve diagnostic accuracy but requires a more complex scoring system [9]. On the other hand, ECHO provides a more complete assessment of the LVH by measuring the thickness and mass of the left ventricle. LVH was defined according to the American Society of Echocardiography as left ventricular mass index (LVMI) >115 g/m2 in men and >95 g/m2 in women [10]. However, although ECHO is the gold standard, its cost and limited availability in some settings highlight the need for reliable ECG criteria that can be easily used in routine practice [11]. Several immunological markers have been found to be associated with LVH, indicating that inflammation is also involved in heart remodeling. These include IL-6, TNF-α, and CRP, which have been implicated in left ventricular hypertrophy, diastolic dysfunction, and other cardiovascular conditions [12, 13]. Also, CRP is a known marker of systemic inflammation and has been linked with LVH and other adverse cardiovascular events [14]. These results imply that inflammation markers can be used not only for diagnostic purposes but also as predictors in LVH patients. Understanding how they interact with LVH could help us better understand the pathophysiology of LVH and develop new treatment targets. In this study, the diagnostic ability of the three voltage criteria, namely Peguero-Lo Presti, Sokolow-Lyon, and Cornell criteria in LVH, is evaluated based on ECHO test, which is the gold standard for the diagnosis of LVH. The factors involved in assessing the diagnostic ability of the three voltage criteria include sensitivity, specificity, positive predictive value, negative predictive value, and accuracy.

AIM

To evaluate the diagnostic performance of ECG criteria and inflammatory markers—interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP)—in detecting LVH.

MATERIALS AND METHODS

This study employs a cross-sectional and retrospective design that examines medical files of patients referred to Al-Hussain Medical City in Kerbala. The Pulmonology and Cardiology Department supplied the patient records, which had information on demographics, body mass index (BMI), smoking habits, and chronic disease history and medication. The Research and Ethics Committee of Al-Hussain Medical City and the college of Medicine at the University of Kerbala granted approval for the study, and informed consent was obtained from the participants. All patient information was kept confidential and managed by the researchers.

STUDY POPULATION

A total of 241 patients diagnosed with concentric LVH via ECHO analysis were selected for the study. Additionally, 50 age-matched participants without LVH, confirmed through ECHO, were recruited as the control group. All participants underwent ECG evaluations after which they were categorized into two groups: (1) those with positive ECG findings for LVH and (2) those with negative ECG results. The inclusion criteria required that patients had an ECHO conducted within three months prior to the ECG. Only adults 20 years and older, as defined by the World Health Organization (WHO), were included. Patients were excluded if they had LVH due to congenital conditions, factors that could prevent appropriate LVH analysis (like left bundle branch block), deposition diseases, incomplete or inadequate medical records or if they were under the age of 20 years of age.

ECHOCARDIOGRAPHIC EVALUATION

The ECHO assessment included measuring the left ventricular diastolic diameter (LVDD), interventricular septal thickness (IVST), posterior wall thickness (PWT), and ejection fraction (EF). These metrics were used to identify the geometric pattern of the left ventricle based on the formulas proposed by Devereux et al [15]. The left ventricular mass calculation was performed using the formula.

The cut-off values for classifying LVH based on left ventricular mass index (LVMI) were set at 95 g/m^2 for women and 115 g/m^2 for men [10]. All ECHO tests were conducted using GE Vivid E9 BT12 Ultrasound System, (USA). For the classification of LVH into mildly, moderately, or severely increased LVMI, the following criteria were utilized (Table 1).

ELECTROCARDIOGRAPHIC EVALUATION

The performance of ECG is according to international standards using graph paper, a thermosensitive machine set to 25 mm/s, and an amplitude of 10 mm/mV, included 12 leads (aVF, aVR, aVL, DI, DII, DIII, V1, V2, V3, V4, V5, and V6). The ECGs of all 241 patients and 50 participants of the control group were evaluated to calculate the ECG criteria for LVH. The diagnostic criteria employed included: (1) Sokolow-Lyon criterion (SV1 + RV5 or V6 ≥ 35 mV) [7]; (2) Cornell voltage criterion (RaVL + SV3 ≥ 20 mV for women and ≥ 28 mV for men) [16]; and (3) Peguero-Lo Presti criterion (deeper S + SV4 ≥ 2.3 mV in women and ≥ 2.8 mV in men) [17].

Table 1. LVMI classification (g/m^2)

Classification	Males (g/m^2)	Females (g/m^2)
Normal	< 115	< 95
Mildly Increased	115 – 130	95 - 105
Moderately Increased	131 – 149	x106 – 120
Severely Increased	≥ 150	≥ 120

Source: compiled by the authors of this study

Table 2. General features of the patients with LVH by ECHO and positive ECG

	LVH (ECHO) - Positive ECG			
	All	**Male**	**Female**	**p-value**
	(n = 93)	**(n = 44)**	**(n = 49)**	
Age, years (mean±SD)	56.06±13.59	55.07±14.41	56.96±12.91	0.253
BMI Categories, n (%)				
Underweight	2 (2.2)	2 (4.5)	0 (0)	
Normal	35 (37.6)	19 (43.2)	16 (32.7)	0.061
Overweight	28 (30.1)	16 (36.4)	12 (24.5)	
Obese	28 (30.1)	7 (15.9)	21 (42.9)	
Smoking status, n (%)				
Smokers	22 (23.7)	17 (38.6)	5 (10.2)	0.001*
Non-smokers	71 (76.3)	27 (61.4)	44 (89.8)	
Chronic Disease, n (%)				
Yes	85 (91.4)	39 (88.6)	46 (93.9)	0.368
No	8 (8.6)	5 (11.4)	3 (6.1)	
Medication, n (%)				
No	30 (32.3)	19 (43.2)	11 (22.4)	0.033
Yes	63 (67.7)	25 (56.8)	38 (77.6)	

LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; BMI: body mass index
*Statistical significance at $p < 0.05$
Source: compiled by the authors of this study

SERUM CYTOKINE ANALYSIS

Blood samples were drawn for all the participants using anticoagulant free vacutainers were allowed rest at room temperature for 15 – 30 minutes. Serum was prepared by centrifugating the blood samples at 10000 g for 10 minutes after that the supernatant was transferred into Eppendorf tubes and stored at -70 °C, thawed under standardized conditions simultaneously. Serum levels of TNF-α, IL-6, and CRP were measured using commercial ELISA kits: the human TNF-alpha ELISA kit (CytImmune Sciences Inc., Rockville, MD), the human IL-6 ELISA kit (Cell Sciences Inc., Canton, MA), and the Human C-Reactive Protein ELISA Kit (CRP) from Sigma-Aldrich (Massachusetts, United States), adhering to the manufacturers' protocols.

STATISTICAL ANALYSIS

Descriptive statistics regarding age, sex, smoking status, presence of chronic diseases, use of medication and the incidence of LVH were analyzed using the Shapiro-Wilk test to examine normality, followed by the Chi-Squared test. One way ANOVA test and Kruskal Wallis test was used to determine statistical significance between the study groups with respect to ECHO findings, serum cytokine levels respectively. For each ECG criterion in the study, sensitivity, specificity, PPV, NPV, and accuracy were assessed in three contexts: mildly increased LVMI, moderately increased LVMI, and severely increased LVMI, utilizing IBM SPSS Statistics v.25.0 (IBM Corporation, Armonk, New York). Statistical significance was set at $p < 0.05$.

Table 3. Patients with negative ECG

	LVH (ECHO) - Negative ECG			
	All	**Male**	**Female**	**p-value**
	(n = 148)	**(n = 57)**	**(n = 91)**	
Age, years (mean±SD)	57.18±10.37	58.49±11.08	56.34±9.78	0.109
BMI Categories, n (%)				
Underweight	0 (0)	0 (0)	0 (0)	
Normal	71 (48.0)	35 (61.4)	36 (39.6)	0.016*
Overweight	36 (24.3)	13 (22.8)	23 (25.3)	
Obese	41 (27.7)	9 (15.8)	32 (35.2)	
Smoking status, n (%)				
Smokers	39 (26.4)	22 (38.6)	17 (18.7)	0.007*
Non-smokers	109 (73.6)	35 (61.4)	74 (81.3)	
Chronic Disease, n (%)				
Yes	116 (78.4)	40 (70.2)	76 (83.5)	0.055
No	32 (21.6)	17 (29.8)	15 (16.5)	
Medication, n (%)				
No	60 (40.5)	30 (52.6)	30 (33.0)	0.018*
Yes	88 (59.5)	27 (47.4)	61 (67.0)	

General features of the patients with LVH by ECHO but negative ECG, LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; BMI: body mass index
*Statistical significance at $p < 0.05$
Source: compiled by the authors of this study

ETHICS

This work complies with the principles of the Declaration of Helsinki.

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

GENERAL CHARACTERISTICS SUBJECTS

Out of the 241 patients included in the study, 93 (38.6%) showed positive ECG outcome, while the remaining 148 patients (61.4%) had negative ECG result. Table 2 shows the general features of the patients with positive ECG which comprised of 44 males and 49 females with the mean age of 55.07±14.41 years and 56.96±12.91 years respectively. Table 3 shows the general features of the patients with negative ECG which comprised of 57 males and 91 females with the mean age of 58.49±11.08 years and 56.34±9.78 years respectively. The general features if the 50 participants that constitute the control group is presented in Table 4. The comprised of 23 males and 27 females, with the mean age of 53.95±8.37 years and 57.55±14.82 years respectively. Table 5 however, shows the distribution of the study participants with respect to the presence of chronic disease(s).

ECHOCARDIOGRAPHIC PARAMETERS OF THE LVH PATIENTS

The ECHO parameters comparing patients with LVH, categorized based on their ECG results is presented in Table 6. In patients with positive ECG findings for LVH, the IVST was 14.09±1.89 mm, which was slightly lower in those with negative ECG results, i.e. 13.65±1.64 mm. The difference is statistically significant with a p-value of 0.027. For PWT, LVH patients with positive had a mean value of 14.09±1.62 mm, compared to 13.92±1.87 mm in the negative ECG group; however, this difference did

Table 4. General features of the non-LVH participants

	Control group			
	All	**Male**	**Female**	**p-value**
	(n = 50)	**(n = 23)**	**(n = 27)**	
Age, years (mean±SD)	55.23±11.27	53.95±8.37	57.55±14.82	1.153
BMI Categories, n (%)				
Underweight	2 (4.0)	0 (0)	2 (7.4)	
Normal	29 (58.0)	12 (52.2)	17 (63.0)	0.178
Overweight	15 (30.0)	10 (43.5)	5 (18.5)	
Obese	4 (8.0)	1 (4.3)	*3 (11.1)*	
Smoking status, n (%)				
Smokers	11 (22.0)	8 (34.8)	3 (11.1)	0.044*
Non-smokers	39 (78.0)	15 (65.2)	24 (88.9)	
Chronic Disease, n (%)				
Yes	*8 (16.0)*	3 (13.0)	*5 (18.5)*	0.599
No	42 (84.0)	20 (87.0)	22 (81.5)	
Medication, n (%)				
No	44 (88.0)	22 (95.65)	22 (81.5)	0.124
Yes	6 (12.0)	1 (4.35)	5 (18.5)	

LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; BMI: body mass index
*Statistical significance at $p < 0.05$
Source: compiled by the authors of this study

not reach statistical significance. The LVDD was greater in the positive ECG group, (44.75± 4.98 mm) versus the negative ECG group (43.39± 5.51 mm), with a p-value of 0.026, indicating a statistically significant difference at $p < 0.05$. The EF was similar between the two groups with the positive ECG group and negative ECG group having an EF value of 67.00±6.87% and 66.90± 5.82%, respectively. The LVMI was significantly higher in patients with positive ECG findings (134.82±26.19 g/m^2) compared to those with negative ECG result 124.42±23.50 g/m^2), ($p = 0.001$). Regarding diastolic function, the majority of both groups exhibited diastolic dysfunction with 91.4% of the positive ECG group and 90.4% of the negative ECG group reporting the condition. The proportion of participant with normal diastolic function was low in both groups (8.6% in positive ECG and 9.6% in negative ECG), and this difference was not statistically significant (0.961).

DIAGNOSTIC PERFORMANCE OF THE ECG CRITERIA

Diagnostic performance of the ECG criteria was described in Table 6.

Table 7 shows the performance of each ECG criteria in the assessment of concentric LVH as well as the different categories of LVH based on sensitivity, specificity, PPV, NPV and accuracy. In diagnosis of concentric LVH (Table 7A), Sokolow-Lyon criteria showed a sensitivity of 13.69% and perfect specificity of 100%. The PPV was also 100%, while NPV was 19.38%, resulting to an overall accuracy of 28.52%. Cornell criteria exhibited a sensitivity of 10.37%, specificity of 92%, with a PPV of 86.21%, an NPV of 17.55% and an accuracy of 24.4%. Peguero-Lo Presti criteria presented a higher sensitivity of 20.75%, an 86% specificity, a PPV of 87.72%, an NPV of 18.37%, and an accuracy of 31.96%.

Regarding diagnosis of mildly increased LVMI (Table 7B), Sokolow-Lyon sensitivity was 10.09% with 100% specificity, a PPV of 100%, NPV of 33.78%, and accuracy of 38.36%. The Cornell criteria indicated a sensitivity of 9.34%, 88.46% specificity, a PPV of 62.5%, an NPV of 32.17%, and an accuracy of 35.22%. Peguero-Lo Presti showed a sensitivity of 18.35%, specificity of 88%, a PPV of 76.9%, an NPV of 33.08%, and an accuracy rate of 40.25%.

Table 5. Distribution of the study subjects with respect to presence of chronic diseases

	Positive ECG	Negative ECG	Control
	(n = 85)	(n = 116)	(n = 8)
Hypertension (HT)	47	49	0
Diabetes (DM)	9	9	0
Cardiovascular accident (CVA)	0	1	3
Cancer (breast)	0	2	0
Asthma	0	0	0
Rheumatoid arthritis	0	0	2
Hypothyroidism	0	5	2
Systemic lupus erythematosus	0	1	0
Valvular heart disease	2	0	1
HT + DM	16	40	0
HT + CKD	3	2	0
HT + CVA	1	0	0
HT + Hypothyroidism	0	1	0
HT + Hyperthyroidism	1	0	0
HT + Hyperlipidemia	1	0	0
HT + Rheumatoid arthritis	0	1	0
HT + DM + CKD	1	1	0
HT + DM + CVA	1	1	0
HT + DM + Asthma	0	1	0
HT + DM + Hypothyroidism	0	1	0
HT + CVA + Cancer (Non-Hodgkin lymphoma)	1	0	0
HT + DM + Cancer (pancreas)	1	0	0
HT + DM + Cancer (breast)	1	0	0
HT + DM + CVA + Hypothyroidism	0	1	0

Source: compiled by the authors of this study

In the assessment of moderately increased LVMI (Table 6C), Sokolow-Lyon with the sensitivity of 12.72%, maintained a 100% specificity, a PPV of 100%, an NPV of 51.02%, and an accuracy of 54.29%. While for Cornell, the sensitivity dropped to 5.45%, specificity remained high at 92%, PPV was 42.86%, NPV was 46.94%, resulting in an accuracy of 46.67%. The Peguero-Lo Presti demonstrated a sensitivity of 20.83%, specificity at 85.96%, a PPV of 55.56%, an NPV of 56.32%, and an accuracy of 56.19%.

In diagnosis of severely increased LVMI (Table 7D), Sokolow-Lyon criteria indicated a sensitivity of 19.74% with 100% specificity, PPV of 100%, NPV of 45.5%, leading to an accuracy of 54.59%. Cornell showed a sensitivity of 14.47%, specificity of 90%, PPV of 68.75%, NPV of 40.91%, and an accuracy of 44.44%. Lastly, Peguero-Lo Presti criteria reported a sensitivity of 26.32%, specificity of 76%, a PPV of 62.5%, an NPV of 40.43%, yielding an accuracy of 46.03%.

SERUM LEVELS OF INFLAMMATORY MARKERS IN RELATION TO CATEGORIES OF LVH

Fig. 1 is the graphical presentation of the mean values for serum IL-6, TNF- α and CRP of the study groups with respect to their LVH categories. For IL-6, the control group showed a mean level of 3.26±0.42 pg/mL. Patients with mildly increased LVMI had a mean IL-6 level 8.11±1.64 pg/mL for those with a positive ECG and 6.14±1.22 pg/mL for those with a negative ECG. Moderately increase LVMI patients exhibited higher levels of IL-6 levels, with averages of 11.20±2.82 pg/mL for positive ECG and 9.47±2.77 pg/mL for negative ECG. In patients with severely increased LVMI, IL-6 levels were 17.23±3.58 pg/mL for positive ECG group and 18.26±3.02 pg/mL for negative ECG. The p-values for both ECG groups ($p < 0.001$) indicated that the differences were statistically significant (Table 8A).

Regarding TNF-α, the control group had a mean level of 4.54±1.15 pg/mL, and in those with mildly increased LVMI, TNF-α levels averaged at 11.51±1.24 pg/mL for

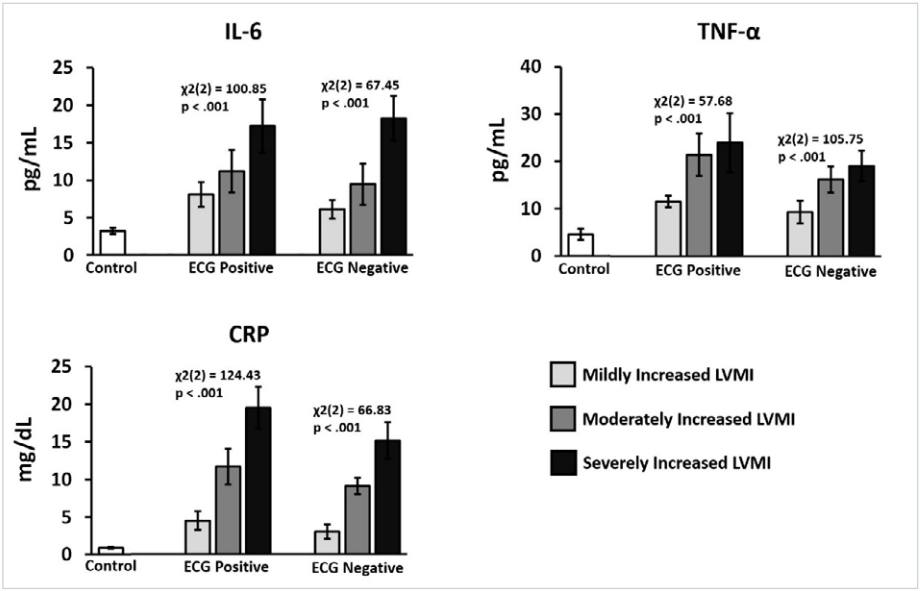

Fig. 1. Serum Levels of IL-6, TNF-α, and CRP in Different LVH Categories
Picture taken by the authors

Table 6. ECHO parameters of the study subjects

	LVH (ECHO)		
ECHO Parameters	**Positive ECG**	**Negative ECG**	**p-value**
IVST (mm)	14.09±1.89	13.65±1.64	0.027*
PWT (mm)	14.09±1.62	13.92±1.87	0.228
LVDD (mm)	44.75±4.98	43.39±5.51	0.026*
EF (%)	67.00±6.87	66.90±5.82	0.456
LVMI (g/m^2)	134.82±26.19	124.42±23.50	0.001*
Diastolic Function, n (%)			
Normal	8 (8.6)	13 (9.6)	0.961
Diastolic dysfunction	85 (91.4)	135 (90.4)	

LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; IVST: interventricular septum thickness; PWT: posterior wall thickness; LVDD: left ventricular diastolic diameter; EF: ejection fraction; LVMI: left ventricular mass index
*Statistical significance at $p < 0.05$x
Source: compiled by the authors of this study

the positive ECG group and 9.33±2.41 pg/mL for the negative ECG group. Patients with moderately increased LVMI presented higher TNF-α levels, with mean values of 21.47±4.52 pg/mL for positive ECG and 16.25±2.78 pg/mL for negative ECG. In patients categorized with severely increased LVMI, TNF-α levels are 24.03±6.27 pg/mL for the positive ECG group and19.09 ±3.24 pg/mL for the negative ECG group. The p-values (< 0.001) confirm that the differences among groups were statistically significant (Table 8B).

Bar graphs illustrating the mean serum levels of IL-6 (top left), TNF-α (top right), and CRP (bottom left) across three groups: Control, ECG Positive, and ECG Negative. Each bar represents the mean ± standard deviation for each group. The colour coding indicates the degree of left ventricular mass index (LVMI): white for Mildly Increased LVMI, light grey for Moderately Increased LVMI, and black for Severely Increased LVMI.

For CRP levels, the control group showed a mean CRP level of 0.88±0.13 mg/dL. For the mildly increased LVMI group, mean CRP levels were 4.51±1.24 mg/dL for those with positive ECG and 3.03±0.95 mg/dL for those with negative ECG. Moderately increased LVMI patients presented even higher CRP levels averaging 11.71±2.38 mg/dL for positive ECG and 9.12±1.08 mg/dL for negative ECG. In the severely increased LVMI category, CRP levels were significantly heightened, with mean values of 19.54±2.78 mg/dL for the positive ECG group and 15.18±2.41 mg/dL for the negative ECG group (Table 7C); the differences among groups were statistically significant with p-value < 0.001.

DISCUSSION

Our study evaluated the characteristic and diagnostic utility of ECG and serum inflammatory markers in pa-

Table 7. Performance of ECG criteria in the assessment of LVH

A.	Concentric LVH				
EGC Criteria	**Sensitivity %**	**Specificity %**	**PPV %**	**NPV %**	**Accuracy %**
Sokolov - Lyon	13.69	100	100	19.38	28.52
Cornell	10.37	92	86.21	17.55	24.4
Peguero-Lo Presti	20.75	86	87.72	18.37	31.96
B.	**Mildly Increased LVMI**				
EGC Criteria	**Sensitivity %**	**Specificity %**	**PPV %**	**NPV %**	**Accuracy %**
Sokolov - Lyon	10.09	100	100	33.78	38.36
Cornell	9.34	88.46	62.5	32.17	35.22
Peguero-Lo Presti	18.35	88	76.9	33.08	40.25
C.	**Moderately Increased LVMI**				
EGC Criteria	**Sensitivity %**	**Specificity %**	**PPV %**	**NPV %**	**Accuracy %**
Sokolov - Lyon	12.72	100	100	51.02	54.29
Cornell	5.45	92	42.86	46.94	46.67
Peguero-Lo Presti	20.83	85.96	55.56	56.32	56.19
D.	**Severely Increased LVMI**				
EGC Criteria	**Sensitivity %**	**Specificity %**	**PPV %**	**NPV %**	**Accuracy %**
Sokolov - Lyon	19.74	100	100	45.05	54.59
Cornell	14.47	90	68.75	40.91	44.44
Peguero-Lo Presti	26.32	76	62.5	40.43	46.03

LVH: left ventricular hypertrophy; ECG: electrocardiography; PPV: positive predictive value; NPV: negative predictive value
Source: compiled by the authors of this study

tients with LVH using ECHO as the gold standard. The findings revealed significant differences in the demographic and clinical features between patients with positive and negative ECG outcomes, particularly in smoking status, BMI and use of medication(s). Notably, smoking status emerged as a statistically significant differentiator, with a higher proportion of smokers in the positive ECG group compared to non-smoking ($p = 0.001$). This aligns with numerous researches that indicate smoking as a known contributor to cardiovascular disease and LVH development [18]. In the control group, smoking was significantly more common among males than females, reflecting sex-related differences in smoking behavior. Additionally, the higher prevalence of obesity in the patients with positive ECG results suggests a correlation between LVH and increase body weight, consistent with findings form previous studies [19, 20], which emphasized the impact of obesity on cardiac load and hypertrophy. Medication use was more common among patients with positive ECG findings than those with negative ECG findings (67.7% vs. 59.5%, $p = 0.033$). This likely reflects the higher burden of underlying cardiovascular comorbidities, particularly hypertension and diabetes, which require long-term pharmacological treatment and are themselves major risk factors for LVH, rather than indicating that medication use is directly associated with the development of LVH. Previous studies have demonstrated that appropriate antihypertensive therapy may improve cardiac remodeling and clinical outcomes in patients with LVH [21].

The control group in this study had a markedly lower prevalence of chronic diseases, while LVH groups exhibited high rates, with the ECG positive group having a higher prevalence than the ECG negative group. This highlights the importance of considering comorbidities in the assessment of LVH, aligning with the meta-analyses conducted by Cuspidi et al. (2018) [22] and Bouthoorn et al. (2018) [23], which respectively highlighted the complicity of hypertension and diabetes in significantly increasing the risk of developing LVH [22, 23] .

The IVST was significantly greater in patients with positive ECG results compare to those with negative ECG results. This is in agreement with a previous study which suggested that IVST is one of the key echocardiographic markers for assessing LVH, supporting its role in

Table 8. Mean serum cytokine levels in relation to LVH categories

A.	IL-6 (pg/mL)		
	LVH (ECHO)		
LVH categories	**Positive ECG**	**Negative ECG**	**Control**
			3.26±0.42
Mildly Increased LVMI	8.11±1.64	6.14±1.22	
Moderately Increased LVMI	11.20±2.82	9.47±2.77	
Severely Increased LVMI	17.23±3.58	18.26±3.02	
p-value	< 0.001	< 0.001	
B.	**TNF-α (pg/mL)**		
	LVH (ECHO)		
	Positive ECG	**Negative ECG**	**Control**
			4.54±1.15
Mildly Increased LVMI	11.51±1.24	9.33±2.41	
Moderately Increased LVMI	21.47±4.52	16.25±2.78	
Severely Increased LVMI	24.03±6.27	19.09±3.24	
p-value	< 0.001	< 0.001	
C.	**CRP (mg/dL)**		
	LVH (ECHO)		
	Positive ECG	**Negative ECG**	**Control**
			0.88±0.13
Mildly Increased LVMI	4.51±1.24	3.03±0.95	
Moderately Increased LVMI	11.71±2.38	9.12±1.08	
Severely Increased LVMI	19.54±2.78	15.18±2.41	
p-value	< 0.001	< 0.001	

LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; LVMI: left ventricular mass index
Source: compiled by the axuthors of this study

the diagnostic process of the disease [24]. These findings highlight the importance of comprehensive ECHO assessment for accurate evaluation of cardiac structure and function. Although PWT did not differ significantly between the groups, its higher value in the positive ECG group supports the role of both IVST and PWT as markers of concentric remodeling, consistent with the findings of Barbieri et al. (2019) [25]. These variables are important to know when trying to understand the pathophysiology of hypertensive heart disease as well as LVH. Moreover, there was a significant difference between the two groups in terms of LVDD, which is higher among those with ECG than those without ECG. This finding is consistent with other literature regarding LVDD [26]. This indicates that patients with positive ECG results may be at an advanced stage of cardiac remodeling. It is interesting to note that while there was no difference in the EF levels between the two groups, our study results corroborate other studies which have shown diastolic dysfunction with normal systolic function [27, 28]. The presence of diastolic dysfunction in the two groups (91.4% of those with positive ECG and 90.4% with negative ECG) indicates that diastolic dysfunction is a common feature in individuals with LVH [28].

Our study indicated that despite the fact that Sokolow-Lyon, Cornell, and Peguero-Lo Presti had very high specificity, sensitivity was still low in all three methods, which raises questions regarding the usefulness of ECG as a means of detecting LVH, especially where there is a need to diagnose LVH accurately. The Sokolow-Lyon criteria exhibited a specificity of 100%, which is in line with earlier studies, as this test is noted for its excellent capability to exclude LVH. Its sensitivity, however, at 13.69%, is quite low, which is

in accordance with other studies [29]. The low NPV of 19.38% and accuracy of 28.52% further accentuate the issue of misdiagnosis, especially among high-risk patients were depending only on ECGs can lead to missing cases of LVH. Also, the Cornell criteria had a low sensitivity of 10.37% but had a comparatively higher specificity of 92%. These results are also supported by a meta-analysis conducted by Zhang et al. (2020) showing that even though the Cornell criteria help in detecting LVH, low sensitivity continues to be an issue [24]. In terms of sensitivity, the Peguero-Lo Presti criteria achieved the highest value (20.75%). Even though it had relatively higher sensitivity compared to the other criteria, its PPV and NPV values were still lower than clinically acceptable values. This means that although the Peguero-Lo Presti criteria have a relatively high sensitivity in diagnosing LVH, it still lacks usefulness because of low PPV and NPV values. This is in line with the study conducted by Grogan et al. (2021) [30]. Likewise, similar trends were identified when assessing the increment in LVMI, where sensitivity was found to improve as the severity of LVH rose. In particular, the Sokolow-Lyon criteria revealed perfect 100% specificity among all categories of LVMI, while sensitivity remained relatively low, illustrating the challenges in recognizing early LVH. The data on mildly and moderately increased LVMI indicate that ECG is more likely to be effective in diagnosing severe LVH but has limited overall effectiveness. This conclusion is supported by the meta-analysis conducted by You et al. (2020) and suggesting that while ECG has good specificity, it cannot be used as a sole diagnostic technique [8]. Additionally, the differences between the criteria used for diagnosing LVH by ECG and the results of ECHOs show the necessity to use a combination of methods for making the diagnosis. The low sensitivity of ECGs is another reason to work on enhancing existing diagnostic criteria or utilizing new technology.

In this study, we also investigated the levels of inflammatory markers - IL-6, TNF-α, and CRP - in relation to LVH and ECG findings. Our results demonstrate a clear association between elevated levels of these inflammatory markers and the severity of LVH which agrees with reports that highlights the relationship between inflammation and cardiac remodeling. IL-6 levels significantly increased with severity of LVMI, as the control participants had normal levels, while patients with mildly increased LVMI demonstrated an increase in the serum levels of the cytokine which increase persisted with moderate and severe LVMI categories. These findings are consistent with previous studies that have illustrated a correlation between IL-6 and cardiac hypertrophy, suggesting that IL-6 might play a role in pathological cardiac remodeling due to its proinflammatory properties. Similarly, TNF-α levels also demonstrated a robust relationship with LVMI severity, starting from a control group mean of 4.54 pg/mL which is slightly above to normal reference range to 24.03 pg/mL in patients with severely increased LVMI with positive ECG results. This finding is paralleled by findings of previous research indicating that TNF-α levels is implicated in myocardial hypertrophy, contributing to the process of cardiac remodeling and dysfunction. The consistently elevated TNF-α levels across all LVMI categories, together with statistically significant p-values, support its potential role as a biomarker for identifying patients at increased risk of progressive cardiovascular disease. The consistently high TNF-α levels among all LVMI groups coupled with significant p-values indicate that TNF-α can be used as a marker to identify individuals who are at a higher risk of developing cardiovascular disease. The clear relationship between increased CRP levels and greater LVH severity further supports the role of inflammation in the pathogenesis of LVH. Although elevated IL-6, TNF-α, and CRP levels were associated with LVH severity, these biomarkers may also be affected by comorbid conditions such as diabetes mellitus, rheumatoid arthritis, systemic lupus erythematosus, and malignancy. Nevertheless, these conditions were present in only a small proportion of the study population and were therefore unlikely to have materially influenced the overall findings. Collectively, the elevated inflammatory marker levels observed in patients with LVH support a close association between inflammation and cardiac hypertrophy, highlighting their potential value as adjunctive biomarkers for diagnosis and risk stratification. Previous studies have also suggested that IL-6, TNF-α, and CRP are not only markers of cardiac stress but may also represent potential therapeutic targets in hypertensive heart disease.

CONCLUSIONS

In conclusion, our findings demonstrate significant clinical and demographic differences among patients with LVH according to ECG findings, highlighting the important role of smoking and obesity in the development and management of cardiac hypertrophy. The high prevalence of chronic diseases in both LVH groups further emphasizes the need for comprehensive patient management that addresses underlying cardiovascular risk factors. The study also highlights the limited diagnostic accuracy of ECG criteria for LVH, particularly in clinical settings with high disease prevalence. Although ECG may be useful

as a screening tool because of its high specificity, its low sensitivity emphasizes the need for comprehensive ECHO evaluation for accurate diagnosis. Furthermore, the higher ECHO parameters observed in ECG-positive patients support the importance of advanced imaging in assessing LVH. In addition, the observed association between elevated inflammatory markers and LVH suggests that these biomarkers may serve as useful adjuncts in diagnosis and future patient management strategies.

Future research should focus on clarifying the molecular mechanisms linking inflammatory markers to the progression of LVH, as our findings suggest that these markers may provide additional insight into the underlying pathophysiology of the condition and help improve diagnostic strategies. Further investigation in this field may contribute to better patient outcomes and more effective management of individuals at risk of LVH.

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The authors wish to thank the Al-Hussain Medical City in Kerbala. The Pulmonology and Cardiology Unit, Iraq for their support.

Source of Funding: University of Al-Ameed.

CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 26.03.2026
ACCEPTED: 08.07.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Gender-specific peculiarities in the manifestation of psychosomatic stress symptoms among law enforcement officers during professional training

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ABSTRACT

Aim: To investigate gender-specific peculiarities in the manifestation of psychosomatic stress symptoms and stress levels among cadets during their training and service activities under martial law.

Materials and Methods: The research involved 134 (71 men and 63 women) cadets. Psycho-emotional and somatic symptoms of stress, as well as the overall level of stress, were assessed using the test proposed by Yu. V. Shcherbatykh twice: before the 4-week field placement in practical police units and after its completion.

Results: It was found that female cadets exhibit more pronounced stress symptoms compared to male cadets, especially after completing their field placements in practical police units. The most pronounced psycho-emotional symptoms of stress in women included anxiety, worry, gloomy mood, difficulty in decision-making; somatic symptoms included pains of an unspecified nature, headaches, low performance, excessive fatigue, and sleep problems. The overall stress level among female cadets was also significantly ($p \leq 0.01$) higher after their field placement than among male cadets, by 3.3 points. During the field placement period, the stress level among male cadets increased by 2.5 points ($p \leq 0.05$), and among female cadets by 5.3 points ($p \leq 0.001$).

Conclusions: The research indicates an urgent need to develop stress resilience among cadets, particularly female cadets, during their professional training to ensure the effectiveness of their academic performance under martial law and their subsequent service activities in practical police units, as well as in developing skills to apply available methods for preventing stress-related phenomena during training and service activities.

KEY WORDS: law enforcement officers, cadets, gender-specific peculiarities, stress, symptoms, health

Wiad Lek. 2026;79(8):1819-1826. doi: 10.36740/WLek/235886 DOI

INTRODUCTION

The war in Ukraine has led to a deterioration in the quality of life for Ukrainians suffering from russian aggression: they are losing loved ones and relatives, their own homes, are forced to move to other regions of Ukraine or abroad, feel the pressure from the destruction of critical infrastructure, which disrupts everyone's comfortable living conditions, unemployment and competition in the labor market are rising, and material well-being is declining [1]. Psychological pressure on people is increasing, anxiety is rising, and this leads to a constant presence of fear, anxiety, nervous tension, uncertainty about the future, and aggression in their lives, while the mind's ability to adapt is diminishing [2]. The forced migration of Ukrainians also leads to conflicts: differences and discrepancies in culture and customs, communication problems, and competition between the local population and internally displaced persons for jobs lead to increased social tension [3]. The issue of stress resilience, which affects an individual's physical and mental health and determines their well-being, is particularly significant in modern society [4-6].

Experts [7] note that law enforcement is one of the most stressful professions, especially under martial law. Given the requirements for gender equality, a significant number of women currently serve in or are training with Ukraine's law enforcement agencies [8]. Therefore, the issue of stress resilience among male

and female law enforcement officers is extremely relevant. At the same time, women and men do not react to stress in the same way. When faced with stressors, men are ready to fight or flee; women, on the other hand, are capable of negotiating in stressful situations [9, 10]. Physiologists note that due to the constant stress women experience, certain processes occur in their bodies related to changes in hormonal balance. Elevated levels of stress hormones weaken the immune system and disrupt hormone production, which in turn accelerates aging and reduces the body's ability to recover. Being in a state of constant psychological stress or experiencing stressful events can alter the endocrine and immune systems, which can exacerbate chronic diseases and/or lead to the development of new ones [11, 12]. This usually leads to additional nervous strain and the subsequent development of new stresses. Law enforcement officers are no exception, as when faced with extreme conditions and various stressful situations, every member of this high-risk profession (both men and women) experiences significant, and at times extreme, stress. A comparative analysis of stress symptoms and stress levels among male and female cadets during training and service activities will inform adjustments to approaches to building stress resilience in law enforcement officers of different genders.

AIM

The aim is to investigate gender-specific peculiarities in the manifestation of psychosomatic stress symptoms and stress levels among cadets during their training and service activities under martial law.

MATERIALS AND METHODS

PARTICIPANTS

The research, conducted in 2025-2026, involved 134 cadets (71 men, 63 women) who were in their fourth training year at Kharkiv National University of Internal Affairs (KhNUIA, Kharkiv, Ukraine), majoring in "Law Enforcement." The cadets' ages ranged from 20 to 22 years. Stress symptoms and overall stress levels among cadets were studied twice: before the start of their field placement in practical police units (Stage 1) and after returning to the HEI (Stage 2). The field placement lasted 4 weeks. No special selection was conducted for the study groups of men and women. Six training groups of KhNUIA cadets majoring in "Law Enforcement" were involved. The inclusion criterion for cadets was their enrollment in a 4th-year training group in the relevant major. The cadets who were on temporary duty leave or receiving inpatient treatment during the research period were excluded. Training conditions, living conditions, food quality, and material and financial support were the same for all cadets. Marital status and the extent to which their parents and relatives were involved in combat missions in the war with russia were not taken into account. The exclusion criterion was the cadet's voluntary desire to withdraw from the research at any time.

RESEARCH METHODS

theoretical analysis and generalization of literature sources, psycho-diagnostic methods, statistical methods. The method of theoretical analysis and generalization of literary sources was used to conduct an analytical review of scientific sources on the outlined range of issues (31 sources (2013-2026) from MedLine, Scopus, Web of Science databases were analyzed).

To identify the characteristics of psychological (intellectual, emotional) and somatic (behavioral, physiological) stress symptoms in cadets while performing training and service tasks under martial law, we used the Stress Level Test (by Yu. V. Shcherbatykh) [13]. The Stress Level Test assesses the degree of manifestation of intellectual, behavioral, emotional, and physiological stress symptoms in respondents, as well as the overall level of stress. The questionnaire form contains 4 sets of 12 symptoms each. If cadets experienced one of the intellectual or behavioral symptoms, they rated it as 1 point; emotional symptoms as 1.5 points; and physiological symptoms as 2 points. Stress levels were assessed as follows: 0-5 points – no stress; 6-12 points – moderate stress; 13-24 points – pronounced stress; 25-40 points – high stress; 41 points and above – excessive stress.

STATISTICAL METHODS

The statistical method was used to process the data obtained. The reliability of the difference was determined using the Student's t-test. The results were presented as Mean ± m, where Mean is the arithmetic mean, m is the standard error. The reliability of the difference was set at $p<0.05$. All statistical analyses were performed using STATISTICA 13.3.1 software package (2018), 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

Table 1. Comparative analysis of psycho-emotional stress symptoms among cadets (n = 134) of different genders before and after their field placement in practical police units, %

Psycho-emotional stress symptoms	Stages of the research					
	Before the field placement			After the field placement		
	Male cadets (n = 71)	Female cadets (n = 63)	Δ	Male cadets (n = 71)	Female cadets (n = 63)	Δ
Predominance of negative thoughts	28.2	30.1	1.9	32.4	39.7	7.3
Difficulty concentrating	14.1	15.9	1.8	16.9	20.6	3.7
Difficulties in decision-making	21.1	23.8	2.7	25.4	31.7	6.3
Impulsiveness, ill-considered decisions	12.7	14.3	1.6	18.3	22.2	3.9
Tendency to shift responsibility	18.3	11.1	7.2	22.5	28.6	6.1
Worry, anxiety	38.1	47.6	9.5	50.7	68.3	17.6
Gloomy mood	25.4	28.6	3.2	30.9	36.5	5.6
Irritability, outbursts of anger	15.5	17.5	2.0	21.1	25.4	4.3

Legend: Δ – the difference between the indicators under study
Source: compiled by the authors of this study

Table 2. Comparative analysis of somatic stress symptoms among cadets (n = 134) of different genders before and after their field placement in practical police units, %

Somatic symptoms	Stages of the research					
	Before the field placement			After the field placement		
	Male cadets (n = 71)	Female cadets (n = 63)	Δ	Male cadets (n = 71)	Female cadets (n = 63)	Δ
Excessive fatigue	12.7	15.9	3.2	18.3	25.4	7.1
A feeling of muscle tension	7.0	7.9	0.9	11.3	14.3	3.0
Digestive disorders	4.2	6.3	2.1	12.7	19.1	6.4
Pain of an unspecified nature, headache	16.9	23.8	6.9	21.1	31.7	10.6
Weakened immune system	8.5	9.5	1.0	11.3	14.3	3.0
Low operational efficiency	15.4	19.1	3.7	19.7	28.6	8.9
Sleep disturbances, insomnia	11.3	15.9	4.6	16.9	25.4	8.5
Heavier smoking and alcohol consumption	9.8	7.9	1.9	12.7	14.3	1.6

Legend: Δ – the difference between the indicators under study
Source: compiled by the authors of this study

the KhNUIA. Also this study followed the regulations of the World Medical Association Declaration of Helsinki. Informed consent was received from all participants who took part in this study.

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

This scientific article was carried out according to the plan of the research work of the Kharkiv National University of Internal Affairs for 2020-2026 "Psychological, pedagogical and sociological support of law enforcement officers" (state registration number 0113U008196).

RESULTS

During the research of psycho-emotional symptoms of stress, it was found that even before the start of their field placement in practical police units, both male and female cadets exhibited symptoms indicating the presence of stress even under the usual conditions of the educational process (Table 1): worry and anxiety was found in 38.1 % of male cadets and 47.6 % of female cadets; the predominance of negative thoughts – in 28.2 % of male cadets and 30.1 % of female cadets; a gloomy mood – in 25.4 % of male cadets and 28.6 % of female cadets; and other symptoms. However, female cadets exhibited a higher level of the vast majority

Table 3. Comparative analysis of stress levels among cadets (n = 134) of different genders before and after their field placement in practical police units, Mean ± SD, points

Research stages	Cadets of different genders		Difference	
	Male cadets (n=71)	Female cadets (n=63)	Δ	t / p
Before the field placement	7.6±0.65	8.1±0.71	0.5	0.52/>0.05
After the field placement	10.1±0.69	13.4±0.75	3.3	3.24/≤0.01
t / p	2.64/≤0.05	5.13/≤0.001		

Legend: Δ – difference between the studied indicators; t – value of Student's t-test; p – level of statistical significance of differences
Source: compiled by the authors of this study

of psycho-emotional stress symptoms (by 1.6-9.5 %) compared to males.

Following the completion of the field placement, there was an increase in the number of cadets of both genders exhibiting psycho-emotional symptoms of stress; however, more pronounced changes were observed specifically among female cadets. Thus, when comparing the increase in the number of male and female cadets with various stress symptoms, it should be noted that among men, the percentage of cadets with the predominance of negative thoughts increased by 4.2 %, and among women – by 9.6 %; with difficulty concentrating – by 2.8 % and 4.7 %, respectively; with difficulty in decision-making – by 4.3 % and 7.9 %; with manifestations of impulsivity and irrational decisions – by 5.6 % and 7.9 %; with the tendency to shift responsibility – by 4.2 % and 17.5 %; with manifestations of anxiety – by 12.6 % and 20.7 %; with a gloomy mood – by 5.5 % and 7.9 %; with manifestations of irritability – by 5.6 % and 7.9 %, respectively. It is worth noting that after completing their field placement in practical police units, female cadets, compared to male cadets, exhibited all psycho-emotional symptoms even more pronounced than before the field placement: the difference ranges from 3.7 % to 17.6 %. All of this indicates that women are more prone to stress and emotional burnout compared to men, and this is particularly acute in the more challenging conditions of law enforcement activities.

When examining somatic symptoms of stress in cadets of different genders, we identified a trend similar to that of psycho-emotional symptoms. In women, both before and after the field placement, symptoms occur more frequently than in men. Moreover, the more stressors are present in training and service conditions, the more frequently and more pronouncedly symptoms manifest in female cadets compared to male cadets (Table 2).

Noteworthy is the high percentage of cadets – both men and women – who, even under normal training conditions, exhibit symptoms such as: pain of an unspecified nature, headaches – 16.9 % of men and 23.8 % of women; low operational efficiency – 15.4 % of men and 19.1 % of women; excessive fatigue – 12.7 % of men and 15.9 % of women; sleep problems (difficulty falling asleep, shallow sleep, insomnia, etc.) – 11.3 % of men and 15.9 % of women. At the same time, for all symptoms (except for smoking intensity and alcohol consumption), the number of female cadets who exhibited them before the field placement was higher compared to men (by 0.9-6.9 %).

After the field placement, the difference between the number of female and male cadets exhibiting somatic symptoms increased in favor of women: 1.6-10.6 %. It should be noted that during the field placement, service-related stressors hurt the manifestation of somatic stress symptoms in both genders; however, more pronounced negative changes were observed specifically among female cadets. Thus, the number of male cadets with excessive fatigue increased by 5.6 %, and among women by 9.5 %; with muscle tension – by 4.3 % and 6.4 %; with digestive disorders – by 8.5 % and 12.8 %; with pains of an unspecified nature – by 4.2 % and 7.9 %; with reduced immunity (manifested in an increase in the number of illnesses) – by 2.8 % and 4.8 %; with low operational efficiency – by 4.3 % and 9.5 %; with sleep disturbances – by 5.6 % and 9.5 %; with signs of increased smoking and alcohol consumption – by 2.9 % and 6.4 %, respectively. The analysis confirms our previous conclusions regarding women's greater susceptibility to stress symptoms, particularly under challenging service-related conditions.

The results of the comparative analysis of stress levels using the test proposed by Yu. V. Shcherbatykh among cadets of different genders before and after their field placement in practical police units is presented in Table 3. It was found that before performing training and service tasks under martial law, stress levels among cadets of both genders were moderate (range: 6-12 points) and did not differ significantly between groups ($p > 0.05$).

During their field placement in practical police units, cadets of both genders experienced a statistically significant increase in stress levels ($p \leq 0.05$-0.001). However,

while the increase was 2.5 points for male cadets, it was 5.3 points for female cadets. It is important to note that after the field placement, female cadets' stress levels were significantly higher than those of male cadets by 3.3 points ($p \leq 0.01$). At the same time, stress levels among male cadets after the field placement were assessed as moderate, while those among female cadets were assessed as pronounced. Our previous findings have been confirmed: female cadets exhibit higher stress levels and more pronounced symptoms compared to male cadets, particularly after prolonged exposure to stressors associated with their service duties.

DISCUSSION

Among the many factors that determine work capacity and other health characteristics of modern individuals, psychological resilience to stressful situations (stress resilience) plays a significant role. A high level of stress resilience is key to maintaining and strengthening an individual's health and professional longevity [14, 15]. Stress resilience is based on the ability to respond appropriately and mobilize in difficult situations, maintain self-efficacy, tolerance, and tact, and filter out unnecessary information or situations [16, 17]. Stress resilience is defined as a complex, integrated personality trait, interrelated with a constellation of intellectual, cognitive, emotional, and personal qualities that enable an individual to endure significant mental, physical, volitional, and emotional stress while maintaining effective functioning in stressful situations [18, 19]. The type of professional activity plays a significant role in the manifestation of this trait – the more extreme the activity, the more pronounced the stress resilience becomes. In particular, the professional activities of law enforcement officers in wartime radically alter their usual way of life, significantly affecting their psycho-emotional state and necessitating adaptation to new working conditions.

Experts have determined that men's stress resilience is higher than women's. While men's stress resilience is more variable due to fluctuations in tension during stressful situations, women react more sharply to such situations [9, 10]. Our research confirms this, as it was found that among female cadets, stress levels and symptoms are more pronounced compared to men, especially after prolonged exposure to stressors associated with their service activities.

Researchers have identified statistically significant differences between men's and women's use of various coping strategies. Women are more emotional under the influence of stressful situations, while men are more likely to avoid stressful situations than women [20, 21]. This is also evident in their behavior. In particular, we found that after female cadets were exposed to extreme conditions during their field placement, their stress levels were significantly higher than those of men by 3.3 points ($p \leq 0.01$). It should also be noted that women exhibit signs of unmotivated anxiety more frequently than men [22]. Researchers [23, 24] have found that indicators of an external locus of control are significantly higher among the women studied: they are more likely to rely on external factors to guide their own behavior and emotional reactions. Internal locus of control is more prevalent among men, who tend to rely on internal resources to manage their behavioral and emotional reactions.

Researchers [25, 26] indicate that differences in stress resilience between men and women depend on individual psychological characteristics. Among respondents with high stress resilience, men differ from women in higher emotional stability, higher levels of self-esteem and self-acceptance, and lower levels of reactive anxiety and emotionality. As our results also show, after exposure to crisis conditions in training and service activities, all psycho-emotional symptoms in female cadets were even more pronounced than before, compared to men: the difference ranges from 3.7 % to 17.6 %. All of this indicates that women are more prone to stress and emotional burnout compared to men, and this is particularly acute in the more challenging conditions of law enforcement service. In turn, among the respondents with low stress resilience, men differ from women in having higher emotional resilience and lower levels of reactive anxiety, emotionality, and social emotionality.

Doctors and physiologists [27, 28] most often observe changes in a woman's body resulting from the negative effects of various stressors. These changes include menstrual cycle irregularities, which result from hormonal shifts triggered by nervous tension. Women are five times more likely to develop diffuse toxic goiter than men. Among the factors that trigger the development of the disease, doctors highlight psychological trauma and prolonged nervous tension. With constant, prolonged nervous stress and exhaustion of the nervous system, illnesses such as acute respiratory viral infections (ARVI), various forms of candidiasis, and cystitis in acute phases or exacerbations of chronic forms occur more frequently than normal. This, in turn, triggers immunodeficiency in women. Women suffer from eating disorders more often than men. Experiencing stress ten times more frequently than men, they tend to engage in emotional eating. Again, the causes of these phenomena are the effects of female hormones: specifically, during stress, estrogen production decreases, levels of the "happiness hormone" serotonin drop, and levels of the "stress hormone" cortisol rise sharply. These physiological processes trigger intense hunger, leading to uncontrolled

consumption of unhealthy foods high in fats and carbohydrates. In women experiencing constant emotional distress, symptoms of nervous reactions and anxiety become increasingly pronounced; somatic reactions appear, and hormonal balance shifts, which in turn trigger the development of diseases and systemic imbalances throughout the body [9, 24]. At the same time, the data we obtained highlight significant prevalence rates of certain symptoms among both male and female cadets: pains of an unspecified nature and headaches – 16.9 % of men and 23.8 % of women; excessive fatigue – 12.7 % of men and 15.9 % of women; sleep problems (difficulty falling asleep, shallow sleep, insomnia, etc.) – 11.3 % of men and 15.9 % of women. As we can see, for various symptoms, the number of female cadets exhibiting them is higher than that of male cadets. This once again underscores women's greater vulnerability compared to men when exposed to stressors.

Thus, our research complements the findings of many scholars [8, 14, 16, 29-31] and expands upon them specifically with results obtained during the assessment of symptoms and stress levels among male and female cadets during training and service activities under martial law.

The development of stress resilience in police cadets should be based on the comprehensive use of preventive and developmental exercises in the educational process, the cultivation of a positive attitude toward situations, the development of skills to reduce the intensity of stressors, and a successful combination of appropriate physical activity and relaxation.

CONCLUSIONS

The research examined gender-specific characteristics of the manifestation of psychosomatic stress symptoms and stress levels among police cadets during their training and service activities under martial law. It was found that female cadets exhibit more pronounced stress symptoms compared to male cadets, particularly after field placements in practical police units. The most pronounced psycho-emotional symptoms of stress in women included anxiety, worry, the predominance of negative thoughts, a gloomy mood, difficulty in decision-making, and the tendency to shift responsibility; somatic symptoms included pains of an unspecified nature, headaches, low operational efficiency, excessive fatigue, and sleep problems. The overall stress level among female cadets was also significantly ($p \leq 0.01$) higher after the field placement than among male cadets, by 3.3 points. During the field placement period, the stress level among male cadets increased by 2.5 points ($p \leq 0.05$), and among female cadets by 5.3 points ($p \leq 0.001$). At the same time, the stress level among men after the field placement is assessed as moderate, and among women as pronounced.

The research indicates an urgent need to develop stress resilience among cadets, particularly female cadets, during their professional training at higher educational institutions to ensure the effectiveness of their academic performance under martial law and their subsequent service activities in practical police units, as well as in developing skills to apply available methods for preventing stress-related phenomena during training and service activities.

PROSPECTS FOR FURTHER RESEARCH

It is planned to investigate the influence of individual psychological characteristics of male and female cadets on the manifestation of stress symptoms and stress levels during training and service activities.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 09.03.2026
ACCEPTED: 10.07.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Conceptual approach to improving dental care under new socio-economic conditions

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ABSTRACT

Aim: To define a conceptual approach to the development of a model for improving dental care under new socio-economic conditions in Ukraine.

Materials and Methods: The study used official statistical data from the Public Health Center of the Ministry of Health of Ukraine, the State Statistics Service of Ukraine, and the Institute for Health Metrics and Evaluation (IHME) regarding the prevalence, incidence, and burden of oral diseases (DALYs) for the period 1991–2023. A sociological survey was conducted among 413 dentists, 360 family physicians, and 368 patients. Bibliographic, descriptive statistical, and analytical methods were applied.

Results: Negative oral health trends, including increased prevalence of dental diseases and a high disease burden, were accompanied by a reduction in public dental infrastructure, insufficient prevention and financing, and decreased access to care, particularly in rural areas. The prevalence of edentulism demonstrated the most pronounced upward trend, particularly among women: by 44% in the 15–49 age group, by 27% in the 50–59 age group, and by 8% among those aged 70 years and older. The incidence of oral diseases among the adult population overall decreased by 5% during the study period, which may indicate a low rate of healthcare utilisation. However, the incidence of edentulism increased, particularly among women aged 15–49 years (by 39%) and 50–69 years (by 18.2%). The prevalence of oral neoplasms rose by 47.5%. 43.3±2.6% of family physicians consider oral health assessment exclusively the responsibility of dentists. Although 42.2±2.6% report examining the oral cavity, this is confirmed by only 23.4±2.2% of patients. Only 27.8±2.4% provide preventive advice on oral health.

Conclusions: Improving the accessibility and quality of dental care requires modernization of the system through diversified financing and a comprehensive conceptual framework encompassing key organizational, financial, technological, educational, preventive, and workforce components.

KEY WORDS: oral cavity, model, organization, indicators, financing

Wiad Lek. 2026;79(8):1827-1833. doi: 10.36740/WLek/235898 DOI

INTRODUCTION

The current stage of development of the dental sector in Ukraine and worldwide is characterised by the search for optimal models of organising dental care that can ensure a balance between economic efficiency and social accessibility [1].

The World Health Organization (WHO) defines key dimensions of the health system as a foundation for ensuring equitable, timely, and effective healthcare, particularly for vulnerable population groups (AAAQ): availability (availability of qualified healthcare professionals, functional infrastructure, and essential medicines); accessibility (access to healthcare facilities and services for all without financial or geographical barriers); acceptability (healthcare services should respect medical ethics and be responsive to gender and life-course requirements of the population); and quality (services must be safe, effective, patient-centred, timely, efficient, and equitable) [2].

In most countries, dental services require substantial co-payments, resulting in high out-of-pocket expenditures for patients. Therefore, socio-economic status is a key determinant of access to dental care, although other factors such as geography, age, and comorbidities may also hinder access and influence outcomes. Furthermore, in most oral healthcare systems, service coverage is predominantly treatment-oriented, with less emphasis on preventive care [3]. This is why the guiding principle of the World Dental Federation (FDI) Vision 2030 programme is the integration of oral health into general health.

To achieve this, three main action areas have been identified: (1) recognition of the need for universal coverage of oral healthcare services, with a focus on prevention and early detection of diseases, bringing dental care closer to patients' places of residence, improving oral health outcomes at lower cost, and creating inte-

grated platforms to increase oral health awareness; (2) recognition that untreated oral diseases constitute a significant share of the burden of noncommunicable diseases; (3) planning resources in oral healthcare in collaboration with governments, educators, and oral health professionals [4].

The transformation of the healthcare system in Ukraine is taking place under conditions of unprecedented socio-economic challenges caused by full-scale military aggression, migration processes, and the transition to a new financing model through the Medical Guarantees Programme. Therefore, the conceptual goal of creating a model for improving dental care for the adult population should be to improve both its accessibility and quality.

AIM

To define a conceptual approach to developing a model for improving dental care under new socio-economic conditions in Ukraine.

MATERIALS AND METHODS

The materials of the study to assess the state of oral health and analyze the performance indicators of dental care institutions, statistical data from the Department of Medical Statistics of the Center for Public Health of the Ministry of Health of Ukraine, the State Statistics Service of Ukraine were used. In this study, data from the Institute for Health Metrics and Evaluation (IHME, USA) were selected and analyzed on the prevalence, primary morbidity and DALY burden of oral diseases (permanent caries, periodontal diseases, adentia) in the world and in Ukraine for the period 1991-2023. The study used a sociological method: to analyze the need, accessibility and quality of dental care, 413 dentists from public and private medical institutions were interviewed; to analyze the interaction between the patient and the family doctor regarding the prevention and treatment of dental diseases, 360 family doctors and 368 patients were interviewed. The analyzed data of the questionnaire survey using specially developed questionnaires by the author allowed to determine the need to improve the model of providing dental care to the adult population in view of the new socio-economic conditions. The work also used bibliographical, descriptive statistical and analytical methods.

ETHICS

During the preparation of the article, the principles of bioethics were observed in accordance with the requirements of the Declaration of Helsinki and the legislation of Ukraine, which was confirmed by the conclusion of the Bioethics Commission of the State Scientific Institution "Center for Innovative Healthcare Technologies" of the State Administration of Health Affairs.

AI STATEMENT

The ChatGPT 5.3 artificial intelligence (AI) tool was used in this work for the formation and formatting of the bibliography under the authors' control. All sections using AI were reviewed and edited personally by the authors. The scientific statements, conclusions, and results are the authors' own intellectual contribution.

FRAMEWORK

The research was conducted as part of the scientific project «Medical and social justification, development and implementation of a modern model of a system for continuous improvement of the quality of integrated medical care in the work of a multidisciplinary healthcare institution» (state registration number 0122U000232; term: 2022-2024) and «Medical and social justification, development and implementation of the «Center of innovative healthcare technologies» model based on the trinity of science, education and practice in the work of a multidisciplinary healthcare institution and determining its role in the formation of a single medical space» (state registration number 0125U000318; term: 2025-2029). The organization and conduct of the study did not require additional funding.

RESULTS

Among the key factors necessitating a revision of the current model of dental care delivery is, first of all, the unsatisfactory state of oral health.

The prevalence of permanent dental caries among the adult population in Ukraine increased across all age and sex groups over the period 1991–2023, with the highest rates observed among women aged 15–49 years (378.0‰) and the lowest among women aged over 70 years (252.3‰). The prevalence of edentulism demonstrated the most pronounced upward trend, particularly among women: by 44% in the 15–49 age group, by 27% in the 50–59 age group, and by 8% among those aged 70 years and older. The incidence of oral diseases among the adult population overall decreased by 5% during the study period, which may indicate a low rate of healthcare utilisation. However, the incidence of edentulism increased, particularly among women aged 15–49 years (by 39%) and 50–69

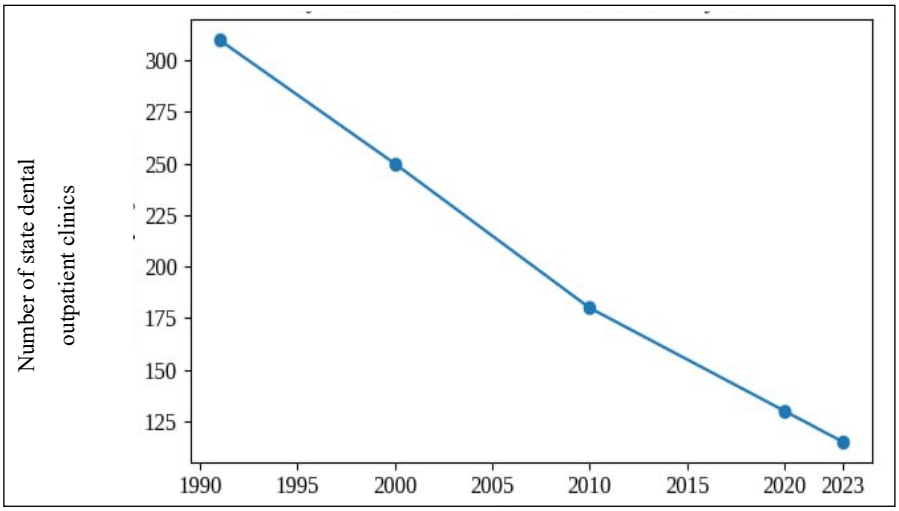

Fig. 1. Dynamics of reduction of state dental outpatient clinics in Ukraine in 1991–2023
Picture taken by the authors

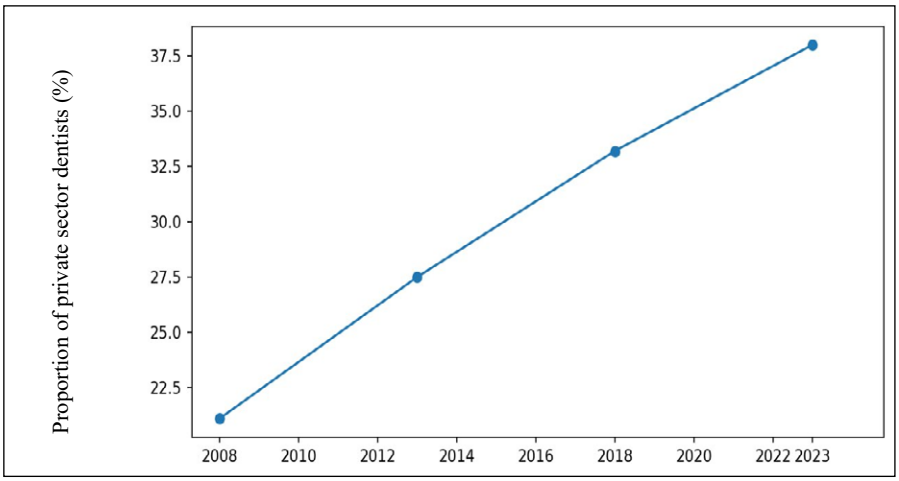

Fig. 2. Growth in the proportion of private sector dentists in 2008–2023
Picture taken by the authors

years (by 18.2%). The prevalence of oral neoplasms rose by 47.5%. The burden of disease due to edentulism remains significant, continuing to result in the loss of years of healthy and quality life to a greater extent than lip and oral cavity cancer (DALY values in Ukraine exceed global estimates by 39.7% and 50.1%, respectively) [5].

Undoubtedly, the increase in dental morbidity in Ukraine has been driven, among other factors, by the reduction and centralisation of dental facilities (Fig. 1), which has negatively affected the territorial and social accessibility of dental care [6]. In recent decades, a significant structural transformation of the dental care network has taken place. As of early 2024, dental care in Ukraine was provided by 1119 public institutions, of which only 115 functioned as independent polyclinics. Over the period 1991–2023, the number of independent public polyclinics decreased 2.7-fold, and the number of public institutions with dental departments or offices decreased 4.7-fold [7].

At the same time, the private sector (Fig. 2) expanded to 3552 facilities (390 dental outpatient clinics and 3162 dental offices) and now dominates the dental care market. However, between 2008 and 2023, the number of private dental outpatient clinics declined by 13.9%, and private dental offices by 4.1% [7].

Structural changes in the sector have also been reflected in the workforce. The number of dentists working in public institutions decreased 2.1-fold, while in the private sector it increased by 5% between 2008 and 2023. The proportion of dentists employed in the private sector rose from 21.1% to 38%. The level of provision of dentists to the population decreased 1.6-fold, reaching 2.3 dentists per 10000 population; for prosthodontists, the decrease was 2.03-fold [7].

In 2021 the frequency of dental visits amounted to 9.5 visits to dentists in public institutions and 9.8 in private institutions per 100 surveyed household members. For urban residents, the respective figures were 9.3 and 10.3, and for rural residents 9.9 and 8.8. The higher utilisation of private dental services in urban areas may be explained by their greater accessibility and perceived quality, despite higher costs. According to official statistics, the total number of visits to private institutions is 2.1 times lower than to public ones. The number of visits per capita to public institutions decreased by 80% to 0.2 per year, and to private institutions by 9.1% to 0.1

per year. The most critical situation regarding access to dental care is observed in rural areas due to the elimination of dentist positions at the primary care level [7].

Against the background of increasing prevalence of edentulism in Ukraine, both the accessibility and the volume of prosthodontic care have declined: the number of individuals receiving dental prostheses (per 100 population) in public institutions decreased by 71.4%. Evidently, prosthodontic care is more accessible to urban populations than to rural populations (2.5 times higher in public institutions and 1.7 times higher in private institutions) [7].

When discussing access to prosthodontic care, it is also important to consider patients' ability to pay, particularly among the elderly, as well as their mobility and transport logistics to remote dental facilities.

Another important factor necessitating improvements in the dental care system is the insufficient level of public healthcare financing (only 2.6% of gross domestic product is allocated to healthcare compared to the WHO-recommended 6.4%), which results in high service costs. According to 75.3±2.1% of dentists and 64.4±2.5% of family physicians, the main barrier preventing patients from visiting a dentist is the high cost of services. However, 60.3±2.4% of dentists consider the cost of services to be adequate for the financial capacity of most patients, whereas 82.2±2.0% of family physicians regard it as excessively high.

Another pressing issue is the critical state of preventive care. In 2023, population coverage with preventive examinations remained extremely low: only 5.3% of the population underwent planned check-ups. Among those examined, 60.6% required oral sanitation/treatment, but only 61.7% received it [7].

The new financial and social mechanisms ensure free access only to emergency dental care for adults, while the minimal base tariff (consultation) for dental services (1,94 – 4,84 Euro) discourages private clinics from contracting with the National Health Service of Ukraine. A positive exception is the pilot project on dental prosthetics for Ukraine's defenders, under which 275 dental care providers were contracted in 2024 (93% of them public and municipal institutions) [8].

The development of dental services is hindered by the lack of widespread implementation of modern technologies based on evidence-based medicine, limited capacity to adhere to clinical protocols, outdated reporting indicators – particularly in public institutions – and the outflow of qualified specialists to the private sector [9].

At the center of a model for improving dental care should be the patient and the health of his oral cavity, since patient-centricity, as a measure of high-quality medical services, is a focus on respecting the individual preferences, needs and values of the patient.

The search for optimal solutions to ensure a balanced coexistence of the public and private dental sectors, and their further regulation at the legislative level, should remain a priority for state authorities. The most likely policy options include [1, 10–12]:

• permitting revenue-generating activities within official working hours to compensate for service volumes and high-cost technologies not covered by budget funding, as well as staff remuneration;

• transitioning to lease-based management of dental facilities by staff collectives, with provision of a defined volume of services to preferential population groups under agreements with local authorities (state procurement), alongside legally regulated paid services for other population groups;

• corporatisation of dental institutions (preferably closed joint-stock companies) with preferential access to state contracts and deferred buyout of fixed assets;

• contracting private companies to manage and operate existing public or municipal healthcare facilities (franchising);

• introduction of universal health insurance.

The proposed model for improving dental care includes informational and analytical, technological, educational and methodological, preventive and health-improving components.

The fundamental block that can ensure optimal accessibility of dental care may be considered the resource and personnel support block, in which three segments should be distinguished: private, public, and family medicine. Private dentistry, as an alternative healthcare sector, creates healthy competition and contributes to improving quality; however, it also exacerbates inequalities by effectively dividing patients according to their financial capacity. Private dental institutions have significantly greater opportunities to utilise modern, high-cost technologies and equipment compared to public facilities.

An important approach is the involvement of family physicians in the prevention and early detection of oral diseases. However, there is often a lack of awareness regarding their role in monitoring and prevention, compounded by insufficient knowledge of dental pathology and preventive care. According to the survey data, it was established that 43.3±2.6% of family physicians consider oral health assessment exclusively the responsibility of dentists. Although 42.2±2.6% report examining the oral cavity, this is confirmed by only 23.4±2.2% of patients. Only 27.8±2.4% provide preventive advice on oral health. For regular visual examination of the oral cavity by family physicians, appropriate conditions

(e.g., lighting and mirrors) must be ensured, along with continuous professional training in oral health.

DISCUSSION

Disparities in oral health reflect inequalities in access to dental care, particularly between urban and rural populations and among low-income communities, due to geographic isolation and financial constraints. These challenges are especially acute for people with special needs. Limited access to dental services significantly contributes to these disparities. Integrating oral health into general medical education and primary healthcare can improve preventive measures and screening, leading to better treatment outcomes and reduced healthcare costs [13–15]. Patient-centred care represents a mutually beneficial partnership between healthcare professionals and patients, enabling shared decision-making [16]. Although most patient visits still occur in public institutions, approximately 10% of citizens have no access to dental care, particularly prosthodontic services. Therefore, new organisational models are required, including public–private partnerships [17, 18].

Accessibility of dental care is reflected in utilisation rates: 24% in India, 20% in Saudi Arabia, 24% in China, and around 20% in developing European countries. In the United States, the presence of health insurance schemes increases utilisation to 92.9% [19]. Resource mobilisation through universal health coverage enables financial risk-sharing across population groups, which is particularly important for low-income populations for whom treatment costs are often prohibitive [20]. Improving dental care is closely linked to the implementation of advanced management technologies that provide analytical information in four key areas: healthcare delivery, staff, patients, and finances [12].

Globally, healthcare quality control systems have evolved into comprehensive quality management systems, encompassing the organisation of care delivery and resource provision (technical, human, financial), and the implementation of modern standards and clinical protocols as essential conditions for ensuring high-quality dental services [21]. Higher education institutions should primarily train general dental practitioners (family dentists), with opportunities for further specialisation after 2–3 years of practice [22]. The FDI promotes the integration of dental care into primary healthcare and universal health coverage to overcome barriers, particularly for low-income, vulnerable populations and refugees [23].

Integration of oral health into primary healthcare represents a strategic approach to improving access, reducing costs, and managing oral diseases as part of overall health, recognising the bidirectional relationship between oral and systemic diseases [24]. Educational efforts are essential to equip all healthcare professionals, particularly family physicians, with the knowledge, skills, and competencies required for effective prevention and management of oral diseases, as well as to improve oral health literacy among patients [4]. In the current context of healthcare reform in Ukraine, the conceptual approach to improving dental care should be based on the principles of patient-centredness, integration, intersectoral collaboration, and social justice. Experience from European Union countries shows that integrated models of dental care involving health insurance mechanisms and public–private partnerships contribute to reducing inequalities in access to dental services and improving population oral health indicators [25–27].

CONCLUSIONS

The state-managed dental care system requires modernisation; however, particularly in wartime conditions, the state lacks sufficient budgetary resources to equip dental facilities with modern equipment, materials, instruments, and technologies. Therefore, additional sources of financing are required, including out-of-pocket payments, employer contributions, and insurance mechanisms. Economic challenges, largely driven by the war, have affected the availability of dental care, especially for low-income groups and rural residents. A conceptual approach to the development of a model for improving dental care will help improve its accessibility and, consequently, its quality.

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CONFLICT OF INTEREST
The Author declare no conflict of interest

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RECEIVED: 10.03.2026
ACCEPTED: 27.07.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Development and validation of a method for determining the quantitative content of amoxicillin in suspensions for injection based on coconut oil and aluminum stearate

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ABSTRACT

Aim of the work was to develop and validate a method for determining the quantitative content of amoxicillin in suspensions for injections by the method of liquid chromatography.

Materials and Methods: The analysis was performed on a Dionex Ultimate 3000 liquid chromatograph, equipped with an LPG-3400SD pump, an ACC-3000 autosampler, and a DAD-3000 diode array detector. The samples were separated on an Acclaim C18 250 × 3.0 mm chromatographic column. The mobile phase was a mixture of 0.01 M potassium dihydrogen phosphate with a pH of 2.5 and acetonitrile in a volume ratio of 4:1. The eluent supply rate was 0.5 ml/min, amoxicillin was detected at an absorption wavelength of 225 nm. The test and standard samples were dissolved in the mobile phase to a concentration of 150 µg/ml of amoxicillin. The results were calculated using the Chromeleon 7.2 software. We determined the overall uncertainty of the analysis, the parameters of the chromatographic peak, and validated the method according to the indicators of accuracy, precision, linearity, robustness (stability of solutions over time).

Results: Under the above conditions, it was possible to completely separate amoxicillin and other components of the studied medicines. It was found that amoxicillin was stable in the test solution for 4 hours, and the suitability parameters of the chromatographic peaks did not exceed the limits specified in the recommendations for analytical research methods. The calibration curve was linear in the recommended range (80–120% of the nominal concentration of the active substance). The coefficient of linearity (R^2) was 0.9997. The extraction of amoxicillin under the conditions of its addition to the matrix and the repeatability of the method were within the limits established by the State Pharmacopoeia of Ukraine.

Conclusion: The method is suitable for routine use in the study of the quantitative content of amoxicillin in suspensions for injections.

KEY WORDS: high-performance liquid chromatography, validation, antibiotics, amoxicillin

Wiad Lek. 2026;79(8):1834-1841. doi: 10.36740/WLek/235902 DOI

INTRODUCTION

Amoxicillin is one of the most common antibacterial substances from the β-lactam group, with a wide spectrum of action, as it exhibits activity against both gram-positive and gram-negative bacteria [1] The effect on target microorganisms is manifested by irreversible binding to membrane proteins, blocking transpeptidation - an important element in the synthesis of the cell wall, leading to the death of bacteria [2]. Amoxicillin (in the form of trihydrate) is used in veterinary medicine in the form of powders for oral use, tablets, antimastitis suspensions and suspensions for injections [3]. The number of veterinary medicinal products on the market of Ukraine, which contain amoxicillin, increases every year, which requires the introduction of fast and accurate methods of quantitative and qualitative control of this substance [4]. Suspensions for injections are one of the most difficult objects for chemical analysis of amoxicillin dosage forms, since the hydrophilic antibiotic is combined with a hydrophobic base - oil and suspension stabilizers, which can make it difficult to extract amoxicillin from the matrix [5], [6]. Among suspensions for injections, the most common base is fractionated coconut oil mixed with a suspension stabilizer - aluminum stearate [7]. That is why veterinary medicines and their basis are taken for research.

The methods of ultraviolet spectrophotometry, electrophoresis, and high-performance liquid chromatography with various types of detectors are used to identify and quantify amoxicillin in medicines [8]. One of the most accurate methods of controlling the identity and quantitative content of active substances is high-performance

Table 1. The studied validation characteristics and their acceptance criteria

Validation characteristics	Criteria
The range of application of the method	80–120%
Tolerances of amoxicillin content in medicines	10%
Maximum test uncertainty	≤3,2%
The number of replicate injections to determine each validation parameter	≤5
Selectivity	Absence of interferences in the retention time zone of the analyte
Linearity	$R^2 \geq 0,997$
The application range	80–120 % of the nominal concentration
Recovery	96–104 %
Accuracy	≤ 3,2 %
Stability /Deviation	Deviation ±1,02 % from the initial value

Note: Statistical data processing was carried out using the StatPlus 7.6.5.0 program package (AnalystSoft Inc., USA).

liquid chromatography with diode-matrix detection. It allows not only to separate the active substance from the matrix, but also to identify the active substance and the purity of its chromatographic peak based on the light absorption spectrum (usually from 195–800 nm) [9].

Therefore, to determine the identity and quantitative content of amoxicillin in suspensions for injections based on coconut oil and aluminum stearate, it was decided to use high-performance liquid chromatography with a diode-matrix detector, and to confirm the quality of the developed method - to validate it according to State Pharmacopoeia of Ukraine.

AIM

Aim of the work was to develop and validate a method for determining the quantitative content of amoxicillin in suspensions for injections by the method of liquid chromatography.

MATERIALS AND METHODS

The laboratory for quality control, safety and registration of veterinary medicines and feed additives of «DEVIE» (Rivne) was the place of research.

The studied medicines are Klamoxyl LA and Amoksidev 15, which are white suspensions. Active substance: amoxicillin - 150.0 mg/ml. Additional substances: aluminum stearate, fractionated coconut oil.

Appearance, density and sterility were determined according to the State Pharmacopoeia of Ukraine.

Determination of the identity and quantitative content of amoxicillin was carried out by the method of ultrahigh-performance liquid chromatography with spectrophotometric detection. A standard sample of amoxicillin trihydrate manufactured by Sigma-Aldrich was used in the work. The initial solution of the standard sample (amoxicillin trihydrate based on the basis) with a concentration of 1.5 mg/ml was prepared taking into account the purity according to the quality certificate, by dissolving it in the mobile phase. The initial solution was diluted with the same solvent to construct the calibration curve in concentrations of the standard sample of 120, 135, 150, 175, 190 µg/ml. The investigated samples of suspensions for injections were dissolved to a concentration of amoxicillin - 150 µg/ml.

The analysis was performed on a Dionex Ultimate 3000 liquid chromatograph equipped with an LPG-3400SD pump, an ACC-3000 autosampler and a DAD-3000 diode array detector. The samples were separated on an Acclaim C 18 250 × 3.0 mm chromatographic column. Detection was carried out at the second absorption maximum of amoxicillin in the ultraviolet part of the spectrum - 225 nm. The results were calculated using the Chromeleon 7.2 software.

The validation of the analytical method was carried out in accordance with the requirements [10] and the guidance on the validation of methods by the method of high-performance liquid chromatography of the FDA [11] (Table 1).

RESULTS

The first key parameter for assessing the suitability of the method is the range of application of the method, which according to [10] for analytical methods in the determination of active substances in medicines is 80–120% of the nominal concentration of the analyte in the working solution of the standard sample and the test sample. This value defines the range of linearity and accuracy.

An extremely important parameter of validation is the tolerances of the substance under investigation (this indicator is determined by the manufacturer of the

Table 2. Components of general uncertainty in tests of Klamoksil LA and Amoksidev 15

Sample preparation	Calculation formula parameter	Uncertainty
Preparation of a working solution of a standard sample of amoxicillin		
1. Selection of the dosage of SZ amoxicillin	m_0	0,40%
2. Bringing to volume in a measuring flask 100 ml	100	0,17%
3. Selection of an aliquot with a pipette of 1 ml	1	0,98%
4. Bringing up to a volume in a measuring flask of 10 ml	10	0,50%
Preparation of the working solution of the test sample		
5. Selection of the mass of the medicines for study	1	0,98%
6. Bringing up to a volume in a volumetric flask of 100 ml	100	0,17%
7. Selection of an aliquot with a pipette 1 ml	1	0,98%
8. Bringing up to a volume in a measuring flask of 10 ml	10	0,50%

medicinal product), since this value further determines the further parameters of the validation of the method, such as the maximum uncertainty of the analysis result, accuracy, precision and robustness. According to the requirements for the drug, the established tolerance limits are 10%. Using the tolerance limits of the active substance according to the formula [10], the maximum permissible uncertainty of the analysis result is calculated, max Δ_{As}:

$$max\,\Delta_{As} \leq B \cdot 0{,}32 = 10 \cdot 0{,}32 = 3{,}2\% \quad (1)$$

The total uncertainty of the analysis shows how large the error of the analysis is and should be less than the maximum permissible uncertainty of the analysis (3.2%). According to [10], the total uncertainty of the analysis includes the uncertainty of the analytical equipment (detector and injector) and the uncertainty of sample preparation (balances, flasks and dispensers). Uncertainty values during sample preparation are given in Table 2.

According to [10], the uncertainty of sample preparation is calculated according to the formula:

$$\Delta_{SP} = \sqrt{n \cdot a^2 + n \cdot b^2 + n \cdot c^2} \quad (2)$$

where, *n* – is the number of uncertainties;
a – uncertainty of each of the used flasks;
b – uncertainty of each of the used dispensers;
c – uncertainty of analytical weights.

According to this formula, the uncertainty of sample preparation will be:

$$\Delta_{SP} = \sqrt{2 \cdot 0{,}17^2 + 2 \cdot 0{,}50^2 + 0{,}4^2 + 3 \cdot 0{,}98^2} = \sqrt{2{,}5206} = 1{,}59\% \leq 3{,}2\% \quad (3)$$

The calculated uncertainty of analytical equipment according to [10]:

Working solution of a standard sample of amoxicillin:

$$\Delta_{FAO,r}^{STD} = \frac{1}{\sqrt{5}} \times 2{,}13 \times 0{,}18 = 0{,}17 \quad (4)$$

Working solution of the test sample:

$$\Delta_{FAO,r}^{SMPL} = \frac{1}{\sqrt{5}} \times 2{,}13 \times 0{,}34 = 0{,}32 \quad (5)$$

The total uncertainty of the analytical equipment according to [10] for the standard and test samples is the root of the sum of the squares of the uncertainties:

$$\Delta_{FAO,r} = (0{,}17)^2 + (0{,}32)^2 = 0{,}13 \quad (6)$$

The total uncertainty of the analysis is the root of the sum of the squares of the uncertainties of sample preparation and analytical equipment:

$$\Delta_{AS,r} = \sqrt{1{,}59^2 + 0{,}13^2} = 1{,}59 \quad (7)$$

So, according to the calculations, the total uncertainty of the analysis is:

$\Delta_{AS,r}$(1,59%)<max $\Delta_{AS,r}$(3,2%)

The total uncertainty is less than the maximum assay uncertainty, and therefore the technique is suitable for further validation and selectivity studies.

One of the key parameters in the validation of an analytical technique is selectivity (specificity), which reflects the ability of the method to reliably determine the substance under study in the presence of impurities, auxiliary substances or decomposition products. The assessment of selectivity allows you to make sure that there is no influence of extraneous components on the accuracy and correctness of the analysis results.

Determination of selectivity was carried out by comparing the chromatograms of RRSZ, RRVP and solution of RMZPl. No peak on the chromatogram of the PMZPl solution should completely or partially overlap with the peaks of amoxicillin on the chromatograms of RRSZ and PMZPl.

Therefore, the time of emergence of peaks of amoxicillin on the chromatogram of RRSZ coincides with the time of emergence of peaks of amoxicillin on the

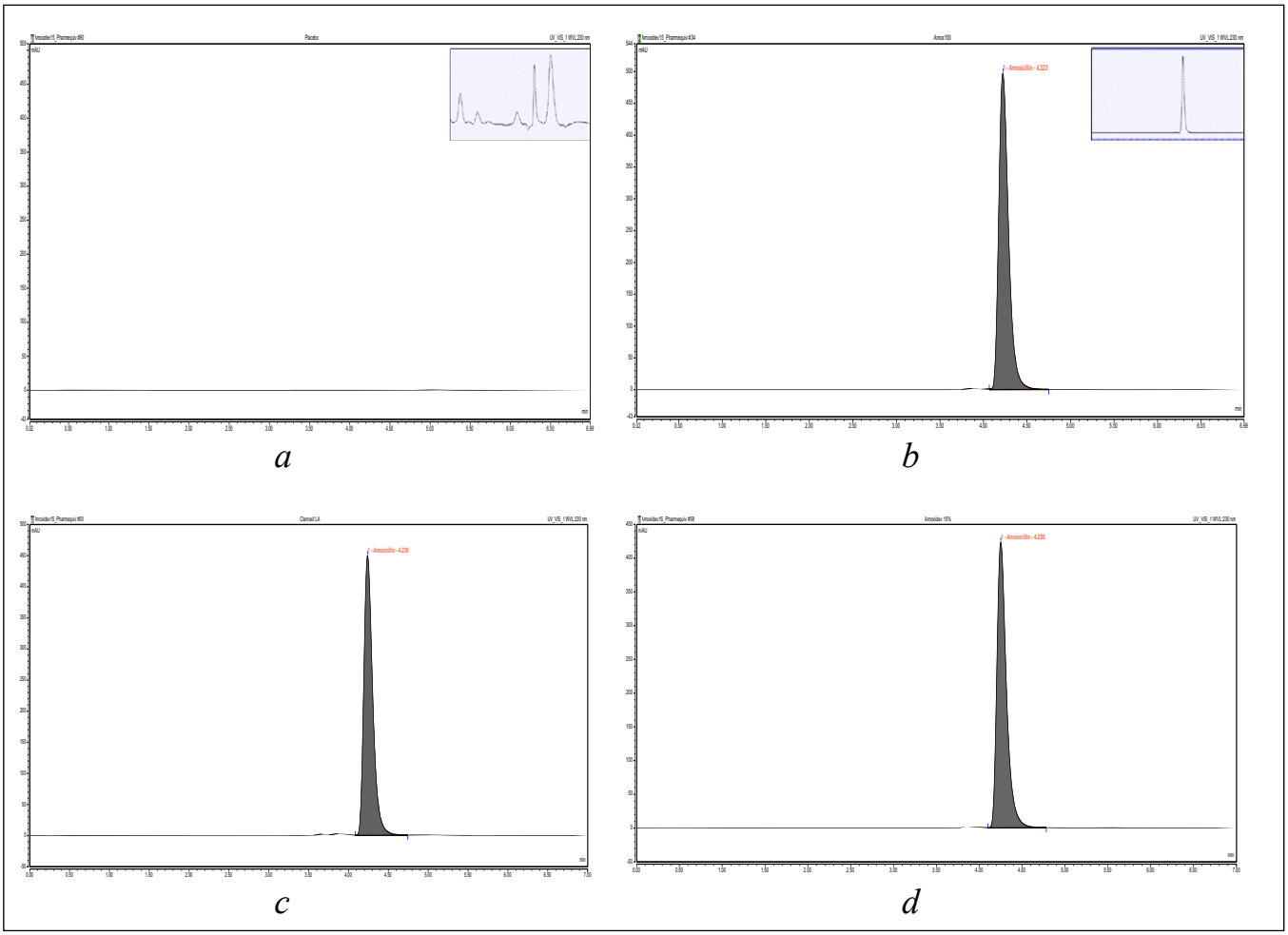

Fig. 1. Chromatograms of placebo solutions (a), a standard sample of amoxicillin (b), «Clamoxil LA» (c) and «Amoksidev 15» (d)

chromatogram of PMZPr, while all the peaks of other components of the solution of PMZPl are sufficiently separated (up to the level of the baseline) from the peaks of amoxicillin, therefore, they do not interfere with the determination.

Standardization for the suitability test of the chromatographic system was established based on the requirements [12] and [10] and FDA recommendations for the liquid chromatography method.

The suitability parameters of the chromatographic system were calculated based on the obtained chromatograms of RRVP and RRSZ.

The relative standard deviation (RSD) was calculated for the chromatograms used to estimate the quantitative content.

In the Table 3 shows the results of checking the suitability of the chromatographic system.

Therefore, the suitability of the chromatographic system meets the established requirements.

After confirming the suitability of the chromatographic system, the next step in analytical method validation is a linearity study. This parameter allows you to evaluate the ability of the technique to give results proportional to the concentration of the analyte in a given range.

The linear dependence was studied within the range of application of the analytical technique, for which 5 solutions were prepared, which were obtained by diluting the solution of RSZ to concentrations of amoxicillin ranging from 80% to 120% relative to the nominal content in RSZ, according to [10]. For clarity, this dependence is presented on the graph (Fig. 2), which shows a direct correlation between the increase in the concentration of amoxicillin and the corresponding increase in the peak area.

Therefore, the R^2 coefficient – 0,9998≥0,997, which meets the requirements [10], regarding the linearity of the technique.

Accuracy is a quality characteristic of measurements that reflects the closeness of the results to the true value. To determine the accuracy of the method, according to [10], amoxicillin trihydrate was added to the medicines matrix (a mixture of aluminum stearate and fractionated coconut oil) in terms of the base within the range of measurements (80–120%) and it was determined how

Table 3. Characteristics of the chromatographic peak of amoxicillin

Parameter	Chromatographic peak characteristics	Normalization range
Output time, min	4,228	-
Chromatographic column efficiency (N)	8200	Not less than 1000
Peak symmetry factor (As)	1,47	0,8 - 1,6
Relative standard deviation (RSD)	0,19	Not more than 1,43 %
Peak width, min	0,63	-
Degree of resolution (R_S)	2,07	Not less than 1,5

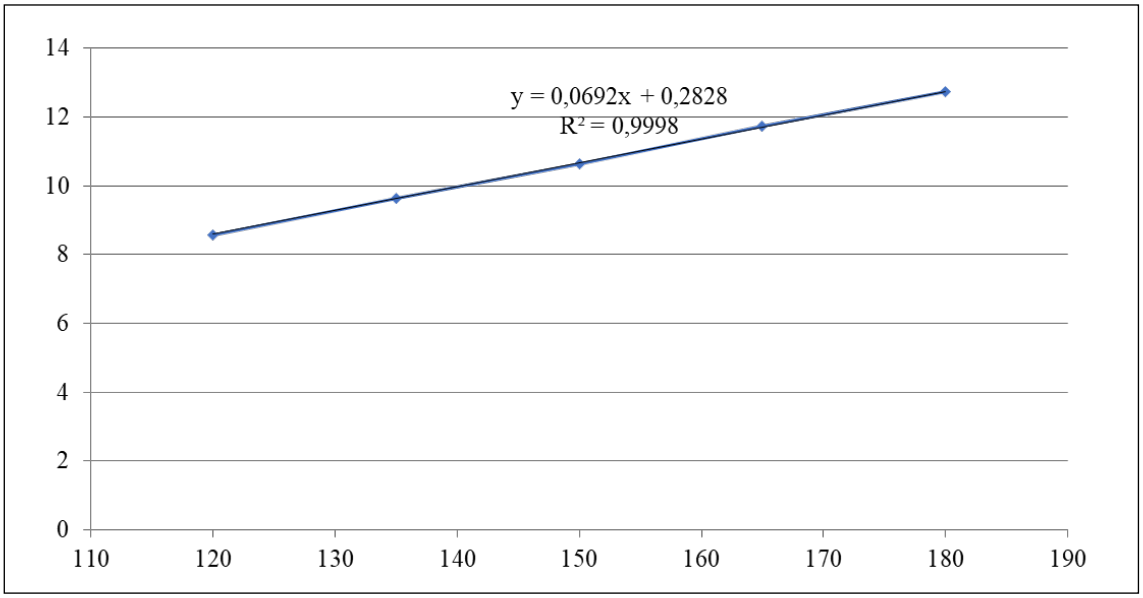

Fig. 2. Dependence of the peak area on amoxicillin concentration

close the found content of amoxicillin is to the theoretical one. Accuracy indicators are given in Table 4.

The precision of the technique is the degree of closeness between the results of a series of measurements obtained from several samples of the same material under established conditions. Precision was determined according to [10] by obtaining five results of measurements of the quantitative content of amoxicillin in the studied drugs on different days.

Metrological characteristics of the precision of the method for determining the quantitative content of amoxicillin in suspensions for injections are given in Table 5.

Accordingly, the Δ_{intra} value calculated during the intra-laboratory precision check is 0.08/0.04%, which meets the requirement:

$\Delta_{intra} \leq \Delta_{As}$=0,08/0,04%≤3,2%

Therefore, the results of intralaboratory precision meet the criteria [10].

For the purpose of the final stage of validation of the analytical technique, after studying the linearity, precision and accuracy, it is advisable to evaluate another important parameter - robustness. This indicator allows you to determine the stability of the results in case of minor changes in the conditions of the analysis, which is critically important for ensuring the reliability of research. One of the parameters of robustness is the stability of solutions over time. The study of this indicator was carried out with the recording of changes 1, 2 and 3 hours after their preparation.

Five chromatograms for RRSZ solutions were obtained every hour for four hours. The results were compared with each other.

The solutions were considered stable over time if the value of the amoxicillin content found did not differ from that of the freshly prepared solution by more than 1.02% (Table 6).

Therefore, the stability of the solution meets the given criterion.

According to the obtained studies, all the characteristics of the method of identification and quantitative determination of amoxicillin content in

Table 4. Results of the study of the accuracy of the method for determining amoxicillin in "Amoksidev 15" and "Clamoxil LA"

Parameters	Amoksidev 15	Clamoxil LA	Criteria	Conclussion
$\bar{Z}$	99,58	99,41	96–104%	Corresponds to the norm
S_Z	1,46	0,81	£ 3,2	Corresponds to the norm
Dz	0,88	0,72	£ 3,2	Corresponds to the norm
d	0,42	0,59	1) d £ 0,204% 2) d £ 1,024%	Corresponds to the norm

Table 5. Results of studies on the precision of the method for determining amoxicillin in the drug «Amoksidev 15» and «Clamoxil LA»

№	m_i, %			
	Clamoxil LA		Amoksidev 15	
	1 day (experiment 1)	2 day (experiment 2)	1 day (experiment 1)	2 day (experiment 2)
	m_i^1	m_i^2	m_i^1	m_i^2
1	14,65	14,75	14,34	14,31
2	14,63	14,71	14,36	14,32
3	14,65	14,73	14,36	14,32
4	14,61	14,75	14,39	14,39
5	14,62	14,62	14,38	14,35
arithmetic mean ($\bar{m}$)	14,63	14,71	14,37	14,34
S_m, %	0,10	0,26	0,11	0,18
S_{intra}, %	0,34		0,17	
Δ_{intra}, %	0,08		0,04	

Table 6. Stability of standard amoxicillin solution

Influence factor	Limits of changes of the influence factor	Limits of changes of the studied parameters				Conclussion
		Peak area, $\bar{X}$	Content found, X, %	δ, %	Criteria	
Time	0	64,84	100,00	0,00	≤|1,02%|	Corresponds to the norm
	1 hour	64,82	99,97	0,03		
	2 hours	64,81	99,95	0,05		
	3 hours	64,79	99,92	0,08		
	4 hours	64,76	99,88	0,12		

the preparations «Amoksidev 15» and «Clamoxil LA» do not go beyond the criteria specified in [10] and [13]. Therefore, the method is considered suitable and accurate and can be used for routine tests to determine the quantitative content of amoxicillin in suspensions for injections based on coconut oil and aluminum stearate.

DISCUSSION

According to the conducted studies, it was found that the method of determining the identity of the quantitative content of amoxicillin in suspensions for injections according to all the studied parameters shows sufficient accuracy when adding the active substance to the matrix at the level of 99.58 and 99.41%, which meets the requirements [10]. The results obtained by us regarding the accuracy in the determination of β-lactam antibiotics by the HPLC method are consistent with those of other authors [8, 11]. This indicates a properly selected solvent that allows the amoxicillin to be extracted from the suspension and eliminates any matrix effects. Analogous approaches to the extraction of active substances from lipid matrices are described in the works of Rahnfeld and Luciani [5, 6]. At the same time, the recovery rate for both drugs does not differ statistically. The absence of the influence of the matrix is evidenced by the placebo chromatogram, which does not contain any significant peaks, and the selected detection wave allows detecting even lower levels of

amoxicillin than indicated in the range of application of the method, which is extremely important when detecting low-quality products.Similar advantages of diode-matrix detection in drug quality control were noted by Snyder and co-authors [9]. The error of the arithmetic mean for determining accuracy is lower than the maximum allowable value, which indicates high reproducibility of research results. High reproducibility and low RSD values are one of the key criteria for the suitability of HPLC methods [11, 12].

This is what the results of the precision study say. The coefficients of Δ_{intra}, % for the study in both drugs are forty times lower than the permissible values. At the same time, the relative standard error of the chromatographic peak area is 0.19%, which is 7.5 times lower than the requirements [10] and FDA recommendations for the liquid chromatography method. Such high accuracy is ensured not only by calibrated equipment, but also by adequate selection of final amoxicillin concentrations for analysis, size of dissolution flasks, and sampling tools. Since amoxicillin is limitedly soluble in water and mixtures with acetonitrile, the selected concentration of 1.5 mg/ml eliminates the risk of analyte not dissolving, and the 100 ml Class A flask ensures a low dilution error. A low error in further dilution was ensured by a 10 ml flask A and a 1 ml dispenser. Any decrease in the volume of dissolution and sample selection increases the uncertainty of the result, and an increase increases the amount of solvent used, and therefore the cost of the analysis, which is consistent with the recommendations of Nazarkin V. and co-authors [12], who emphasize the importance of optimizing sample preparation volumes to reduce analytical error.The selected conditions of chromatographic separation allow you to quickly obtain research results (total analysis time - 2 hours), with minimal error, and the parameters of chromatographic peaks meet the requirements of FDA recommendations for the liquid chromatography method, which eliminates errors in the integration of chromatographic peaks. Similar criteria for evaluating the parameters of chromatographic peaks are given in the works of Rozet and co-authors [11], and the data obtained by us expand and complement these studies. At the same time, the linearity of the method is confirmed by calculating the R^2 coefficient, which according to the requirements [10, 13] is higher than 0.997, and amoxicillin solutions are stable during the analysis. Therefore, the developed method is accurate, robust and fast and is suitable for routine analyzes for the determination of amoxicillin in suspensions for injections.

CONCLUSIONS

The developed method for determining the identity and quantitative content of amoxicillin in suspensions for injections based on coconut oil and aluminum stearate meets the requirements and guidelines for the validation of methods by the high-performance liquid chromatography method of the FDA according to the parameters of chromatographic peaks, linearity, accuracy, precision, robustness (stability of solutions over time), so it can be used in routine studies.

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The work is a fragment of the research work of the Rivne State University for the Humanities "Innovative technologies of teaching natural sciences in institutions of general secondary and higher education" (0121U112774).

CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 18.03.2026
ACCEPTED: 29.07.2026

CREATIVE COMMONS 4.0

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ORIGINAL ARTICLE

Assessment of subjective and objective health indicators in cadets during professional training

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ABSTRACT

Aim: To investigate the prevalence of healthy lifestyle skills and physical health indicators among future law enforcement officers during their professional training under martial law.

Materials and Methods: Conducted between 2025 and 2026, this research involved 171 male cadets enrolled in the first (n = 59), second (n = 57), and third (n = 55) academic years. Subjective health indicators were assessed based on the level of health-promoting skills development using the "Health-Promoting Lifestyle Profile, Adult Version" questionnaire. In contrast, objective health indicators were determined via Professor G. L. Apanasenko's rapid assessment method.

Results: It was found that the overall level of health-promoting skills development among cadets is average. Statistically significant differences were found in the development of healthy lifestyle skills between third- and junior-year cadets ($p \leq 0.05$). The application of the rapid method for determining somatic health levels in cadets confirmed the consistency between survey data and objective indicators. The increase in the level of health-promoting skills development among senior-year cadets is accompanied by improvements in somatic health indicators, indicating a correlation between subjective and objective characteristics.

Conclusions: An average level of healthy lifestyle skills development was observed among cadets, with significant improvements in indicators during the academic training process. A positive trend in cadets' physical health was observed, indicating improved functional capabilities and suggesting directions for optimizing the professional training system for future law enforcement officers.

KEY WORDS: health, health-promoting, healthy lifestyle, cadet, law enforcement officer, physical training

Wiad Lek. 2026;79(8):1842-1849. doi: 10.36740/WLek/235879 DOI

INTRODUCTION

Human health is shaped by the complex interactions among social, biological, psychophysiological, and behavioral factors, which, in contemporary scientific discourse, are integrated into the concept of a healthy lifestyle as a systemic determinant of an individual's life-sustaining activities [1, 2]. In today's context, the issue of developing healthy lifestyle habits among the population has become particularly relevant. This is due to the influence of a complex of destabilizing factors, including full-scale war, post-pandemic consequences, and the intensive processes of globalization, digitalization, and technological advancement, accompanied by physical inactivity, stress, increased psycho-emotional tension, and disruption of established patterns of life [3, 4].

Consequently, the issue of developing healthy lifestyle habits among cadets – future law enforcement officers – takes on particular significance. The professional activities of this category of specialists are characterized by high stress levels, significant physical and psycho-emotional strain, the need for rapid decision-making, and the performance of service duties under extreme conditions, particularly during martial law. Under such circumstances, health-promoting skills development is not only an individual characteristic but also an important component of professional readiness, directly influencing the effectiveness of service duties, the level of occupational capacity, and the functional reliability of future police officers.

An analysis of scientific sources indicates that developing healthy lifestyle skills among future professionals across various fields is the subject of interdisciplinary research that examines the topic from the perspectives of medical, psychological-pedagogical, social, and physical education and health sciences [5]. Scholars note that the health status of higher education students is

an integral indicator of the effectiveness of the educational process and a determining prerequisite for their future professional success [6, 7]. At the same time, the modern higher education system is designed to ensure not only the development of professional competencies but also the cultivation of a sustained motivation for health preservation, the ability to self-regulate, and responsible behavior regarding one's own health [8].

Despite extensive scientific research, theoretical analysis suggests no unified approach to defining the essence of a healthy lifestyle for cadets – future law enforcement officers. Its structure includes interrelated components, the leading ones being physical activity, a balanced diet, the absence of harmful habits, psycho-emotional stability, a culture of safe behavior, and adherence to hygiene standards [9, 10].

At the same time, empirical studies indicate a significant discrepancy between higher education students' awareness of the principles of a healthy lifestyle and the actual development of the corresponding skills. This discrepancy manifests as insufficient physical activity, disruption of work-rest patterns, harmful habits, and low self-monitoring of the body's functional state [11, 12]. In this context, the issue of appropriately assessing the level of development of health-promoting skills among cadets becomes particularly relevant. In scientific and educational practice, the use of questionnaires and self-assessment methods is widespread, as they allow for the determination of students' subjective perceptions of their own lifestyles. At the same time, such data do not always correlate with objective indicators of physical health obtained through standardized physiological and functional methods.

In light of this, there is a scientifically grounded need to conduct a comparative analysis of the level of development of healthy lifestyle skills, as determined by questionnaires, and the actual level of health, as established by objective diagnostic results. The analysis of these indicators in the context of professional training under martial law – particularly across academic years – also gains additional significance, as it will help identify trends in the development of relevant skills.

Implementing this approach will help establish the degree of alignment between subjective self-assessment and objective health characteristics, identify problematic aspects, determine the level of development of health-promoting behavior among future law enforcement officers, and identify areas for improving their professional training system.

Thus, the insufficient development of issues regarding the comprehensive comparison of subjective and objective indicators of a healthy lifestyle, as well as the lack of systematic studies of their dynamics during professional training under martial law, determine the relevance and practical significance of the chosen research direction.

AIM

The aim is to investigate the prevalence of healthy lifestyle skills and physical health indicators among future law enforcement officers during their professional training under martial law.

MATERIALS AND METHODS

PARTICIPANTS

The research, conducted in 2025-2026, involved 171 male cadets from the National Academy of Internal Affairs (NAIA, Kyiv, Ukraine) majoring in "Law Enforcement Activities" specialty. The sample consisted of future law enforcement officers in their first (n = 59), second (n = 57), and third (n = 55) academic years. The processing and analysis of the results were carried out at the Department of Special Physical Training of the National Academy of Internal Affairs. No special selection of research participants was conducted; therefore, the inclusion criteria were: male cadets, enrollment in a specific academic year, and the major they were pursuing at the higher educational institution ("Law Enforcement Activities"). Each cadet provided voluntary written consent to participate in the research. The exclusion criterion was the cadet's desire to withdraw from the research at any point during the research. Research limitations: the research focused exclusively on subjective indicators related to professional training at the higher educational institution; we did not set out to assess the cadets' subjective health indicators outside the educational institution.

METHODS

The research used a combination of theoretical, empirical, and statistical methods. Theoretical methods included the analysis and generalization of literary sources. Analysis and generalization of literary sources were used to conduct an analytical review of scientific sources on the outlined range of issues (23 sources from PubMed, Scopus, Web of Science, and Index Copernicus were analyzed).

Empirical methods were used to assess subjective and objective health indicators. Subjective health indicators were assessed based on the level of development of health-promoting skills using the "Health-Promoting Lifestyle Profile, Adult Version" questionnaire. In

contrast, objective somatic health indicators were determined via Professor G. L. Apanasenko's rapid assessment method.

The "Health-Promoting Lifestyle Profile, Adult Version" questionnaire contains 52 statements and six scales: responsibility for health, physical activity, nutrition, spiritual development, interpersonal relationships, and stress management [13, 14]. Responses were rated on a four-point scale ("never,""sometimes,""often,""systematically"); the respondent's average score determined the level of development of healthy lifestyle skills: up to 1.5 – insufficient, 1.6-2.0 – low, 2.1-2.5 – satisfactory, 2.6-3.0 – average, over 3.1 – high.

The level of cadets' somatic health was determined using the rapid assessment method proposed by Professor G. L. Apanasenko. The method is based on anthropometric indicators and the condition of the cadets' cardiovascular system. During professional training, the following parameters of cadets were examined: body weight, body height, vital lung capacity (VLC), dynamometry of the dominant hand, resting heart rate (HR), blood pressure, body mass index (BMI), vitality index (VI), strength index (SI), Robinson index (RI), Martine-Kushelevsky index (MKI), and somatic health level (SHL). According to the method of G. L. Apanasenko, cadets' somatic health level (SHL) was determined by the sum of points received by cadets for each of the 5 indices. If the total score was less than 3 points, the SHL was assessed as "low"; 4-6 points – "below average"; 7-11 points – "average"; 12-15 – "above average"; 16-18 – "high."

STATISTICAL METHODS

The methods of mathematical statistics were used to process the data obtained. The reliability of the difference between the indicators was determined using the Student's t-test. The results were presented as Mean ± m, where Mean is the arithmetic mean, m is the standard error. The reliability of the difference was set at $p<0.05$. All statistical analyses were performed using STATISTICA 6.1 software package (number AGAR909E-415822FA), 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 NAIA. Also this study followed the regulations of the World Medical Association Declaration of Helsinki. Informed consent was received from all participants who took part in this study.

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

This scientific article was carried out according to the plan of the research work of the National Academy of Internal Affairs for 2020-2026 "Psychological, pedagogical and sociological support of law enforcement officers» (state registration number 0113U008196).

RESULTS

Based on the analysis of empirical data, cadets from all three academic years who participated in the survey rated the development of healthy lifestyle skills at an average level. Specifically, the overall index of health-promoting skills development was as follows: for first-year cadets – 2.61 ± 0.03 points, for second-year cadets – 2.63 ± 0.05 points, and for third-year cadets – 2.84 ± 0.05 points (Table 1). The results of the mathematical analysis of the data revealed a statistically significant difference between third-year cadets and first- and second-year cadets ($p \leq 0.05$), indicating a positive trend in the development of healthy lifestyle skills during professional training. At the same time, no significant differences were found between first- and second-year cadets ($p \geq 0.05$), suggesting relative stability in these indicators during the initial stages of training. The obtained values generally support the conclusion that the majority of respondents possess basic health-promoting concepts and behavioral models; however, their insufficient stability and awareness limit the effectiveness of implementing a healthy lifestyle in daily activities.

A comparative analysis of indicators across individual scales revealed structural features of the development of health-promoting skills among cadets. Thus, on the "Responsibility for Health Status" scale, the lowest mean scores were recorded among first- (2.32 ± 0.08 points) and second-year (2.34 ± 0.06 points) cadets, which corresponds to a satisfactory level. This may indicate a predominance of external regulation of health-promoting behavior, in which responsibility for maintaining one's own health is partially attributed to the organization of the educational process, the activities of the medical service, or the regulatory requirements of the educational institution. At the same time, among third-year cadets, this indicator is significantly higher – 2.89 ± 0.05 points ($p \leq 0.05$) – which is assessed as an average level and reflects an increase in personal responsibility for one's own health during the process of professional development.

Table 1. Level of development of healthy lifestyle skills (subjective indicators) and somatic health (objective indicators) among cadets in different academic years (n = 171), points

Indicators	Years of study			Significance of the difference		
	1st (n=59)	2nd (n=57)	3rd (n=55)			
	Mean ± m	Mean ± m	Mean ± m	t_{1-2} (p)	t_{1-3} (p)	t_{2-3} (p)
Level of development of healthy lifestyle skills (based on "Health-Promoting Lifestyle Profile, Adult Version" questionnaire)						
Responsibility for Health Status	2.32±0.08	2.34±0.06	2.89±0.05	0.20 p≥0.05	6.042 p≤0.001	7.042 p≤0.001
Physical Activity	2.71±0.10	2.76±0.07	2.93±0.07	0.410 p≥0.05	1.802 p≥0.05	1.717 p≥0.05
Nutrition	2.44±0.06	2.46±0.05	2.47±0.07	0.256 p≥0.05	0.384 p≥0.05	0.116 p≥0.05
Spiritual Development	2.93±0.09	2.94±0.08	3.09±0.09	0.083 p≥0.05	1.257 p≥0.05	1.246 p≥0.05
Interpersonal Relationships	2.84±0.11	2.88±0.06	3.04±0.09	0.319 p≥0.05	1.407 p≥0.05	1.479 p≥0.05
Stress Management	2.40±0.10	2.44±0.06	2.78±0.04	0.343 p≥0.05	3.528 p≤0.001	4.715 p≤0.001
Overall indicator of health-promoting skills	2.61±0.09	2.63±0.05	2.84±0.05	0.194 p≥0.05	2.234 p≤0.05	2.970 p≤0.05
Somatic health level (according to Professor G. L. Apanasenko's method)						
BMI, kg/m^2	23.18±0.09	23.29±0.1	23.61±0.1	0.818 p≥0.05	3.196 p≤0.01	2.263 p≤0.05
VI, ml/kg	56.13±0.46	56.93±0.44	58.22±0.48	1.257 p≥0.05	3.144 p≤0.01	1.981 p≥0.05
SI, %	64.94±0.32	65.56±0.31	66.28±0.29	1.392 p≥0.05	3.103 p≤0.05	1.696 p≥0.05
RI, c. u.	86.61±0.45	87.15±0.46	87.79±0.46	0.839 p≥0.05	1.834 p≥0.05	0.984 p≥0.05
MKI, s	120.57±1.39	117.85±1.44	115.74±1.37	1.359 p≥0.05	2.475 p≤0.05	1.062 p≥0.05
SHL, points	2.46±0.28	4.22±0.27	5.24±0.25	4.525 p≤0.001	7.406 p≤0.001	2.772 p≤0.01

Legend: Mean – arithmetic mean; m – standard error; t – Student's test value; p – level of significance of the differences between studied indicators
Source: compiled by the authors of this study

On the "Physical Activity" scale, the highest scores were recorded among third-year cadets (2.93 ± 0.07 points), while first- and second-year cadets scored 2.71 ± 0.10 points and 2.76 ± 0.07 points, respectively. However, the observed differences are not statistically significant (p ≥ 0.05). These results are likely due to the specific nature of cadet training, which includes mandatory specialized physical training sessions and a sufficient level of physical activity within the educational process. At the same time, the average level of this indicator suggests that physical activity is largely regulated and does not always translate into an internal need for independent exercise during extracurricular activities.

An analysis of the "Nutrition" scale revealed a satisfactory level of development of relevant skills among cadets in all three academic years, with no statistically significant differences (p ≥ 0.05). On the one hand, these results may be due to limited opportunities for individual dietary choices under a centralized meal plan. On the other hand, they indicate insufficient awareness of the role of a balanced diet in maintaining occupational capacity, recovery, and the body's adaptation to physical and psycho-emotional loads.

Relatively higher indicators were recorded on the "Spiritual Development" scale; however, no statistically significant differences were found among cadets in different academic years (p ≥ 0.05). The average level of development of this component attests to the positive influence of the higher educational institution's educational and social environment on the formation of value orientations and moral-ethical attitudes among future police officers.

For representatives of all academic years, the "Interpersonal Relationships" indicator also corresponds to

the average level. The observed positive trend reflects the gradual improvement of cadets' communication skills and social cohesion, which are important factors for psychological resilience, teamwork, and professional adaptation in the context of service activities.

The results on the "Stress Management" scale deserve special attention. For first- and second-year cadets, this indicator is at a satisfactory level, which may indicate insufficient development of psycho-emotional self-regulation skills and stress resilience. Under conditions of martial law, intensive academic training, and heightened demands for discipline and responsibility, these conditions can increase the risk of overexertion, emotional exhaustion, and reduced occupational capacity. At the same time, third-year cadets showed significantly higher values ($p \leq 0.001$), corresponding to the average level and indicating the gradual development of stress management skills during professional training.

The BMI analysis revealed statistically significant differences among cadets in different academic years. Specifically, a significant difference was found between the indicators of first- and third-year cadets ($p \leq 0.01$), as well as between second- and third-year cadets ($p \leq 0.05$). The mean BMI values were 23.18 ± 0.09, 23.29 ± 0.10, and 23.61 ± 0.10, respectively, indicating the average level. The observed trend toward a gradual increase in the BMI during academic training may indicate adaptive changes in the body, particularly an increase in muscle mass due to systematic physical exercise; however, this requires a comprehensive interpretation that takes into account other indicators of physical condition.

Assessment of the VI, calculated as the ratio of VLC to body weight, revealed a positive trend in its changes during professional training. A statistically significant difference was found between cadets in the first and third academic years ($p \leq 0.01$), indicating an improvement in respiratory system functional capacity. Nevertheless, the VI level among cadets across all academic years is assessed as average, indicating reserves for further improvement in functional fitness.

An analysis of the SI, determined by the ratio of the dynamometric indicators of the stronger hand to body weight, revealed significant differences only between the first- and third-year cadets ($p \leq 0.05$). For first-year cadets, this indicator was 64.94 ± 0.32 % and was assessed as below average, whereas for second- and third-year cadets, it was 65.56 ± 0.31 % and 66.28 ± 0.29 %, respectively, indicating an average level of development. Thus, a positive trend in muscle strength development is observed during the academic training process, likely due to the influence of systematic, specialized physical training sessions.

The RI was used to determine the functional state of the cardiovascular system and the efficiency of cardiac function. The results of the analysis confirm a positive trend toward improvement in indicators during the academic training process; however, no statistically significant differences were found between the academic years ($p \geq 0.05$). In all study groups, the RI level is at the average, indicating a relatively stable cardiovascular system without pronounced adaptive changes.

The MKI, which characterizes the rate at which heart rate returns to normal after a standard physical exercise, proved to be more sensitive to changes in functional status. Among the first-year cadets, this indicator was 120.57 ± 1.39 s and was assessed as below average. For the second-year cadets, it was 117.85 ± 1.44 s (average level), and for the third-year cadets, 115.74 ± 1.37 s, which is significantly better compared to the first-year cadets. This trend indicates an increase in the cardiovascular system's adaptive capacity and more effective recovery after physical exertion during professional training.

The comprehensive SHL assessment enabled us to summarize the results and identify general trends. Among the first-year cadets, the average score was 2.46 ± 0.28 points, indicating a low level. The second- and third-year cadets' scores were higher – 4.22 ± 0.27 and 5.24 ± 0.25 points, respectively – which are assessed as below average. At the same time, a statistically significant improvement in the SHL was observed during the academic training process, indicating a positive impact of the professional training system on the health of future law enforcement officers.

A comparative analysis provides grounds for concluding that there is general consistency between cadets' subjective assessments of their own health (based on survey results) and objective indicators of somatic health (according to Professor G. L. Apanasenko's method). Thus, the increase in the level of health-promoting skills development among senior-year cadets is accompanied by improvements in somatic health indicators, indicating a correlation between subjective and objective health indicators. At the same time, first-year cadets tend to overestimate their own health-promoting skills relative to objectively recorded indicators, which may be due to insufficient development of reflective assessment and practical experience in applying these skills.

Overall, the research results demonstrate heterogeneity in the dynamics of individual indicators of physical and functional condition: alongside significant improvements in strength, respiratory, and recovery characteristics, some indicators (in particular, the RI) remain relatively stable. This points to the complex, multi-component nature of somatic health development and the need for its comprehensive assessment. The identified differences among cadets from different

academic years provide grounds for asserting positive changes in the process of professional training; however, they also indicate insufficient development of certain health components, necessitating further improvement of the physical training system and health-promoting technologies at the higher educational institution.

DISCUSSION

The results obtained are consistent with current scientific understanding [2, 15] regarding the multifaceted nature of a healthy lifestyle and its close connection to somatic health level. The positive trend in indicators observed during professional training demonstrates the effectiveness of the educational environment in shaping cadets' basic health-promoting attitudes as future law enforcement officers. At the same time, the absence of significant changes in certain functional indicators (in particular, the Robinson index) suggests a limited impact on the cardiovascular system's adaptive mechanisms, warranting further scientific research.

A contradiction was noted between the relatively stable average values of subjective indicators in the junior academic years and the dynamics of objective somatic health characteristics. The data obtained suggest that physiological adaptation to academic and training loads occurs more rapidly than the development of conscious health-promoting behavior. This asynchrony in development underscores the need to strengthen educational interventions that foster intrinsic motivation and responsibility for one's own health [16, 17].

An important finding is the establishment of consistency between subjective and objective indicators, which indirectly confirms the validity of the questionnaire used to assess healthy lifestyle skills. At the same time, the absence of high levels of development, even among senior-year cadets, indicates that existing educational and training programs primarily provide an average level of development in the relevant competencies.

Overall, the research results confirm the feasibility of a comprehensive approach to health assessment that combines subjective (questionnaire-based) and objective (physiological) methods. Such an approach provides a comprehensive reflection of the actual state of health-promoting skills development. It helps justify directions for optimizing the professional training system for future law enforcement officers. The data we obtained confirm the conclusions of many scholars who have addressed the issue of preserving and strengthening cadets' health during professional training [9, 10, 18-23], and supplement and expand upon them.

CONCLUSIONS

Based on the research conducted, the average level of development of healthy lifestyle skills among cadets was established, with statistically significant improvements in indicators during the academic training process ($p \leq 0.05$). It was found that the least developed components were those related to responsibility for one's health, nutrition, and stress management. A positive trend in the somatic health of future law enforcement officers was recorded ($p \leq 0.05$-0.001), indicating an improvement in the body's functional capabilities. A comparative analysis revealed a general consistency between the cadets' subjective and objective health indicators. At the same time, first-year cadets tended to overestimate their own health-promoting skills relative to objectively recorded indicators.

PROSPECTS FOR FURTHER RESEARCH

Prospects for further research should be linked to an in-depth analysis of the relationships between individual components of a healthy lifestyle and indicators of the body's functional state, as well as to the development and implementation of programs to foster health-promoting competence under martial law conditions.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 18.03.2026
ACCEPTED: 27.07.2026

CREATIVE COMMONS 4.0

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ORIGINAL ARTICLE

Systemic disorders of the oxidant-antioxidant system of the brain and kidney in scopolamine-induced Alzheimer's disease and their correction with carbacetam

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ABSTRACT

Aim: To assess the state of the oxidant-antioxidant system of the hippocampus and kidneys of rats with scopolamine-induced Alzheimer's disease and with the administration of carbacetam, as a GABA receptor modulator, and to clarify the possible systemic oxidative process.

Materials and Methods: The experiments were carried out on mature and old male rats. Alzheimer's disease was simulated by scopolamine hydrochloride (Sigma, USA). It was introduced into the peritoneum in a dose of 1 mg/kg of the body weight once a day during 27 days. On the 28th day, carbacetam was administered in a dose of 5 mg/kg once a day during 14 days. Intensity of lipid peroxide oxidation (LPO) was evaluated by the content of products reacting with 2-thiobarbituric acid reactive substances (TBARS). The content of protein oxidation modification (POM), also known as protein oxidation, in homogenates was determined by the amount of their oxidative modification products with the help of spectrophotometric method. The state of antioxidant protection was assessed by catalase and SOD activity.

Results: Simulated Alzheimer's disease was found to cause affliction of the protein amino groups in the hippocampal neurons and endotheliocytes, and in the mesangial matrix of non-collapsed renal glomeruli of rats of different ages with more pronounced changes in brain cells. At the same time, there is a clear existing relationship between affliction of the nerve cells and kidneys, which makes a foundation for further study of pathogenic processes and interrelations in neurodegenerative processes.

Conclusions: Thus, the group of rats of different ages with experimental Alzheimer's disease presented increase of the lipid and protein peroxidation products with more pronounced lesion in the hippocampal cells than those of the kidneys. Moreover, decrease of the lipid and protein peroxidation products in the examined organs of rats with scopolamine-induced Alzheimer's disease after administration of carbacetam indicates the involvement of the GABA-ergic system in the pathogenesis of damage to hippocampal neurons and kidney cells.

KEY WORDS: scopolamine-induced Alzheimer's disease, carbacetam, lipid and protein peroxide oxidation, antioxidants, hippocampus, kidneys

Wiad Lek. 2026;79(8):1850-1858. doi: 10.36740/WLek/222257 DOI

INTRODUCTION

Globally, dementia has become one of the most important social, economic and public issues of health care, which is associated with increasing human lifespan. Epidemiological studies have estimated that about 50 million people worldwide suffer from dementia. Alzheimer's disease accounts for 60 to 80% of all cases. According to forecasts, this number will triple by 2050 [1, 2]. The main risk factor of Alzheimer's disease incidence is old age [3]. However, recently kidney diseases have been suggested as a modified risk factor promoting the development of Alzheimer's disease. The foundation for this is the fact that kidneys and brain are the organs with similar anatomical and vascular systems, hemodynamic specific features, which make them prone to vascular damage [4]. Therefore, Alzheimer's disease and kidney damage may have common risk factors and potential basic mechanisms.

The physiological function of the kidney is to maintain the stability of the internal environment, including cerebrovascular circulation, while impaired renal function often leads to ischemia and hypoxia. The high blood flow rate in the kidneys significantly exceeds the needs of their own metabolism. At the same time, oxygen consumption by the human brain is approximately 1/5 from oxygen consumption by the whole body. The amount of blood reaching the human brain is approximately 15% of total cardiac output. Normal blood pressure allows the brain to receive sufficient cerebral blood supply. Blood pressure balance depends on complicated regulatory mechanisms of the neurohumoral systems involving all the body organs, and the kidney is a center of the blood pressure regulation system [5].

From pathophysiological view, Alzheimer's disease is known to contain a vascular component, and the cause of cognitive decline is multifaceted. Contrary to this, individuals with kidney failure present a disproportionately high degree of cerebrovascular diseases, which can be a significant cause of development and advance of cognitive decline [5].

According to the scientific evidence, gamma-aminobutyric acid (GABA) is the major inhibitory neurotransmitter of the central nervous system. The acid plays a key role in the CNS physiology, simulating various processes, participates in many pathological processes: sleep disorders, depression, anxiety, alcohol abuse, and premenstrual syndrome [6, 7]. The same subtype of GABA receptors is known to possess a different nature of the cellular population and subcellular expression in different portions of the brain, stimulating excitability and neuronal synchronization in various pathologies and conditions [8]. The scientific literature presents evidence concerning their considerable presence in the kidneys [10]. For example, activation of endogenous GABA and glutamate receptors in the kidneys is known to significantly change the diameter of microvessels alternating renal blood flow [9]. GABA effect produced on the renal capillaries is very much alike the effect, which is the central one to regulate the central nervous system capillaries. Since regulatory disorders of the renal blood flow are associated with chronic kidney diseases and changes in the renal GABA system, possibly by means of prescription drugs, long-term kidney function can be significantly affected.

In recent decades, numerous hypotheses have made attempts to explain interrelationship between these two diseases (Alzheimer's disease and kidney dysfunction), which are multifactorial by their nature. However, irrespective of the facts, the underlying mechanisms of this correlation remain unclear. At the same time, the scientific literary sources available do not contain information about Alzheimer's disease effect of kidney condition.

AIM

Therefore, the aim of our study was to assess the state of the oxidant-antioxidant system of the hippocampus and kidneys of rats with scopolamine-induced Alzheimer's disease and with the administration of carbacetam, as a GABA receptor modulator, and to clarify the possible systemic oxidative process.

MATERIALS AND METHODS

The experiments were performed on male rats of mature (0.21-0.24 kg) and old (0.41-0.44 kg) age, which were kept under standard vivarium conditions at a temperature of 18-22 °C and a relative humidity of 40-60%, on a balanced diet with free access to water under conditions of natural day and night cycles. Twenty-two mature and 23 old rats were used for this study. All the experimental procedures were carried out according to the main principles of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes.

Given the general acceptance of the cholinergic hypothesis in the pathogenesis of Alzheimer's dementia, studies were conducted in rats with a scopolamine-induced model [10]. The model we used focuses on reproducing cognitive impairments and specific behavioral deficits. It allows us to assess the consequences of the disorders, but does not fully reproduce the pathogenesis of the neurodegenerative disease. It was modeled by the administration of scopolamine hydrochloride (Sigma, USA) intraperitoneally at a dose of 1 mg/kg body weight once a day for 27 days [11]. On the 28th day, carbacetam was administered in a dose of 5 mg/kg once a day during 14 days. Euthanasia of rats was performed under light chloroform narcosis. The brain and kidneys were removed in the cold and thoroughly washed with cooled 0,9 % NaCl solution. The hippocampus was isolated using a stereotaxic atlas [12]. Cytoplasmic fraction was isolated by means of differential centrifugation of homogenate of the examined structures in a refrigerated centrifuge at 1000 g for 10 min, followed by 1400 g for 10 min at the temperature of 4°C. LPO intensity was evaluated by the content of products reacting with 2-thiobarbituric acid reactive substances (TBARS) [13]. TBARS amount was calculated in μmol per 1 g of tissue. The content of protein oxidation modification (POM), also known as protein oxidation, in homogenates was determined by the amount of their oxidative modification products with the help of spectrophotometric method. At a wavelength of λ=370 nm, ketone dinitrophenyl hydrozones of neutral character were determined, at λ=430 nm – aldehyde dinitrophenyl hydrozones of basic character were determined [14]. POM content was expressed in units per g of tissue. The state of the antioxidant defense system was assessed by the activity of superoxide dismutase (SOD) and catalase [15].

Brain samples for histological examination were fixed in 10 % neutral formalin solution and after standard histological processing the tissue was embedded in paraffin. Paraffinic histological sections of the hippocampal and kidney tissues 5 μm (microns) thick were made with a sled microtome MS-2. Quantitative assessment of the protein state in histochemical samples stained with bromophenol blue according to Mikel Calvo was carried out by computer microspectrophotometry based on the R/B ratio [16].

Table 1. Effect of carbaracetam on indices of the prooxidant system of the hippocampus and kidneys of rats of different ages with scopolamine-induced Alzheimer's disease, M±m

Indices	Age	Control	Scopolamine-induced Alzheimer's disease	Scopolamine-induced Alzheimer's disease + carbacetam
hippocampus				
TBA AP mcmol/gof tissue	mature	42.965±1.272	76.371±1.792*	58.019±1.085**
	old male	46.665±1.419	81.901±0.795*	71.609±0.897**
POM, λ=370, units/g of tissue	mature	24.014±1.992	38.686±0.654*	29.329±1.128**
	old male	39.129±1.246	50.443±0.938*	44.329±0.869**
POM, λ=430, units/g of tissue	mature	20.243±0.699	28.543±0.714	24.657±0.830
	old male	34.4±0.721	48.843±0.905	36.4±0.683
kidneys				
TBA AP mcmol/gof tissue	mature	45.017 ±1.627	64.979±1.116	55.749±0.708
	old male	46.555±0.980	71.719±0.778	57.727±1.008
POM, λ=370, units/g of tissue	mature	22.357±0.718	37.786±0.823	26.143±0.781
	old male	38.457±0.596	48.343±0.976	42.5±0.896
POM, λ=430, units/g of tissue	mature	18.743±0.619	26.543±0.678	21.957±0.966
	old male	36.057±0.637	55.671±3.215	43.586±1.039

Notes:* – reliability of differences compared with the control group of rats,
** – reliability of differences compared with the group of rats with scopolamine-induced Alzheimer's disease.
Source: compiled by the authors of this study

Table 2. R/B coefficient in the hippocampus and kidneys (histochemical method for "acidic" and "basic" proteins with bromophenol blue by Mikel Calvo) of rats of different ages with scopolamine-induced Alzheimer's disease and after carbacetam administration

Organs under investigation	Age	Research groups		
		Control	Scopolamine-induced Alzheimer's disease	Scopolamine-induced Alzheimer's disease + carbacetam
hippocampus	mature	1.09±0.008	1.89±0.012	1.33±0.012
	old male	1.38±0.022	1.98±0.021	1.21±0.016
endotheliocytes of non-collapsed renal glomeruli	mature	1.04±0.012	1.38±0.019	1.18±0.014
	old male	1.18±0.014	1.68±0.024	1.47±0.021
mesangial matrix of non-collapsed renal glomeruli	mature	1.06±0.013	1.38±0.021	1.18±0.015
	old male	1.19±0.016	1.72±0.026	1.52±0.022

Source: compiled by the authors of this study

Experimental data were processed on personal computers using the EXCEL-2010 statistical program package (Microsoft Corp., USA). Statistical processing of the research results was carried out using the Student's t-test. A preliminary check of the distribution of values in the samples was carried out to confirm the adequate method of statistical assessment of the average difference between the study groups. According to the Shapiro-Wilk test [17], data on the deviation of the distribution in the samples from normal ($p>0.05$) were obtained. Taking into account the above, the use of the Student's t-test was considered sufficient to obtain valid conclusions. To confirm the reliability of the conclusions, the non-parametric Mann-Whitney comparison test was used in parallel, which showed similar results to calculations using the Student's t-test regarding the value of p. Therefore, $p\leq0.05$ was considered a sufficient level of probability of differences.

RESULTS

All the biological systems are known to exist in reduction-oxidation (redox) equilibrium, balancing oxidation and reduction reactions to achieve favorable conditions for life. Disturbance of this homeostasis

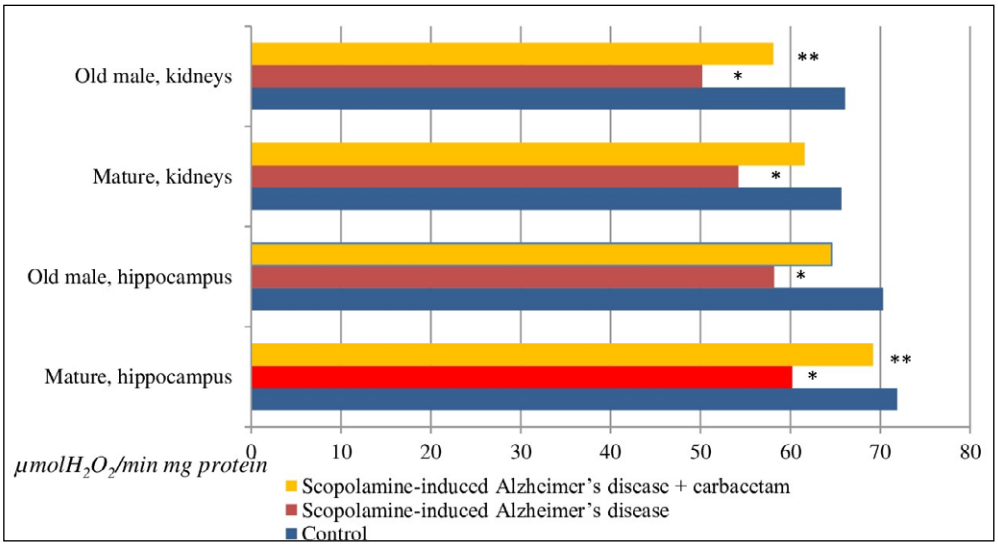

Fig. 1. Effect of carbacetam on catalase activity in the hippocampus and kidneys of rats of different ages with scopolamine-induced Alzheimer's disease, M±m
Notes:* – reliability of differences compared with the control group of rats,
** – reliability of differences compared with the group of rats with scopolamine-induced Alzheimer's disease.
Picture taken by the authors

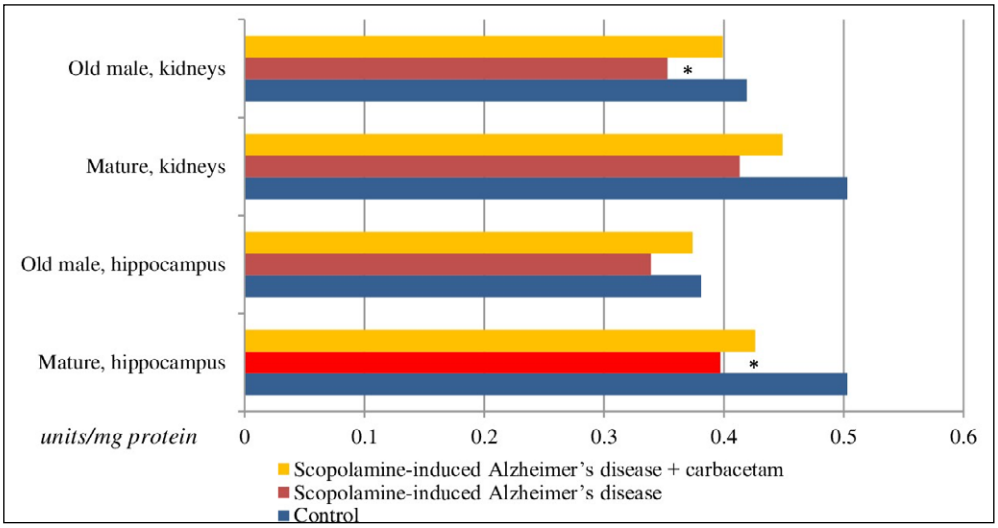

Fig. 2. Effect of carbacetam on SOD activity indices of the hippocampus and kidneys of rats of different ages with scopolamine-induced Alzheimer's disease, M±m
Notes:* – reliability of differences compared with the control group of rats,
** – reliability of differences compared with the group of rats with scopolamine-induced Alzheimer's disease
Picture taken by the authors

promotes oxidation of DNA, proteins and lipids, and thus changing their structure, activity and physical properties. Oxidation damage and reduction-oxidation equilibrium disorders are known to promote imbalance in the biological homeostasis resulting in diseases or even death. Alzheimer's disease is no exception. This pathology is characterized by progressive loss of neuronal structure and function caused by such mechanisms as oxidative stress, mitochondrial dysfunction, and chronic neuritis [18]. Oxidative damage has become a crucial factor. More and more evidences emphasize its key role in pathophysiology and advance of this pathology.

That is why the first stage of our research was to examine the state of lipid and protein peroxide oxidation in the hippocampus and kidneys of rats with an experimental model of Alzheimer-like cognitive dysfunction (Table 1). Thus, TBARS content increases both, in the hippocampus and kidneys of mature and old rats with experimental pathology. As we can see, in the hippocampus, this indicator increased by 77.8% in sexually mature animals and by 75.5% in old ones. At the same time, an increase in the content of lipid peroxidation products was also observed in kidney homogenates. In the group of sexually mature rats TBARS content increased by 44,3%, and in old rats – by 54,1%. Thus, hippocampal lipids are more damaged. Nevertheless, against the ground of brain damage we see kidney damage as well, which is indicative of interrelationships between these examined structures.

Analyzing the results of LPO after carbacetam administration, we see a decrease in the content of TBARS in the hippocampus and kidneys of sexually mature and old rats. In particular, in the hippocampus, TBARS content decreased by 24,1% in sexually mature rats and by 14,2% in old ones, and in the kidneys by 12,6% and 19,9%, respectively.

No less significant are changes in protein peroxidation (Table 1). Thus, in the groups of sexually mature

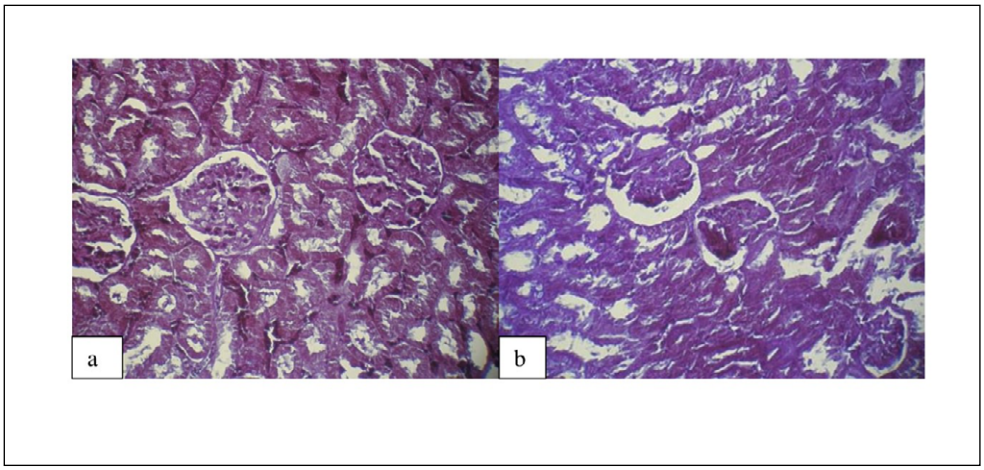

Fig. 3. R/B coefficient in endothelial cells of uncollapsed renal glomeruli of sexually mature (a), old male (b) males (when stained with bromophenol blue according to Mikel Calvo)
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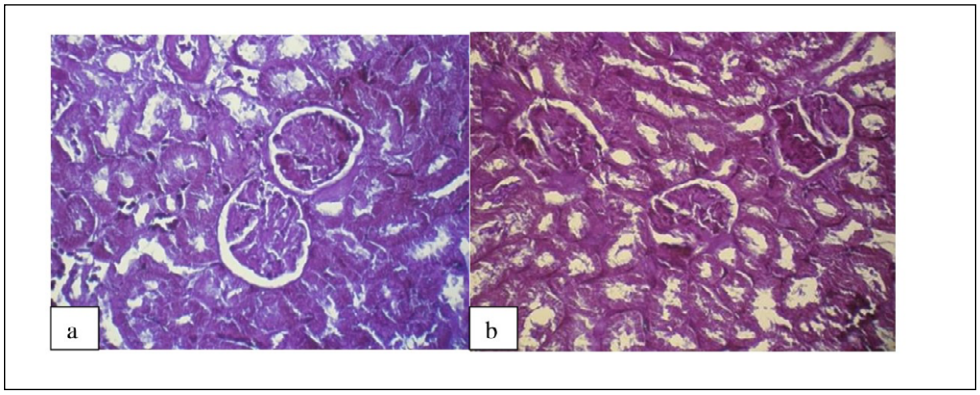

Fig. 4. R/B coefficient in endothelial cells and mesangial matrix of uncollabsed renal glomeruli of mature (a) and old male rats (b) with scopolamine-induced Alzheimer's disease (when stained with bromophenol blue according to Mikel Calvo)
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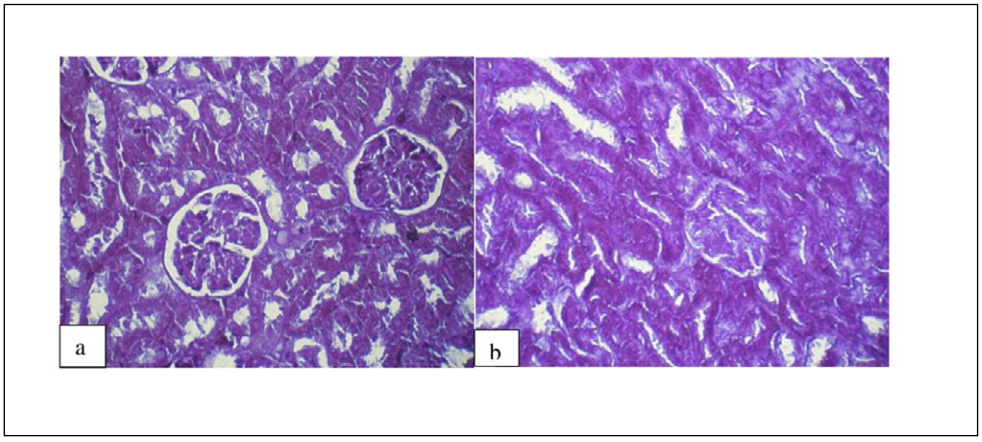

Fig. 5. R/B coefficient in endothelial cells and mesangial matrix of uncollapsed renal glomeruli of sexually mature (a) and old male (b) rats with scopolamine-induced Alzheimer's disease and upon administration of carbacetam (when stained with bromophenol blue according to Mikel Calvo).
Obj. 40x Oc. 10x
Picture taken by the authors

and old rats with a model of cognitive impairment induced by scopolamine, the content of ketone dinitrophenyl hydrozones of neutral character and aldehyde dinitrophenyl hydrozones of basic character increased in the hippocampus and kidneys. At the same time, protein content both neutral and basic by character increased in the hippocampus of sexually mature rats with model pathologyby 61,1% and 41,1% respectively compared to the control group. When comparing the same indicators in the group of old rats, we observe an increase in the content of both groups of proteins: of neutral character by 28,9% and basic – by 41,9%.

The changes in the values of POM indicators in the kidneys of the examined groups were similar. In particular, the products of protein peroxide oxidation increased: those of neutral character in sexually mature rats – by 69% and basic character – by 41,6%; in the group of old rats – by 25,7% and by 54,4% respectively.

Increasing processes of protein peroxide oxidation observed in our research is one of the early markers of oxidative stress, since POM products are more stable compared to LPO metabolites, which are rapidly oxidized under the action of peroxidases. At the same time, destructuring of protein molecules can cause the damage of DNA-apparatus of cells, disturbances of

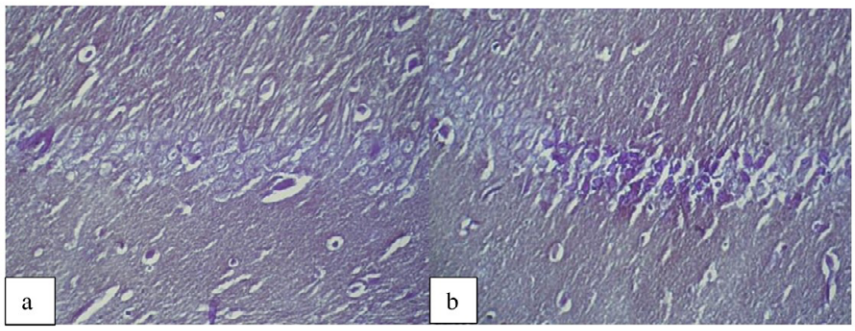

Fig. 6. R/B coefficient in hippocampal neurons of sexually mature (a) and old (b) rats (when stained with bromophenol blue according to Mikel Calvo).
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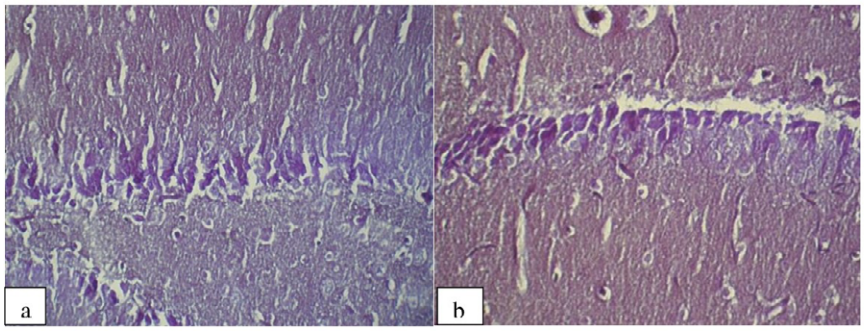

Fig. 7. R/B coefficient in hippocampal neurons of sexually mature (a) and old (b) rats with scopolamine-induced Alzheimer's disease (when stained with bromophenol blue according to Mikel Calvo).
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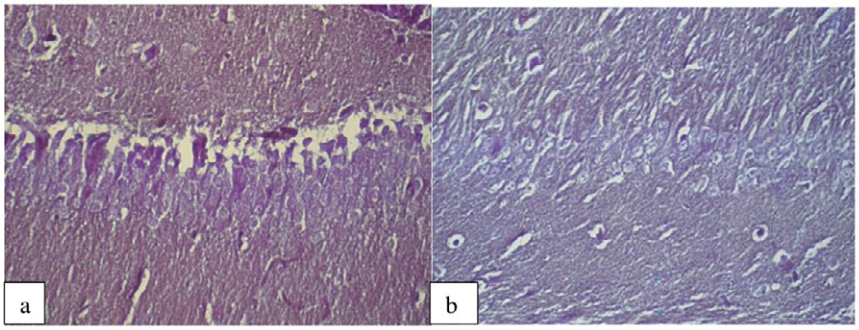

Fig. 8. R/B coefficient in hippocampal neurons of sexually mature (a) and aged (b) rats with scopolamine-induced Alzheimer's disease and carbacetam administration (when stained with bromophenol blue according to Mikel Calvo)
Obj. 40x Oc. 10x
Picture taken by the authors

respiratory and phosphorylation processes in the mitochondria, and blocking ATP synthesis [19]. Significant protein modification is a signal for changing cellular metabolism. The intensity of protein peroxidation reflects not only the degree of oxidative damage to tissues, but reserve-adaptive possibilities of the body as well [20].

14-day carbacetam administration decreased POM content in the hippocampus and kidneys of rats of different ages. Thus, in sexually mature rats, the content of ketone dinitrophenyl hydrozones of neutral character decreased by 24,2% in the hippocampus and by 30,3%% in the kidneys, and the content of aldehyde dinitrophenyl hydrozones of basic character by 13,6% and 17,3%% respectively. In the group of old rats, the content of protein peroxidation products decreased as well in both examined organs. In the group of old rats, the content of ketone dinitrophenyl hydrozones of neutral character decreased by 12,1% in the hippocampus and kidenys, a the content of aldehyde dinitrophenyl hydrozones of basic character by 25,5% and 21,7% respectively.

As is known, the enzymatic activity of SOD is aimed at detoxifying superoxide anion radicals by converting them into a more stable compound - hydrogen peroxide, which is critically important for the functioning of the antioxidant system. In the hippocampus and kidneys of rats with scopolamine-induced Alzheimer's disease (Fig. 1), a decrease in the activity of this enzyme was found in

both age groups: in the hippocampus of sexually mature individuals - by 21.1%; and in the kidneys of old individuals - by 15.8%. However, when a GABA receptor modulator is administered, we observe only a tendency to increase SOD activity in sexually mature and old rats both in the hippocampus and in the kidneys.

Considering that the neutralization of hydrogen peroxide, which is formed as a result of the dismutation of the superoxide radical, is carried out by catalase, we checked the state of this enzyme in the groups of rats under study. In rats with scopolamine-induced Alzheimer's disease, catalase activity (Fig. 2) compared to the control decreased on average by 16.9% in the hippocampus and by 20.6% in the kidneys of rats of different ages. At the same time, the administration of carbacetam increased the activity of this enzyme in the hippocampus of sexually mature and kidneys of old rats by 14.8% and 15.7%, respectively. In other groups, there is a tendency to increase the activity of this enzyme. That is, the administration of carbaracetam, as a GABA receptor modulator, in experimental scopolamine-induced Alzheimer's disease promotes the restoration of antioxidant protection, significantly increasing catalase activity in the hippocampus and kidneys, while SOD activity demonstrates only a positive trend towards growth.

Since POM reflects changes in the ratio between amino- and carboxyl groups, which can be estimated by means of histochemical method for "acidic" and "basic" proteins with bromophenol blue by Mikel Calvo, when proteins are stained in different colors depending on their properties according to the ratio of amino- and carboxyl groups [17]. For example, with a clear predominance of amino groups in proteins, they are stained blue, and with a clear predominance of carboxyl groups, they are stained red. In practice, combined staining always occurs due to the presence of a "mixture" of proteins in the tissues, which prompts the use of not only visual but also quantitative assessment of POM degree.

We used this method in our research as well. After processing the data obtained, we were interested in studying the quantitative assessment of the state of the hippocampal and kidney proteins in rat histochemical samples stained with bromophenol blue according to Mikel Calvo (Fig.3.a,b, Fig 6.a.b). The findings obtained in our research are in Table 2. In the group of sexually mature and old rats with a model of cognitive impairment, induced by scopolamine increasing R/B coefficient was detected both in the hippocampal neurons and endotheliocytes, and in the mesangial matrix of non-collapsed renal glomeruli by 73,4%; 43,5%; 32,7%; 42,4%; 30,2%; 44,5% respectively (Fig. 4.a, b, Fig 7.a, b). The results obtained by means of this method correlate with the findings of the biochemical examination.

In sexually mature rats with simulated pathology that received carbacetam, the examined coefficient decreased by 29,6% and by 14,5% in the kidneys; by 14,5% in the endotheliocytes, and in the mesangial matrix of non-collapsed renal glomeruli (Fig. 5.a., Fig 5.b) In the group of old rats R/B coefficient decreased as well: in the hippocampus and kidneys by 38,9%, 12,5%, 11,6% respectively (Fig. 8.a., Fig 8.b).

Thus, when modeling scopolamine-induced Alzheimer's disease, we observe damage to the amino groups of proteins in the hippocampal neurons and in the endotheliocytes, and in the mesangial matrix of non-collapsed renal glomeruli of rats of different ages having more pronounced changes in the brain cells. At the same time, there is an existing interrelationship between damage to neurons and kidney cells, which makes a foundation for further investigation of pathogenic processes and interrelations in neurodegenerative processes.

DISCUSSION

In our opinion, the obtained data are the basis for studying the possible new functional role of GABA receptors in the mechanisms of kidney damage. However, our studies used a pharmacological model of cognitive disorders with animal studies and the mechanistic pathways involving GABA receptors were not directly studied.

However, when analyzing the obtained data, it was found that modeling scopolamine-induced Alzheimer's disease in rats of all age groups triggers a cascade of pathobiochemical reactions that initiate the development of a pronounced systemic oxidative process. This is manifested by the intensification of peroxidative damage to lipids and proteins against the background of critical suppression of the endogenous antioxidant system. During the study, a clear tissue specificity of the lesion was established, in particular, hippocampal cells show significantly higher vulnerability to free radical damage compared to kidney tissues. This selectivity of neuronal damage directly correlates with a deeper depletion of the enzymatic reserve in the nervous tissue, which is probably due to the high density of GABAergic receptors, intense oxygen consumption, and relatively low levels of protective enzymes in the hippocampus [21].

At the same time, the use of carbaracetam as a positive modulator of GABA receptors opens up new prospects for the correction of these disorders. Presumably, activation of GABAergic signaling contributes to the restoration of excitatory-inhibitory balance[22], which limits the phenomena of excitotoxicity and secondary oxidative stress. Based on the conducted study, a relationship was recorded between the neuroprotective

effect of the drug and its ability to modulate the activity of key antioxidant enzymes - SOD and catalase.

Of particular interest are parallel changes in enzymatic activity in the hippocampus and kidneys. The ability of carbaracetam to reduce the amount of oxidation products in both types of tissues indicates the involvement of the GABAergic system in the common mechanisms of neuro- and renoprotection. This suggests that the drug not only locally protects the hippocampus from atrophy [21], but also has a systemic detoxification effect, supporting the functional state of the kidneys as a key organ for the elimination of metabolites [23].

However, based on a review of the literature, it is possible to hypothesize a possible brain-kidney interaction that is critical for maintaining homeostasis. For example, according to [20], a decrease in GABA receptor activity leads to activation of the renin-angiotensin-aldosterone system, which stimulates NADPH oxidase, which leads to excessive production of reactive oxygen species and the development of a systemic prooxidant state. In this case, systemic inflammatory markers and reactive oxygen species resulting from renal dysfunction increase the permeability of the blood-brain barrier. At the same time, prooxidants reduce the activity of glutamate decarboxylase, which is involved in the synthesis of GABA in the brain [24]. As a result, the excitation/inhibition balance is disturbed with an increase in neurodegeneration or cognitive deficit. That is, a "vicious circle" is formed.

Thus, the obtained data confirm that the limitation of systemic oxidative stress under the influence of carbaracetam is a pathogenetically justified basis for its further study as a means of complex therapy of neurodegenerative disorders, regardless of the age factor. It also acts as a new potentially effective direction of preventive therapy and treatment of kidney diseases.

CONCLUSIONS

1. Modeling scopolamine-induced Alzheimer's disease leads to the development of pronounced oxidative stress in the hippocampus and kidneys of rats of all age groups, which is manifested by the intensification of peroxidative damage to lipids and proteins and the suppression of antioxidant defense mechanisms.
2. The tissue specificity of the pathological process has been established: hippocampal cells exhibit higher vulnerability to free radical damage compared to kidney tissues, which correlates with a deeper suppression of the enzymatic link of antioxidant defense in nervous tissue.
3. The ability of carbaracetam to reduce the amount of oxidation products indicates the involvement of the GABAergic system in the mechanisms of neuro- and renoprotection, which is the basis for further study of their feasibility in neurodegenerative disorders.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 10.06.2025
ACCEPTED: 20.05.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Determinants of stress resilience enhancement in female students during "power step" resistance fitness training sessions

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ABSTRACT

Aim: To investigate the determinants of stress resilience enhancement and their relationship to indicators of physical fitness among female students during "Power Step" resistance fitness training sessions.

Materials and Methods: The research, conducted during the 2024-2025 academic year, involved 40 female students aged 17-18 with no health issues engaged in "Power Step" resistance fitness training sessions. Stress resilience was assessed using the Boston Method; among volitional qualities, decisiveness, perseverance, and self-control were assessed. Physical fitness was evaluated using the following indicators: 4x9 m shuttle run, 30 m sprint, 1500 m run, standing long jump, 10-second Burpee test, and jump rope test.

Results: This research examined the determinants of stress resilience enhancement and their relationship to physical fitness indicators among female students engaged in "Power Step" resistance fitness training sessions. It was found that the markers of stress resilience are volitional qualities: decisiveness and self-control. It was established that the main markers of decisiveness among female students are those physical indicators that require the simultaneous demonstration of speed-strength qualities, speed, and endurance. In contrast, the markers of self-control are various types of endurance.

Conclusions: The volitional structure of stress resilience has been identified, along with statistically significant correlations of varying strength between specific indicators of physical fitness and stress resilience among female students during "Power Step" resistance fitness training sessions, confirming the possibility of influencing the volitional sphere and enhancing stress resilience in female students through specifically targeted exercise workloads during resistance fitness training sessions.

KEY WORDS: female students, physical fitness, volitional qualities, stress resilience, resistance fitness, Power Step, physical education

Wiad Lek. 2026;79(8):1859-1864. doi: 10.36740/WLek/235881 DOI

INTRODUCTION

The physical education system in higher education institutions (HEIs) is subject to constant change and innovation, driven by global trends, sector-specific reforms, and today's socio-political challenges. Contemporary realities emphasize the development of individuals who are intellectually, psychologically, physically, and spiritually prepared for independent life and professional activities [1].

The main guidelines for students' physical education under martial law and other stressors of modern life in Ukraine are an emphasis on maintaining and restoring physical and mental health through physical culture, increasing students' motor activity and their motivation to engage in physical exercise through the introduction of popular and effective forms of motor activity in group training sessions, which can have a comprehensive impact on improving the physical and psycho-emotional well-being of young people [2, 3].

Aerobic and coordination-strength exercises can be particularly beneficial for young people, especially girls, as they have the greatest health-improving and developmental effect [4, 5]. One such type of physical exercise is Power Step – a high-intensity group fitness program that combines cardio on a step platform with coordination and strength exercises. The workout consists of various steps and jumps on the step platform in different directions, combined with swings, squats, bends, and active arm movements [6]. Thus, aerobic workloads optimize the functioning of the cardiorespi-

ratory system: they train the heart and blood vessels, improve lung ventilation, increase physical performance, accelerate calorie burning, and help control body weight [7]. Coordination exercises improve intermuscular coordination and balance, helping to keep the body toned without exhausting workouts [8]. Strength exercises build muscle definition and improve physique, and performing group exercises to music invigorates, creates a good mood, promotes emotional release, and reduces stress levels [9].

Furthermore, according to many scientists [10, 11], in today's world, the development of volitional qualities is crucial for successfully coping with environmental stressors. Contemporary studies have demonstrated a direct, bidirectional relationship between volitional qualities and physical abilities: enhancing physical capacities is impossible without volitional effort. In contrast, physical exercise is a powerful tool for developing will [12].

Many scientific works are devoted to developing students' physical and volitional qualities in physical education [13-15]. However, not all physical and volitional qualities are equally effective for managing stress and enhancing students' stress resilience while studying in wartime conditions. Therefore, research on volitional qualities – which are key determinants of stress resilience enhancement – and the examination of the relationship between the developmental levels of motor and volitional qualities in female students practicing Power Step are timely topics.

AIM

The aim is to investigate the determinants of stress resilience enhancement and their relationship to indicators of physical fitness among female students during "Power Step" resistance fitness training sessions.

MATERIALS AND METHODS

PARTICIPANTS

The research, conducted during the 2024-2025 academic year, involved 40 first- and second-year female students (aged 17-18) from Dragomanov Ukrainian State University who had no health issues and who engaged in the "Power Step" resistance fitness training sessions. The inclusion criteria for female students in the study group were age 17-18 years (first- or second-year students) and voluntary enrollment in the Power Step sports club. The research was open-ended; the girls were informed in advance and consented to participate. Testing of the girls' volitional and physical qualities was conducted in a gym in March-April 2025 by a physical education instructor. The exclusion criterion was the girls' own desire to withdraw from the research at any time.

METHODS

Analysis and generalization of the literature, pedagogical testing of physical fitness indicators, psycho-diagnostic methods, and methods of mathematical statistics. A total of 25 scientific sources from various scientometric databases were reviewed on the selected research topic.

The level of stress resilience was examined using the Boston University Medical Center Stress Vulnerability Scale [16]. The questionnaire designed for this purpose contains 18 questions, with answers scored on a 1-3 points scale; the total score determines the level of stress resilience: the lower the total score, the higher the level of stress resilience. The manifestation level of such volitional qualities as decisiveness, perseverance, and self-control was assessed using the Volitional Organization of Personality Questionnaire by A. Khokhlov [17]. The questionnaire consists of 56 questions, the answers to which were used to determine the levels of decisiveness, perseverance, and self-control separately. The higher the score a respondent receives, the higher the level of these volitional qualities.

Physical fitness was assessed using the following indicators: 4x9 m shuttle run (agility), 30 m sprint (speed), 1500 m run (aerobic endurance), standing long jump (speed-strength qualities), 10-second Burpee test (squat, extend legs back into a push-up position, return to a squat, vertical jump; coordination-strength abilities and speed (anaerobic) endurance), and jump rope (number of jumps per minute; speed-strength endurance, coordination of movements).

METHODS OF MATHEMATICAL STATISTICS

To investigate the relationship between physical fitness indicators and volitional qualities in female students practicing Power Step, we used Pearson's linear correlation analysis. The existence of a relationship and the differences between individual variables were considered statistically significant at a 95 % significance level ($p \leq 0.05$). The data were analyzed at the Department of Theory and Methods of Physical Education at Dragomanov Ukrainian State University.

COMPLIANCE WITH ETHICAL STANDARDS

The participants were informed of the research aim and

Table 1. The relationship between stress resilience and volitional qualities among female students engaged in "Power Step" resistance fitness training sessions (n = 40)

Volitional qualities	Level of stress resilience
Decisiveness	-0.38
Perseverance	-0.19
Self-control	-0.44

Notes: statistically significant correlations are indicated in bold
Source: compiled by the authors of this study

Table 2. The relationship between the level of development of volitional and physical qualities in female students who practice "Power Step" resistance fitness (n = 40)

Physical qualities	Volitional qualities	
	Decisiveness	Self-control
Agility (4x9 m shuttle run)	-0.07	-0.13
Speed (30 m sprint)	-0.11	0.03
Speed-strength qualities (standing long jump)	0.24	0.19
Aerobic endurance (1500 m run)	-0.16	-0.37
Speed endurance (Burpee test)	0.42	0.29
Speed-strength endurance (jumping rope)	0.34	0.39

Notes: statistically significant correlations are indicated in bold
Source: compiled by the authors of this study

voluntarily agreed to participate. The research results were reviewed and approved by the Academic Integrity Committee of the Dragomanov Ukrainian State University (Minutes No. 5 dated April 20, 2026)

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

This study was carried according to the research plan of the Faculty of Physical Education, Sports and Health of the Dragomanov Ukrainian State University in 2023-2027 in accordance with the theme "Monitoring, control and evaluation of learning results in physical culture, the basics of healthy lifestyle" (state registration number 0113U009185).

RESULTS

Stress resilience is shaped by volitional mechanisms that serve as internal regulators, enabling individuals to control their emotions, maintain an optimal level of anxiety, and inhibit negative impulsive reactions. A correlation has been established between stress resilience and specific volitional qualities in 17- to 18-year-old female students who practice "Power Step" resistance fitness (Table 1).

The correlation analysis enabled the identification of the volitional structure of stress resilience among female students who practice the "Power Step" resistance fitness. It was found that the markers of stress resilience are decisiveness ($r = -0.38$) and self-control ($r = -0.44$) at $p \leq 0.05$, while no significant relationship was found between the level of stress resilience and perseverance ($p > 0.05$).

The analysis of the relationships between volitional qualities and physical fitness indicators in 17- to 18-year-old female students engaged in "Power Step" resistance fitness training sessions revealed significant correlations among some of these factors (Table 2).

It has been found that the level of decisiveness among female students engaged in "Power Step" resistance fitness correlates significantly with speed-strength indicators ($r = 0.24$, at $p \leq 0.05$), with speed and speed-strength endurance indicators ($r = 0.42$ and $r = 0.34$, respectively, at $p \leq 0.05$). No significant correlations were found between other physical qualities and decisiveness ($p > 0.05$).

Regarding self-control, significant correlations were found between this volitional quality and various types of endurance in female students engaged in "Power Step" resistance fitness, specifically aerobic endurance ($r = -0.37$ at $p \leq 0.05$), speed endurance ($r = 0.29$ at

$p \leq 0.05$), and speed-strength endurance ($r = -0.39$ at $p \leq 0.05$); other correlations between self-control and physical fitness indicators were not significant ($p > 0.05$).

Thus, the main markers of decisiveness among female students are those physical indicators that require the simultaneous manifestation of speed-strength qualities, speed, and endurance. In contrast, the markers of self-control are various types of endurance.

Establishing a relationship between stress resilience and volitional manifestations made it possible to identify the volitional structure of stress resilience, and the established correlation between volitional and specific physical qualities of 17- to 18-year-old female students engaged in "Power Step" resistance fitness will allow for influencing the volitional sphere of these students through specifically targeted physical exercises.

DISCUSSION

Martial law and other contemporary crises place an additional strain on the mental well-being of Ukrainian students, leading to increased anxiety, emotional instability, and behavioral reactions, which underscores the importance of developing stress resilience as an individual personality trait for maintaining mental and somatic health [18]. Stress resilience ensures the preservation of the body's psycho-functional resources under stress, and the volitional sphere of the personality serves as the primary instrument for controlling and regulating the psyche and behavior, enabling the body to function at an optimal level of performance [19].

Psychological research devotes significant attention to individual volitional qualities of personality that can influence stress resilience in various ways; among these are decisiveness, perseverance, and self-control [10, 11]. Decisiveness characterizes an individual's ability to make quick decisions and choose the optimal course of action in response to a stressor. Perseverance ensures the consistency of the behavior adopted by the individual. Self-control involves the individual's ability to maintain control over their actions and behavior in critical situations. Understanding the contribution of volitional manifestations to overall stress resilience allows for a deeper understanding of the structure of this integral psychological construct [20].

A sufficient level of motor abilities serves as the biological foundation of stress resilience, as they enhance the adaptive capacity of the nervous system and internal organs, enabling the body to process stress hormones more effectively, maintain emotional stability, and recover more quickly from psycho-emotional stressors [1, 21]. Thus, endurance enhances the functional capacity of the cardiovascular and respiratory systems and improves the body's overall resistance to prolonged psychological stress. Strength and speed-strength qualities can raise the pain threshold and relieve muscle tension caused by suppressed emotions and anxiety. Agility and coordination require maximum concentration, which distracts the brain from obsessive thoughts and resets the nervous system [7, 22].

The results of our research are consistent with existing data in psychological and pedagogical theory, which establishes a correlation between volitional and physical qualities [4, 12, 13]. The modern view of stress resilience lies in the interconnection between volitional manifestations and motor activity, and in exploring the possibility of developing these qualities through targeted influence on physical fitness during training sessions [3, 23]. It is known that various types of fitness generate high interest among female students. Power step is a high-intensity aerobic-resistance fitness activity that involves various variations of jumps and steps on a step platform, combined with active arm movements, and comprehensively develops physical qualities by integrating cardio and strength training. It requires concentration and the ability to overcome fatigue through complex coordination exercises [6, 7, 24]. Power step is an ideal tool for developing volitional qualities and improving physical fitness. Thus, the development of strength and speed-strength endurance is facilitated by repeated lifts, jumps, and strength exercises (squats, lunges), which target the muscles of the legs, glutes, and core, thereby increasing their ability to work for extended periods without a decline in efficiency. The emphasis on strength training can be adjusted by using dumbbells of varying weights (typically 1.5-3.0 kg). The intense training rhythm builds resistance to physical fatigue, promoting aerobic endurance. Working on an elevated platform, changing direction, and varying movement pace improve spatial orientation, overall coordination, and body balance. Focusing on the rhythm of the music and precise movement technique helps train emotional resilience [8, 13, 25].

A relationship has been confirmed between indicators of volitional qualities and motor abilities in 17- to 18-year-old girls during "Power Step" resistance fitness training sessions. A correlation has been established between decisiveness and the expression of speed-strength qualities, and the corresponding type of endurance, which allows one to trace the influence of decisiveness on the execution of movements requiring maximum muscular effort in the minimum time. A connection was found between self-control and the expression of various types of endurance: aerobic, speed (anaerobic), and speed-strength (aerobic-anaerobic), indicating the contribution of self-control to the ability to overcome physical fatigue and maintain a high level of physical performance. It has been found that decisiveness and self-control constitute the volitional structure of stress resilience, thereby allowing pedagogical influence to increase stress resilience in girls during "Power Step" resistance fitness training sessions. It has been established that the

comprehensive development of coordination and speed-strength qualities, as well as various types of endurance, which constitute the content of "Power Step" resistance fitness training sessions, contributes to increased stress resilience by influencing the corresponding volitional determinants of improvement: decisiveness and self-control.

CONCLUSIONS

The volitional structure of stress resilience has been determined among female students engaged in "Power Step" resistance fitness during group training sessions at a higher education institution. It was found that the determinants of increased stress resilience are decisiveness ($r = -0.38$ at $p \leq 0.05$) and self-control ($r = -0.44$ at $p \leq 0.05$). In contrast, no significant correlation was found between the level of stress resilience and perseverance ($p > 0.05$).

It was found that the main markers of decisiveness among female students are those motor performance indicators that require the simultaneous manifestation of speed-strength qualities, speed, and endurance. In contrast, the markers of self-control are various types of endurance: the level of decisiveness exhibited by female students engaged in "Power Step" resistance fitness significantly correlates with speed-strength indicators ($r = 0.24$ at $p \leq 0.05$), with indicators of speed endurance and speed-strength endurance ($r = 0.42$ and $r = 0.34$, respectively, at $p \leq 0.05$), and self-control significantly correlates with various types of endurance, specifically aerobic ($r = -0.37$ at $p \leq 0.05$), speed ($r = 0.29$ at $p \leq 0.05$), and speed-strength endurance ($r = -0.39$ at $p \leq 0.05$). Other relationships between physical fitness indicators and volitional qualities were not significant ($p > 0.05$).

The data obtained confirm the possibility of influencing the volitional sphere and increasing stress resilience among female students through specifically targeted physical exercises during "Power Step" resistance fitness training sessions.

PROSPECTS FOR FURTHER RESEARCH

We see opportunities for further research into developing and refining methods to build stress resilience in female students during the "Power Step" resistance fitness training sessions.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 09.03.2026
ACCEPTED: 22.07.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Gender-specific determinants of the cardiorespiratory system and energy supply for working capacity in sport dance athletes

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ABSTRACT

Aim: To identify specific functional characteristics of male and female partners in the semi-finals and finals of the standard European program.

Materials and Methods: Twenty-one professional standard European dance couples were assessed during semifinal and final performances; VO_2, VCO_2, VE, and lactate were measured using MetaMax 3B and Biosen+. To compare independent samples, the Mann–Whitney U test was applied; data are presented as mean, median, SD, min–max, Q1–Q3, and IQR.

Results: No significant differences were found between SF and F in VO_2max, VO_2max/kg, VE, EqO_2, VCO_2, VCO_2/kg, or $EqCO_2$. A significant difference was observed for lactate ($p<0.05$). These findings indicate stable functional support across competitive rounds, while higher lactate values in the final reflect greater glycolytic load, particularly in female partners.

Conclusions: In most dancers, in F SEP, there was found an increase in aerobic metabolism in partners and glycolytic capacity in female partners. The reactive properties of the cardiorespiratory system are reflected in the efficiency of oxygen consumption per unit of pulmonary ventilation (EqO2) and the stability of the respiratory compensation response to metabolic acidosis.

KEY WORDS: energy supply, sport dances, functional capabilities, Standard European Program

Wiad Lek. 2026;79(8):1865-1872. doi: 10.36740/WLek/222255 DOI

INTRODUCTION

Studies conducted over three decades show high requirements to the level and large specific features of the functional support of competitive activity of dancers [1, 2]. There is a clear understanding that the level of physiological stress of dancers that occurs during the performance of dance programs reaches a limit, which affects the level of demonstration of technical, artistic and choreographic skills of dancers [3, 4]. This puts forward certain requirements for the functional orientation of special physical training. Most of the means of special physical training of other sports [5-7] contradict the target guidelines for the functional provision of special working capacity of dancers. Contradictions cause physiological states that arise under the influence of work modes that are inadequate to the physiological stress of the competitive activity [8-11]. Means that develop specialized manifestations of neurodynamic functions and properties of the musculoskeletal system are in a significant deficit [12, 13]. In most cases, the training system for athletes uses exercises that do not correspond to the static and dynamic stresses of the dancers' posture [14, 15].

A particular problem is the uncertainty of functional training target guidelines in sport [16-19]. Orientation to the generalized factors of functional preparedness forms an energy supply structure that is inadequate to the requirements of the special working capacity of dancers, which significantly affects the effectiveness of competitive activity. The presence of high VO_2max and La concentration is often misleading in assessing the effectiveness of functional preparedness of dancers. The uncertainty of the conditions for the development and implementation of VO_2 max and La max, in real practice, often leads to the rapid development of fatigue and overstrain of the body. The functions of endurance are transformed into "functions of the ability to tolerate fatigue", which does not contribute much to the realization of the existing special skills of dancers.

At the same time, research in recent years has contributed to understanding the structural requirements for the functional support of competitive activity [20, 21,

22]. The outlined factors that influence the structure of energy supply of competitive activity of dancers form the functional focus of the training process of dancers. Data from specialized literature indicate special conditions for the implementation of VO_2 max, glycolytic power and capacity, and mechanisms for regulating functions during competitive activity [23-25]. Identifying quantitative and qualitative characteristics that reflect these processes remains relevant. Contradictions are caused by the quantitative characteristics of the energy supply of dancers' competitive activity, which determine the quality and functional orientation of the training process.

AIM

To identify specific functional characteristics of male and female partners in the semi-finals and finals of the standard European program.

MATERIALS AND METHODS

Material: Qualified athlete dancers specializing in the standard European prograzm (SEP). Age of male partners is 25,3±2,2 y. o. and female partners – 23,4±2,2 y. o.; the body weight and height of male partners were 78,1±3,0 kg and 181,8±2,1 cm, female partners – 51,8±1,5kg and 162,2±1,9 cm.

Quantity of dancers: 21 male partners and 21 female partners (21 couple). All couples are highly qualified athletes, prize-winners and winners of prestigious tournaments in Ukraine and abroad.

RESEARCH ORGANIZATION

The study was conducted at the end of the special training period. Before the start of the study, voluntary written consent from the athletes and approval by the local bioethics committee for scientific research were obtained. Simulation of the competitive activity was held in a dance hall of the National University of Ukraine on Physical Education and Sport; the registration of cardiorespiratory system and energy supply indicators was carried out by employees of the university's functional diagnostics laboratory.

All athletes confirmed their willingness to participate in the study. They declared the absence of the use of additional means of stimulating work capacity, in particular drugs of any origin, doping, etc.

RESEARCH PROGRAM AND INDICATORS

The modulation of dancers' competitive activity included the simulation of semi-final and final (with 20 minutes break) of SEP. This allowed to identify reaction characteristics, adequate to physiological stress of the competitive load.

During the performance of Slow Waltz, Tango, Viennese Waltz, Foxtrot and Quickstep, within SF and F SEP, the indicators of CRS and energy supply were registered in real time.

The procedure and course of the study complied with the ethical standards of the Helsinki Declaration. The study program was submitted to the local Biomedical Ethics Committee of National University of Ukraine on Physical Education and Sport (Dated 15.12.2025, Protocol No. 6).

EQUIPMENT AND INDICATORS

The consumption of O_2 (VO_2), release of CO_2 (VCO_2), level of pulmonary ventilation (V_E), blood lactate concentration were registered using MetaMax 3B gas analyser and Biosen+ device for biochemical research. Blood sampling to determine the lactate concentration level was performed at the 3rd and 5th minutes of the recovery period after the SF and F simulation. The highest indicators were registered.

Maximum aerobic capacity (VO_2 max), maximum pulmonary ventilation (V_E max), respiratory compensation reaction of metabolic acidosis ($EqCO_2$), oxygen utilization efficiency (EqO_2), anaerobic glycolytic capacity (La) were measured.

STATISTICAL ANALYSIS

To compare two independent samples, a Mann–Whitney U test criterion was applied – this is a nonparametric statistical test used to compare two independent samples of semifinal (SF) and final (F) indicators. There were used calculated statistical characteristics , Me (the median), S (the standard deviation), Max (the maximal indicator), Min (minimal indicator), percentiles Q1 (25%) and Q3 (75%); IQR – interquartile range (IQR – Interquartile Range).

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

Quantitative and qualitative functional characteristics of male partners are represented in Table 1, female partners – in Table 2.

The control was carried out upon completion of pre-competition training, when the dancers reached

Table 1. Characteristics of the cardiorespiratory system response and energy supply of male partners

Statistics	VO_2 max, l•min^{-1}	VO_2 max / kg, ml•min^{-1}•kg^{-1}	V_E, l•min^{-1}	EqO_2	VCO_2, l•min^{-1}	VCO_2 / kg, ml•min^{-1}•kg^{-1}	$EqCO_2$	La, mmol•l^{-1}
Data semifinal								
	4.4	55.6	146.8	33.6	4.5	56.7	33.0	9.6*
Me	4.4	55.0	146.0	34.2	4.4	56.4	33.2	9.8
S	0.2	3.6	5.8	1.9	0.2	3.6	1.8	0.8
Max	5.0	61.3	157.0	37.5	5.0	61.9	36.5	11.0
Min	4.0	49.8	135.0	30.4	4.1	51.0	29.9	8.0
Q1 (25%)	4.2	53.1	144.0	32.3	4.3	54.0	31.8	9.0
Q3 (75%)	4.5	59.7	150.0	34.8	4.6	61.1	34.1	10.1
IQR	0.2	6.6	6.0	2.5	0.3	7.1	2.3	1.1
Data final								
	4.6	58.8	149.5	32.4	4.6	58.6	32.5	12.5*
Me	4.6	58.7	149.0	32.2	4.5	58.7	32.4	12.8
S	0.3	4.2	5.7	1.8	0.2	4.1	1.6	0.7
Max	5.1	65.3	161.0	36.1	5.1	64.5	36.1	14.0
Min	4.2	50.6	141.0	30.0	4.2	49.4	30.0	10.9
Q1 (25%)	4.4	55.2	146.0	31.3	4.5	56.3	32.0	11.9
Q3 (75%)	4.9	62.8	151.0	32.9	4.8	62.8	33.1	12.9
IQR	0.5	7.6	5.0	1.6	0.3	6.6	1.1	1.0

*– the differences are statistically reliable $p<0,05$

Source: compiled by the authors of this study

the competitive level of functional and special preparedness. This gives reason to interpret the obtained functional characteristics as a generalized model of energy supply of competitive activity in SEP. The model range is based on the indicators of the Q1 – Q3 range.

The data presented in the table and schematically in Fig. 1, Fig.2, Fig.3, Fig.4, Fig.5 indicate the absence of statistically significant differences in most indicators of SF and F of male and female partners. Statistically significant differences are noted between La indicators, registered in SF and F of SEP.

The results of statistical analysis indicate the stability of the functional support of competitive activity in changing conditions of SF and F. Differences in La of SF and F indicate rational use of anaerobic reserve during SEP and an increase in glycolytic load in F. This phenomenon is especially evident in female partners.

The presence of general positive conclusions of the statistical analysis is confirmed by the data of empirical reasoning, which indicate tendencies towards certain functional shifts, which affect the effectiveness of the functional support of the special working capacity of dancers. This is especially true for the increased level of F indicators.

It is important to note that the increase in CRS response and energy supply occurred within reference values in response to the increase in physiological stress of load in F. The increase in response is considered as compensation for increasing metabolic shifts and progressive fatigue. This is naturally observed in the ratio of respiratory compensation indicators of metabolic acidosis ($EqCO_2$) and efficiency of oxygen consumption (EqO_2).

Consideration of individual functions allowed us to identify the same and individual features of functional support in SEP. On the Fig. 1, Fig.2, Fig.3, Fig.4, Fig.5 in the boxslots there schematically presented the statistical ranges, which provide opportunities to identify general trends and differences in functional support in SF and F for male and female partners.

Statistical distribution of VO_2 max / kg indicators in SF and F is presented on Figure I. In the absence of statistically significant differences in indicators, there is a tendency for aerobic power increase while performing F. The model range of Q1 – Q3 (IQR) corresponds to the generalized norms of aerobic energy supply capacity in professional dancers.

The characteristics of blood lactate concentration have static differences that characterize the redistribution of glycolytic load between SF and F of SEP is presented on Figure II. Changes in the median, reduced

Table 2. Characteristics of the cardiorespiratory system response and energy supply of female partners

Statistics	VO_2 max, l•min^{-1}	VO_2 max / kg, ml•min^{-1}•kg^{-1}	V_E, l•min^{-1}	EqO_2	VCO_2, l•min^{-1}	VCO_2 / kg, ml•min^{-1}•kg^{-1}	$EqCO_2$	La, mmol•l^{-1}
Data semifinal								
	2.8	49.7	102.5	36.8	3.2	56.7	32.5	7.8*
Me	2.8	50.0	102.0	36.1	3.2	56.4	31.9	8.0
S	0.2	4.0	3.1	2.2	0.2	3.6	2.8	0.5
Max	3.0	58.0	109.0	41.6	3.6	61.9	38.2	8.6
Min	2.5	42.4	98.0	34.1	2.8	51.0	28.1	7.0
Q1 (25%)	2.6	47.3	100.0	34.8	3.0	54.0	30.9	7.6
Q3 (75%)	2.9	52.7	104.0	38.8	3.4	61.1	34.3	8.1
IQR	0.3	5.5	4.0	4.0	0.4	7.1	3.4	0.5
Data final								
	2.9	51.7	104.8	36.2	3.1	55.1	31.41	12.1*
Me	2.9	51.7	107.0	36.3	3.0	54.5	31.25	12.0
S	0.1	3.5	4.1	2.3	0.1	3.2	1.39	0.5
Max	3.0	60.0	109.0	40.0	3.3	61.5	33.75	13.1
Min	2.5	44.6	100.0	33.3	2.9	50.8	28.57	10.9
Q1 (25%)	2.8	49.2	101.0	34.8	3.0	51.8	30.61	11.9
Q3 (75%)	3.0	54.5	109.0	37.6	3.2	57.1	32.26	12.2
IQR	0.2	5.4	8.0	2.8	0.2	5.4	1.7	0.3

*– differences are statistically reliable $p<0,05$

Source: compiled by the authors of this study

IQR, and min–max range in female partners in F indicate a significant factor of the dancers' preparedness. These data confirm the results of the static comparison of glycolytic reserve indicators, corresponding to the assessment of the ratio of La SF and La F (%) given below.

The results of the statistical analysis of the ratio of La SF and La F (%) in male and female partners are schematically presented in the Figure III. According to the data presented on the Figure, the given differences are not statistically reliable. However, the general trend of Me redistribution and regulatory ranges Q1 – Q3 (IQR) indicates a persistent trend towards differences in the majority of dancers who participated in the study. The lack of reliable connections is due to the presence of a significant range of min-max, indicators that form highly individual manifestations of energy reactions. This is natural for the high-class athletes.

The results of the statistical analysis presented in Fig. 4 and in Fig. 5 indicate a significant range of differences in SF and F indicators in male and female partners. The general tendency towards a decrease in Me, a redistribution of the Q1 – Q3 and min – max ranges, indicates a decrease in the specific characteristics of the pulmonary ventilation response and oxygen consumption in the final part of the competitive activity.

The results of the statistical analysis also did not reveal statistically significant differences in SF and F indicators in male and female partners. The above differences are based on individual manifestations of the reaction, which is confirmed by the wide range of Q1 – Q3 and min – max and the stability of the median among the SF and F indicators in male and female partners. Certain differences of F indicators in male and female partners are connected with a more pronounced pulmonary ventilation response in men.

The presented results of functional control confirm the known data on regulatory requirements for potential aerobic (VO_2 max) and anaerobic (La max) reserve, at the same time, they provide grounds for reflection on ways to optimize the structure of energy supply for competitive activities of dancers.

DISCUSSION

In modern sports, there is a clear understanding that the capacity of aerobic energy supply is a potential functional reserve of the special performance of athletes in most sports. However, the importance of maximal oxygen consumption for dancers is actively discussed in the specialized literature. There are reasons to claim

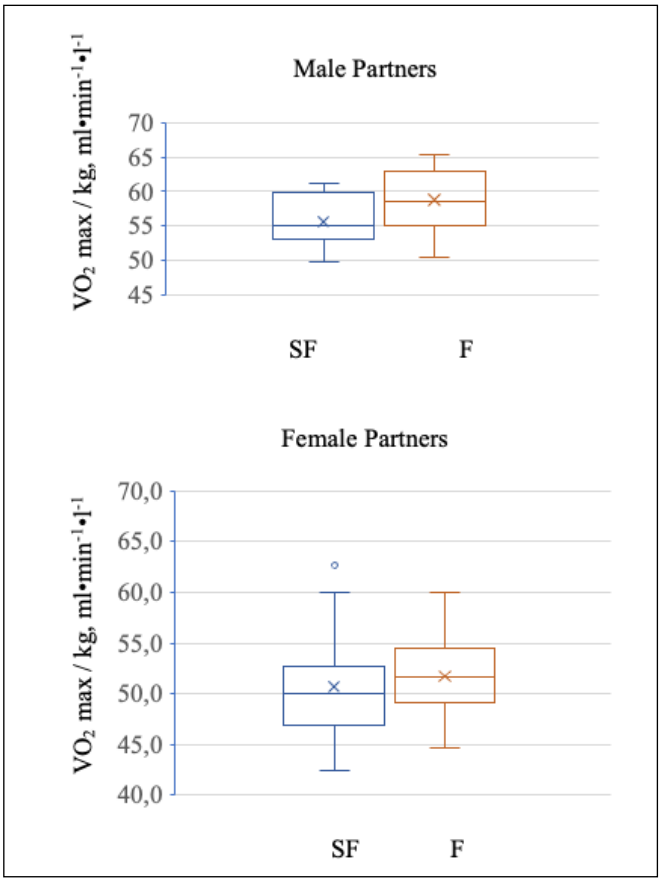

Fig. 1. Statistical characteristics of maximal oxygen consumption in the semi-final and final of the standard European program
Picture taken by the authors

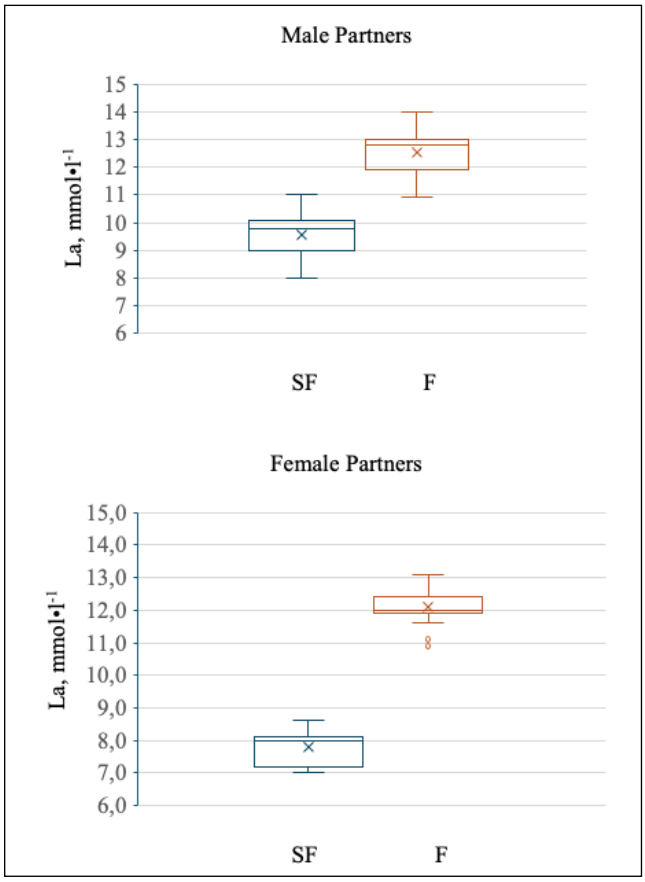

Fig. 2. Statistical characteristics of blood lactate concentration in the semifinal and final of the standard European program
Picture taken by the authors

that the debatable issues arise due to the unsuccessful interpretation and normative uncertainty of this component of preparedness. It is obvious that the statement of high VO_2 max provides certain characteristics of the energy capabilities of athletes, but it does not indicate much about the effectiveness of its use during competitive activity, especially when it goes about absolute indicators of (VO_2 max, l•min^{-1}) reaction. In this work, the increase in absolute aerobic power indicates the preservation of effective aerobic performance in the final. More informative indicator of aerobic power is its modification in relation to body weight (VO_2 max / kg, ml•min^{-1}•kg^{-1}), which indicates the degree of oxygen consumption efficiency in relation to body weight. This characteristic is much more informative for determining the aerobic capacity of female partners.

Glycolytic reactions play a significant role in the overall energy balance of special performance of dancers. Modern concepts of the structure of anaerobic glycolytic reactions in professional dancers separate the characteristics of power and capacity [26, 27]. The redistribution of the load between SF and F forms the prerequisites for the rational use of glycolytic reactions throughout the dance program, which requires appropriate characteristics of the anaerobic glycolytic capacity. This is proven in this study. Statistically significant differences between La SF and F correspond to the conditions of rational distribution of glycolytic reactions during SEP performance. An increase in the lactate concentration level in F (La, mmol•l^{-1}) indicates the presence of glycolytic capacity reserve to maintain the level of performance of dancers in the final part of the competition. According to the data, represented in Figure 2, this component of functional preparedness is more pronounced in female partners.

The special literature provides data on the reactive properties of the cardiorespiratory system, which reflect adaptive processes and have a direct impact on the structure of energy reactions according to the requirements of competitive activity [28, 29, 30]. In sports dance, the reactive properties of CRS are manifested in the efficiency of breathing regulation according to the power of oxygen consumption (EqO_2) and respiratory compensation of metabolic acidosis ($EqCO_2$) [31,32].

Data presented in the literature indicate the specificity of the pulmonary ventilation response in dancers. There is an opinion, that the frequency of respiratory cycles affects the aesthetic perception of dancing and the judges'

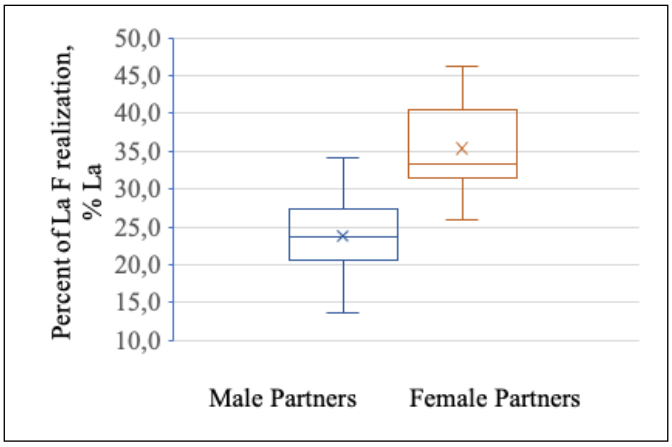

Fig. 3. Statistical characteristics of glycolytic reserve in the final of the standard European program
Picture taken by the authors

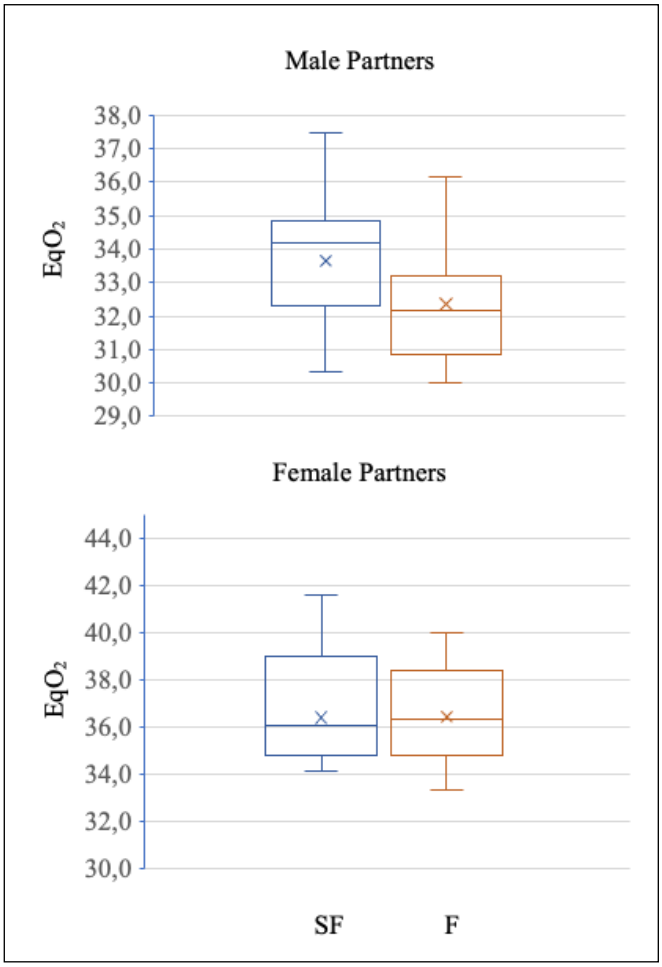

Fig. 4. Statistical characteristics of pulmonary ventilation for oxygen consumption
Picture taken by the authors

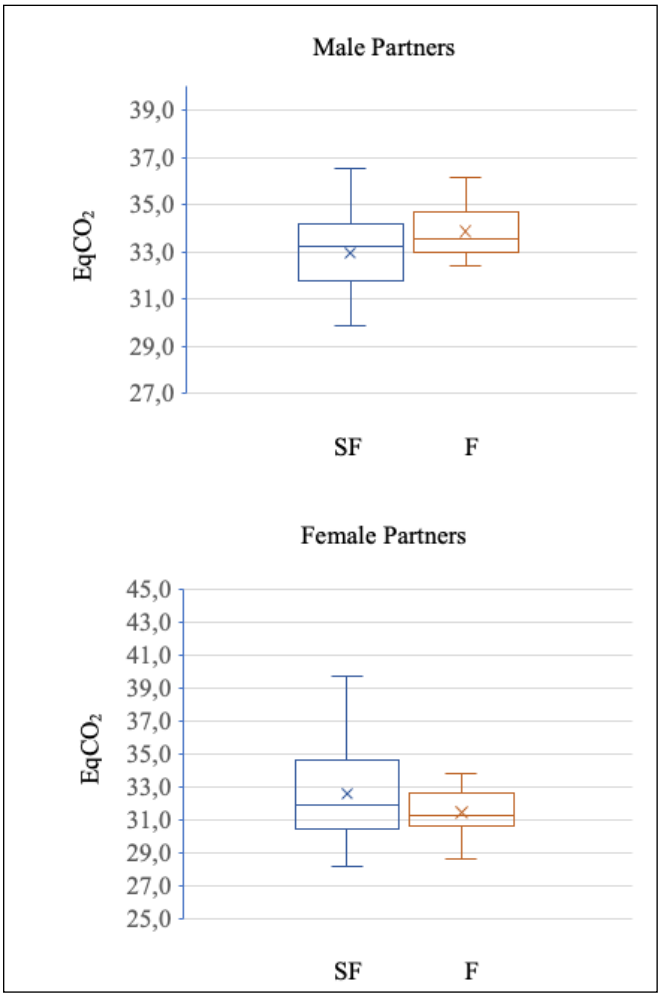

Fig. 5. Statistical characteristics of pulmonary ventilation to remove carbon dioxide
Picture taken by the authors

assessment of dance performance. In practice, dancers "artificially" regulate breathing functions, which reflects the specifics of adaptation processes. This is especially evident in the degree of increase in the pulmonary ventilation response in the final part of the competition. This is certainly a debatable issue and requires more detailed study based on identifying different types of responses to increased physiological stress of load. Monitoring of pulmonary ventilation indicators in real time made it possible to make assumptions about the higher significance of the stability of the respiratory response than its power.

At the same time, the presented research results indicate certain patterns that accompany the correlation of the processes of pulmonary ventilation, oxygen consumption and glycolytic reactions. The increase in the peak values of pulmonary ventilation in the final is consistent with an increase in aerobic power and glycolytic capacity. The increased response of pulmonary ventilation to increased metabolism that accompanies higher VCO_2 ($EqCO_2$) is interpreted as an increased response of respiratory compensation of metabolic acidosis, the decrease of EqO_2 indicators in F shows reduction of ventilation load per unit of oxygen consumption. This factor becomes especially important in the final part of competitive activity.

CONCLUSIONS

In the final of the standard European program, in most dancers, an increase in aerobic metabolism was found in male partners and glycolytic capacity in female partners. The structure of energy supply is influenced by the reactive properties of the cardiorespiratory system. The reactive properties of cardiorespiratory system are reflected in the efficiency of oxygen consumption per unit of pulmonary ventilation (EqO_2) and the stability of the respiratory compensation response to metabolic acidosis ($EqCO_2$).

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We express our gratitude to the athletes of the national teams of Ukraine in sport dance and the professional sports club in sport dance Supadance.

CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 25.12.2025
ACCEPTED: 20.05.2026

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ORIGINAL ARTICLE

Health-promoting technologies for enhancing students' motor activity during online learning

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ABSTRACT

Aim: To investigate the impact of health-promoting technologies designed to increase students' motor activity during online learning on their level of physical fitness and health status.

Materials and Methods: The research, conducted in 2025-2026, involved 70 students aged 17-19 (first-year students). Two groups were formed: an experimental group (EG, n = 33) and a control group (CG, n = 37). During online learning, the EG students followed a newly developed health-promoting program designed to increase their motor activity; the CG students participated only in remote physical education training sessions (twice a week).

Results: The effectiveness of the developed health-promoting program in maintaining and improving students' physical fitness and preserving their health has been demonstrated. After completing the online learning, the EG students showed significantly ($p < 0.05$) better results than those in the CG in the following tests: push-ups in 1 minute – by 3.8 reps, sit-ups in 1 minute – by 3.6 reps, in the sit-and-reach test – by 1.2 cm, and in plank holding – by 13.1 sec. HR indicators, which characterize students' health status, were also better than those in the CG after online learning.

Conclusions: The results indicate that the systematic implementation of a health-promoting technology program into the educational process at HEIs contributes to maintaining and even increasing students' levels of motor activity and physical fitness, as well as improving their health indicators in an online learning environment, compared to the traditional organization of physical education in an online format.

KEY WORDS: health, health-promoting technologies, physical fitness, motor activity, students, online learning, martial law

Wiad Lek. 2026;79(8):1873-1880. doi: 10.36740/WLek/235882 DOI

INTRODUCTION

The current transformation of Ukraine's higher education system is taking place amid profound socio-political changes, martial law, and the rapid digitization of the educational process [1. 2]. The transition of higher education institutions (HEIs) to online learning is driven by security challenges, primarily air raid alerts, limited access to educational infrastructure, the need to reallocate instructional time, an increase in the proportion of independent student work, as well as the need to ensure the continuity of the educational process in wartime [3, 4]. Under such conditions, the risk of reduced motor activity among students increases significantly, which negatively affects their physical fitness, functional status, and health [5].

In online learning, the volume and intensity of motor activity necessary to preserve students' health and maintain their psychological well-being are not always provided [6]. Students are forced to spend long periods in front of digital screens, which leads to physical inactivity, poor posture, reduced tolerance for physical exertion, increased fatigue and anxiety, and decreased motivation for physical exercise and self-improvement [7].

The issue of motor activity among young people and its impact on physical and mental health is reflected in numerous studies. However, according to many researchers [8, 9], implementing a set of health-promoting technologies is particularly significant under martial law, as these technologies enable targeted maintenance of students' motor activity levels during the online format of the educational process at HEIs.

AIM

The aim is to investigate the impact of health-promoting technologies designed to increase students' motor activity during online learning on their level of physical fitness and health status.

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 70 students aged 17-19 (first-year students in the faculties of "Management and Marketing" and "Software Systems and Applied Mathematics"). Two groups were formed: an experimental group (EG, n = 33) and a control group (CG, n = 37). During online learning, the EG students followed a newly developed health-promoting program designed to increase their motor activity. In contrast, the CG students participated only in remote physical education training sessions (twice a week for 2 hours each).

In the context of this research, health-promoting technologies are understood as a specially organized set of pedagogical, physical education, health-related, motivational, and digital tools aimed at preserving, maintaining, and strengthening students' health by increasing their daily motor activity. Unlike traditional online physical education training sessions, health-promoting technologies were systematic and focused not only on completing a specific set of motor tasks but also on changing students' attitudes toward motor activity and on developing skills in self-control, self-organization, self-regulation, and a responsible attitude toward their own physical condition.

Inclusion criteria: all students involved in the research belonged to the general health group (had no health issues or contraindications for motor activity); before on-line learning, all 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 students were instructed on the importance of motor activity for maintaining health during on-line learning under martial law. There was no special selection of students for the EG and the CG: all first-year students of the Management and Marketing Faculty were included in the EG and were asked to follow the developed health-promoting program during online learning; all first-year students of the Software Systems and Applied Mathematics Faculty were included in the CG. 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 on-line learning, Phase 2 (end) – after the completion of on-line learning). The research lasted 3 months (December 2025 – February 2026). Research limitations: students who regularly attended sports clubs for various sports and held sports ranks and titles did not participate in the research.

RESEARCH METHODS

bibilosemantic, testing, biomedical, statistical. The bibilosemantic method was aimed at studying the state of the problem, identifying the main trends and systematizing the accumulated knowledge on the topic of research (18 sources from MedLine, Scopus, Web of Science databases were analyzed).

Testing was used to assess students' physical fitness levels. Tests that can be performed without special equipment, in a relatively confined space while adhering to safety requirements, were used: push-ups in 1 minute (to assess the speed-strength endurance of the shoulder girdle muscles); sit-ups in 1 minute (to determine the strength endurance of the abdominal muscles); sit-and-reach test (to determine flexibility); the prone plank test (to assess the static endurance of the trunk muscles).

Biomedical methods were used to assess students' functional status and health using indicators that students could measure independently: resting heart rate (HR) in the morning, a 20-squat test with HR measured before and after exercise, and HR recovery rate.

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 Academic Council of 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.

AI STATEMENT

The author states that no AI tools were used in writing this article.

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

Based on the findings of numerous scholars and our own research, we have developed and implemented a set of health-promoting technologies to optimize motor activity, improve physical fitness, maintain health, and enhance students' well-being during online learning under martial law. The formative approach combined physical education with health-promoting, organizational, methodological, motivational, and digital support tools, which together were intended to ensure more effective engagement of the EG students in systematic motor activity. As part of the research, the EG students were provided with individualized exercise programs, the content and scope of which were selected based on their baseline levels of physical fitness, functional capabilities, daily routines, and the availability of conditions for independent training sessions. Such individualization was particularly important in the context of online learning, where students were in different living situations, had varying access to sports equipment, and had different opportunities for organizing motor activity. The exercise programs included morning calisthenics routines; exercises to develop strength, endurance, flexibility, and coordination; elements of functional training; and compensatory exercises to reduce the negative effects of prolonged sitting at a computer.

An important component of the experimental program was the use of digital tools to monitor students' physical activity. This made it possible to systematically track students' motor activity levels, the frequency and duration of exercise, and the dynamics of individual workload, as well as to foster a more conscious attitude toward their own motor activity regimen. The use of digital tools not only facilitated the recording of results but also enhanced students' self-control, discipline, and responsibility for maintaining an appropriate level of physical fitness within the online learning format.

In addition to direct physical exercise, regular online support was provided to students throughout the online learning process. This support was provided through consultations, thematic webinars, online discussions, individual recommendations, and ongoing feedback between instructors and students. Its goal was not only to adjust the physical workload but also to support student motivation, help overcome difficulties with self-organization, foster a consistent commitment to regular motor activity, and raise awareness of its role in maintaining health. Motivational and informational support also played a significant role, including explaining the importance of motor activity for physical and mental well-being, preventing overfatigue, and maintaining work capacity and functional readiness under increased academic workload.

The implementation of health-promoting technologies into the educational process during online learning was carried out with key conditions in mind. First, all exercises were designed to be performed independently without special sports equipment or with minimal use of it. Second, exercises and workloads were selected with consideration for the limited space available to students. Third, special emphasis was placed on the safety of performing physical exercises, the clarity of instructions, and the ability to self-monitor workload intensity. Fourth, the entire system of formative influence was designed not to overload students with an excessive number of tasks, but rather to integrate motor activity into their daily routine as a natural, regular component of a healthy lifestyle. The structure of the health-promoting technology program to increase students' motor activity in an online learning environment is presented in Table 1.

The results of the comparative analysis of the physical fitness indicators for the EG and the CG students before and after online learning are presented in Table 2.

The analysis of the physical fitness of the EG and CG students before online learning revealed no significant differences between the groups on any measured indicator ($p > 0.05$). After online learning, certain changes occurred in the indicators: in the EG, there was a significant improvement across all tests, while in the CG, the results remained virtually unchanged (with non-significant improvements or declines). Thus, in the push-up test, results in the EG improved significantly by 4.4 repetitions ($p < 0.01$), while in the CG, they deteriorated insignificantly by 0.2 repetitions ($p > 0.05$). At the end of the research, the EG showed significantly better results in this test than the CG, by 3.8 repetitions ($p < 0.05$). A similar trend was observed in the 1-minute sit-ups test: in the EG, performance improved by 3.5 repetitions during the online training period ($p < 0.05$), whereas in the CG, it improved by 0.5 repetitions ($p > 0.05$). After completing the online learning, the EG's indicators on this test were significantly better than those of the CG by 3.6 repetitions ($p < 0.05$). In the sit-and-reach test, flexibility improved in both groups during the

Table 1. The structure of the health-promoting technology program to increase students' motor activity in an online learning environment

Program module	Goal	Content	Frequency of execution	Duration
1. Morning motor activity	Waking up after sleep, boosting overall energy levels, and getting ready for the academic day	March in place for 1-2 minutes; rotate your head, shoulders, and wrists; swing your arms; bend forward and to the sides; rotate your hips; do 10-15 squats; do 8-10 lunges on each leg; run in place for 30-60 seconds.	Daily	10-15 minutes
2. Active breaks during study sessions	Reducing the negative effects of prolonged sitting, preventing fatigue, and static strain	Stand up every 45-60 minutes; walk around the room; rotate your shoulders in circles; do 10 squats; do 10-12 push-ups against a table or wall; rise onto your toes 15-20 times; do eye exercises; do breathing exercises.	2-3 times a day	3-5 minutes
3. Strength module	Developing speed-strength endurance and strength in major muscle groups	Push-ups; squats; lunges; sit-ups; bicycle crunches; forearm plank; side plank; "superman" (lying on your stomach).	3 times a week	20-25 minutes
4. General endurance training module	Improving aerobic capacity and cardiovascular function	Brisk walking; jogging; running in place; stepping onto a platform or step; interval training: 30 seconds of active exercise / 30 seconds of walking; cardio exercise routines.	2-3 times a week	20-30 minutes
5. Flexibility and mobility module	Improving joint mobility, preventing muscle stiffness, and addressing posture problems	Forward bends from a standing and sitting position; calf and quadriceps stretches while standing; trunk twists while sitting; shoulder girdle stretches.	Daily or after your main workout	10-15 minutes
6. Static endurance and core stabilization module	Strengthening the core muscles, improving postural stability	Prone plank test; side plank; holding the "chair against the wall" position; holding the "boat" position; balancing on one leg.	Twice a week	10-15 minutes
7. Functional rehabilitation module	Restoring normal functional status after exercise, reducing stress	A leisurely walk, relaxing the neck and shoulder muscles, gentle bends and stretches, breathing exercises, and monitoring your heart rate before and after exercise.	After every workout	2-3 minutes
8. Self-monitoring and digital support	Developing self-awareness skills, improving discipline, and motivation	Keeping a motor activity log, recording the number of workouts per week, tracking steps, measuring resting heart rate, and conducting a brief self-assessment of well-being.	Daily / weekly	3-5 minutes
9. Motivational and educational module	Developing a conscious approach to health and motor activity	Online consultations; lectures on the importance of motor activity; recommendations for a daily routine; personalized messages; discussions of interim results.	Once a week	10-15 minutes

Source: compiled by the authors of this study

research period: in the EG by 1.8 cm ($p < 0.01$), and in the CG by 0.2 cm ($p > 0.05$). However, at the end of the research, the results in the EG were significantly better than in the CG by 1.2 cm ($p < 0.05$). In the prone plank test, both groups showed an improvement in the duration of maintaining a horizontal static trunk position: in the EG by 19.4 s ($p < 0.01$), and in the CG by 4.4 s ($p > 0.05$). At the same time, after the completion of online learning, the results for holding the plank in the EG were significantly better than in the CG by 13.1 s ($p < 0.05$). The results indicate that the proposed health-promoting technology program is superior to the traditional physical education program in HEIs in improving students' physical fitness during online learning.

The results of the comparative analysis of health indicators for the EG and the CG students before and after online learning are presented in Table 3.

Before online learning, none of the health indicators differed significantly between the EG and the CG students ($p > 0.05$). After the research, the resting HR in the EG improved by 0.7 bpm ($p > 0.05$), while in the CG it worsened by 0.3 bpm ($p > 0.05$). At the end of the research, the resting HR in the EG was 0.8 bpm better than in the CG; however, no significant difference was found ($p > 0.05$). Assessment of HR before exercise (20 squats in 30 seconds) shows a trend similar to that of resting HR: an improvement in HR in the EG by 1.0 bpm ($p > 0.05$), a decrease of 0.5 bpm in the CG ($p > 0.05$), and a 1.4 bpm advantage of the EG over

Table 2. The results of the comparative analysis of the physical fitness indicators for the EG (n=33) and the CG (n=37) students before and after online learning (M±m)

Research stages	Groups of students		Significance of the difference	
	EG (n=33)	CG (n=37)	Difference	t; p
Push-ups in 1 minute, reps				
Beginning	27.3±1.07	28.1±0.99	0.8	0.55; >0.05
End	31.7±0.98	27.9±0.97	3.8	2.76; <0.05
t; p	3.03; <0.01	0.14; >0.05		
Sit-ups in 1 minute, reps				
Beginning	35.9±1.14	35.3±1.06	0.6	0.39; >0.05
End	39.4±1.11	35.8±1.05	3.6	2.36; <0.05
t; p	2.20; <0.05	0.33; >0.05		
Sit-and-reach test, cm				
Beginning	7.8±0.39	8.2±0.32	0.4	0.79; >0.05
End	9.6±0.41	8.4±0.34	1.2	2.25; <0.05
t; p	3.18; <0.01	0.45; >0.05		
Prone plank test, sec				
Beginning	107.5±3.71	109.4±3.52	1.9	0.37; >0.05
End	126.9±3.84	113.8±3.61	13.1	2.49; <0.05
t; p	3.63; <0.01	0.87; >0.05		

Notes: M – arithmetic mean; m – error of arithmetic mean; n – number of students; t – Student's test value; p – reliability value
Source: compiled by the authors of this study

Table 3. The results of the comparative analysis of health indicators for the EG (n=33) and the CG (n=37) students before and after online learning (M±m)

Research stages	Groups of students		Significance of the difference	
	EG (n=33)	CG (n=37)	Difference	t; p
Resting HR, bpm				
Beginning	71.5±1.28	71.3±1.21	0.2	0.11; >0.05
End	70.8±1.30	71.6±1.24	0.8	0.45; >0.05
t; p	0.38; >0.05	0.17; >0.05		
HR before exercise, bpm				
Beginning	71.9±1.31	71.8±1.22	0.1	0.66; >0.05
End	70.9±1.32	72.3±1.25	1.4	0.77; >0.05
t; p	0.54; >0.05	0.29; >0.05		
HR after exercise, bpm				
Beginning	99.5±1.42	101.3±1.28	3.6	1.86; >0.05
End	97.3±1.37	103.1±1.32	5.8	3.05; <0.01
t; p	1.10; >0.05	0.98; >0.05		
HR 1 minute after recovery, bpm				
Beginning	78.1±1.35	80.5±1.27	2.4	1.29; >0.05
End	76.6±1.34	81.2±1.29	4.6	2.47; <0.05
t; p	0.79; >0.05	0.28; >0.05		

Notes: M – arithmetic mean; m – error of arithmetic mean; n – number of students; t – Student's test value; p – reliability value
Source: compiled by the authors of this study

the CG after online learning ($p > 0.05$). The analysis of HR immediately after exercise indicates that in the EG, the indicators were significantly better than in the CG by 5.8 bpm ($p < 0.01$). At the same time, in the EG, the studied indicators tend to improve over the course of the study, whereas in the CG, they tend to worsen. The analysis of HR 1 minute after recovery shows that, at the end of the research, the HR recovery rate in the

EG was significantly higher than in the CG by 4.6 bpm ($p < 0.05$). Furthermore, during the online learning period, the duration of recovery processes in the EG decreased, whereas in the CG it increased. All of this also confirms the effectiveness of the health-promoting technology program in preserving and strengthening students' health during online learning under martial law.

DISCUSSION

The development of Ukraine's higher education system under martial law is accompanied by large-scale digitization of the educational process in HEIs and the introduction of distance and blended learning formats. While in the early stages of the COVID-19 pandemic, online learning was viewed primarily as a necessary, temporary measure, it is now being gradually integrated into HEIs' curricula as a tool for ensuring the continuity of professional training for future specialists [6, 10]. At the same time, the transition to distance learning formats significantly alters the structure of students' academic days, their motor activity patterns, and the conditions for organizing physical education.

Studies [11] examining the lifestyles of university students during the COVID-19 pandemic and prolonged remote learning document a systematic decline in motor activity, an increase in sedentary behavior duration, and a related deterioration in students' subjective health indicators. Analyzing the characteristics of students' lifestyles under online learning conditions, researchers [12] note that the transition to online formats was accompanied by increased time spent at the computer, decreased physical activity, and a blurring of structured daily routines. Similar results have been obtained in other studies [13], which show that among students who studied remotely, the proportion of individuals with insufficient motor activity is increasing, while the proportion of those who regularly engage in physical exercise is decreasing. Analyzing the educational process during wartime, researchers [14] emphasize that remote learning formats, amid air raid alerts, movement restrictions, and unstable energy supplies, further exacerbate the trend toward a sedentary lifestyle among students. In studies on students' motor activity during the war in Ukraine [15], it was found that the combination of pandemic and war-related factors creates a "double challenge" for young people's health: on the one hand, access to infrastructure (gyms, stadiums, parks) is limited, and on the other, psycho-emotional stress intensifies, which also reduces motivation for regular motor activity. Summarizing the results of surveys of students across various fields of study, researchers [16] note that distance learning fosters a specific "screen-centered" lifestyle, in which a significant portion of time is spent using devices, and physical activity is often limited to brief daily movements. Researchers [17] emphasize that online learning has altered the content, location, and structure of physical education for students. Most exercises are performed at home, and a significant portion of physical education training sessions consists of video tutorials, online classes, and self-monitoring via mobile apps. Under these conditions, the demands on students' self-discipline, intrinsic motivation, and ability to plan their own motor activity increase significantly. In the absence of external supervision, a clearly defined sports infrastructure, and group dynamics (competitions, joint training sessions), there is a high risk of a reduction in the actual volume of physical activity, even if the curricula are formally "fulfilled." At the same time, researchers [18] emphasize that negative trends are not fatally inevitable. With purposeful organization of the educational process and the implementation of health-promoting technologies, the distance learning format can be combined with sufficient daily motor activity among students.

Our research found that implementing a set of health-promoting technologies within the educational processes of HEIs during online learning increased students' motor activity and, in turn, helped maintain and improve their physical fitness and health. The results obtained confirm the conclusions of many researchers and expand upon them.

CONCLUSIONS

A program (set) of health-promoting technologies has been developed and implemented in the educational process to optimize motor activity, improve physical fitness, and maintain students' health during online learning under martial law. The program combined physical education with health-promoting, organizational, methodological, motivational, and digital support tools, which together were intended to ensure more effective student engagement in systematic motor activity.

The effectiveness of the developed health-promoting program in maintaining and improving students' physical fitness and preserving their health has been demonstrated. After completing the online learning, the EG students showed significantly ($p < 0.05$) better results than those in the CG in the following tests: push-ups in 1 minute – by 3.8 repetitions, sit-ups in 1 minute – by 3.6 repetitions, in the sit-and-reach test – by 1.2 cm, and in plank holding – by 13.1 seconds. HR indicators, which

characterize students' health status, were also better than those in the CG after online learning: resting HR – by 0.8 bpm ($p > 0.05$), HR before and after exercise – by 1.4 bpm ($p > 0.05$) and 5.8 bpm ($p < 0.01$), respectively, and HR recovery time – by 4.6 bpm ($p < 0.05$).

The results indicate that the systematic implementation of a health-promoting technology program into the educational process at HEIs – which includes rationally planned individualized exercise programs, the use of digital tools for monitoring motor activity, online guidance, and motivational and informational support, contributes to maintaining and even increasing students' levels of motor activity and physical fitness, as well as improving their health indicators in an online learning environment, compared to the traditional organization of physical education in an online format.

PROSPECTS FOR FURTHER RESEARCH

It is planned to investigate the impact of a set of health-promoting technologies on students' mental health during online learning.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 07.03.2026
ACCEPTED: 25.07.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Why early preventive check-ups matter: Unmasking subclinical abnormalities in adults aged 18–45 via systemic ultrasound phenotyping (the LUMINA score)

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ABSTRACT

Aim: To evaluate systemic multi-organ ultrasound phenotyping using VScan Air™ CL for detecting subclinical abnormalities in healthy adults aged 18–45 years and develop an integrated scoring system (LUMINA System) for early risk stratification.

Materials and Methods: A prospective cohort study (2010–2025) enrolled 188 clinically healthy adults with normal biochemical markers, stratified into three age groups (18–26, 27–35, 36–45 years). Standardized ultrasound assessments of liver, kidneys, carotid arteries, heart, and thyroid were performed. The LUMINA System (score range: 0–29) integrated findings across organ systems.

Results: Subclinical abnormalities were detected in 79.8% of participants despite normal laboratory values. Early liver steatosis occurred in 20.7%, correlating with higher BMI, triglycerides, and HOMA-IR. Increased renal echogenicity was found in 28–35% despite preserved kidney function. Carotid intima-media thickness exceeded the 75th percentile in 22.6%, with progressive vascular stiffness. Thyroid abnormalities appeared in 47.35%, suggesting autoimmune activation. Mean LUMINA scores increased from 0.44±0.31 (18–26 years) to 12.12±3.68 (27–35 years), strongly correlating with BMI (r=0.68), waist circumference (r=0.71), and HOMA-IR (r=0.54).

Conclusions: Systemic ultrasound phenotyping enables early detection of multi-organ abnormalities in young adults with normal laboratory profiles. The LUMINA System provides unified preclinical risk stratification, revealing that metabolic, vascular, and endocrine remodeling coexist years before disease onset, enhancing preventive medicine through personalized intervention.

KEY WORDS: Vascular Remodeling, Ultrasonography, Risk Assessment, Young Adult, Preventive Medicine

Wiad Lek. 2026;79(8):1881-1898. doi: 10.36740/WLek/222260 DOI

INTRODUCTION

Cardiovascular diseases, diabetes (DM), and chronic kidney and liver disorders remain leading causes of mortality despite major diagnostic and therapeutic advances [1]. Most individuals seek medical care only when pathology becomes clinically apparent, although its biological onset begins years earlier [2]. Among young adults, the prevalence of metabolic and behavioral risk factors is steadily increasing, yet conventional HCE-based risk models substantially underestimate their long-term vulnerability, creating a diagnostic gap and contributing to therapeutic inertia in the 18–45 age group [3]. The subclinical period—the "blind zone" of medicine—therefore represents a critical stage for transitioning from reactive treatment to proactive metaphylaxis.

Pathomorphological evidence shows that microcirculatory, parenchymal, and vascular alterations precede biochemical and clinical manifestations. Early hepatic steatosis predicts insulin resistance and T2DM [4]; subtle renal echogenicity changes indicate early nephropathy [5,6]; increased carotid intima–media thickness (CIMT) reflects endothelial dysfunction [7]; and reduced global longitudinal myocardial strain predicts future heart failure [8]. The thyroid gland is similarly sensitive to metabolic–immune imbalance, with diffuse hypoechogenicity, structural heterogeneity, or micro-nodules appearing before TSH or free T4 abnormalities [9]. Collectively, these alterations correlate with low-grade inflammation, cytokine dysregulation, impaired insulin sensitivity, altered lipid profiles, and endothelial reactivity, forming a unified multiorgan subclinical risk phenotype [10]. Detecting such changes in asymptomatic individuals provides a critical "window of opportunity" for early intervention.

This framework supports the hypothesis that multiorgan ultrasound phenotyping represents a universal

"ultrasound risk biomarker." The integration of conventional ultrasound with elastography, strain imaging, and vascular sonography enables preclinical stratification by aggregating minimal multiorgan deviations as sensitive indicators of systemic metabolic and endothelial stress. Within this paradigm, SUP (Sonographic Ultrasound Phenotyping) is proposed as a multimodal quantitative approach capable of detecting early multiorgan structural and functional alterations. To translate these findings into an integrative vulnerability metric, the LUMINA framework (Long-term Ultrasound-Metabolic Integrated Assessment) shifts risk assessment from traditional HCE models toward estimating Biological Age or a consolidated Phenotypic Risk Score (PRS) based on previous publications [11-16]. The scientific novelty lies in the transition from organ-centric diagnostics to preclinical multisystem phenotyping and metaphylaxis, enabling risk modification before symptom onset. An individualized "ultrasound passport" for young adults, with regular monitoring of key quantitative parameters, may enhance primary care by enabling early risk identification and timely personalized prevention, ultimately reducing the long-term burden of chronic diseases.

AIM

To evaluate systemic multi-organ ultrasound phenotyping using VScan Air™ CL for detecting subclinical abnormalities in healthy adults aged 18–45 years and develop an integrated scoring system (LUMINA System) for early risk stratification.

MATERIALS AND METHODS

This prospective longitudinal cohort study (2010–2025) progressed over the years through sequential stages refining systemic ultrasound phenotyping and integrating accumulated data into the final protocol. The analysis included 188 clinically healthy adults aged 18–45 meeting strict inclusion criteria, the population study was conducted on Caucasians. Laboratory parameters (glucose, creatinine, ALT, AST, lipid profile) were within reference ranges; manifest chronic somatic disease led to exclusion. In a small subgroup, additional biomarkers—ApoB, TNF-α, IL-6—were measured using high-sensitivity ELISA (see Supplementary Materials). The population was stratified by age: 1-st group — 18–26 years (n = 68; 36.2%), 2-nd group — 27–35 years (n = 70; 37.2%), 3-rd group — 36–45 years (n = 50; 26.6%), enabling analysis of age-related subclinical dynamics within a homogeneous young adult cohort and ensuring adequate statistical power to detect age-dependent changes. All participants signed informed consent (Declaration of Helsinki and GDPR, Art. 6 Abs. 1 lit. a). The study was approved by the Ethics Committee of Kharkiv National Medical University (approval No. 4, date: 01.04.2026).

All participants underwent standardized anthropometric assessment (BMI, waist circumference), blood pressure measurement, and comprehensive ultrasound using the portable expert-class VScan Air™ CL system (GE Healthcare). All scans were performed by a single researcher to minimize variability, digitally stored, and independently reviewed by two blinded experts. The ultrasound protocol covered five organ systems. Liver echogenicity, structure, and steatosis were assessed, with elastography when feasible. Kidney evaluation included size, parenchymal thickness, cortico-medullary differentiation, echogenicity, and resistive index as a marker of microvascular dysfunction. Carotid arteries and jugular veins were examined for intima–media thickness and focal remodeling. Standard echocardiography assessed diastolic function (E/A and E/e' ratios) and included strain analysis. The thyroid gland was evaluated for volume, echostructure, vascularity, and asymptomatic nodules according to TIRADS criteria [17].

Data processing was performed centrally. Quantitative variables were described as mean values and standard deviations (mean ± SD), Median (IQR) and qualitative variables as percentage frequencies. Comparisons between groups were carried out using the Student's t-test for independent samples or the χ^2 test. Correlation analysis was performed using Pearson's or Spearman's method (ρ). The statistical significance was set at $p < 0,05$.

SUPPLEMENTARY MATERIALS

https://docs.google.com/document/d/1ty1UhuS1--l-5xmcYsJ2S-S94RkXvHKXsj6MYooHbQ/edit?usp=sharing

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

THE LIVER AS AN EARLY ULTRASOUND MARKER OF METABOLIC RISK

The liver is a key organ of metabolic regulation that responds sensitively to changes in lipid and carbohydrate metabolism, and increased echogenicity of

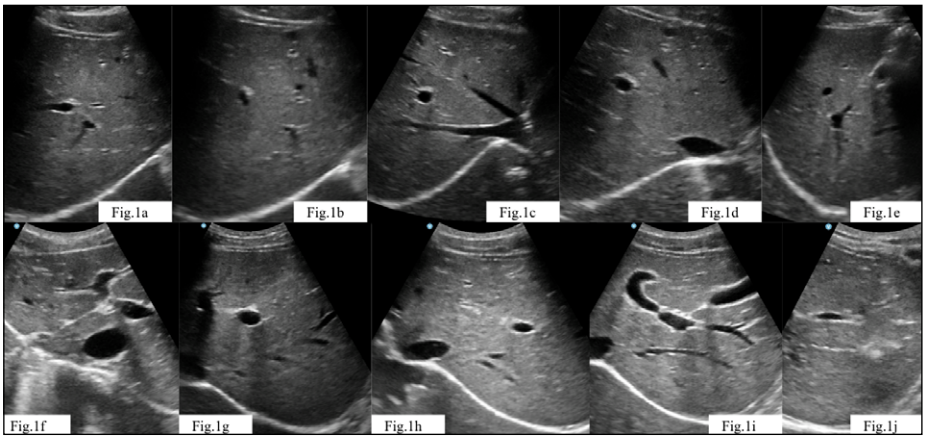

Fig. 1. Ultrasound features of the liver in the 18–26 age group
Picture taken by the authors

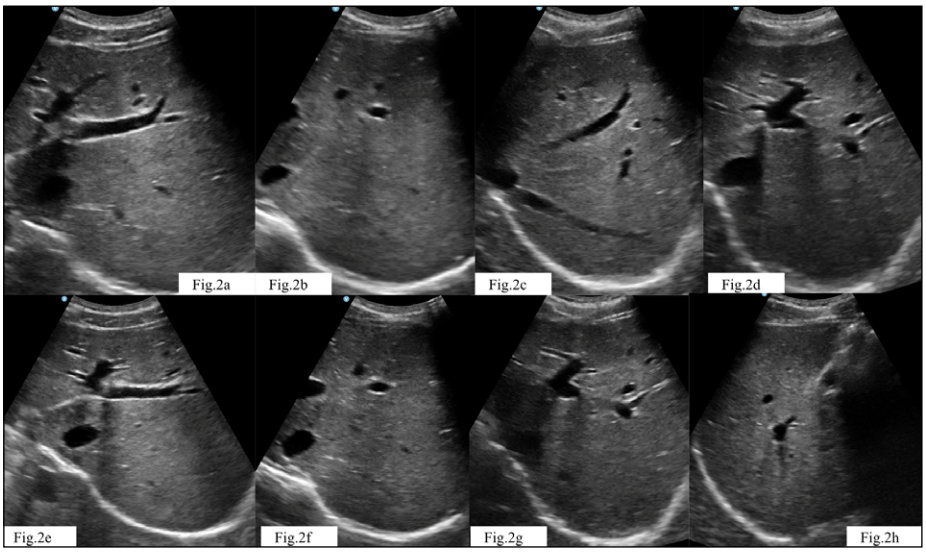

Fig. 2. Ultrasonic features of the liver in the 27–35 age group
Picture taken by the authors

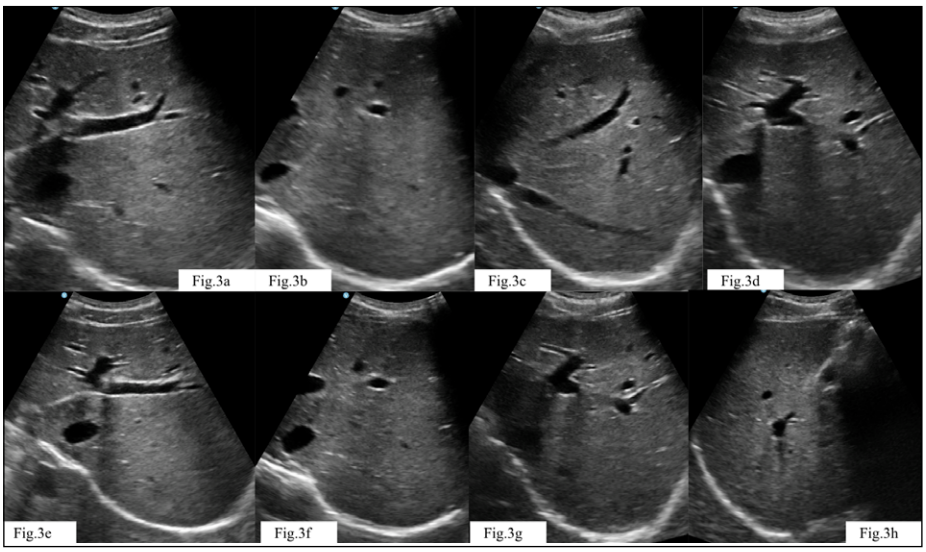

Fig. 3. Ultrasound features of the liver in the 36–45 age group
Picture taken by the authors

its parenchyma serves as one of the earliest markers of metabolic disturbances [18]. This phenomenon reflects the accumulation of TG in hepatocytes, which alters the acoustic properties of the tissue, and can be detected by ultrasound even before laboratory abnormalities appear [19]. In a cohort of 188 participants, increased parenchymal echogenicity, consistent with early hepatic steatosis, was detected in 39 individuals (20.7%). In addition, increased liver echogenicity was connected with early insulin resistance despite normal fasting glucose and HbA1c levels [20]. Subclinical steatosis was accompanied by higher fasting insulin

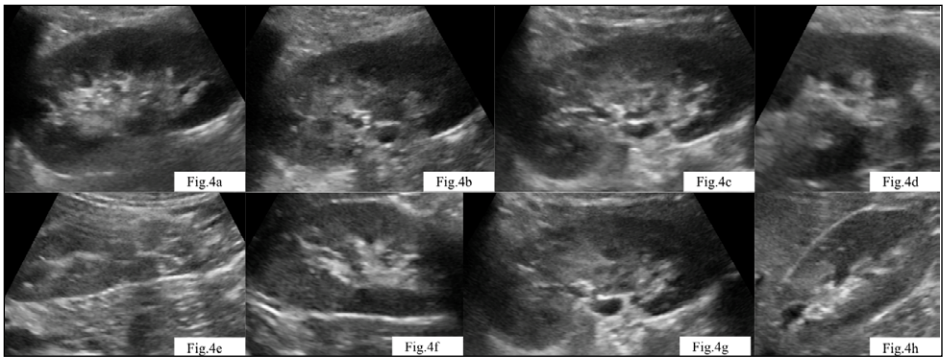

Fig. 4. Morphometric and microvascular characteristics of kidneys in young adults (18–26 yrs)
Picture taken by the authors

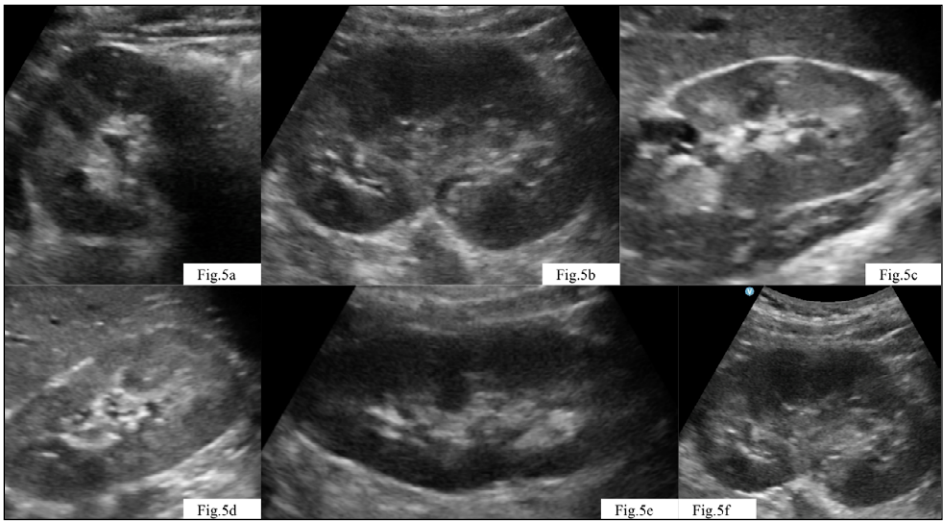

Fig. 5. Morphometric and microvascular characteristics of kidneys in middle-aged adults (27–35 yrs)
Picture taken by the authors

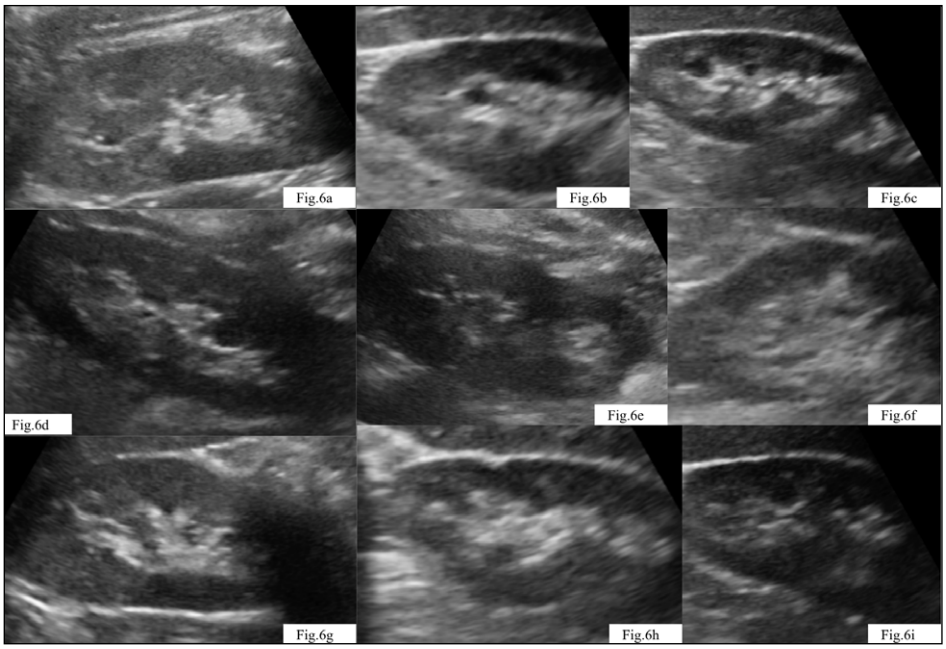

Fig. 6. Morphometric and microvascular characteristics of kidneys in older adults (36–45 yrs)
Picture taken by the authors

(4.44–20.28 μIU/mL), elevated HOMA-IR (1.09–4.74), and increases in TG (1.84±0.40 mmol/L), LDL-C (3.66±0.57 mmol/L), and pro-inflammatory cytokines (TNF-α 3.75±0.60 pg/mL; IL-6 12.56±0.88 pg/mL), indicating low-grade inflammation that promotes insulin resistance [4, 21, 26].

The 2-nd group demonstrated a statistically significant increase in BMI and waist circumference compared with the 1-st group ($p<0.05$), that indicates early development of the abdominal component of metabolic syndrome. In this group, moderate hepatic echogenicity corresponded to early subclinical steatosis and was consistent with ele-

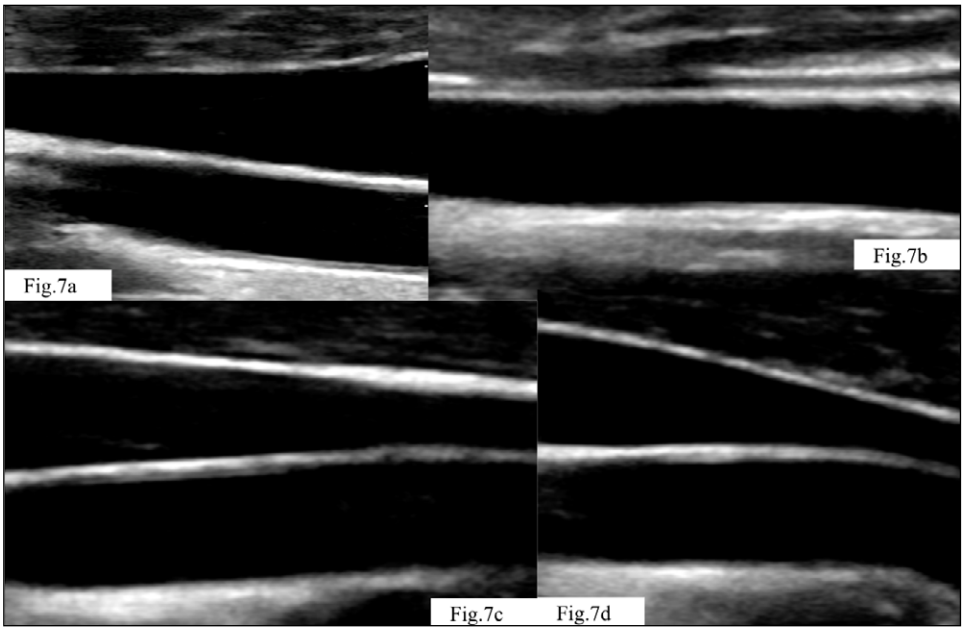

Fig. 7. Morphometric and hemodynamic characteristics of the common carotid arteries in the 18–26-year age group (control phenotype)
Picture taken by the authors

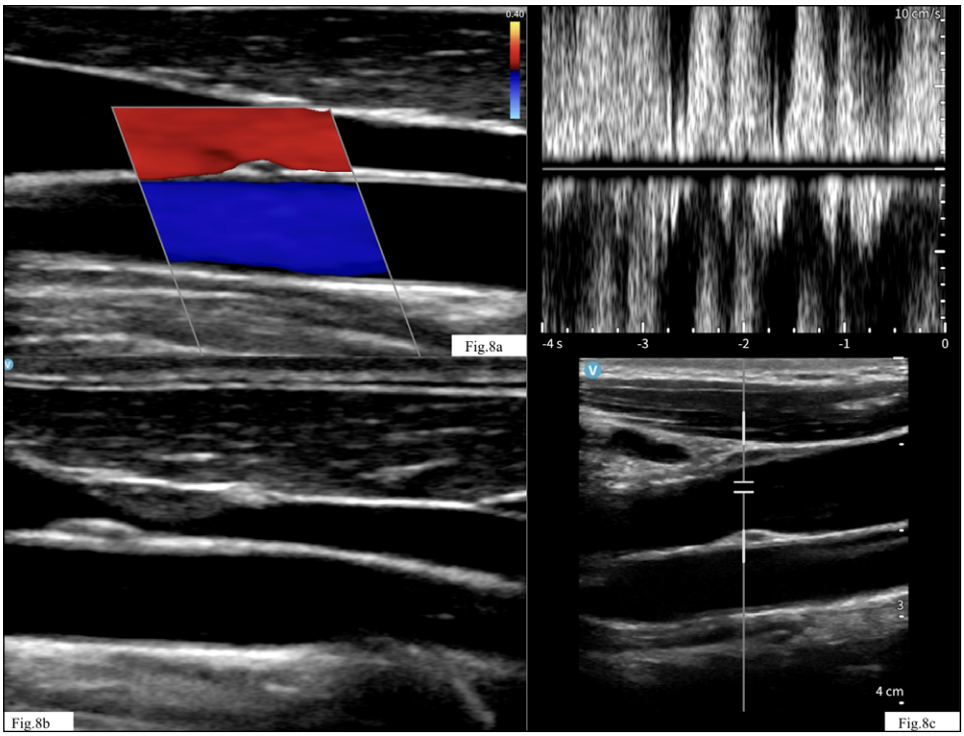

Fig. 8. Ultrasound documentation of early atherogenic mass formation with minimal stenotic changes (<25%)
Picture taken by the authors

vated BMI and waist circumference. Despite the increased anthropometric indices, glycemia, liver enzymes, and lipid profile remained normal, suggesting preserved metabolic compensation [28]. Ultrasound findings confirmed increased echogenicity characteristic of early steatosis with maintained liver function, as described by Mathiesen et al. (2002) [22]. This stage likely reflects a "window of metabolic vulnerability," during which structural liver alterations precede detectable biochemical disturbances. In the 1-st group, no structural liver abnormalities were identified. Echostructure remained homogeneous with a preserved vascular pattern, confirming intact hepatocellular homeostasis. These findings reflect the high adaptive capacity of the young liver, supported by efficient antioxidant defense and fatty-acid oxidation systems, serving as a physiological benchmark of early metabolic stability. In the 3-rd group, increased liver echogenicity was observed in only ~6% of participants and corresponded to minimal steatosis with preserved hepatic function. These individuals had borderline-normal anthropometric parameters without abdominal obesity. The low prevalence of steatosis in this group suggests a shift in systemic metabolic regulation: enhanced β-oxidation and activity of the AMPK–SIRT1–PPAR-α axis limit hepatic lipid accumulation, while the

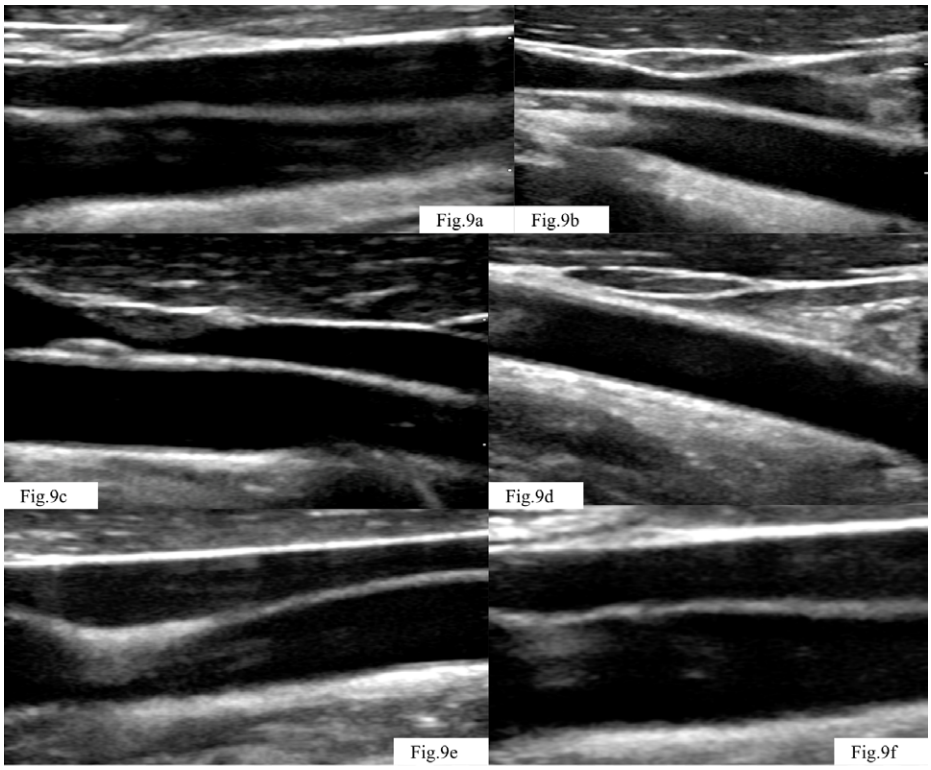

Fig. 9. Early morphologic alterations in the 27–35-year age group
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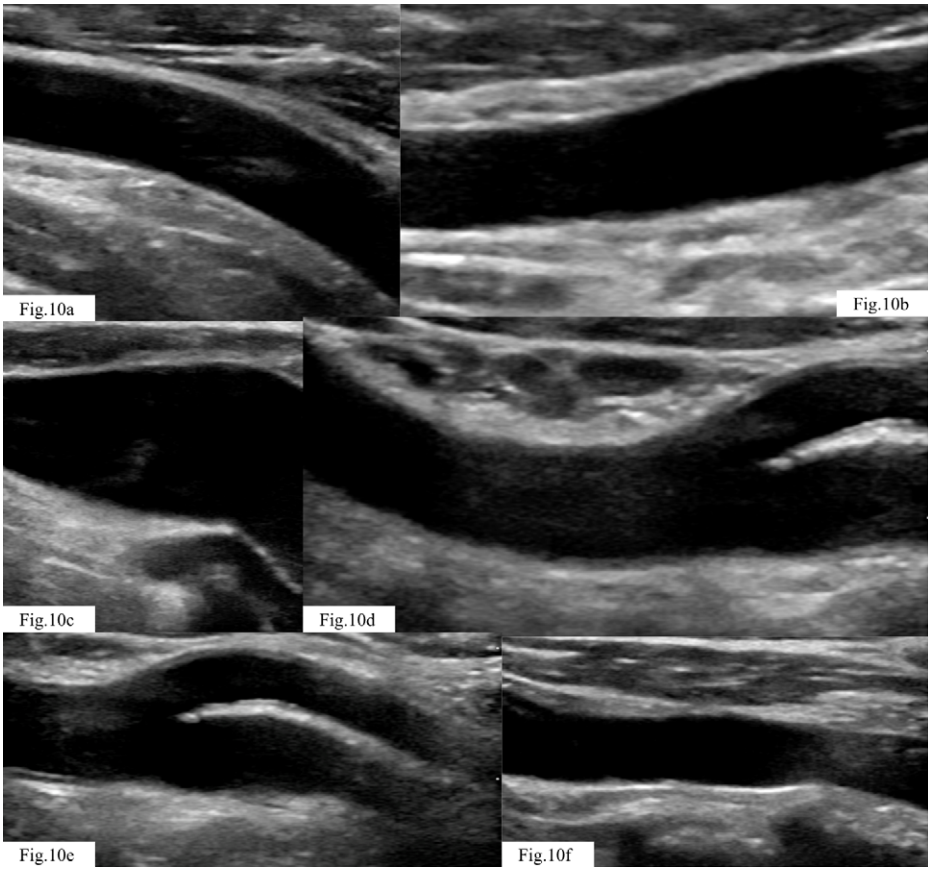

Fig. 10. Structural and hemodynamic alterations in the 36–45-year age group
Picture taken by the authors

metabolic load increasingly affects endothelial and renal microcixrculation [23, 24]. This "metabolic adaptation" phenotype reflects effective interorgan regulation and balanced redox status, representing a model of healthy early aging. In the majority of participants in the 3-rd group, minimal echogenicity had no clinical or biochemical significance, indicating compensatory metabolic adaptation. Age-related ultrasound patterns are presented in Supplementary Materials: Fig. 1a–j (18–26 years), Fig. 2a–h (27–35 years), Fig. 3a–h (36–45 years).

Table 1. Age-related Ultrasound results

Parameters	Group 1 (18–26 yrs, n=68)	Group 2 (27–35 yrs, n=70)	Group 3 (36–45 yrs, n=50)	p G1 vs G2	p G2 vs G3	p G1 vs G3
Kidney Patterns						
Length, cm	10.5 ± 0.8	11.2 ± 0.6	11.0 ± 0.7	<0.001	0.105	<0.001
Width, cm	5.3 ± 0.3	5.6 ± 0.3	5.8 ± 0.3	<0.001	<0.001	<0.001
Parenchymal thickness, mm	18.5 ± 2.5	19.2 ± 3.8	21.5 ± 2.5	0.202	<0.001	<0.001
Increased echogenicity, %	0	28	35	<0.001	0.430	<0.001
Ultrasound findings of the internal jugular vein / common carotid artery						
CIMT, mm	0.48 ± 0.05	0.62 ± 0.08	0.72 ± 0.09	<0.001	<0.001	<0.001
Arterial diameter, mm	6.6 ± 0.5	6.9 ± 0.5	7.1 ± 0.5	<0.001	0.033	<0.001
Peak velocity, cm/s	50 ± 5	75 ± 5	87 ± 2	<0.001	<0.001	<0.001
Mean velocity, cm/s	8.2 ± 0.8	6.5 ± 0.5	6.5 ± 0.7	<0.001	1.000	<0.001
Additional findings	No stenosis or plaques	Early jugular wall masses; minimal stenosis (5–15%)	Stenosis up to 25%, plaques; flow 0.1–0.3 L/min	—	—	—
Echocardiographic data						
LVEDD, cm	4.7 ± 0.3	4.8 ± 0.3	4.9 ± 0.4	0.052	0.139	0.004
LVESD, cm	3.0 ± 0.2	3.1 ± 0.3	3.2 ± 0.3	0.023	0.075	<0.001
IVSd, cm	0.85 ± 0.08	0.95 ± 0.08	0.98 ± 0.10	<0.001	0.082	<0.001
LVPWd, cm	0.85 ± 0.08	0.95 ± 0.08	0.98 ± 0.10	<0.001	0.082	<0.001
Ejection fraction (EF), %	66 ± 2	64 ± 3	63 ± 3	<0.001	0.075	<0.001
Left atrium (LA), cm	3.1 ± 0.2	3.3 ± 0.3	3.4 ± 0.3	<0.001	0.075	<0.001
E/A ratio	2.1 ± 0.3	1.9 ± 0.3	1.7 ± 0.4	<0.001	0.004	<0.001
E/e' ratio	6.3 ± 0.8	6.8 ± 1.0	7.2 ± 1.2	0.002	0.057	<0.001
Thyroid Patterns						
Normal structure, %	94.1	32.9	6	<0.001	0.003	<0.001
Diffuse hypoechogenicity, %	0	41.1	8	<0.001	<0.001	0.030
Small nodules ≤5 mm, %	5.9	18.9	24	0.036	0.501	0.006
Cysts, %	0	0	6	1.000	0.070	0.073

Source: compiled by the authors of this study

Thus, data highlight liver echogenicity as an early marker of metabolic dysregulation preceding biochemical abnormalities and underscore the value of integrating imaging with anthropometric and laboratory assessments for timely preventive interventions.

KIDNEYS — PRECLINICAL CHANGES IN PARENCHYMA AND MICROVASCULATURE

Preclinical parenchymal and microvascular kidney changes are increasingly recognized as early markers of future nephropathy [16, 25]. In our cohort, all functional indicators were within reference ranges (Supplementary Materials) despite structural ultrasound variations. Average kidney size corresponded to physiological norms across age groups, with age-related morphometric and echogenic features (Table 1).

In the 1st group, kidney size parameters indicated preserved nephron and microvascular integrity, supporting effective perfusion and filtration. Mild parenchymal thickening (2–3 mm) in some participants likely reflected benign anatomical variability, including increased mesangial volume and endothelial proliferative changes not detected by laboratory tests. In the 2nd group, increased parenchymal echogenicity was observed in 28% of participants, indicating early preclinical microvascular alterations [26]. Within our proposed model, these findings may represent an early marker of systemic endothelial stress, remaining clinically silent and without laboratory abnormalities. The ultrasound features suggest mild, compensated glomerular and tubular dysfunction supported by intact nephrons and adaptive mechanisms [27]. In the 3rd group, 35% demonstrated increased echogenicity,

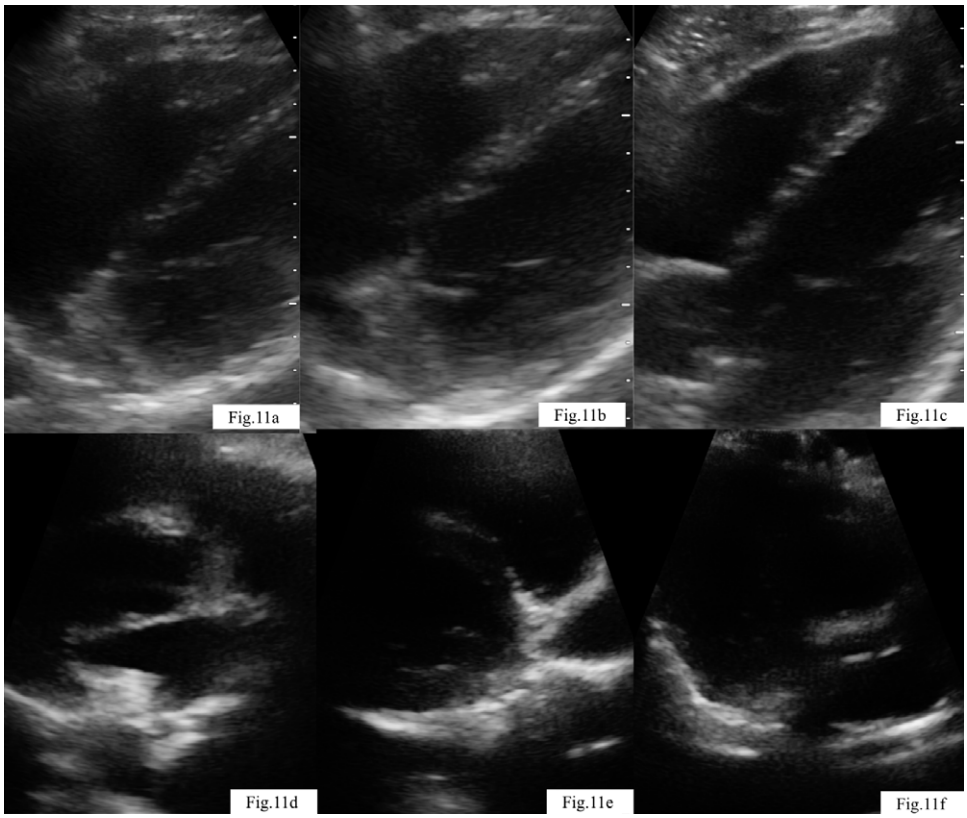

Fig. 11. Echocardiographic profile of young adults
Picture taken by the authors

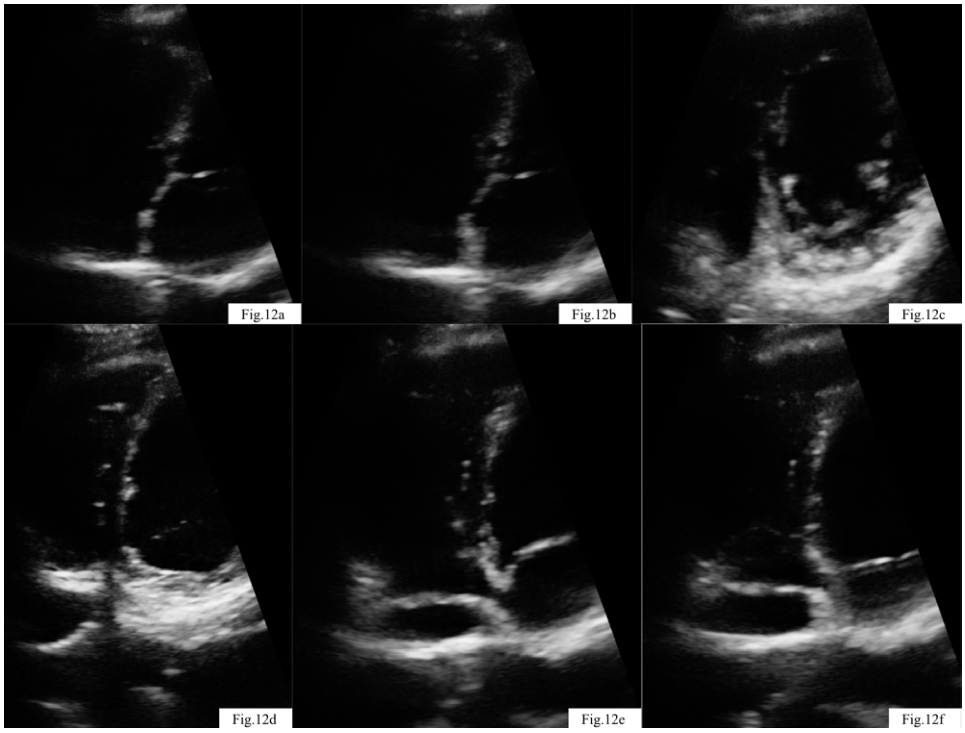

Fig. 12. Echocardiographic parameters in adults aged 27–35 demonstrating preserved functional stability and normal early diastolic filling
Picture taken by the authors

consistent with progressive mesangial and interstitial changes and subtle perfusion disturbances preceding overt nephropathy. Age-related ultrasound patterns are shown in Supplementary Materials: Fig. 4a–h (18–26 years), Fig. 5a–f (27–35 years), Fig. 6a–i (36–45 years).

***Arteria carotis and vena jugularis* — markers of endothelial dysfunction.** Ultrasound examination of the common carotid artery and internal jugular vein in 188 young adults revealed early markers of endothelial dysfunction. Mean CIMT was 0.58±0.07 mm, with 22.6% of patients exceeding the 75th percentile for age and sex. Two individuals showed bilateral focal intimal thickenings (up to 1.15 - 1.18 mm), surpassing the recommended 0.9 mm limit. These findings we consider as

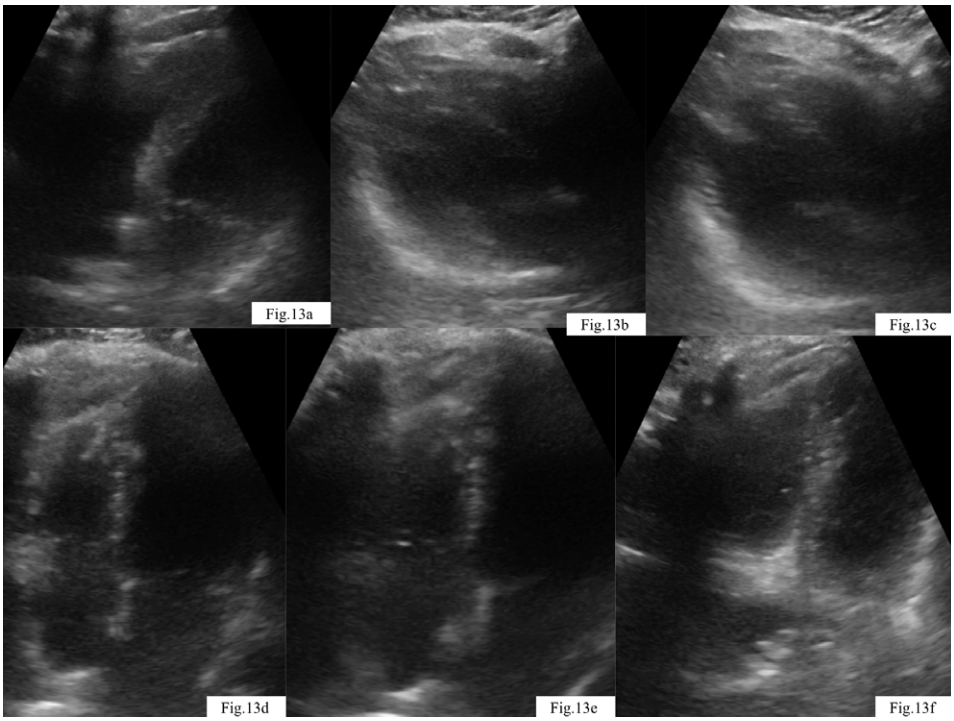

Fig. 13. Echocardiographic parameters in adults aged 36–45 showing normal cardiac function without signs of dysfunction
Picture taken by the authors

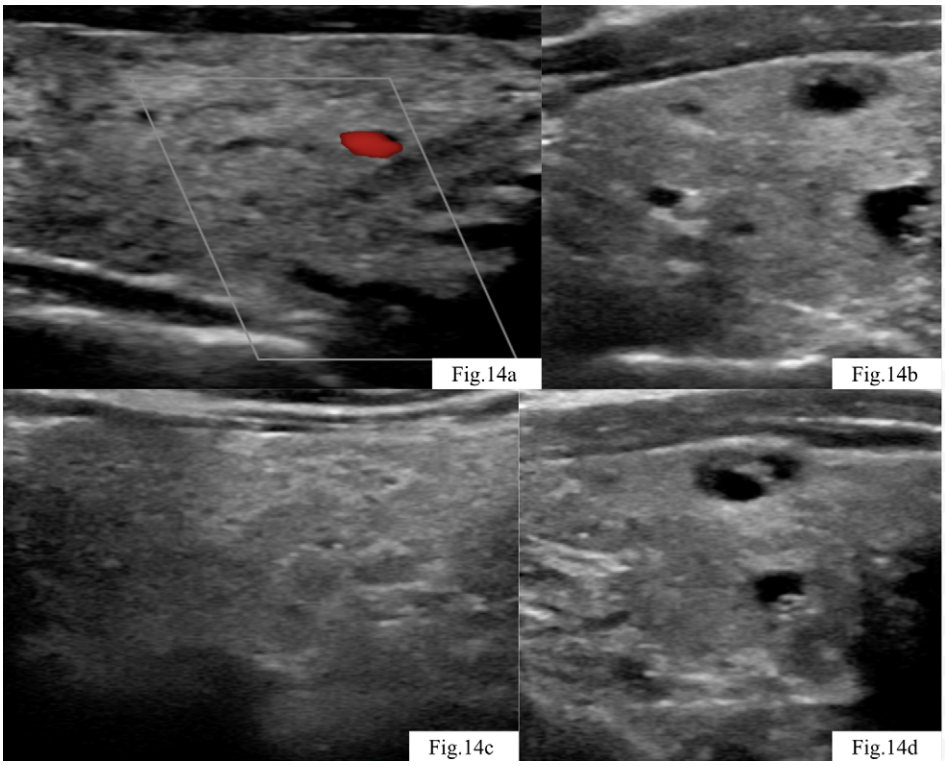

Fig. 14. Ultrasonographic patterns of the thyroid gland in clinically and laboratory 'healthy' young adults
Picture taken by the authors

early morphological predictors of vascular remodeling [11]. CIMT correlated significantly with BMI ($\rho = 0.41$; $p < 0.001$), waist circumference ($\rho = 0.44$; $p < 0.001$), and systolic blood pressure ($\rho = 0.36$; $p < 0.01$), which corresponds to the findings of our previous studies and underscores the contribution of metabolic risk factors to early arterial changes. CIMT was selected as the primary vascular parameter given its established validity as a surrogate marker for subclinical atherosclerosis and its demonstrated correlation with metabolic risk factors in young adults.

In the 1-st group all vascular parameters remained within physiological norms, with no plaques or stenosis, indicating preserved endothelial function (Table 1). This allows considering this group as a control phenotype with fully preserved endothelial function. In the 2nd group, early structural changes were observed (Table 1), including CIMT elevation in 13 participants, early

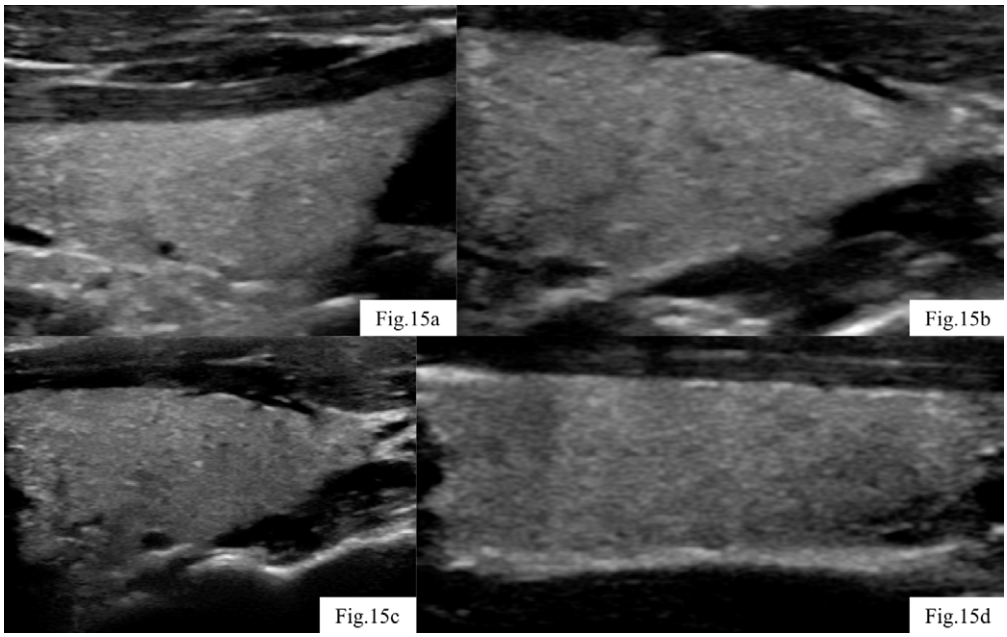

Fig. 15. Ultrasonographic patterns in adults aged 18–26
Picture taken by the authors

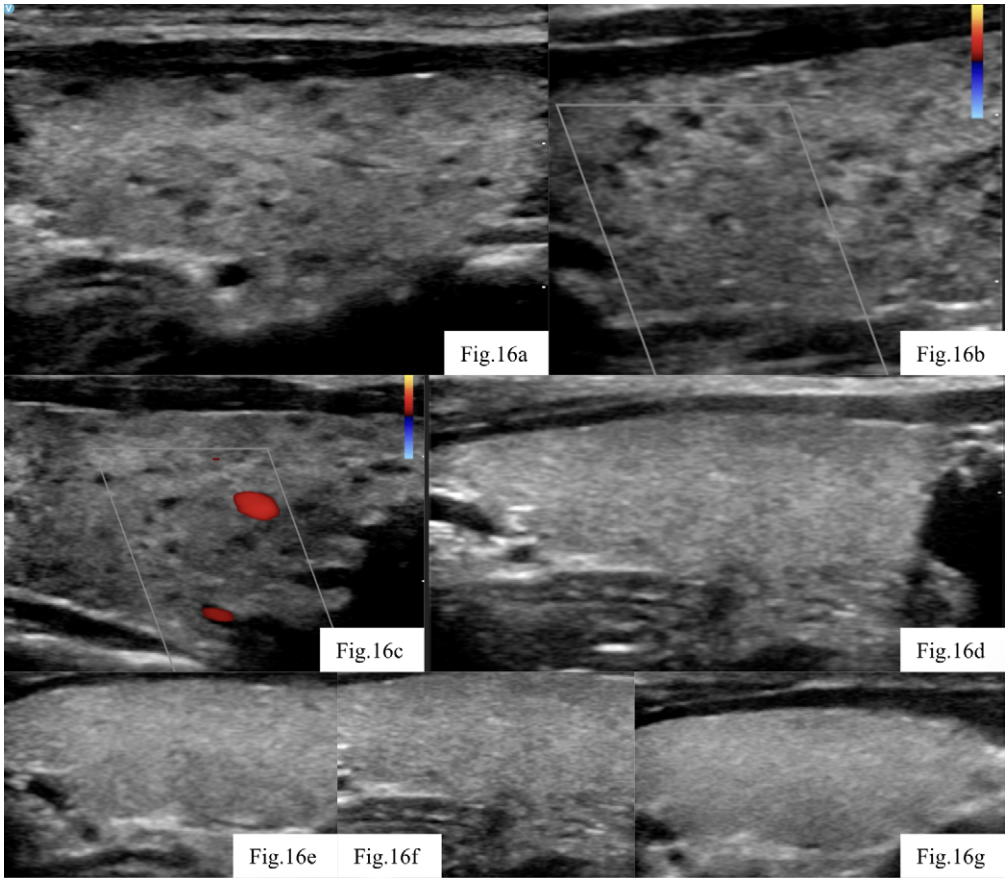

Fig. 16. Ultrasonographic patterns in adults aged 27–35
Picture taken by the authors

jugular wall masses, and minimal hemodynamically insignificant stenosis (<25%). These findings indicate that plaque formation can be detected at an early, preclinical stage. Hemodynamically, this group showed a moderate increase in peak blood flow velocity (up to 70–80 cm/s) and a decrease in mean velocity (6–7 cm/s), suggesting increased vascular wall stiffness [28,29]. In some patients, minimal stenosis (5–15%) and small echogenic areas were also noted. In the 3-rd group, the average CIMT value was higher, plaques and stenoses up to 25% were detected, and peak blood flow velocities approached 85–89 cm/s, while the mean velocity remained at 6–7 cm/s (Table 1), reflecting reduced arterial elasticity and early hemodynamic disturbance. The volumetric blood flow in this group demonstrated the greatest variability, from 0.1 to 0.3 L/min. Age-related

ultrasound data are presented in Supplementary Materials: Fig. 7a–d, Fig. 8a–c, Fig. 9 a–f, Fig. 10 a–f.

Combined morphometric and hemodynamic ultrasound parameters enable sensitive detection of subclinical endothelial dysfunction, reflecting early inflammatory remodeling and loss of vascular elasticity [30]. Carotid and jugular vessels thus serve as early biomarkers of preclinical atherogenesis in young adults, allowing identification of vascular changes before clinical or laboratory signs appear, as also noted by Jones DL et al. [30]. Detection of an atherogenic mass in a group-2 patient underscores the need for regular preventive ultrasound monitoring.

Heart — early echocardiographic changes. Across all age groups, cardiac chamber dimensions and functional indices remained within physiological limits, with no evidence of dilation, hypertrophy, remodeling, or systolic/diastolic dysfunction; NT-proBNP levels were well below pathological thresholds. Detailed data are provided in Supplementary Materials Table 2.

In the 1st group, echocardiographic parameters reflected optimal myocardial elasticity and reserve. The 2nd group maintained comparable functional stability without signs of impaired early diastolic filling. Similarly, the 3rd group showed no abnormalities, with all parameters remaining within normal limits (Table 1). Age-related ultrasound patterns are presented in Supplementary Materials Fig. 11a–f (18–26 years), Fig. 12a–f (27–35 years), and Fig. 13a–f (36–45 years).

Overall, all cohorts demonstrated a stable diastolic profile and preserved cardiovascular homeostasis. Nevertheless, reports of increasing early-onset cardiac pathology in young adults [31] emphasize the role of echocardiography in early risk stratification and prevention.

The thyroid gland — markers of hidden endocrine dysfunctions. Thyroid ultrasound evaluation revealed two main preclinical phenotypes in a cohort of 188 clinically healthy adults: minimal diffuse echostructural changes (47.35%) and small ≤5 mm iso- or hypoechoic nodules (7.44%) (Fig.14). Simple colloid cysts were found in 4.3% of participants. All nodular findings corresponded to benign patterns requiring periodic follow-up [17].

In the 1st age group, almost all scans showed normal echostructure, with only minor variants and no laboratory abnormalities (Table 1). This reflects the physiological state of young age with stable hormonal and neuro-immune balance. In the 2nd group, Hashimoto-like features were more frequent, mainly diffuse hypoechogenicity and small nodules. The predominant phenotype was diffuse hypoechogenicity, sometimes with nodules up to 5 mm; isolated small nodules were less common, and cystic formations were rare (Table 1). These changes indicate early inflammatory activity and initial thyroid remodeling [17]. The nodules typically appeared iso- or hypoechoic with thin peripheral vascularization, indicating active tissue remodeling [17, 32]. Clinically, this pattern is associated with a higher likelihood of emerging antibodies and progressive autoimmune involvement [17, 32], making regular ultrasound and antibody monitoring advisable for this age group. In the 3-rd group, the ultrasound pattern demonstrated considerable variability (Table 1). Most participants had a normal thyroid pattern, while others demonstrated small nodules (≤5 mm) or minimal parenchymal alterations without significant hypoechogenicity or fibrosis. Some presented with early diffuse heterogeneity or simple cystic formations. Nodules classified as benign by EU-TIRADS (10%) required only routine follow-up. Vascularization was normal, with no clinical or laboratory signs of thyroid dysfunction. Participants with suspicious ultrasound features (14%) were referred for specialist evaluation despite normal thyroid function. Age-related ultrasound data are presented in Supplementary Materials: Fig. 15 (18–26 years), Fig. 16 (27–35 years), Fig. 17 (36–45 years).

Our analysis indicates that thyroid diffuse hypoechogenicity reflects early morphological changes of autoimmune thyroiditis, including mild lymphocytic infiltration, follicular loss, and colloid disruption. These changes likely result from Th1/Th17 activation, impaired T-regulatory function, local cytokine production (IL-6, IFN-γ, TNF-α), and B-cell autoantibodies [17, 32]. Ultrasound hypoechogenicity usually precedes changes in TSH, free T4, or antibody levels and is therefore an early sensitive marker, while serological abnormalities appear later [17, 32].

The comprehensive "ultrasound risk phenotype" and the LUMINA System. By integrating the results of our 11 sub-studies [11-16, 33-35, 37,38] we developed a unified system of early multi-organ stratification of subclinical risk — the LUMINA System (Ultrasound Multi-Organ Risk Stratification), which is based on the principle of a single pathological continuum, within which minimal structural deviations in different organs reflect early phases of metabolic, microvascular, and immuno-endocrine remodeling. The system integrates ultrasound findings of the liver, kidneys, heart, carotid arteries, and thyroid into a single indicator of preclinical systemic–metabolic risk, reflecting early structural and functional changes. Only 20.2% (n = 38) of participants showed no subclinical abnormalities, whereas 79.8% (n = 150) had ultrasound markers of early systemic disturbances, including multi-organ involvement in 48.9% (n = 92) and three or more markers in 21.8% (n = 41). Early changes predominantly affected the liver, kidneys, ves-

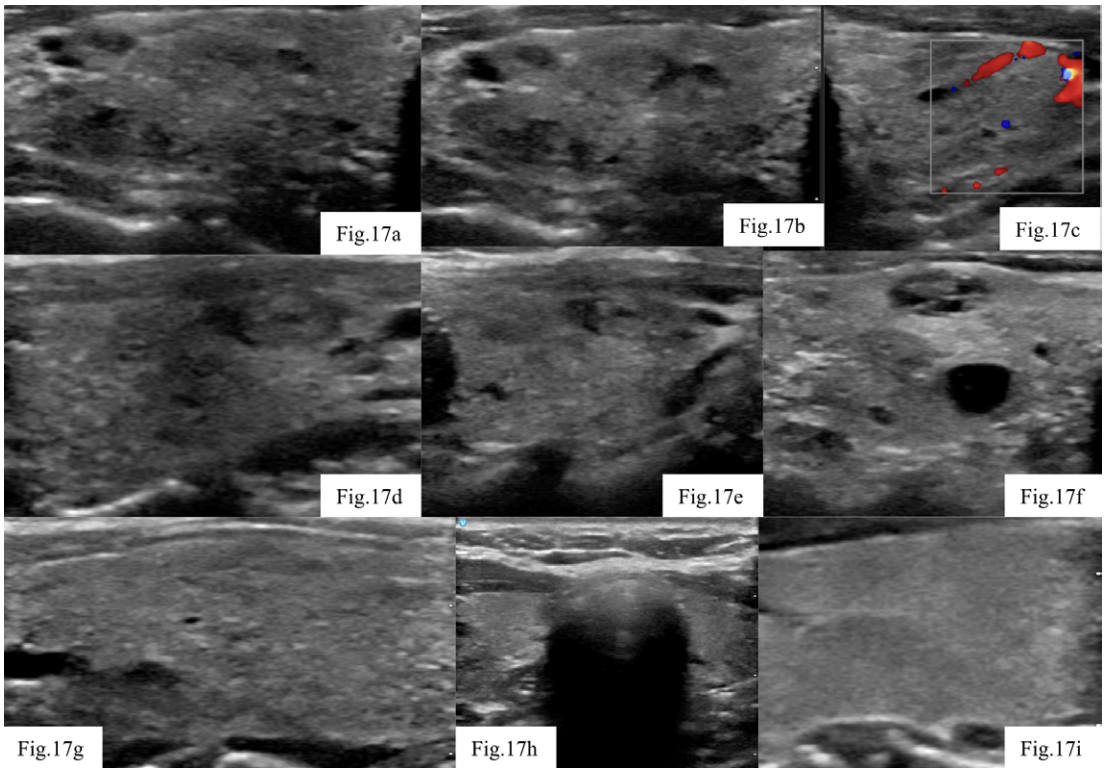

Fig. 17. Ultrasonographic patterns in adults aged 36–45
Picture taken by the authors

sels, and thyroid, while cardiac involvement was absent, suggesting a later onset. The coexistence of metabolic, microvascular, endothelial, and endocrine alterations at the preclinical stage highlights early multi-organ risk. Thus, the integrated ultrasound phenotype serves as a sensitive marker of systemic stress, preceding biochemical and clinical manifestations and enabling early prevention. The LUMINA System includes five domains:

1. **The hepatic domain** serves as an early marker of metabolic load: focal heterogeneity and mild echogenicity increase suggest steatogenic changes, while diffuse echogenicity reflects insulin resistance. Combined with BMI and waist circumference, these patterns represent the core axis of metabolic stress.
2. **The renal domain** captures early parenchymal remodeling associated with metabolic dysfunction. Increased echogenicity, reduced cortico-medullary differentiation, microcystic or echo-negative inclusions indicate initial structural changes, whereas minor size asymmetry reflects adaptation; renal size is considered a risk factor rather than a diagnostic criterion.
3. **The vascular domain** reflects early atherogenesis, including intima–media thickness above the 75th percentile, focal non-stenotic thickening, increased wall stiffness or heterogeneity, and isolated hyperechoic inclusions, consistent with endothelial dysfunction and reduced elasticity.
4. **The cardiac domain** includes subtle echocardiographic changes: early LV wall thickening, mild LV dilation within normal limits, minimal physiological regurgitation, and slightly increased myocardial echogenicity.
5. **The thyroid domain** reflects early immuno-endocrine remodeling, with diffuse hypoechogenicity or heterogeneity indicating initial autoimmune activity, small nodules (<10 mm) early proliferation, gland enlargement compensatory response, and moderately increased vascularization.

All five domains are evaluated using four unified criteria forming an integral subclinical risk scale. Table 3 summarizes organ-specific criteria (liver, kidneys, carotid arteries, heart, thyroid), each scored 1–2 points. The total score defines four risk levels: 0–4 low, 5–11 moderate, 12–20 high, 21–29 very high. This system standardizes multi-organ subclinical assessment and guides further monitoring or intervention. The LUMINA System, through its unified multi-organ structure, allows early detection of potentially reversible pathological phenotypes in young adults, supports personalized risk correction, and forms a basis for standardized preclinical monitoring.

MOLECULAR–BIOCHEMICAL PANEL: AN EMPIRICAL–MECHANISTIC MODEL OF THE MOLECULAR–IMAGING CONTINUUM

The molecular–biochemical panel is presented separately as a hypothetical tool requiring validation in larger cohorts. Early morphological changes may reflect underlying metabolic–immune remodeling. In

Table2. Baseline characteristics of the study cohort (N = 188)

Category	Parameter	Mean ± SD / %		
Demographics	Age, years	31.8 ± 6.7		
	Male sex, %	46.3		
	Female sex, %	53.7		
Anthropometry	Body mass index, kg/m²	18–26 years	27–35 years	36–45 years
	p< 0.05	23.1 ± 3.2	31.8 ± 6.1	25.0 ± 0.6
	Waist circumference, cm male female	85.1 ± 11.4 79.2 ± 10.5		
	Waist-to-hip ratio male female	0.90 ± 0.07 0.81 ± 0.07		
Hemodynamics	Systolic blood pressure, mmHg	122.3 ± 11.4		
	Diastolic blood pressure, mmHg	78.1 ± 8.6		
	Heart rate, bpm	74 ± 9		
Biochemistry	Fasting glucose, mmol/L	5.1 ± 0.6		
	Fasting insulin, µU/mL	11.2 ± 3.7		
	HOMA-IR	2.4 ± 0.9		
	Total cholesterol (TC), mmol/L	5.7 ± 0.8		
	HDL-C, mmol/L	Female	Male	
		1.05 ± 0.15	0.89 ± 0.12	
	LDL-C, mmol/L	3.3 ± 0.7		
	Triglycerides (TG), mmol/L	1.6 ± 0.5		
	Atherogenic index (TC/HDL-C)	3.8		
	Creatinine, µmol/L	82 ± 12		
	ALT, U/L	22 ± 9		
	AST, U/L	20 ± 6		
	creatinine, µmol/L	78.4±12.6		
	urea, mmol/L	5.2±0.9		
	serum albumin, g/L	42.3±3.1		
	Glomerular filtration rate (GFR), mL/min/1.73 m²	96.8±8.4		
urinary test	microalbuminuria, mg/L,	18.2±6.4		
	urine protein, g/day.	0.08±0.03		
	urine creatinine, mg/dl	99.3±55		
	albumin-to-creatinine ratio (ACR), mg/mmol	2.07±0.87		
Lifestyle factors	Regular physical activity, %	64		
	Daily fruits and vegetables, %	58		
Ultrasound examination of the arteria carotis communis and vena jugularis	CIMT, mm	0.58 ± 0.07		
Cardiac Structural and Functional Parameters	LVEDD, cm	4.8 ± 0.4		
	LVESD, cm	3.1 ± 0.3		
	IVSd, cm	0.9 ± 0.1		
	LVPWd, cm	0.9 ± 0.1		
	Ejection fraction (EF), %	64 ± 3		
	Left atrium (LA), cm	3.3 ± 0.3		
	E/A ratio	1.9 ± 0.4		
	E/e' ratio	6.8 ± 1.2		
	NT-proBNP, pg/mL	42.5 ± 14.3		
Thyroid gland	Minimal diffuse echostructural changes, %	47.35		
	Small iso-/hypoechoic nodules ≤5 mm, %	7.44		
	Simple cysts, %	4.3		

Source: compiled by the authors of this study

Table 3. LUMINA System: Integrated risk assessment & Scoring

Organ specific changes and scoring		
Organ	Finding / Description	Score
Liver	Local heterogeneity / minimal echogenicity	1
	Diffuse changes (Marked increase in echogenicity)	2
	BMI ≥25 kg/m²	1
	Waist circumference >90/80 cm	2
Kidneys	Increased Echogenicity	2
	Partial reduction of cortico-medullary differentiation	1
	Local changes (Microcysts / echonegative areas)	1
	Size (Mild asymmetry)	1
Carotid arteries	CIMT >75 percentile	2
	Focal Thickening, without stenosis	1
	Wall Stiffness / heterogeneity	2
	Findings (Hyperechoic foci)	1
Heart	Local LV wall thickening	2
	LV at the upper limit of normal	1
	Valves (Minimal regurgitation)	1
	Increased echogenicity of Myocardium	2
Thyroid gland	Echotexture (Hypoechogenicity / heterogeneity)	1
	Nodules ≤10 mm	1
	Volume >18/25 ml	2
	Doppler (Increased vascularization)	2
Total Score & Risk Interpretation		
Total score	Risk level	Interpretation
0–4	Low	Preclinical changes are minimal or absent.
5–11	Moderate	Subclinical changes in 1–2 organs; monitoring is recommended.
12–20	High	Multi-organ changes; active risk correction is required.
21–29	Very high	Early systemic dysfunctions; multidisciplinary management required.

\Source: compiled by the authors of this study

a small subgroup, ApoB (n=3, 1.15 ± 0.26 g/L), TNF-α (n=24, 3.87 ± 0.96 pg/mL), and IL-6 (n=24, 12.25 ± 2.23 pg/mL) were assessed. Although the data are insufficient for statistically robust conclusions, they indicate a tendency toward elevated cytokines and atherogenic particles, consistent with previous studies [35, 36]. The model is based on the following mechanisms: ApoB reflects atherogenic particles and affects the intima–media complex [37]; TNF-α increases vascular tone and contributes to microvascular injury [38, 39]; IL-6 coordinates low-grade inflammation and metabolic integration [40]. These findings remain preliminary and require validation in larger, dynamically monitored cohorts.

An age-stratified analysis of subclinical risk using the LUMINA system was conducted based on quantitative ultrasound assessment of five organ systems (liver, kidneys, carotid arteries, heart, thyroid), with a maximum score of 29 points.

In the 18–26 yrs cohort, the mean LUMINA score was 0.44 ± 0.31, representing a reference phenotype, with 94% showing no structural abnormalities. Only minimal thyroid changes (1 point in 5.9%) were observed, while all other domains remained within physiological limits. The 27–35 yrs group demonstrated a marked shift toward multisystem involvement, with a mean score of 12.12 ± 3.68, significantly higher than in the youngest cohort ($p < 0.001$); 87% fell into high or very high risk categories. Liver and thyroid domains contributed most to the burden, alongside vascular remodeling and moderate renal changes, while cardiac function remained preserved. The LUMINA

Table 4. Core LUMINA Risk Metrics Across Age Cohorts

Metric	18–26 yrs (n = 68)	27–35 yrs (n = 70)	36–45 yrs (n = 50)	p between groups (G1 vs G2 vs G3)
Mean LUMINA score	0.44 ± 0.31	12.12 ± 3.68	8.67 ± 2.80	<0.0001
Risk category	Very Low / Reference	High / Very High	Moderate / High	—
BMI (kg/m^2)	23.1 ± 3.2	31.8 ± 6.1	25.2 ± 2.8	<0.0001
Liver score	0	3.71 ± 0.26	0.96 ± 0.15	<0.0001
Renal score	0	1.39 ± 0.20	1.74 ± 0.24	<0.0001
Vascular score	0	3.61 ± 0.37	4.16 ± 0.41	<0.0001
Cardiac score	0	0	0	0 in all groups
Thyroid score	0–1	3.41 ± 0.30	1.81 ± 0.38	—

Source: compiled by the authors of this study

index correlated with BMI, waist circumference, and HOMA-IR (all $p < 0.01$). In the 36–45 yrs cohort, the mean score decreased to 8.67 ± 2.80, indicating a metabolic adaptation phenotype. Hepatic burden declined, whereas vascular remodeling and renal involvement increased; cardiac parameters remained normal and thyroid changes moderate. These data are summarized in Table 4.

DISCUSSION

This study shows that a high proportion of clinically healthy young adults exhibit subclinical multi-organ structural changes detectable by ultrasound despite normal laboratory findings. These data indicate that early metabolic, microvascular, endothelial, and immuno-endocrine remodeling develops long before clinical disease and remains largely invisible to conventional risk assessment models.

The distribution of ultrasound findings suggests an age-dependent and organ-specific continuum. Increased liver echogenicity predominated in early adulthood and correlated with anthropometric and insulin-resistance markers, supporting the role of the liver as an early indicator of systemic metabolic stress. Greber-Platzer et al. (2019) arrived at similar conclusions. [41] They found that increased liver echogenicity predominated in adolescents aged 14–18 years (49% among those with pathological echogenicity vs. 34% with normal echogenicity, $P < 0.0001$) and correlated with anthropometric markers, particularly extreme obesity (OR = 3.45, 95% CI: 1.9–6.1, $P < 0.0001$) and elevated BMI (34.0 ± 6.2 kg/m^2 vs. 31.2 ± 5.9 kg/m^2, $P < 0.0001$). [41] Furthermore, the authors confirmed a significant association between increased liver echogenicity and insulin resistance markers: impaired glucose metabolism was associated with elevated liver enzymes > 50 U/L (OR = 4.4, 95% CI: 1.6–11.8, $P < 0.005$). [41] The researchers emphasized that NAFLD serves as an early mediator of metabolic disturbance, supporting the role of the liver as an early indicator of systemic metabolic stress in obese youth. [41] With increasing age, renal parenchymal echogenicity and carotid vascular remodeling became more prevalent, reflecting a shift toward microvascular and endothelial involvement. These findings align with our conclusions. Siddappa et al. (2013) reported consistent findings regarding progressive parenchymal changes. [42] They demonstrated that increased renal cortical echogenicity correlated with disease progression ($P = 0.004$), with echogenicity representing irreversible structural damage. [42] The authors cited evidence that renal echogenicity has the strongest correlation with histologic parameters including glomerular sclerosis, tubular atrophy, interstitial fibrosis, and interstitial inflammation, supporting the concept that increasing echogenicity reflects underlying microvascular and tissue involvement in chronic disease. [42] Thyroid hypoechogenicity, particularly in the 27–35-year group, occurred in the absence of hormonal abnormalities and likely represents early immune-mediated tissue remodeling. These findings are consistent with our observations. Vejbjerg et al. (2006) demonstrated in a large cross-sectional study of 4,649 randomly selected adults that thyroid hypoechogenicity occurs as an early sign of thyroid dysfunction even in subjects without overt thyroid disease. [43] Participants with decreased echogenicity had a higher mean TSH (1.65 mU/l) compared with subjects with normal echogenicity (1.21 mU/l, $P<0.0001$), with this association being stronger in subjects with markedly decreased echogenicity (4.20 mU/l, $P<0.0001$). [43] Importantly, subjects with decreased echogenicity had a higher risk of having thyroid autoantibodies than subjects without decreased echogenicity ($P<0.0001$), and this association was stronger when echogenicity was

markedly decreased. [43] The authors concluded that decreased echogenicity and irregular echo pattern represent early markers of thyroid dysfunction, supporting the concept that structural tissue changes reflect immune-mediated remodeling occurring before the development of overt hormonal abnormalities.

Integration of these findings into the LUMINA system revealed a non-linear risk pattern, with the highest burden of subclinical alterations in the 27–35-year cohort and partial redistribution of organ involvement thereafter. This suggests a critical window in early adulthood characterized by maximal phenotypic instability, during which structural changes may still be modifiable. The absence of cardiac involvement across cohorts is consistent with later myocardial engagement in the pathological cascade and supports the value of upstream detection. Clinically, these results underscore the limitations of laboratory-based and short-term risk models in young adults. Systemic ultrasound phenotyping provides a practical, non-invasive method for identifying discordance between structural remodeling and biochemical normality, enabling earlier individualized prevention. The study is limited by its single-center design, sample size, and observational nature, and the molecular biomarker data remain exploratory. Longitudinal studies are required to validate the prognostic significance of the LUMINA score.

CONCLUSIONS

Systemic multi-organ ultrasound phenotyping of young adults enables the detection of subclinical structural and functional changes in the liver, kidneys, vessels, and thyroid gland even in the absence of laboratory and clinical abnormalities. Since individuals in this age group rarely undergo preventive examinations, such changes often remain undetected until clinically manifest pathology develops. The identification of a universal "ultrasound risk phenotype" supports the rationale for implementing preventive ultrasound screening in young adults and opens opportunities for proactive metaphylaxis, personalized prevention, and the advancement of preventive medicine.

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A complete list of references can be requested from the Authors.

CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 19.01.2026
ACCEPTED: 20.05.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Comparative analysis of stress resilience indicators in law enforcement officers of different genders

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ABSTRACT

Aim: To conduct a comparative analysis of stress resilience indicators in future law enforcement officers of different genders during their professional training.

Materials and Methods: The research, conducted in 2025-2026, involved 134 cadets (71 men, 63 women) in their fourth training year and majoring in the "Law Enforcement" program. Three methods were used to assess the cadets' stress resilience: the Reactive Anxiety Scale, the Method for Assessing Neuro-Emotional Tension, and the Perceived Stress Scale (PSS-10).

Results: It has been established that female cadets exhibit lower levels of stress resilience across all measured indicators (anxiety levels, neuro-emotional tension, and stress) compared to male cadets. At the same time, the greater the impact of stress factors in professional activities, the more pronounced the difference in indicators becomes. After the field placement in practical police units, female cadets were found to have significantly ($p \leq 0.05–0.01$) worse indicators than those of male cadets in reactive anxiety (by 4.4 points), neuro-emotional tension (by 4.8 points), and stress (by 3.9 points).

Conclusions: The results of the research should be taken into account when developing and implementing preventive and corrective programs, as well as when conducting counseling and educational-psychological activities among law enforcement cadets, thereby enhancing their stress resilience and strengthening their psychophysical health.

KEY WORDS: stress, anxiety, stress resilience, law enforcement officers, cadets, gender, mental health

Wiad Lek. 2026;79(8):1899-1905. doi: 10.36740/WLek/235885 DOI

INTRODUCTION

In the current conditions of war in Ukraine, nearly 90 % of Ukrainians live in a state of high stress caused by threats to life, separation from loved ones, financial instability, and daily shelling [1]. Stress has evolved from a temporary reaction into a chronic condition, leading to mental exhaustion, somatic illnesses, and premature aging [2]. Numerous studies indicate that stress negatively affects both the mental and physical health of modern individuals [3, 4]. At the same time, a person with a resilient psyche fully fulfills their social roles, carries out their professional and civic duties for the common good, is an effective worker and a good family member, continually improves themselves, and harmonizes their interactions with the surrounding world [5].

One of the most intense and stress-filled types of activity is law enforcement. Stress is an integral part of law enforcement officers' professional activities, as their work is constantly marked by high psycho-emotional tension, life-threatening risks, and the need to make quick decisions under extreme conditions [6, 7]. During the war in Ukraine, the level of stress associated with law enforcement activities has significantly increased, in part due to a substantial expansion of law enforcement officers' powers [8]. Cadets – future law enforcement officers – are no exception; their professional training takes place under the challenging conditions of martial law, amid heightened responsibility and strict discipline. The modern educational process for law enforcement cadets involves: high physical and psychological demands; a combination of intensive study, physical training, and the performance of service duties (while on duty in patrols, on shifts, during practical training, and field placements); psychological readiness of cadets to face danger and work with offenders; performing tasks under time constraints and in situations requiring rapid decision-making [9, 10].

At the same time, today, higher educational institutions (HEIs) that train future law enforcement officers have a large number of female cadets, whose stress levels differ from those of male cadets [11, 12]. Research into the stress resilience of male and female law enforcement cadets during training in wartime conditions is relevant to developing effective strategies to prevent stress-related phenomena among cadets, foster stress-coping skills, and strengthen their psychosomatic health, thereby improving their professional performance.

AIM

The aim is to conduct a comparative analysis of stress resilience indicators in future law enforcement officers of different genders during their professional training.

MATERIALS AND METHODS

PARTICIPANTS

The research, conducted in 2025-2026, involved 134 cadets (71 men, 63 women) who were in their fourth training year at Kharkiv National University of Internal Affairs (KhNUIA, Kharkiv, Ukraine), majoring in "Law Enforcement." The cadets' ages ranged from 20 to 22 years. The cadets' stress resilience indicators were assessed twice: before the start of their field placement in practical police units (Stage 1) and after returning to the HEI (Stage 2). The field placement lasted 4 weeks. No special selection was conducted for the study groups of men and women. Six training groups of KhNUIA cadets majoring in "Law Enforcement" were involved. The inclusion criterion for cadets was their enrollment in a 4th-year training group in the relevant major. The cadets who were on temporary duty leave or receiving inpatient treatment during the research period were excluded. Training conditions, living conditions, food quality, and material and financial support were the same for all cadets. Marital status and the extent to which their parents and relatives were involved in combat missions in the war with russia were not taken into account. The exclusion criterion was the cadet's voluntary desire to withdraw from the research at any time.

RESEARCH METHODS

theoretical analysis and generalization of literature sources, psycho-diagnostic methods, statistical methods. The method of theoretical analysis and generalization of literary sources was used to conduct an analytical review of scientific sources on the outlined range of issues (24 sources (2013-2026) from MedLine, Scopus, Web of Science databases were analyzed).

Psycho-diagnostic methods were used to study stress resilience indicators among cadets of different genders. Three methods were used to study the cadets' stress resilience: the Reactive Anxiety Scale (Ch. D. Spielberger, Yu. L. Khanin); the Method for Assessing Neuro-Emotional Tension (T. A. Nemchyn); the Perceived Stress Scale, PSS-10 (J. M. Taylor) [13, 14].

The Reactive Anxiety Scale consists of 20 questions, through which the cadets assessed their state at the time of testing. Response options: no, that is not true; probably true; true; completely true. Scores were calculated using the formula: $RA = \Sigma 1 - \Sigma 2 + 50$, where RA is reactive anxiety, $\Sigma 1$ is the sum of the numbers marked on the form for items 3, 4, 6, 7, 9, 12, 13, 14, 17, and 18; $\Sigma 2$ is the sum of the numbers marked on the form for scale items 1, 2, 5, 8, 10, 11, 15, 16, 19, 20. The level of reactive anxiety was assessed as follows: 30 points or below – low anxiety level; 31-45 points – average level; 46 points or above – high level.

The Method for Assessing Neuro-Emotional Tension (NET) includes 30 characteristics of this state, divided into three levels of severity (a – low, b – average, c – high). By selecting one of the three response options (a, b, c), cadets assessed their state at the time of testing. Data processing was performed by summing the points: 1 point for response a, 2 points for b, and 3 points for c. The level of neuro-emotional tension was assessed as follows: 30-50 points – low NET; 51-70 points – average NET; 71-90 points – high NET.

The "Perceived Stress Scale, PSS-10" method consists of 10 questions with the following response options: never – 0 points, rarely – 1 point, sometimes – 2 points, quite often – 3 points, very often – 4 points. Stress levels were assessed as follows: 0-13 points – low level (mild stress); 14-26 points – average level (moderate stress); 27-40 points – high level (severe stress).

STATISTICAL METHODS

The statistical method was used to process the data obtained. The reliability of the difference was determined using the Student's t-test. The results were presented as Mean ± m, where Mean is the arithmetic mean, m is the standard error. The reliability of the difference was set at $p<0.05$. All statistical analyses were performed using STATISTICA 13.3.1 software package (2018), 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 KhNUIA. Also this study followed the regulations of

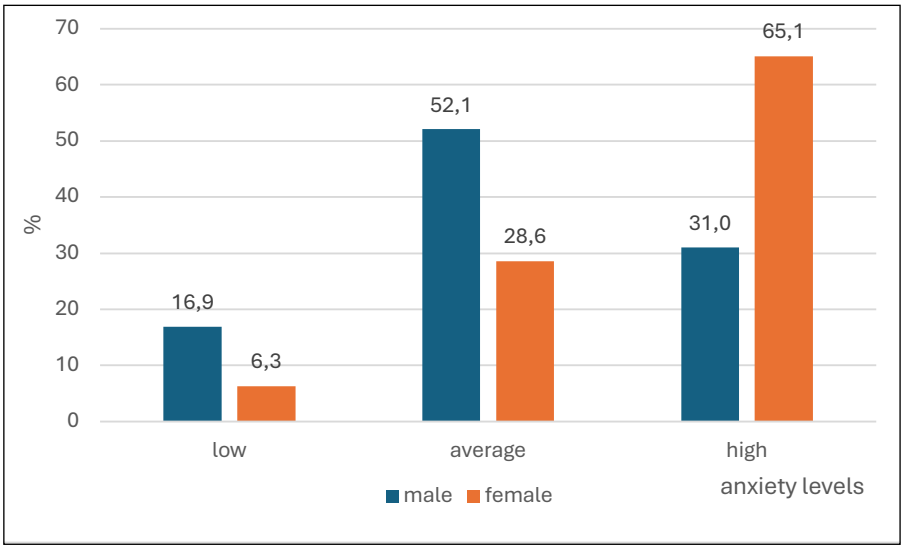

Fig. 1. The ratio of reactive anxiety levels among male (n=71) and female (n=63) cadets after the field placement, %
Picture taken by the authors

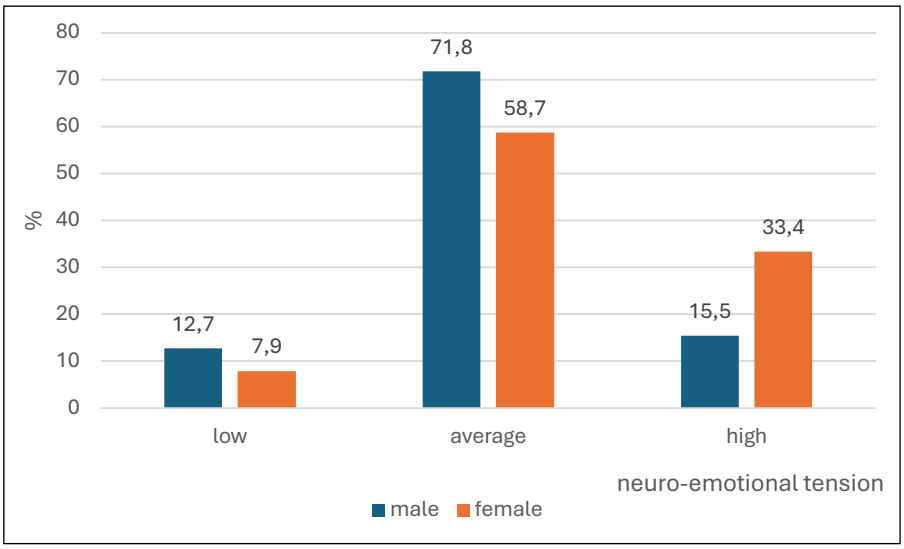

Fig. 2. The ratio of neuro-emotional tension levels among male (n=71) and female (n=63) cadets after the field placement, %
Picture taken by the authors

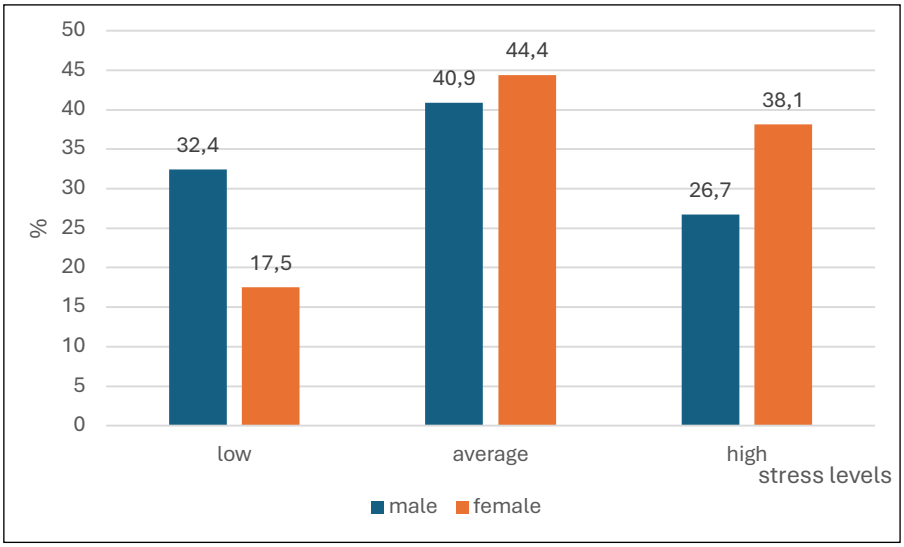

Fig. 3. The ratio of stress levels among male (n=71) and female (n=63) cadets after the field placement, %
Picture taken by the authors

the World Medical Association Declaration of Helsinki. Informed consent was received from all participants who took part in this study.

AI STATEMENT

The author states that no AI tools were used in writing this article.

Table 1. The comparative analysis of stress resilience indicators in cadets of different genders (n = 134) before (Stage 1) and after (Stage 2) their field placement in practical police units, Mean±m, points

Research stages	Cadets of different genders			
	Male cadets (n=71)	Female cadets (n=63)	Δ	t / p
Reactive anxiety				
Stage 1	41.7±0.95	43.6±0.99	1.9	1.38/>0.05
Stage 2	44.2±0.98	48.6±1.02	4.4	3.11/≤0.01
t / p	1.83/>0.05	3.52/≤0.001		
Neuro-emotional tension				
Stage 1	52.5±1.07	55.1±1.12	2.6	1.68/>0.05
Stage 2	54.9±1.09	59.7±1.14	4.8	3.04/≤0.01
t / p	1.57/>0.05	2.88/≤0.05		
Stress level				
Stage 1	21.2±1.15	23.5±1.19	2.3	1.39/>0.05
Stage 2	24.3±1.18	28.2±1.21	3.9	2.31/≤0.05
t / p	1.88/>0.05	2.77/≤0.05		

Legend: Δ – difference between the studied indicators; t – value of Student's t-test; p – level of statistical significance of differences
Source: compiled by the authors of this study

FRAMEWORK

This scientific article was carried out according to the plan of the research work of the Kharkiv National University of Internal Affairs for 2020-2026 "Psychological, pedagogical and sociological support of law enforcement officers" (state registration number 0113U008196).

RESULTS

The results of the comparative analysis of stress resilience indicators in cadets of different genders before and after their field placement in practical police units are presented in Table 1.

Assessment of the level of reactive anxiety indicates that before the field placement, anxiety among cadets of both genders was at an average level. Among female cadets, the level of reactive anxiety before the field placement was 1.9 points higher than among male cadets; however, no statistically significant differences were found ($p > 0.05$). During the performance of law enforcement duties while on field placement in practical units, the anxiety level among both male and female cadets increased by 2.5 and 5.0 points, respectively; however, the changes among men were not statistically significant ($p > 0.05$), while the increase in anxiety among women was statistically significant ($p \leq 0.001$). A comparison of cadets' anxiety levels after the 4-week field placement revealed that female cadets' anxiety levels were significantly higher than those of male cadets by 4.4 points ($p \leq 0.01$). Moreover, while male cadets' anxiety levels remained unchanged (at an average level) at the end of the research, those of female cadets worsened to a high level. The ratio of reactive anxiety levels among male and female cadets after the field placement is shown in Fig. 1.

As shown in Fig. 1, after the field placement, the proportion of women with high levels of reactive anxiety (65.1 %) is more than twice that of men (31.0 %). In comparison, only 6.3 % of women have low levels of reactive anxiety, compared to 16.9 % of male cadets. This indicates that female cadets experience the stressful conditions of law enforcement work more acutely than men and are more prone to anxiety and distress.

The analysis of cadets' NET before their field placement revealed no statistically significant differences between genders – the difference was 2.6 points ($p > 0.05$). At the same time, the NET level before the field placement was assessed as average for both men and women. The study of the dynamics of NET indicators among cadets of different genders reveal negative changes in the indicators of both male and female cadets during their field placement in practical police units. However, the decline among male cadets is 2.4 points ($p > 0.05$), while among female cadets it is 4.6 points ($p \leq 0.05$). It is worth noting that after the field placement, female cadets showed significantly worse NET indicators (59.7 points) than male cadets (54.9 points), a difference of 4.8 points ($p \leq 0.01$). These findings are supported by the male-to-female ratio of cadets across different NET levels after the field placement (Fig. 2).

The study of stress levels among male and female cadets before the field placement indicates that the indicators for both genders do not differ significantly

and correspond to the average level (moderate stress). During the field placement period in practical police units, stress levels worsened for cadets of both genders (by 3.1 points for men and 4.7 points for women); however, statistically significant differences were found only for female cadets ($p \leq 0.05$). It was found that after performing service duties during the field placement, the stress level among male cadets remained unchanged (moderate stress). At the same time, for women, it worsened to a high level (severe stress), which underscores the negative impact of law enforcement stressors on cadets' stress resilience, particularly among female cadets. After the field placement, female cadets' stress levels were significantly higher than those of male cadets by 3.9 points ($p \leq 0.05$). The ratio of stress levels among male and female cadets after the field placement is shown in Fig. 3.

The studies conducted showed that, across all indicators examined, stress resilience among female cadets is lower than that of male cadets. At the same time, the greater the impact of stressors related to professional activities, the more pronounced the difference in indicators becomes.

DISCUSSION

Currently, Ukraine is experiencing a deterioration in its social, economic, and political situation, along with increasing external pressure on individuals, resulting in significant stress among Ukrainians. High levels of anxiety about the future – both for one's family and loved ones and for the country as a whole – the constant threat to life and health, frequent sirens warning of missile danger and air raid alerts, power outages, disruptions in mobile communications, and the necessity to work or study remotely – are far from an exhaustive list of the causes of stress among Ukrainians [15].

The concepts of "stress" and "stress resilience" are now widely discussed in the scientific literature [16, 17]. When studying this phenomenon, the focus is most often on the development of its individual aspects or on the psychological rehabilitation of those who have experienced stress. At the same time, questions regarding manifestations of stress resilience influenced by gender differences – including among law enforcement personnel during wartime – remain understudied. This issue is of particular scientific interest because, as our research confirms, a thorough examination of it will enable the development of effective approaches to gender-based prevention of stress-related phenomena, stress-coping skills, and so on.

Experts use the term "stress resilience" to refer to emotional stability, psychological resilience to stress, stress resistance, frustration tolerance, and other related concepts. Stress resilience is equated with emotional stability and the ability to control emotions, the ability to cope with heavy workloads and effectively solve tasks under extreme circumstances; the ability to independently calm emotional arousal while performing complex activities; a temperamental trait that allows one to successfully achieve one's goals through the optimal use of reserves of neuropsychological and emotional energy; the ability to direct one's emotional experiences toward positive solutions to future tasks; a consistent predominance of positive psycho-emotional states; an integrative personality trait characterized by the interaction of emotional, volitional, intellectual, and motivational components of human mental activity, which ensure the optimal and successful achievement of activity goals in a complex emotional environment [18].

The analysis of scientific sources [3, 4, 19] indicates that, to date, there is no consensus in the scientific community regarding differences in stress resilience indicators between men and women. At the same time, studies are being conducted on gender-related factors in stress resilience, self-actualization, gender stereotypes, personality traits, behavioral characteristics, motivation, vital capacity, self-realization, and other areas. However, many studies present conclusions that men have higher stress resilience than women [6]. Our research results also confirm this trend. It was found that, compared to men, women experience a significant increase in stress levels (severe stress) after performing professional tasks in crisis conditions, which underscores the negative impact of work-related stressors on stress resilience indicators among women.

As scientists note [20], stress resilience levels in men and women differ due to biological and social factors, with men more often demonstrating higher resilience, which is attributed to lower impulsivity. At the same time, women have better emotional adaptation and the ability to maintain social bonds, thanks to oxytocin (the "love" or "trust" hormone), which plays a key role in forming emotional bonds and social interactions. Women more often use emotional support (coping strategies), while men tend to analyze problems, avoid stress, or hide their emotions [21]. The results of our research confirmed the findings of scientists [3, 4, 22], who noted higher stress resilience in men than in women. Across all measured indicators (levels of anxiety, neuro-emotional tension, and stress), male cadets demonstrated better results than female cadets. Moreover, after a 4-week field placement in practical police units, the indicators among female cadets became even more pronounced. This once again confirms our scientific position that, across all indicators studied, stress resilience among female cadets is lower than that of male cadets.

Researchers also note that women demonstrate better adaptation to prolonged stress. Thus, studies [23, 24] indicate that women cope better with prolonged stress due to hormonal characteristics (estrogen, progesterone, oxytocin) that promote adaptive flexibility. However, the degree of influence of professional activity stressors is significant: the higher the stress level, the more pronounced the personality indicators become. In contrast, men tend to exhibit higher "combat readiness" and "fight-or-flight" responses. To confirm these findings, further research is needed involving longer-term exposure of participants to constant stressors.

CONCLUSIONS

It has been established that female cadets exhibit lower levels of stress resilience across all measured indicators (anxiety levels, neuro-emotional tension, and stress) compared to male cadets. At the same time, the greater the impact of stress factors in professional activities, the more pronounced the difference in indicators becomes. After the field placement in practical police units, female cadets were found to have significantly ($p \leq 0.05–0.01$) worse indicators than those of male cadets in reactive anxiety (by 4.4 points), neuro-emotional tension (by 4.8 points), and stress (by 3.9 points). At the same time, the level of anxiety and stress shifted from average to high, indicating that female cadets experience the stressful conditions of law enforcement work more acutely than their male counterparts and are more prone to emotional distress. The obtained data are confirmed by the established correlation between the levels of the studied indicators in male and female cadets after their field placement.

The results of the research should be taken into account when developing and implementing preventive and corrective programs, as well as when conducting counseling and educational-psychological activities among law enforcement cadets, thereby enhancing their stress resilience and strengthening their psychophysical health.

PROSPECTS FOR FURTHER RESEARCH

It is planned to investigate the dynamics of somatic and mental health indicators among law enforcement officers of different genders under prolonged exposure to stressors.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 11.03.2026
ACCEPTED: 17.07.2026

CREATIVE COMMONS 4.0

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ORIGINAL ARTICLE

Relationship between physical development and coordinative abilities in adolescent girls with low adaptive capacity

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ABSTRACT

Aim: To investigate the relationship between physical development and coordinative abilities in adolescent girls aged 16-17 with low adaptive capacity.

Materials and Methods: The research involved 48 female students aged 16-17 from general secondary schools with low adaptive capacity (Ruffier test scores ranging from 10.1 to 15.0 c. u.). The girls' physical development was assessed using the following indicators: 30-meter sprint (speed), standing long jump (speed and strength), push-ups (strength), 4x9-meter shuttle run (agility), and Harvard step test (endurance). Coordinative abilities were assessed using the following tests: the "Flamingo" balance test – standing on one leg on a limited surface (static balance), walking in a straight line with eyes closed (spatial orientation), jumping rope (motor coordination), target-throwing accuracy test with a tennis ball (spatial-dynamic accuracy), and the tapping test (movement frequency). To achieve the research aim, Pearson's linear correlation analysis was applied.

Results: Significant correlations of varying degrees were established between individual parameters of physical development and the coordinative abilities of 16- to 17-year-old girls with low adaptive capacity. These findings indicate that, due to the phenomenon of positive transfer, it is possible to contribute to improving the physical fitness of girls with medical restrictions on certain exercises, specifically by enhancing endurance, speed, and speed and strength qualities through coordination training.

Conclusions: The results obtained allow for the use of more accessible physical exercise parameters to improve physical qualities that are otherwise limited for girls with low adaptive capacity, specifically by developing the most informative types of coordinative abilities based on the phenomenon of positive transfer.

KEY WORDS: girls aged 16-17, adolescents, low level of adaptive capacity, physical education, physical fitness, physical development, coordinative abilities

Wiad Lek. 2026;79(8):1906-1912. doi: 10.36740/WLek/235883 DOI

INTRODUCTION

The low level of adaptive capacity in modern adolescents is a pressing issue, leading to insufficient adaptation to physical exertion, reduced physical fitness and development, and a decline in functional status, often manifested through cardiorespiratory criteria [1, 2]. Low adaptive capacity of the body results in the inability of the cardiovascular, respiratory, and muscular systems to effectively respond to physical exertion and recover quickly afterward, thereby reducing the health-promoting, developmental, and training benefits of physical exercise [3, 4]. A low level of the body's adaptive capacity is often a direct consequence of physical inactivity – an extremely low level of motor activity, which is a side effect of modern conditions of distance learning and excessive gadget use, is typical of the leisure time of modern children and youth, and can lead to deteriorating health, serious impairments in the functions of the musculoskeletal system, circulation, respiration, metabolism, hormonal status, and more [5]. Unfortunately, a sedentary lifestyle has become prevalent among modern adolescents, affecting, according to various data, between 75 % and over 80 % of students who do not meet the recommended level of motor activity [6, 7]. However, for a fulfilling life and education, today's youth must have sufficient health reserves to cope with the negative impacts of the physical and social environments.

Physical education in general secondary schools, in various organizational forms, offers certain opportu-

nities to address the deficit in students' motor activity [8]. However, it is known that for schoolchildren with low adaptive capacity (classified into special medical groups), restrictions on the volume and intensity of physical exertion are mandatory. In particular, endurance, high-intensity, and certain strength exercises should be used cautiously and in moderation [9].

It is possible to develop certain physical qualities and indirectly enhance students' physical development through positive transfer, whereby targeted development of one physical quality contributes to increased manifestation of another [10-12]. The task of developing physical qualities, the influence of which is limited for schoolchildren with low adaptive capacity, can be addressed by studying the interrelationships between them and other motor abilities available for development, in particular coordinative abilities.

AIM

The aim is to investigate the relationship between physical development and coordinative abilities in adolescent girls aged 16-17 with low adaptive capacity.

MATERIALS AND METHODS

PARTICIPANTS

The research, conducted during the 2025-2026 academic year, involved 48 girls aged 16-17 who were enrolled in grades 10-11 at Lyceum No. 17 "Kyrylivskyi," Lyceum No. 183 "Fortuna," and Lyceum "Dominanta" in Kyiv (Ukraine). All girls had low adaptive capacity: a low level of adaptive capacity was defined as a Ruffier test score of 10.1-15.0 c. u. according to age norms. Girls with a Ruffier test score above 15.0 c. u. were not allowed to participate in the research, as this level of adaptive capacity indicates serious problems with the cardiorespiratory system.

The inclusion criteria for girls in the study group were age 16-17 years (10th-11th grades of secondary schools), and a low level of adaptive capacity. The research was open-ended; the girls and their parents were informed in advance and consented to participate. Testing of the girls' coordinative abilities and physical qualities was conducted in a gym in October-December 2025 by a physical education teacher in the presence of the school physician. The exclusion criterion was the girls' own desire to withdraw from the research at any time.

METHODS

Analysis and generalization of the literature, testing of physical development indicators and coordinative abilities, and methods of mathematical statistics. A total of 22 scientific sources from various scientometric databases were reviewed on the selected research topic.

The physical development of the girls was assessed using the following tests: 30-meter sprint (speed qualities), standing long jump (speed and strength qualities), bench push-ups (strength qualities), 4x9-meter shuttle run (agility), and a modified (simplified) Harvard step test (endurance) [13]. Coordinative abilities were assessed using the following tests: the "Flamingo" balance test – standing on one leg on a limited surface (static balance), walking in a straight line with eyes closed (spatial orientation), jumping rope (motor coordination), target-throwing accuracy test with a tennis ball (spatial-dynamic accuracy), and the tapping test (movement frequency) [14]. The "Flamingo" balance test was used to assess the level of static balance. The starting position is standing on a limited surface on one leg, with the other leg bent at the knee and pulled up to the buttocks, held by the corresponding arm. Using the other hand to hold onto a support, the girl assumes a stable position. As soon as the girl removes her hand from the support and can maintain the static pose on her own, the stopwatch is started. The stopwatch is stopped when balance is lost and restarted as soon as the girl regains a stable position. The number of attempts the girl made to maintain stable balance on the surface within 1 minute is counted. The fewer attempts required to maintain balance, the better the test result. The test is performed once. The level of spatial orientation was assessed by having participants walk in a straight line. The girls were asked to walk at a normal pace along a path, first with their eyes open and then with their eyes closed. Normally, when walking with eyes closed, deviation from a straight line does not exceed 10-15 cm. With insufficient vestibular stability, a zigzag gait is observed with deviations from a straight line of up to 30-50 cm or more. The level of motor coordination was assessed using two-footed jumping with a jump rope. The level of spatial-dynamic accuracy (precision) was assessed by throwing a tennis ball at circles of varying diameters. The width of each circle was 10 cm, and the diameter ranged from 10 to 30 to 50 cm. The quality of ball throws at circles of various diameters, drawn on a wall at a height of 2 m from a distance of 3 m, was scored as follows: 3 points for hitting the center, 2 points for the second sector, 1 point for the third sector, and 0 points for landing outside the third circle. The level of movement frequency was assessed using the tapping test. It consisted of the girls, upon the command "go," using a pencil to make as many taps as possible with

Table 1. Relationships between physical development indicators (level of physical qualities development) and coordinative abilities in 16- to 17-year-old girls with low adaptive capacity (n = 48)

Physical development indicators	Coordinative abilities				
	Static balance	Spatial orientation	Motor coordination	Spatial-dynamic accuracy	Movement frequency
Speed	-0.349	0.119	0.425	-0.016	-0.524
Speed and strength qualities	0.086	-0.015	-0.179	0.235	0.193
Strength	-0.016	-0.122	-0.116	-0.214	0.045
Agility	0.467	0.247	0.397	-0.042	-0.319
Endurance	-0.034	0.019	-0.389	-0.001	-0.081

Notes: Statistically significant correlations are indicated in bold
Source: compiled by the authors of this study

their dominant hand within 10 seconds in two squares (50 cm apart), moving as quickly as possible from one square to the other.

METHODS OF MATHEMATICAL STATISTICS

To determine whether there is a relationship between physical development indicators and coordinative abilities in adolescent girls with low adaptive capacity, we used Pearson's linear correlation analysis. The existence of a relationship and differences between individual variables were considered significant at a 95 % significance level ($p \leq 0.05$). The data were analyzed at the Department of Theory and Methods of Physical Education of Dragomanov Ukrainian State University.

COMPLIANCE WITH ETHICAL STANDARDS

The participants and their parents were informed of the research aim and voluntarily agreed to participate. The research results were reviewed and approved by the Academic Integrity Committee of Dragomanov Ukrainian State University (Approval Protocol No. 4, issued on March 18, 2026).

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

This study was carried according to the research plan of the Faculty of Physical Education, Sports and Health of the Dragomanov Ukrainian State University in 2023-2027 in accordance with the theme "Monitoring, control and evaluation of learning results in physical culture, the basics of healthy lifestyle" (state registration number 0113U009185).

RESULTS

The relationship between physical development indicators and coordinative abilities in adolescent girls is complex and interdependent, and it plays a decisive role in the effectiveness of any motor activity. Coordinative abilities serve as the foundation for providing targeted and safe pedagogical guidance in the development of physical qualities. The correlation analysis revealed varying degrees of relationship between specific physical qualities and coordinative abilities in 16- to 17-year-old girls. Thus, in adolescent girls with low adaptive capacity, certain relationships were found between various types of coordinative abilities and physical qualities (Table 1).

Significant relationships were found between the level of speed and indicators of static balance ($r = -0.349$), motor coordination ($r = 0.425$), and movement frequency ($r = -0.524$) at $p \leq 0.05$. It was established that the agility level significantly correlates with indicators of motor coordination ($r = 0.397$), spatial orientation ($r = 0.247$), static balance ($r = 0.467$), and movement frequency ($r = 0.319$) at $p \leq 0.05$. It was found that the level of endurance is associated with motor coordination ($r = 0.389$) at $p \leq 0.05$; no other relationships were found between these physical qualities and any of the types of coordinative abilities ($p > 0.05$).

At the same time, a weak but significant correlation was observed between speed and strength ability levels and the spatial-dynamic orientation indicator ($r = 0.235$; $p \leq 0.05$); no statistically significant correlations were found between strength performance and indicators of various types of coordinative abilities ($p > 0.05$).

These relationships between physical development indicators and coordinative abilities in 16- to 17-year-old girls with low adaptive capacity can be interpreted as follows: an increase in running speed occurs in parallel with the development of motor coordination;

to improve endurance, motor coordination should be developed; to develop speed and strength qualities, spatial-dynamic accuracy should be improved. Regarding the 4x9 m shuttle run, this test requires running short distances at high speed with multiple changes in direction; therefore, its result depends on the combined level of speed, agility, and speed and strength qualities. Therefore, to improve performance in the shuttle run, it is advisable to promote the development of spatial orientation, movement frequency, and motor coordination. Regarding balance, this indicator has an inverse relationship with speed and agility: in the "Flamingo" balance test, the lower the result, the more points the participant receives; therefore, the better the result in the speed run, the poorer the display of static balance.

The data reveal the nature of positive transfer of physical qualities, where the development of certain aspects of motor skills contributes to the improvement of others. This allows for the rational planning of physical exercise sessions for 16- to 17-year-old girls with low adaptive capacity, by planning physical activity parameters appropriate to their capabilities and ensuring the best health-promoting and developmental effects in line with their functional abilities.

Thus, to develop speed in 16- to 17-year-old girls with low adaptive capacity, it is advisable to include exercises aimed at developing motor coordination, balance, and movement frequency, specifically dance exercises, exercises on limited support, maintaining a stable posture, shuffling, intense arm and leg swings while standing, exercises on a coordination ladder, and, to a limited extent, jumping rope, etc. To develop speed and strength in physical education, accuracy exercises should be planned, such as throwing and tossing balls of various sizes and weights at horizontal and vertical targets. To improve endurance, it is advisable to include dance exercises, simultaneous movements of different body parts in various directions, walking in place, and walking while moving with random changes in direction. In addition to these exercises, given the wide variety of motor actions and the accessibility of these activities for individuals with varying levels of fitness, it is advisable to use a variety of sports games to develop the physical fitness of 16- to 17-year-old girls with low adaptive capacity.

DISCUSSION

The direction, magnitude, and level of the significant correlation coefficients indicate that several physical development indicators – on which direct pedagogical influence is limited due to girls' low adaptive capacity – can be improved through the indirect development of coordinative abilities. This is explained through the biomechanical and physiological mechanisms underlying various aspects of motor function [15, 16].

Thus, the strength of the correlation between different types of coordinative abilities and speed depends on the specifics of the movements. Motor coordination is the foundation for speed, as it ensures precise muscle contractions, reduces resistance from antagonist muscles, and allows the nervous system to transmit impulses accurately. From a biomechanical perspective, as the demands on movement speed increase, the coordination complexity of their execution rises; therefore, higher motor skill is required to maintain accuracy [17]. This is explained by the inhibition factor (Fitts' law): speed and accuracy are inversely proportional; the higher the movement speed, the greater the likelihood of coordination errors [18]. To act quickly, the brain must coordinate muscle activity effectively. High speed is impossible without coordination (the ability to control one's body movements and to coordinate muscle activity to perform precise, complex movements). The better one's coordination is developed, the less effort and attention the nervous system expends on performing a motor act. This allows one to safely increase speed without losing quality. The development of these aspects of motor skills occurs in parallel: from slow, conscious execution of exercises (building neural connections and perfect coordination) to a gradual increase in speed to consolidate high-intensity automated movement [19].

Movement frequency is a basic manifestation of speed. At the same time, movement frequency is determined by the ability to control movement and by a high level of coordination between alternating excitation and inhibition processes in the cerebral cortex, thereby enabling the muscles to contract rapidly and relax instantly [20]. At the same time, in the context of human biomechanics, there is a relationship between movement speed and static balance. As the speed of any movement increases, the body's center of mass moves beyond the base of support more rapidly, which critically reduces static balance and requires a transition to dynamic balance. That is, the higher the movement speed, the less important static balance is for successful task completion [21].

The comprehensive expression of physical qualities during shuttle runs requires an understanding of the physiological mechanisms underlying various forms of coordinative ability. Thus, performing the shuttle run exercise involves running short distances at high speed, repeated abrupt stops, rapid 180° turns, and

rapid muscle re-engagement [8]. These phases require a high level of movement frequency and motor coordination. At the same time, the sudden change in direction forces the body to balance and maintain equilibrium, which contributes to the exercise's effectiveness. At the same time, to perform the exercise effectively, the brain must constantly calculate the distance to the turning line, assess speed, and select the optimal angle for the turn. This requires spatial orientation – the ability to assess and differentiate the spatial characteristics of movements [10].

There is a weak positive correlation between long jump results and accuracy test scores (spatial-dynamic accuracy), which can be explained by the fact that both tests are based on the demonstration of coordination – the ability to synchronize movements. The long jump requires a quick takeoff and the ability to maintain balance in space during the flight phase. This same control helps in making precise movements when throwing or aiming at a target. From a physiological perspective, the development of explosive strength, as a component of speed and strength qualities, simultaneously influences improvements in the overall coordination of the central nervous and peripheral neuromuscular systems [1, 22]. Accuracy requires a delicate balance, precise aiming, and excellent muscle control; therefore, the lack of a direct correlation with strength is explained by the fact that strength can reduce movement precision, as strength exercises induce physiological arousal that interferes with fine motor skills and movement precision [9].

A significant correlation has been observed between endurance and motor coordination, which can be explained as follows: a high level of motor coordination reduces the body's energy expenditure. In contrast, high endurance enables the maintenance of precision and coordination of movement even under fatigue, thereby optimizing overall performance.

Thus, the research results confirm that performance in exercises requiring unidirectional or complex manifestations of speed, speed and strength abilities, and endurance can be improved through the targeted development of specific types of coordinative abilities. Although the observed correlations are statistically significant, they are relatively weak, indicating a specific pattern of physical development among 16- to 17-year-old girls with low adaptive capacity.

CONCLUSIONS

Significant correlations were found between the level of speed and the indicator of motor coordination ($r = 0.425$), balance ($r = -0.349$), and movement frequency ($r = -0.524$) at $p \leq 0.05$; the level of agility with the indicator of motor coordination ($r = 0.397$), the indicator of spatial orientation ($r = 0.247$), the indicator of balance ($r = 0.467$), and the indicator of movement frequency ($r = 0.319$) at $p \leq 0.05$; the level of endurance with the motor coordination indicator ($r = 0.389$) at $p \leq 0.05$. At the same time, a weak but significant correlation was found between the level of speed and strength abilities and the spatial-dynamic orientation indicator ($r = 0.235$) at $p \leq 0.05$; no statistically significant correlations were found between strength performance and indicators of various types of coordinative abilities ($p > 0.05$).

The results obtained allow for the use of more accessible physical training parameters to improve the level of those physical qualities (speed, strength, endurance, speed and strength qualities), the influence on which is limited for adolescent girls with low adaptive capacity, particularly to develop the most informative types of coordinative abilities based on the phenomenon of positive transfer.

PROSPECTS FOR FURTHER RESEARCH

Future research will focus on developing a comprehensive program to improve the physical qualities of 16- to 17-year-old girls with low adaptive capacity.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 11.03.2026
ACCEPTED: 28.07.2026

CREATIVE COMMONS 4.0

ORIGINAL ARTICLE

Morphofunctional features of small intestine remodeling under the influence of cadmium chloride in an experiment

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ABSTRACT

Aim: The aim of the study was to determine the characteristics of structural changes in the jejunum and ileum of experimental animals of different ages following cadmium chloride intoxication.

Materials and Methods: Experimental studies were conducted on 60 white laboratory male rats, both prepubertal and pubertal, with body weights of 80–100 g and 190–220 g, respectively. All animals were divided into three groups. Of these, 12 animals constituted the intact control group, which was divided into two subgroups: 6 sexually immature white rats and 6 sexually mature animals. The experimental animals comprised two groups, each with two subgroups. The second group included 24 immature rats, of which 12 were removed from the experiment on the 7th day and 12 on the 14th day after cadmium chloride poisoning. Group 3 consisted of 24 experimental animals, of which 10 were removed from the experiment on day 7 and 14 two weeks after cadmium intoxication. Poisoning of the experimental white rats with a cadmium chloride solution was performed intraperitoneally at a dose of 6 mg/kg body weight. It was used electron microscopic examination.

Results: Cadmium chloride exposure causes structural changes in the jejunum and ileum. The observed phenomena are more pronounced in the jejunum, which is explained by its greater functional activity compared to the ileal segment of the small intestine. Exotoxin disrupts the function of proteins and cell membranes, affects metabolic processes in the small intestine and its epithelium. Under electron microscopy, the surface of the ciliated epithelial cells appeared as a series of microvilli closely arranged next to one another. A functional feature of the apical membrane of epithelial cells is a pronounced endocytosis, manifested by the detachment of endocytic vesicles containing substrates from the base of the microvilli. Changes in the ultrastructure of the microvilli of the brush border at the apical pole of columnar epithelial cells may indicate disturbances in parietal digestion and absorption processes. On the 7th day after cadmium chloride poisoning, exposure to exogenous factors results in thickening of the subepithelial mucus layer, which may be interpreted as the organ's protective response to a chemical irritant. Cadmium chloride intoxication in experimental animals leads to the suppression of regenerative processes against the background of morphological changes in the structure of ciliated epithelial cells, which is associated with cadmium accumulation in the cells.

Conclussion: The destructive changes in the organization of organelles, the cytoplasmic membrane of epithelial cells, and the basement membrane indicate disturbances in intracellular bioenergetics, the protein-synthesizing apparatus, and the transcellular transport of substances through the capillary network, leading to changes in the properties of the capillaries themselves.

KEY WORDS: small intestine, jejunum, cadmium chloride, ileum, morphology, electron microscopy, experiment

Wiad Lek. 2026;79(8):1913-1921. doi: 10.36740/WLek/235903 DOI

INTRODUCTION

The adverse environmental conditions in Ukraine's regions have led to an increase in the number of pathological lesions of the gastrointestinal tract, one of the main causes of which is the impact of environmental chemical factors on the body, particularly heavy metals and their salts, since the digestive system is one of the primary routes through which they enter and are excreted from the body [1, 2].

Cadmium ranks first in terms of toxicity and danger; once it enters the body, it is characterized by extremely slow excretion and accumulates in various organs [3, 4]. It is known that cadmium cations are capable of interacting with biomolecules, causing damage to their structure, exerting a destructive effect on nuclear components, biomembranes, and cytoplasmic structures of cells, and influencing the processes of proliferation and apoptosis [5, 6, 7].

The small intestine plays an extremely important role in the digestive process and is therefore almost always involved in the pathological process when pollutants affect the body. The local effect on the organ is due to

the fact that most toxic chemical complexes enter the body through active absorption in the jejunum and ileum, thereby exerting a destructive effect on the morphological state of the organ walls, resulting in functional disorders [8, 9, 10].

A prerequisite for the disruption of metabolic processes in tissues and organs is impaired blood supply. In the event of any toxic effect on the gastrointestinal tract, the pathological process involves not only the structures of the mucosa, submucosa, muscular layer and serosa of the small and large intestines, but also the vessels of the microcirculatory bed, which constitute an important functional system that fully ensures homeostasis in accordance with the morphological characteristics and physiological or pathological states of the tissue or organ [11]. It is extremely important in morphological and toxicological studies to consider the age-related aspect, as each life stage is characterized by specific features of the action, distribution, and accumulation levels of chemical substances. With age, the body's resistance, sensitivity, and adaptation to the effects of xenobiotics change [12].

Thus, studying the process of structural changes in the small intestine wall during pathological conditions resulting from the influence of exogenous factors, as well as across different age periods, remains a relevant issue in experimental and clinical medicine.

AIM

To determine the characteristics of structural changes in the jejunum and ileum of experimental animals of different ages following cadmium chloride intoxication.

MATERIALS AND METHODS

Experimental studies were conducted on 60 white laboratory male rats, both prepubertal and pubertal, with body weights of 80–100 g and 190–220 g, respectively.

The care and handling (experimental studies and euthanasia), morphological and biochemical invwstigations of laboratory animals were conducted in accordance with the "Scientific and Practical Recommendations for the Care and Handling of Laboratory Animals" and Order No. 690 of the Ministry of Health of Ukraine dated September 23, 2009 in accordance with the provisions of the "General Ethical Principles for Animal Experiments," adopted by the First National Congress on Bioethics (Kyiv, 2001), and in compliance with the rules established by the European Commission for the Supervision of Laboratory and Other Experiments Involving Experimental Animals of Various Species (European Convention, 1986) [13].

All animals were divided into three groups. Of these, 12 animals constituted the intact control group, which was divided into two subgroups: 6 sexually immature white rats and 6 sexually mature animals. The experimental animals comprised two groups, each with two subgroups. The second group included 24 immature rats, of which 12 were removed from the experiment on the 7th day and 12 on the 14th day after cadmium chloride poisoning. Group 3 consisted of 24 experimental animals, of which 10 were removed from the experiment on day 7 and 14 two weeks after cadmium intoxication.

Poisoning of the experimental white rats with a cadmium chloride solution was performed intraperitoneally at a dose of 6 mg/kg body weight. Animals in the control and experimental groups were kept under identical conditions, and the material collected from them for electron microscopic examination was processed simultaneously.

For electron microscopic examination, tissue sections from the specified parts of the small intestine were taken from the animals immediately after respiratory and cardiac arrest. The small intestine section was fixed in a 2% solution of osmium tetroxide in phosphate buffer with a pH of 7.4 and a molar concentration of 0.1 M. Initially, semi-thin sections were prepared to supplement the histological examination of the material, and sites for electron microscopic examination were selected from these sections. Ultrathin sections were prepared on an UMTP-7 ultramicrotome and mounted on 1-mm-diameter copper blanks with a Formvar base. Sections 30–50 nm thick were contrasted in a 2% solution of uranyl acetate in 70% ethanol and Reynolds' mixture and examined using a PEM-125K electron microscope.

RESULTS

Electron microscopic studies of the jejunum wall in sexually immature white rats on the 7th day after cadmium intoxication revealed destructive changes in its structure. The height and number of damaged microvilli on the apical surface of columnar epithelial cells were noticeably reduced. In the cytoplasm, organelles were destroyed, the endoplasmic reticulum became heteromorphic, and enlarged vacuoles were observed in some areas.

Plasmocytes were detected in the lamina propria of the mucosa, indicating an immune response by the body. The presence of damaged fibroblasts indicated a decrease in the regenerative capacity of the tissues of the organ under study (Fig. 1).

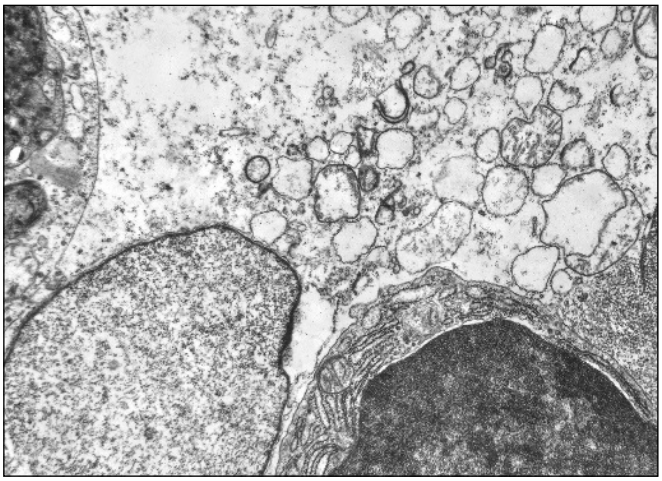

Fig. 1. Ultrastructural changes in the lamina propria of the small intestine mucosa of a sexually immature animal on the 7th day of observation. Cytoplasm of a damaged fibroblast with destructively altered organelles. Magnification: ×14,000.

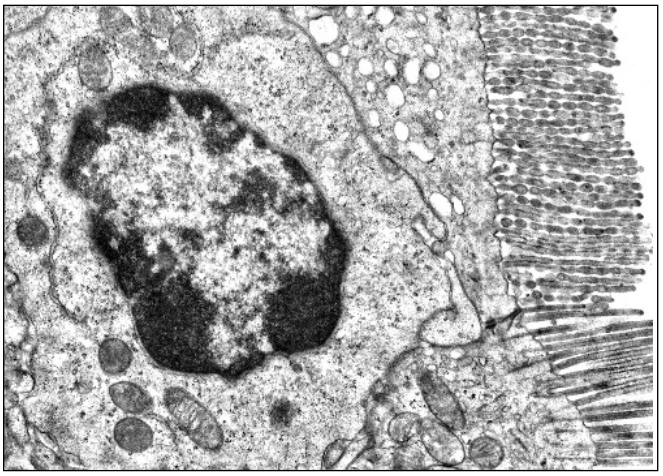

Fig. 3. Submicroscopic changes in the columnar epithelial cells of the ileal villi of a sexually immature animal 7 days after exposure to cadmium chloride. Partially fragmented microvilli, a nucleus with heterochromatin clusters, mitochondria. Magnification: ×15,000.

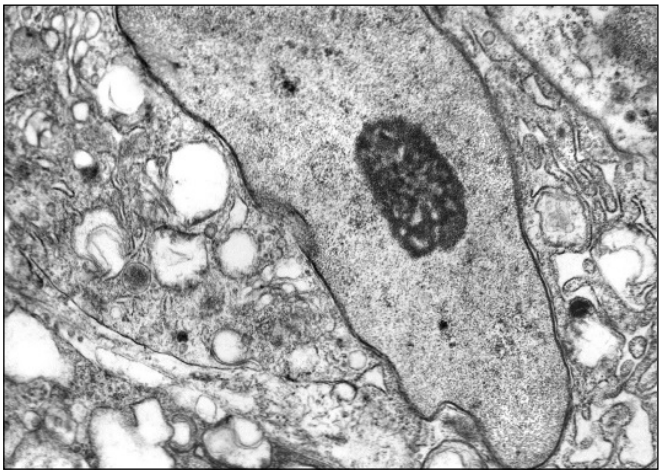

Fig. 2. Submicroscopic view of the lamina propria of the jejunum mucosa in a sexually immature white rat on the 14th day of observation. A nucleus with large nucleolus of a fibroblast, cytoplasm, and tubules of the granular endoplasmic reticulum. Magnification: ×21,000.

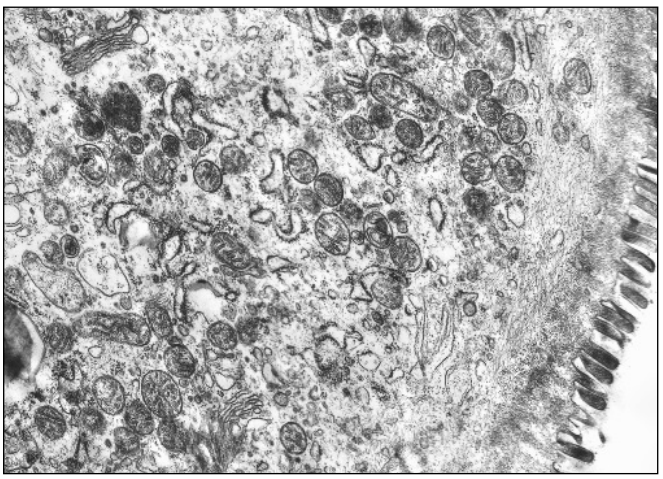

Fig. 4. Submicroscopic structure of a columnar epithelial cell in the lower part of a villus of the ileum of a sexually immature animal on the 14th day of observation. Short microvilli, epithelial cell cytoplasm, mitochondria, and a canaliculus of the granular endoplasmic reticulum. Magnification: ×14,000

On the 14th day following cadmium chloride poisoning in sexually immature white rats, signs of improvement in the condition of ciliated epithelial cells were observed. The plasma membranes were thickened and exhibited higher electron density, and the intercellular spaces were widened. Partial restoration of epithelial cell microvilli was observed, although signs of destructive processes were still present.

Organelle destruction was less pronounced: moderately dilated tubules of the granular endoplasmic reticulum were identified, and hypertrophy of the Golgi complex and primary lysosomes was detected. An increase in the number of mitochondria was observed, with organelles having a condensed matrix and a large number of cristae. The elongated-oval nuclei were displaced apically. Euchromatin predominated in the karyoplasm. Leukocyte infiltration was observed near the damaged columnar epithelial cells (Fig. 2).

Morphometric, microscopic, and ultrastructural data on the condition of the epithelial cells of the villi in the mucosa of the affected small intestine indicated disturbances in the processes of parietal digestion and absorption.

Electron microscopic studies of the ileal wall in sexually immature animals poisoned with cadmium chloride revealed pronounced structural changes on the 7th day of observation. The intercellular spaces widened, leading to the extrusion of damaged cells

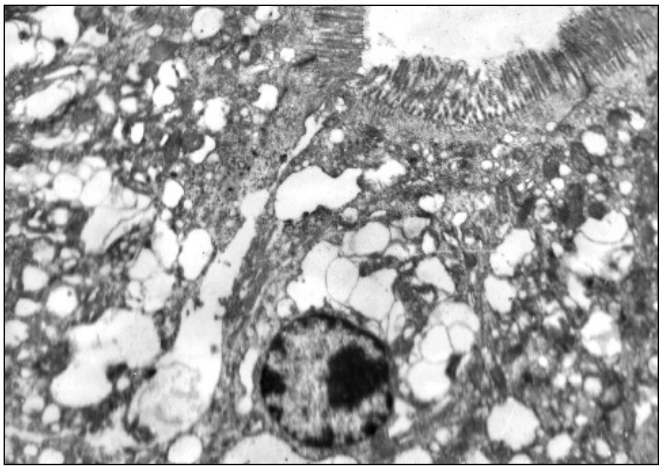

Fig. 5. Submicroscopic changes in the columnar epithelial cells of the villi of the small intestine mucosa of a sexually mature animal on the 7th day of observation. Fragmented microvilli, a nucleus with heterochromatin clumps, significantly dilated canaliculi of the granular endoplasmic reticulum, and an enlarged intercellular space. Magnification: ×7000.

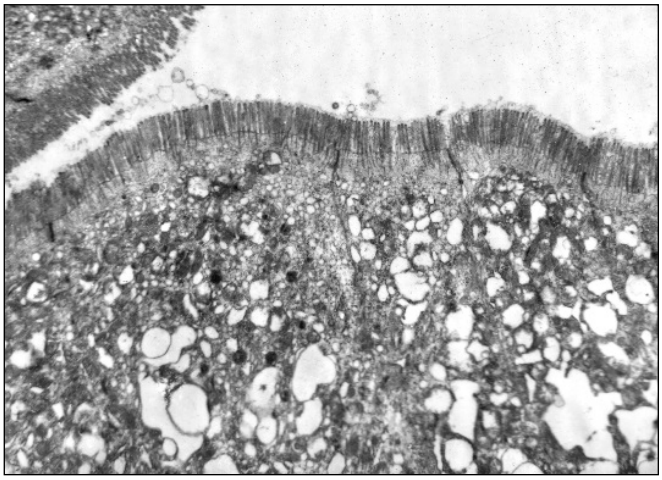

Fig. 6. Submicroscopic appearance of columnar epithelial cells in the villi of the small intestine of a sexually mature animal 14 days after exposure to cadmium chloride. The apical surface of the cell with microvilli. Magnification: ×7000.

from the epithelial layer and, consequently, its destruction. Submicroscopic changes in columnar epithelial cells manifested as partial fragmentation of microvilli, thickening of the basement membrane, destruction of individual organelles, and an increase in the number of lysosomes (Fig. 3).

The basal orientation of the nucleus, characteristic of the cells under study, was lost. Clusters of heterochromatin were observed along the periphery of the nuclear matrix. Mitochondria were present in the nuclear zone, exhibiting the most significant changes. Mitochondrial membranes were preserved, but the cristae were not tightly arranged, and the mitochondrial matrix was

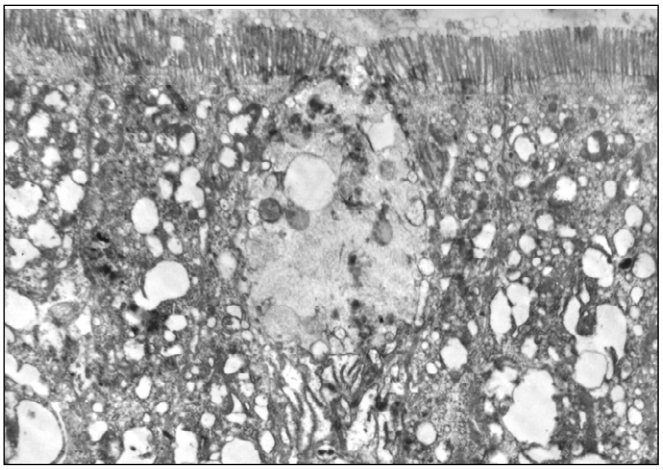

Fig. 7. Ultrastructural picture of the epithelial layer of the ileum mucosa villi in the sexually mature rat 7 days after exposure to cadmium chloride. Damaged microvilli on the apical surface of columnar epithelial cells, significantly dilated, vacuole-like tubules of the granular endoplasmic reticulum, damaged mitochondria, goblet cell. Magnification: ×8000.
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pale. Fine granulation was present in the cytoplasm, indicating protein dystrophy.

During the observation period, a large number of lysosomes appeared in the cytoplasm of epithelial cells, digesting organelles damaged and destroyed as a result of intoxication. Their appearance triggered the activation of the Golgi complex. The presence of autophagosomes in the cells indicated toxic stress, since autophagy is one of the ways cells rid themselves not only of damaged organelles but also remove dead cells from tissues. The appearance of lysosomes and autophagosomes in the cytoplasm indicated the activation of protective mechanisms in the studied organ. As a result of the studies, necrobiotically altered cells were identified among the epithelial cells.

On the 14th day after cadmium chloride poisoning of sexually immature white rats, signs of improvement in the condition of bordered epithelial cells were observed. Plasma membranes had higher electron density, and intercellular spaces were widened.

During this study period, partial restoration of epithelial cell microvilli was observed, but signs of destructive processes still persisted (Fig. 4).

The destruction of organelles displaced closer to the basal pole was less pronounced. Here, moderately dilated tubules of the granular endoplasmic reticulum were identified, and hypertrophy of the Golgi complex and primary lysosomes was observed. Mitochondrial hyperplasia was observed, with a condensed matrix and a large number of cristae. Nuclei were displaced apically, and euchromatin predominated in the karyoplasm. Lymphocytes were detected among the columnar epithelial cells.

In the intestinal villi, electron microscopy revealed columnar epithelial cells in which destructive changes were developing. Disruption of cell contouring and the basal arrangement of nuclei was observed; as a result of cadmium chloride exposure in sexually mature animals, the nuclei were localized in the center of the cell. Lymphocytes were detected near the altered cells.

The interconnection of columnar epithelial cells was maintained by a system of intercellular junctions, the spaces of which were locally expanded by the 7th day of the experiment.

A significant sign of impaired parietal digestion is a change in the structure of microvilli. On the apical surface of the examined cells, areas with deformation and destruction of microvilli were detected, manifested by their swelling and shortening, as well as partial fragmentation (Fig. 5).

Some of the microvilli underwent lysis, resulting in the complete exposure of certain areas. One of the functions of the apical membrane of columnar epithelial cells is endocytosis, which occurs through the budding of endocytic vesicles containing a specific substrate from the base of the microvilli. Lysis, fragmentation of the microvilli, and exposure of areas of the apical membrane led to a partial loss of its function.

Intestinal epithelial cells were in a state of protein dystrophy. An increased number of organelles was observed in the cytoplasm, concentrated in the perinuclear zone of the epithelial cells. Mitochondria were swollen, contained an electron-light matrix, and had isolated transparent vesicles. The cristae were damaged, and their number had significantly decreased; however, the mitochondrial membranes remained intact.

The Golgi apparatus was hypertrophied in some cells. Vacuole-like dilated cisternae were detected in this organelle. The vacuoles surrounding this structure had increased in size.

The granular endoplasmic reticulum underwent significant changes: the tubules were partially degranulated, fragmented, significantly dilated, and filled with a substance characterized by low electron density. On the 7th day of the experimental study, a significant decrease in the number of ribosomes localized on the membranes of the granular endoplasmic reticulum was observed, indicating a disruption in the functions of this cellular structure; its volume decreased at the basal poles of the cell. The membrane of this organelle lost its sharply defined outline and appeared thickened.

An increase in the number of lysosomes and autophagosomes was observed in the cytoplasm. In some intestinal columnar epithelial cells, large autophagosomes were observed on the 7th day of the experimental study, inside which remnants of destroyed organelles were detected.

The oval-shaped nuclei increased in size. The nuclear envelope formed deep invaginations. In the partially disrupted nucleolus, areas undergoing lysis were observed. The perinuclear space was unevenly expanded. The nucleoplasm of the nuclei of the studied cells on the 7th day of the experimental study, under the influence of cadmium chloride, became diluted and lost its electron density. Clusters of condensed chromatin were concentrated along the periphery of the nuclear matrix.

On the 14th day of the experimental study, following the exposure of sexually mature animals to cadmium chloride, a partial restoration of the size of the microvilli of the mucosal epithelial cells of the hollow intestine was microscopically observed (Fig. 6).

Signs of destructive processes were observed in the epithelial layer of the villi: areas of epithelial detachment were found at the apical pole, and subepithelial edema was observed on the lateral surfaces and partially at the apex.

During this period of the study, heterogeneous changes in the columnar epithelial cells of the small intestine mucosa were observed. In a significant portion of the cells, the structural organization improved, although a large number of them remained significantly damaged.

The condition of the microvilli of some epithelial cells within the epithelial layer of the villi improved noticeably. Electron microscopic examination revealed that on the apical surface of the studied cells, the microvilli showed a tendency toward recovery, although some of them remained sparse and shortened. The intercellular spaces were not widened.

The cytoplasm of columnar epithelial cells, as the experimental study progressed, became fine-grained and clarified. Less pronounced destruction of organelles was observed within it, with these organelles displaced toward the basal pole of the columnar epithelial cells. Expanded tubules of the granular endoplasmic reticulum and cisternae of the Golgi complex are present. The cisternae of the endoplasmic reticulum varied in shape and size. Damaged mitochondria with a condensed matrix and a large number of cristae were observed. Primary lysosomes were present. The plasma membranes were thickened and had a higher electron density.

The elongated-oval nuclei were displaced apically. Euchromatin predominated in the karyoplasm. Morphological and ultrastructural changes in the villus epithelial cells indicated disturbances in paracellular digestion and absorption.

Electron microscopic studies of the ileal wall of sexually mature white rats on the 7th day after cadmium chloride exposure showed that destructive changes were observed in the epithelial lining of the villi (Fig. 7). As a result of intoxication, the nuclei of columnar epithelial cells were localized in the center of the cells. On the apical surface of the examined structures, areas with destruction of microvilli were detected, manifested by partial fragmentation, lysis, and exposure of certain zones of the apical membrane. The above indicates a disruption of paracellular digestion in the examined organ.

As of the 7th day of the study, the cytoplasm of the columnar epithelial cells is fine-grained and cloudy. Organelles are concentrated near the nucleus, which has increased in size. Certain areas of the karyolem have undergone lysis. As a result of the effect of cadmium chloride on cellular structures, the karyoplasm is diluted and has lost its electron density. An increased number of free ribosomes was detected in the cytoplasm of columnar epithelial cells, resulting from the degranulation of the granular endoplasmic reticulum. These changes indicate a dysfunction of the cellular structure under study. In certain areas, the tubules of the endoplasmic reticulum are dilated. Mitochondria, whose matrix is condensed, showed signs of swelling. The cristae of the studied cellular structures are partially destroyed, and, as a result, their number is reduced. The Golgi complex is surrounded by enlarged vesicles.

As of the 7th day after cadmium chloride intoxication in sexually mature animals, an increased number of autophagosomes and lysosomes was observed in the cells of the columnar epithelium of the ileum, indicating significant changes in the structure and disruption of the functions of cellular organelles. In particular, deformed and partially destroyed mitochondria were detected in some large autophagosomes.

On the 14th day of the experimental study, heterogeneous changes persisted in the epithelial cells with microvilli. In a certain portion of the cells, the structural organization improved, while signs of destructive processes persisted in a significant portion of the epitheliocytes.

On the apical surface of the studied cells with a microvilli, a tendency toward recovery was observed, indicating the restoration of epithelial cell functions, although a significant portion of the microvilli remained swollen, shortened, and partially fragmented. By the 14th day of observation, the cytoplasm was clear, with less pronounced destruction of organelles.

The mitochondria had partially restored their structure, as evidenced by an increased number of cristae compared to the previous stage of the experiment. The plasma membranes were thickened and exhibited higher electron density. The nuclei occupied a basal position. Euchromatin predominated in the nucleoplasm.

Thus, the phenomena under study were more pronounced in the jejunum, which is explained by its greater functional activity compared to the ileum.

DISCUSSION

According to the literature, it is known that the environment is constantly subjected to heavy metal pollution, which affects the human and animal organisms [14]. A common characteristic of heavy metals is their ability to slowly accumulate in living organisms [15, 16]. Excessive amounts of heavy metals can alter the structure and function of all body systems [17]. This disrupts the function of proteins and cell membranes, affects metabolic processes in the body, and has the potential to cause cellular mutations. It is also known that if the concentration of heavy metals in the body is higher, it is the great risk of viral activation [18]. Researchers have experimentally established that the intestinal epithelium is affected by the exotoxin [19]. This is confirmed by the data obtained in our study. Under electron microscopy, the surface of the ciliated epithelial cells appeared as a series of microvilli closely arranged next to one another.

A functional feature of the apical membrane of epithelial cells is a pronounced endocytosis, manifested by the detachment of endocytic vesicles containing substrates from the base of the microvilli. Changes in the ultrastructure of the microvilli of the brush border at the apical pole of columnar epithelial cells may indicate disturbances in parietal digestion and absorption processes [20].

The surface of the microvilli membrane is covered by the glycocalyx, which is the first structure to come into contact with intestinal contents; its glycoproteins serve as receptors for toxins, hormones, and antibodies, possess barrier properties, and retain a layer of mucus on the surface of the intestinal epithelium. The destruction of microvilli under the influence of exogenous factors indicates damage to the glycocalyx, which is an additional risk factor and creates conditions for the penetration of bacteria from the lumen of the small intestine into the mucosal tissue.

On the 7th day after cadmium chloride poisoning, edema of the villus stroma and increased desquamation of epithelial cells at their apical poles were observed in the mucosa of the jejunum and ileum of the experimental animals. According to scientific studies, exposure to exogenous factors results in thickening of the subepithelial mucus layer, which scientists interpret

as the organ's protective response to a chemical irritant [21, 22].

Some of the heavy metal salts in the lysosomes of bordered epithelial cells bind to metalloproteins to form complexes; these complexes, along with cells desquamated from the surface of the villi, enter the intestinal lumen, where some are reabsorbed and the rest are excreted in the feces. In addition, the thickened supramucosa layer of mucus, which plays a protective role by binding excess heavy metal salts in the lumen of the small intestine, prevents their absorption. According to researchers when the body is exposed to heavy metal compounds, particularly cadmium, hypertrophy and hyperplasia of goblet cells are observed, along with a significant thickening of the supraepithelial mucus, which plays a protective role by preventing further absorption of xenobiotics [16, 23].

Our results indicate that cadmium chloride intoxication in experimental animals leads to the suppression of regenerative processes against the background of morphological changes in the structure of ciliated epithelial cells, which is associated with cadmium accumulation in the cells.

As a result of electron microscopic studies of the walls of the jejunum and ileum in sexually immature and sexually mature white rats on the 7th day after cadmium chloride exposure, we observed destructive changes in the mitochondria, heteromorphism of the endoplasmic reticulum, an increase in the number of lysosomes, and damage to microvilli. According to researchers, morphological and functional disturbances of plasma and intracellular membranes are detected almost immediately upon exposure to external agents, even at relatively low doses [24]. The cause of impaired metabolic activity in epithelial cells may be structural disturbances in the elements of the endoplasmic reticulum during the course of intoxication. The detected destruction of the membranes of the granular endoplasmic reticulum indicates the predominance of catabolic processes over synthetic ones; disruption of the internal structural organization of mitochondria leads to the suppression of enzyme activity and a decrease in redox reactions occurring within the organelles. This, in turn, leads to an energy deficiency in the synthetic processes of intracellular metabolism. Disruption of mitochondrial function leads to a decrease in cytosolic ATP content and to an energy deficit in cells, causing their necrosis.

The described destructive changes in the organization of organelles, the cytoplasmic membrane of epithelial cells, and the basement membrane indicate disturbances in intracellular bioenergetics, the protein-synthesizing apparatus, and the transcellular transport of substances through the capillary network, leading to changes in the properties of the capillaries themselves.

Electron microscopic examination of the walls of the jejunum and ileum of sexually immature and sexually mature white rats on the 14th day after cadmium chloride poisoning showed that the microvilli on the apical surface of columnar epithelial cells were clearly defined and closely adjacent to one another, indicating a probable improvement in membrane digestion and absorption.

During this observation period in experimental white rats of various age groups, we noted less pronounced destruction of organelles in the cytoplasm of bordered epithelial cells, indicating the predominance of anabolic processes over catabolic ones, as well as improvements in intracellular bioenergetics and the protein-synthesizing apparatus. However, data from electron microscopic studies of the structural components of the cell wall indicated that during the specified experimental period, the presence of free ribosomes, hypertrophic changes in the Golgi complex, and the granular endoplasmic reticulum - structures where the synthesis of enzymes, structural proteins, and other substances takes place - had not completely disappeared, which still indicated impaired intracellular digestion. The reactive changes we observed are consistent with the data of other authors [18, 24, 25].

The described dynamics indicate that by the 14th day of observation, a trend toward a decrease in destructive processes and an increase in regenerative processes was noted in the mucous membrane of the jejunum and ileum of experimental animals in various age groups.

CONCLUSIONS

Cadmium chloride exposure causes structural changes in the jejunum and ileum. The observed phenomena are more pronounced in the jejunum, which is explained by its greater functional activity compared to the ileal segment of the small intestine.

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The work is carried out within the framework of the initiative research work of the I. Horbachevsky Ternopil National Medical University "0124U00061 Peculiriaties of the structural reorganization of blood vessels of the abdominal cavity and retroperitoneal space under the conditions of modeling different blood circulation states".

CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 18.03.2026
ACCEPTED: 29.07.2026

CREATIVE COMMONS 4.0

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ORIGINAL ARTICLE

Psychological and sports-based rehabilitation of combatants through adaptive strength sports

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ABSTRACT

Aim: To investigate the impact of strength sports (using kettlebell lifting as an example) on the effectiveness of psychological and sports-based rehabilitation for combatants.

Materials and Methods: The research, conducted in 2025-2026, included 63 combat veterans who had undergone limb amputations and sustained various traumatic injuries resulting from shrapnel and gunshot wounds. The participants were divided into three groups based on the type of injuries sustained. The dynamics of the combat veterans' psychological state were assessed using the "Assessment of Neuro-Emotional Stress" method; somatic health was assessed using the self-assessment of health status method proposed by V. P. Voitenko. The research was conducted using Google Forms.

Results: The research results showed a statistically significant decrease in neuro-emotional stress across all groups ($p \leq 0.01$), as well as a reduction in the number of individuals with high levels of psycho-emotional workload. A reduction in intergroup differences was observed, indicating an improvement in the psycho-emotional state of combat veterans. Assessment of somatic health confirmed a significant improvement in indicators across all groups ($p \leq 0.001$). A positive effect of kettlebell exercises on the effectiveness of psychological and sports-based rehabilitation for combat veterans was established, attributable to the combined action of physiological, psychological, and socio-adaptive factors.

Conclusions: The results obtained provide grounds for considering kettlebell exercises as an effective means of psychological and sports-based rehabilitation for combat veterans, as well as for their social reintegration, and it is advisable to incorporate them into adaptive sports and veteran sports programs.

KEY WORDS: health, strength sports, kettlebell exercises, neuro-emotional stress, psychological rehabilitation, sports-based rehabilitation, combatants, combat veterans.

Wiad Lek. 2026;79(8):1922-1929. doi: 10.36740/WLek/235892 DOI

INTRODUCTION

In the current context of the military conflict between Ukraine and russia, the number of combat veterans who have suffered injuries and limb amputations as a result of blast and shrapnel wounds is on the rise. Under these circumstances, the issue of their comprehensive rehabilitation – which involves restoring both physical and mental health – takes on particular significance [1, 2]. This is due to the multifaceted nature of combat injuries, which are accompanied not only by somatic impairments but also by significant psycho-emotional disorders that substantially complicate the process of social adaptation [3, 4].

Under such conditions, the consequences of combat experience – including injuries, prolonged exposure to stressors, post-traumatic disorders, and reduced physical fitness – objectively highlight the need for the implementation of effective rehabilitation technologies [5, 6]. Modern approaches to the rehabilitation of wounded military personnel are primarily focused on integrating physical education and sports as a means of restoring the body's functional capabilities and normalizing the psycho-emotional state [7, 8]. The use of strength sports, which combine the development of strength, endurance, and coordination of movement while fostering willpower, self-regulation, and stress resilience, is

promising [9, 10]. In the system of physical rehabilitation for military personnel, the implementation of strength and function-oriented training methods is becoming increasingly significant, aimed not only at restoring the body's functional state but also at enhancing its overall adaptive capacity. In light of this, particular attention should be paid to various types of functional training, specifically programs such as "CrossFit," which combine strength, aerobic, and coordination workloads, provide a comprehensive effect on the body, and contribute to the restoration of work capacity, the development of endurance, and the formation of psychological resilience [11, 12].

Strength-based forms of physical activity are increasingly being integrated into rehabilitation programs for combat veterans, as they contribute not only to the restoration of lost functions but also to the development of a sense of control over one's own body, increased self-esteem, and motivation for further recovery and improvement [13, 14]. The variability of loads and the possibility of applying an individualized approach to exercise execution ensure that such methods are accessible to individuals with varying levels of functional limitation. Against this backdrop, the use of kettlebell exercises as an effective and accessible means of strength training becomes particularly relevant [15]. They have become widely used in both training and competitive practice in adaptive and veteran sports. In particular, such exercises are actively incorporated into competition programs organized by institutions such as the Kettlebell Lifting Union and the Strongman Federation, which attests to their significant potential in the system of physical rehabilitation and social adaptation for military personnel. Kettlebell modalities are widely used during strength and functional training for participants in the Invictus Games (Invictus Games Foundation) [16]. Within this framework, kettlebell exercises are adapted to accommodate individuals with various functional limitations, including combat veterans with amputations and other disabilities. This practice demonstrates the versatility and adaptability of kettlebell training as a tool for physical rehabilitation, allowing for the customization of exercise intensity according to an individual's functional capabilities [17].

Despite the existence of a significant number of studies in the field of combat veterans' rehabilitation [1, 2, 18], the issue of the comprehensive impact of kettlebell sport on the psychological state and physical health of individuals with various types of combat injuries (amputations, shrapnel wounds) remains under-researched. Scientific justification for the effectiveness of such modalities, using both objective and subjective assessment methods, is becoming increasingly relevant. At the same time, the differential impact of kettlebell training on individuals with different types of combat injuries remains insufficiently studied.

The analysis of scientific sources indicates that the issue of rehabilitation for combat veterans is addressed within the framework of medical, psychological, and physical education and health research [9, 19, 20]. Researchers emphasize the need for a comprehensive approach that combines physical activity with psychological support and social adaptation for these individuals [21]. Research in the field of physical rehabilitation provides grounds for concluding that systematic physical activity improves the functional state of the cardiovascular and respiratory systems, increases work capacity, and restores motor functions [22]. At the same time, psychological studies have demonstrated the positive impact of physical exercise on reducing anxiety levels, depressive symptoms, and symptoms of post-traumatic stress disorder [5]. Researchers highlight the significance of strength sports in developing willpower, self-control, and confidence in one's abilities [13]. In addition, kettlebell lifting is an effective means of developing strength endurance, coordination, and functional fitness [15, 16].

The analysis of competition programs and regulations for kettlebell exercises demonstrates their adaptive nature and the potential for varied applications depending on participants' functional status. In particular, individuals with lower-limb impairments (amputations, severe injuries, impaired leg function) perform kettlebell exercises primarily in a seated position (kettlebell press). Still, they can also be performed in a standing position (press, long-cycle clean and jerk, kettlebell snatch). Competitors with upper limb impairments (amputation of one arm or significant functional limitations), or the consequences of injuries without amputation (soft tissue injuries, effects of concussions, traumatic brain injuries, etc.) may perform exercises in both positions [21].

Kettlebell exercises are also used for functional rehabilitation in individuals with neurological disorders [19]. However, their application requires an individualized approach, gradual progression of the workload, and mandatory medical and pedagogical supervision. With appropriate adaptation, such exercises contribute to the development of muscle strength and endurance, improved intermuscular coordination, stimulation of compensatory motor mechanisms, and increased overall functional fitness [23]. These findings demonstrate the significant potential of kettlebell lifting as a universal means of physical training and adaptation for individuals with various types of impairments. At the same time, its potential within the rehabilitation

system for combat veterans remains insufficiently studied, particularly in terms of its impact on psychological characteristics. This creates a scientific need for comprehensive research to study the impact of kettlebell lifting on the physical and psycho-emotional states of combat veterans, using valid diagnostic methods.

AIM

The aim is to investigate the impact of strength sports (using kettlebell lifting as an example) on the effectiveness of psychological and sports-based rehabilitation for combatants.

MATERIALS AND METHODS

PARTICIPANTS

The research was conducted between 2025 and 2026 with the participation of 63 combat veterans (men) who had limb amputations (n = 37) or various traumatic injuries resulting from shrapnel and gunshot wounds (n = 26). To systematize the results, they were divided into 3 groups. To standardize the research, a proprietary group coding system was used, developed in accordance with the approaches of the International Classification of Functioning, Disability, and Health. Group 1 (LL-A) included individuals with lower limb amputations (n = 19): LL-A1 – amputation of one lower limb (n = 12), LL-A2 – amputation of both lower limbs (n = 7). Group 2 (n = 18) comprised individuals with significant functional impairment or amputation of an upper limb (UL-A1). Group 3 (NA) consisted of individuals without amputations (n = 26), among whom the following subgroups were identified: NA-NEU (individuals with neurological sequelae of injuries (n = 15)) and NA-MSK (participants with musculoskeletal injuries (n = 11)).

The testing involved participants who, during 2025-2026, competed for the first time in Ukrainian kettlebell lifting championships and cups, as well as in events organized by the Ukrainian Strongman Federation, whose programs included kettlebell strength exercises. Retesting was conducted after the completion of a one-year cycle of systematic training, competition participation, and sports rehabilitation activities.

The inclusion criteria were defined as follows: male gender; participants' membership in one of the study groups based on the type of injury; participation in competitions and events involving kettlebell exercises (at least 3 times a year); and the participants' voluntary consent to take part in the research (each participant provided written consent). Exclusion criteria were the participant's personal desire to withdraw from the research at any time or a deterioration in health that prevented the participant from continuing training and competing. Research limitations: participants' age, duration of combat service, military and athletic rank, prior experience in training and competition in any sport, marital status, education, and financial status were not considered. We also did not monitor the number of competitions and other sports- and health-related events in which the participant took part during the year, nor the methodology of the training process (number, duration, and focus of sessions, and the presence of a coach/rehabilitation specialist).

The results were processed at the Department of Physical Education and Sports Rehabilitation of S. P. Koroliov Zhytomyr Military Institute (Zhytomyr, Ukraine) and the Department of Special Physical Training of the National Academy of Internal Affairs (Kyiv, Ukraine).

METHODS

The research used a combination of theoretical and empirical methods, as well as mathematical statistics. Analysis and generalization of literary sources were used to conduct an analytical review of scientific sources on the outlined range of issues (28 sources from PubMed, Scopus, Web of Science, and Index Copernicus were analyzed).

To assess the dynamics of the psychological state of combat veterans, we applied the "Assessment of Neuro-Emotional Stress" method (proposed by T. A. Nemchyn), which enables the precise determination of the level of psycho-emotional workload among the subjects. Indicators of this method should be interpreted as markers of functional mental state and neuropsychological tension that indirectly reflect participants' adaptive capabilities. The method includes 30 state characteristics, categorized into three levels of manifestation: A – low, B – average, C – high. By selecting one of the response options, the respondents assessed their own level of neuropsychological tension during the research period. The results were processed by summing the points: response "A" was assigned 1 point, "B" – 2 points, and "C" – 3 points. The interpretation of the total indicators was based on the following ranges: 30-50 points – low level of neuropsychological tension; 51-70 points – average level; 71-90 points – high level [24].

To determine the dynamics of combat veterans' health indicators, V. P. Voitenko's self-assessment method for somatic health was used. The test contains 29 questions: the first 28 are answered with "yes" or "no," while the last one is rated on a scale of "good," "satisfactory," "poor," and "very poor." The first 28 questions were scored using a point system: for each "yes" answer, the respondent re-

Table 1. Dynamics in psychological and somatic health indicators among combat veterans (n = 63) during kettlebell training sessions, X ± m, points

Studied groups	Stages of the research		Significance of the difference	
	Initial	Final	t	p
Indicators of neuro-emotional stress (according to T. A. Nemchyn's method)				
Group 1 (n=19) (LL-A1, n=12; LL-A2; n=7)	72.85±1.77	63.66±1.86	3.579	≤0.01
Group 2 (UL-A1; n=18)	69.74±1.87	61.39±1.90	3.132	≤0.01
Group 3, (n=26) (NA-NEU, n=15; NA-MSK, n=11)	67.42±1.81	58.39±1.85	3.489	≤0.01
Indicators of somatic health (according to V. P. Voitenko's method)				
Group 1 (n=19) (LL-A1, n=12; LL-A2; n=7)	21.16±0.87	12.23±0.69	7.863	≤0.001
Group 2 (UL-A1; n=18)	18.74±0.81	10.42±0.83	7.174	≤0.001
Group 3, (n=26) (NA-NEU, n=15; NA-MSK, n=11)	17.93±0.78	6.57±0.84	9.910	≤0.001

Legend: X – arithmetic mean, m – error of arithmetic mean, t – value of Student's t-test, p – level of statistical significance of differences
Source: compiled by the authors of this study

ceived 1 point; for a "no" answer, 0 points. An additional 1 point was awarded if the respondent selected "poor" or "very poor" for the final question. The final indicator reflected a quantitative self-assessment of health status. The results were interpreted according to the following criteria: 0-3 points – excellent health; 4-7 points – good; 8-13 points – fair; 14-20 points – satisfactory; 21-29 points – poor health [25]. The survey was conducted using the specified methods via an electronic form (Google Forms).

STATISTICAL METHODS

The methods of mathematical statistics were used to process the data obtained. The reliability of the difference between the indicators was determined using the Student's t-test. The results were presented as X ± m, where X is the arithmetic mean, m is the standard error. The reliability of the difference was set at $p<0.05$. All statistical analyses were performed using STATISTICA 6.1 software package (number AGAR909E415822FA), 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 National Academy of Internal Affairs. Also this study followed the regulations of the World Medical Association Declaration of Helsinki. Informed consent was received from all participants who took part in this study.

AI STATEMENT

The author states that no AI tools were used in writing this article.

FRAMEWORK

This scientific article was carried out according to the plan of the research work of the National Academy of Internal Affairs for 2020-2026 "Psychological, pedagogical and sociological support of law enforcement officers» (state registration number 0113U008196).

RESULTS

The research results showed that regular kettlebell training sessions, combined with competitive activities, led to a statistically significant improvement in the psychophysical status of combat veterans across all study groups. A statistically significant decrease in neuropsychological tension ($p \leq 0.01$) and an improvement in self-assessment indicators of somatic health ($p \leq 0.001$) were observed. At the same time, a reduction in the number of individuals with high levels of neuro-emotional stress and in those with poor or satisfactory health status, and a decrease in intergroup differences in the studied indicators were observed (Table 1). The obtained data should be considered evidence of the optimization of the subjects' current mental state, which may be due to the systematic influence of dosed physical exercise, an increase in functional fitness, and involvement in competitive activities, which have significant motivational and social-adaptive potential.

At the initial stage of the research, the neuropsychological tension indicator for participants in Group 1 (LL-A1/LL-A2) was 72.85 ± 1.77 points, indicating a high level and significant psycho-emotional workload. After completing a year-long training cycle and systematic participation in competitions involving kettlebell strength exercises, the indicator decreased significantly by 9.19 points to 63.66 ± 1.86 points ($p \leq 0.01$), revealing an average level of neuropsychological tension. At the same time, the number of individuals with a high level of tension decreased from 52.6 % to 21.1 %. The analysis of participants' self-assessments of somatic health also revealed a positive trend: the health status indicator decreased from 21.16 ± 0.87 points (poor level) to 12.23 ± 0.69 points ($p \leq 0.001$), indicating an average level of somatic health. The results indicate an improvement in the psycho-emotional state, a reduction in physical and psychological discomfort, and an increase in the body's adaptive capabilities, despite severe functional impairments.

In individuals in Group 2 (UL-A1), who had undergone amputation or had functional impairments of the upper limb, the neuropsychological tension indicator at the initial stage was 69.74 ± 1.87 points and was assessed as average. The results of the follow-up examination revealed a significant decrease in this indicator to 61.39 ± 1.90 points ($p \leq 0.01$). At the same time, the number of individuals with a high level of neuropsychological tension decreased from 44.4 % to 16.7 %. Positive dynamics were also observed using V. P. Voitenko's method: the self-assessment indicator for somatic health improved significantly from 18.74 ± 0.81 points (satisfactory level) to 10.42 ± 0.83 points ($p \leq 0.001$), indicating a transition to an average level of somatic health. The results obtained may be associated with improved functional capacity, increased physical fitness, and the development of more stable adaptive mechanisms.

The representatives of Group 3 (NA-NEU, NA-MSK), who had musculoskeletal system injuries and neurological consequences of injuries without amputations, also showed a significant improvement in the studied indicators. In particular, the level of neuropsychological tension decreased from 67.42 ± 1.81 points at the initial stage to 58.39 ± 1.85 points at the final stage ($p \leq 0.01$), and the number of individuals with high tension levels decreased from 34.6 % to 7.7 %, which is the most pronounced positive change among the study groups.

The average self-assessment of somatic health improved significantly from 17.93 ± 0.78 points (satisfactory) to 6.57 ± 0.84 points (good; $p \leq 0.001$). The results indicate the high effectiveness of systematic kettlebell exercises in optimizing the psycho-emotional state and improving subjective perception of health in individuals with preserved functional reserves.

The comparative analysis of the results showed that, at the initial stage, the least favorable indicators of psychophysical state were observed among individuals with lower-limb amputations. In contrast, the best results were observed in the group without amputations. After completing the one-year exercise cycle, all groups showed improvements, with indicators shifting toward more favorable levels of neuropsychological tension and somatic health. At the same time, intergroup differences decreased, suggesting a positive impact of systematic kettlebell training sessions, regardless of injury type.

DISCUSSION

The results of the studies confirm the effectiveness of the systematic use of kettlebell exercises as a means of psychological and sports-based rehabilitation for combat veterans with limb amputations, musculoskeletal disorders, and neurological sequelae of combat injuries [19]. The statistically significant reduction in neuro-emotional stress and improvements in somatic health indicators observed across all study groups demonstrate the positive impact of training and competitive activities on the psychophysiological state of combat veterans.

The combined effect of several factors can explain the results obtained. First, systematic physical exercise improved the functional state of the cardiovascular, respiratory, muscular, and nervous systems, and increased strength, endurance, and overall working capacity. Second, participation in the training and competition process positively affected the subjects' psychological and emotional state, reducing anxiety, building self-confidence, and increasing motivation for an active lifestyle. Third, the social adaptation component is of significant importance, as it involves integrating combat veterans into a sports environment, expanding social interaction, and restoring social activity. The combination of these factors led to positive changes in participants' subjective perceptions of their health and overall psychophysical status.

Particular attention is drawn to the fact that the most pronounced positive changes were observed in groups with more severe functional impairments, primarily among individuals with lower-limb amputations. Although the members of this group exhibited the worst baseline indicators in both neuropsychological tension levels and self-assessment of somatic health, a significant improvement in the studied parameters was observed after completing a one-year cycle of

kettlebell training. This may indicate the body's significant adaptive potential, even in the presence of severe structural and functional impairments, as well as the high efficiency of dosed strength loads during recovery.

At the same time, the group of individuals without amputations (NA-NEU, NA-MSK) showed the most pronounced positive trends in health indicators and the greatest reduction in the number of individuals with high levels of neuropsychological tension. This is likely due to greater preservation of the body's functional reserves, a greater capacity for physical exercise, and faster development of adaptive mechanisms. The results obtained are consistent with the current understanding, according to which the effectiveness of physical rehabilitation depends to a significant extent on the degree of functional limitations and the body's initial condition [5, 7, 22].

The combined effect of physiological, psychological, and social factors can explain the observed reduction in neuro-emotional stress. From a physiological perspective, systematic strength training helps optimize cardiovascular and nervous system function, increase endurance, improve neuromuscular coordination, and develop stable adaptive responses to stressors [15]. In addition, regular physical activity is associated with reduced levels of anxiety, emotional exhaustion, and mental stress, which is particularly important for individuals with combat experience.

Positive changes in psycho-emotional state may also be linked to the psychological benefits of sports participation. Participation in training and competitions contributed to increased self-esteem, greater confidence in one's physical abilities, restored motivation for an active lifestyle, and improved self-control [7, 23, 26]. For individuals who have suffered combat injuries and amputations, not only physical recovery but also the restoration of a sense of personal efficacy and social significance becomes crucial, which directly influences the overall perception of one's own health [3, 4, 27, 28].

The social adaptation component of the research likely played a significant role as well. Engaging combat veterans in a sports environment created conditions for expanding social contacts, mutual support, and integration into a community of individuals with similar experiences. This helped reduce social isolation, increase emotional resilience, and foster a positive psychological and emotional state. It is also important that participation in competitions provides an additional motivational incentive for regular training and self-improvement.

The results obtained provide grounds for asserting that kettlebell exercises should be viewed not only as a means of developing strength, but also as an effective tool for the psychological and sports-based rehabilitation of combat veterans. Their use contributes to improving the body's functional state, optimizing the psycho-emotional state, and increasing the subjective assessment of health status, regardless of the nature of the injuries sustained. At the same time, the research results should be interpreted with certain limitations in mind. In particular, the research included a relatively small sample of participants, and the assessment of health status was partly based on self-reports, which may introduce subjectivity into the data.

CONCLUSIONS

The systematic use of kettlebell strength exercises, combined with training and competitive activities, results in a statistically significant reduction in neuro-emotional stress among combat veterans, regardless of the nature of their injuries ($p \leq 0.01$). A reduction in the number of individuals with high levels of neuropsychological tension and an improvement in their psycho-emotional state were observed. Health assessment results confirmed a significant improvement in all study groups ($p \leq 0.001$). The positive effects of kettlebell exercises stem from the combined action of physiological, psychological, and socio-adaptive factors, including improved functional fitness, increased motivation, the development of self-confidence, and the integration of combat veterans into a sports environment.

The results provide grounds for considering kettlebell exercises as an effective means of psychological and sports-based rehabilitation for combat veterans, and for incorporating them into adaptive and veteran sports programs.

PROSPECTS FOR FURTHER RESEARCH

Promising areas for further research include studying the long-term effects of kettlebell exercises on the functional status of veterans, analyzing the dynamics of specific psychophysiological indicators, and developing differentiated physical and sports rehabilitation programs based on the nature of combat injuries and the level of functional limitations.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 16.03.2026
ACCEPTED: 29.07.2026

CREATIVE COMMONS 4.0

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REVIEW ARTICLE

Psychophysiological and medical indicators in determining police officers' professional suitability

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ABSTRACT

Aim: To assess the significance of medical and psychophysiological indicators in the selection of police.

Materials and Methods: The study is based on a comprehensive comparative, analytical, and content review of modern approaches to the professional psychophysiological selection of police officers in international practice and in Ukraine. A systematic literature search was conducted across the Scopus, Web of Science, PubMed, and Google Scholar databases for publications profile spanning from 2010 to 2025 inclusive. Out of 87 initially identified scientific publications, 41 sources met the strict inclusion criteria (focus on psychophysiological screening, cognitive testing, and law enforcement selection systems) and were selected for final detailed scientific analysis.

Conclusions: The introduction of modern assessment technologies reduces the risks of professional maladaptation and supports the development of high-quality human resource potential within law enforcement agencies. A systemic approach to evaluating psychophysiological indicators is therefore essential for improving the overall efficiency and safety of police service.

KEY WORDS: personnel selection, professional fitness, medical screening, stress, «Psyholot»

Wiad Lek. 2026;79(8):1930-1939. doi: 10.36740/WLek/224379 DOI

INTRODUCTION

The police profession belongs to the category of activities associated with a high level of risk and significant psychophysiological demands, which requires specific individual psychological and medical-physiological characteristics. In many countries around the world, including the United States [1; 2] and member states of the European Union [3; 4], recruitment to police units involves intense competition and multi-level assessment procedures aimed at evaluating a candidate's ability to function effectively under stress, risk, and high responsibility. Such an approach is driven by the need to ensure not only the professional reliability of police officers but also the safety of citizens with whom they interact in their daily work.

In Ukraine, the system of professional psychophysiological selection (PPS) is undergoing modernization. The key challenges remain the renewal of technical and material resources, the introduction of modern hardware–software complexes, and the enhancement of objectivity in candidate assessment. Under these circumstances, particular importance is attached to determining the role of medical and psychophysiological indicators that can serve as reliable predictors of professional suitability and forecast the effectiveness of future police activity.

In this regard, it is essential to conduct a systematic study of how medical, cognitive, and psychophysiological parameters are integrated into the personnel selection process, as well as to identify modern tools that allow for their most accurate and reliable assessment.

Contemporary research on police professional suitability emphasizes the importance of comprehensively considering motivational, psychophysiological, medical, and socio-psychological factors. Candidate motivation is one of the key predictors of professional resilience. Summarizing the findings of 22 empirical studies, Franklin F. and Alves A. [5] stress that motivation for police service is multidimensional, and that intrinsic motives (public service, professional self-realization) have a more sustainable influence than extrinsic ones. Studies by Vermeer S.-J. et al. [6] and Reny T.T. et al. [7] complement this topic, indicating that social orientations, trust in the police, and perception of the profession are decisive in shaping the intention to join law enforcement agencies.

Mental health of law enforcement officers is critically important both at the selection stage and throughout their service. An analytical review by Casas J.B. and Kegel A. [8] shows that police officers face numerous occupational stressors that often lead to mental health problems, while stigma and a «toughness culture» hinder help-seeking behavior. The practice of annual psychological evaluations described by Panza N.R. et al. [9] demonstrates the importance of prevention but highlights the need for standardized procedures, particularly regarding the depth of testing and the protection of confidentiality.

Stress acts as a central psychophysiological factor in police activity. In a study of Lebanese officers, Fayyad F.A. et al. [10] identified six key stressor groups, including excessive workload, work-life conflict, insufficient training, and poor health conditions. New methods of assessing psychophysiological reactions are actively developing through the use of VR technologies. Gamito P. et al. [11] and Muñoz J.E. et al. [12] confirm that VR-based scenarios with biometric monitoring (SCL, PT, HRV) allow for precise measurement of officers' reactivity and can be integrated into systems of professional selection and de-escalation training.

Medical screening traditionally forms the foundation of professional selection. The classical approach by Mostardi R.A. et al. [13] describes the development of age-related physical performance standards for police officers and demonstrates that appropriate medical criteria reduce the risk of injury and occupational disease. The system of police recruitment described by Pepper I. and McGrath R. [14] in the United Kingdom involves a comprehensive assessment of cognitive, psychological, and physiological characteristics in accordance with the National Police Training Programme.

Gatto J. and Dambrun M. [15], in their research, outlined the relationship between socio-psychological factors and an individual's psychophysiological characteristics. They demonstrated that authoritarianism, social dominance, and prejudice among young police officers are largely shaped by normative context and group socialization – factors that must be taken into account during police recruitment.

A synthesis of the existing studies indicates that professional police selection should be based on the integration of medical, psychophysiological, motivational, and socio-psychological indicators. Such an approach ensures more accurate prediction of performance effectiveness, stress resilience, and operational safety among police officers.

AIM

To assess the significance of medical and psychophysiological indicators in the selection of police.

MATERIALS AND METHODS

The study is based on a comprehensive comparative, analytical, and content review of modern approaches to the professional psychophysiological selection of police officers in international practice and in Ukraine. A systematic literature search was conducted across the Scopus, Web of Science, PubMed, and Google Scholar databases for publications profile spanning from 2010 to 2025 inclusive. The search strategy utilized targeted keyword combinations, including "psychophysiological selection", "professional suitability", "police officers", "medical screening", "stress resistance", "cognitive assessment", "VR technologies", "biosensory systems", "heart rate variability", and "occupational safety". Out of 87 initially identified scientific publications, 41 sources met the strict inclusion criteria (focus on psychophysiological screening, cognitive testing, and law enforcement selection systems) and were selected for final detailed scientific analysis.

The study is based on a comprehensive analysis of modern approaches to professional psychophysiological selection of police officers in both international practice and Ukraine. The research employs methods of theoretical analysis, synthesis, generalization, and a comparative–analytical review of scientific sources published in international databases such as Scopus and Web of Science. Particular attention is given to studies examining the psychophysiological reactions of police officers in stressful situations, methods of medical and psychophysiological screening, and the use of VR technologies and biosensory systems in personnel training and selection.

The analysis includes data on the operation of hardware–software complexes used in professional selection, such as Psyholot, TAP (Test Battery for Attention Performance), E-Prime a software platform for conducting psychological experiments, including tests assessing a variety of cognitive abilities [3], CVSA (Computer Voice Stress Analyzer) and VR systems with sensory monitoring (SCL (Skin Conductance Level), PT (Peripheral Temperature), HRV (Heart Rate Variability)). The research material also comprises descriptions of police recruitment requirements in the United States, United Kingdom, and EU countries, which made it possible to compare international standards with the existing practices of the National Police of Ukraine.

A professionographic analysis was applied to determine professionally important psychophysiological qualities (PIPQ) for various types of police activities. Additionally, a qualitative content analysis was used to examine research related to stress resistance, mental health, and the impact of occupational stressors on police officers.

ETHICS

This study is a theoretical and analytical review based on previously published scientific literature and does not involve direct research involving human participants, biological samples, or confidential personal data. Therefore, according to international ethical standards, formal approval by an ethics committee was not required

AI STATEMENT

The author states that no AI tools were used in writing this article.

REVIEW AND DISCUSSION

The analysis of scientific studies and professionographic data has shown that medical and psychophysiological indicators are among the key factors in determining the professional suitability of police officers. It was found that modern technologies – particularly VR modeling, biosensory systems, and computerized test batteries – significantly enhance the accuracy of assessing a candidate's functional state.

As a result of the study, the following findings were established:

1) psychophysiological qualities (PIPQ) clearly correlate with the type of police activity.

For special units, the most important traits include balance of nervous processes, reaction speed, and the ability to act effectively under extreme conditions; for patrol officers – attention, stress resilience, and operational thinking; for drivers – sensorimotor coordination and resistance to monotony;

2) VR technologies and biosensors demonstrated high efficiency in identifying individual differences in stress response. Experienced police officers showed lower SCL levels, more stable HRV (Heart Rate Variability), and better PT (Peripheral Temperature) regulation, confirming the relationship between professionalism and stress tolerance;

3) medical screening remains the foundation of selection, as somatic, neurological, and psychological conditions significantly affect the safety of service performance. The results of previous studies and current methodologies indicate the need to apply age-specific standards and to conduct regular re-evaluations of the health status of both candidates and active police officers;

4) international experience demonstrates a growing emphasis on cognitive testing, mental health assessment, and automated reaction analysis systems. According to the British model, the evaluation of psychophysiological parameters is integrated into a long-term system of professional development;

5) analytical synthesis has shown that the integration of medical, cognitive, and psychophysiological criteria makes it possible to form a reliable profile of professional suitability, reduce the risks of professional maladaptation, and improve the overall effectiveness of personnel selection;

6) the obtained results confirm the necessity of modernizing the system of professional psychophysiological selection within the National Police of Ukraine, particularly through the implementation of modern hardware-software solutions, standardization of procedures, and adaptation of best international practices.

For effective adaptation to service, a police officer must possess specific psychophysiological qualities inherent to this profession. This creates the need for modern and reliable methods of professional selection, the foundation of which is psychophysiological assessment of candidates, a practice relevant for any country.

In a number of developed countries, the issue of professional psychophysiological selection of personnel potential has been the subject of extensive research by specialized institutions. Western psychologists emphasize the undeniable economic benefits of conducting effective psychophysiological selection to determine candidates' suitability for police service, as well as the significant financial losses resulting from its absence or errors in the process.

The personnel selection systems used in foreign armed forces enable a rational distribution of servicemen, which reduces the time required to admit them to responsible types of activity, decreases training costs, and lowers accident rates caused by human error [16]. Well-founded requirements for operator specialists include emotional stability under pressure, sustained attention during standby periods before emergency action, and the ability to adapt to complex informational environments.

In the United States, a catalog of standard tests is used, including 33 tests to assess general intellectual abilities and 19 tests to evaluate specific skills. To predict professional suitability, various questionnaires (such as the Minnesota Multiphasic Personality Inventory, Woodworth Personal Data Sheet, etc.), demonstration tests (abstract tests in the form of tables, drawings, and gaming programs), hardware-based tests evaluating psychomotor and other psychophysiological characteristics, as well as individual and group practical sessions and simulation training systems reproducing real working conditions are widely used [17].

Through the widespread use of automated hardware–software complexes, the efficiency of testing, data processing, and evaluation of psychophysiological assessments is significantly increased, enabling the

testing of larger groups of respondents within shorter time frames.

The effectiveness of professional selection is beyond doubt and is supported by extensive data. For example, psychophysiological selection of candidates for operator specialties can reduce the rejection rate of unfit individuals from 23–30% to 5–8%, decrease accidents caused by human error by 40–70%, improve the reliability of control systems by 10–25%, and reduce training costs for military specialists by 30–40% [18].

The European model of occupational safety clearly defines measures to improve workplace safety and health protection. According to Directive 89/391/EEC, employers must consider an employee's suitability for the assigned work in terms of occupational safety and health protection. At the same time, improving human safety in the workplace remains an ongoing state priority [19].

The application of psychophysiological professional selection leads to a reduction in technical system accidents by 40–70%, depending on the type and conditions of activity, a decrease in the number of technogenic disasters by 20–25%, and a reduction in injury rates caused by the «human factor» by 40–45% [20]. Professional psychophysiological selection and psychophysiological expertise (as its final stage) are measures aimed precisely at addressing the «human factor» problem in production, significantly improving safety levels and preserving workers' health.

Currently, in the vast majority of foreign countries, a professional selection system has been established that takes into account the requirements of each profession for an individual's psychophysiological characteristics. A transition has been made to scientific methods of selection and training. Selection work is carried out both in state institutions and in private independent centers of psychophysiological expertise.

Worldwide, numerous programs are used to assess psychophysiological qualities and conduct professional selection of police officers for vacant positions, among which are:

– CANTAB (Cambridge Neuropsychological Test Automated Battery) – a program designed to assess various cognitive functions such as attention, memory, and visuospatial perception [3].

– Vienna Test System – a program including over 100 tests to evaluate mental qualities such as reaction speed, motor coordination, and decision-making ability.

– Psytoolkit – a program containing a set of tests measuring psychological attributes such as attention, memory, and reaction speed.

– E-Prime – a software platform for conducting psychological experiments, including tests assessing a variety of cognitive abilities [3].

– Test Battery for Attention Performance (TAP) – a program comprising tests that measure different aspects of attention, such as selective and divided attention [21].

CANTAB (Cambridge Neuropsychological Test Automated Battery) is a computer-based program designed to assess a range of cognitive functions such as memory, attention, information processing speed, and others. The program is widely used in many countries around the world, including the United States, the United Kingdom, the European Union, and Australia, and has several advantages over traditional assessment methods, as it provides more precise information about an individual's mental state [3]. In addition, this program allows for faster acquisition of test results, thereby contributing to more efficient psychophysiological professional selection.

Vienna Test System (VTS) is a computerized software product used for psychological testing in various fields, including professional psychophysiological selection. Developed in Austria in 1994, it offers extensive capabilities for evaluating different mental processes such as attention, memory, perception, comprehension, and logical reasoning. VTS includes over 80 tests that can be used to assess reaction speed, motor coordination, concentration, perception, and analytical abilities [22]. Most of the tests are administered via computer using specialized equipment such as motion sensors, keyboards, and mice.

Psytoolkit is a free web-based application that enables the creation of tests to measure reactions to stimuli, memory, attention, emotions, and other indicators of cognitive functioning. It is a powerful tool for assessing cognitive performance and can be used both in scientific research and in professional psychophysiological selection processes.

E-Prime (Experiment Builder) is a well-known software program for conducting psychological experiments. E-Prime allows researchers to design complex experiments with high precision and provides accurate measurement of reaction times. It includes a built-in editor and a data recording function [3]. The program contains more than 2,000 pre-installed commands and components for creating complex experiments, including visual and auditory stimuli, as well as keyboard and mouse responses. E-Prime also allows users to add custom scripts to create their own elements and commands. Within the program, researchers can set various experimental conditions such as stimulus size and shape, reaction pace, and task duration. E-Prime is used to study a wide range of psychological phenomena, including perception, attention, memory, language, and

others. Furthermore, it provides accurate and reliable data for studies requiring high temporal precision in reaction time measurement.

Test Battery for Attention Performance (TAP) is a software suite for assessing attention and memory. It includes tests that measure cognitive functions such as reaction speed, sensorimotor coordination, attention shifting, concentration, symbol recognition, and other cognitive abilities [21]. TAP is used to detect neuropsychiatric disorders, as well as in professional selection, for example, to assess the level of attention and other cognitive functions in police officers.

In addition to the software complexes discussed above, there are a number of other automated testing techniques used to select police officers and military personnel for service. The most common are:

– MMPI (Minnesota Multiphasic Personality Inventory) – a multifactor personality test used to assess emotional stability, interpersonal relationships, and social adaptation.

– GATB (General Aptitude Test Battery) – a test designed to measure general abilities, including verbal and non-verbal logic, analytical skills, and memory.

– OPQ (Occupational Personality Questionnaire) – a test aimed at identifying personality traits that influence professional performance and predicting a candidate's potential success in a specific occupation [23].

– PF16 (Personality Factor 16) – a sixteen-factor personality questionnaire assessing such qualities as stress tolerance, emotional stability, openness to new experiences, and self-confidence.

– ASVAB (Armed Services Vocational Aptitude Battery) – a test for determining general abilities and vocational interests, used in the selection of military personnel for the U.S. Armed Forces.

In practice, the selection process for police officers in different countries has its own characteristics and depends on many factors. These include historical traditions of legislation and law enforcement, the socio-economic and cultural development of the country, the structure of national police systems, the material support of the police, etc. [24].

The high level of competition for positions in the police forces of EU countries and the US creates the authority of this profession, which is achieved through a decent level of social and material support and forms a positive image of law enforcement agencies. The social orientation of police activities towards meeting the needs and requests of citizens is of considerable importance, with the aim of constantly increasing the level of trust on the part of the population [25].

Developed countries devote a lot of effort and resources to creating an image of prestige for work in law enforcement agencies. This contributes to improving the quality of personnel and makes it possible to select the best of the best. One of the most important means of achieving such high goals is professional psychophysiological selection.

Foreign countries have a carefully thought-out and well-established procedure for recruitment (i.e., attracting candidates for employment) and selection. Applicants undergo a two-stage selection process to ensure compliance with the requirements: minimum standards and competitive professional selection [26]. Minimum standards are understood to mean compliance with certain key requirements: citizenship, place of residence, minimum age, education, appropriate physical characteristics, no criminal record, computer skills, good eyesight, driver's license, ability to swim, etc. [4].

A traditional example to follow is the experience of the USA, which has achieved significant success in establishing a system of professional selection of police officers and has achieved significant results in this area.

An example of this is the requirement of the Buffalo Police Department, according to which a candidate for police service must have lived in the county for at least two years [27]. Professional selection includes the following stages: preliminary interview; study and analysis of information contained in the personal file; verification of information received about the candidate; polygraph examination; psychological testing; medical examination; physical fitness test; written and oral exams; final interview, after which a final decision is made on the candidate's suitability for police service [28].

In the USA, the police profession is one of the most dangerous because it is associated with constant physical and emotional stress and requires appropriate psychophysiological readiness to perform functional duties. That is why the system of recruitment to law enforcement agencies involves a complex competition, and 20-40 people can compete for one place in a large police department [1].

In the USA, various software and hardware complexes are used to assess the psychophysiological qualities of police candidates during recruitment, one of which is the Computerized Voice Stress Analyzer (CVSA). CVSA is a system that uses a voice analyzer to measure psychophysiological indicators, in particular stress and nervous tension levels, during interviews with candidates. CVSA helps to identify signs of dishonesty or psychological instability in candidates. The system is based on the assumption that changes in the voice may indicate a state of stress or unreliability of responses [2]. However, CVSA is the subject of debate and criticism regarding its scientific basis and accuracy.

Another example of a well-designed professional selection system in Europe is the experience of the United Kingdom. There, the National Recruitment Assessment Centre (NRAC) is responsible for assessing the psychophysiological qualities of police candidates during the recruitment process. The NRAC is a candidate assessment centre that uses various methods and tools to assess their ability to work in the police force. The NRAC provides various stages of assessment, such as psychological tests, physical tests, situational exercises, and observations, which allow the psychophysiological qualities of candidates to be assessed. This complex is focused on identifying the key skills and characteristics necessary for successful work in the police, such as communication skills, stress resistance, decision-making, and emotional intelligence [29].

The most common tools for assessing the aptitude of British police officers are: IRT (Inductive Reasoning Test – a test of logical and methodical thinking under time constraints), VRT (Verbal Reasoning Test – a psychometric test that assesses the ability to understand and analyze written information) and NRT (Numerical Reasoning Test – a psychometric test that identifies a candidate's ability to perform calculations and interpret and evaluate numerical information to solve work-related tasks) [30]. The second stage of the examination to identify physical and medical contraindications generally coincides with the model used in other countries and is aimed at screening out candidates who have developmental disabilities or chronic diseases that may interfere with the successful performance of their duties.

Another example of a country with a well-established professional psychophysiological selection system is Germany. The main components of this system are the Federal Ministry of the Interior (Bundesministerium des Innern) and the Federal Police (Bundespolizei) [31].

In Germany, various software and hardware complexes are used to assess the psychophysiological qualities of police candidates during the recruitment process. One of them is known as the Polizeipsychologisches Eignungsauswahlverfahren (PEAV) [22]. PEAV is a comprehensive system that includes psychological tests, physical tests, and interviews.

The system of training and selection of police officers in France also has its own organizational features. Its work at the legislative level is ensured by the so-called General Directorate and its subordinate Directorate of Education of the French National Police (La direction de la formation de la police nationale – DFPN). The psychophysiological selection of candidates for the police in France is based on an assessment of psychological and physiological characteristics. Various methods are used for this purpose to determine the candidate's abilities and level of intelligence, personal characteristics, physical endurance, and ability to work under stress. The test results are considered in conjunction with medical records, criminal background checks, interviews with the candidate, and their references. All these indicators are used to create a complete picture of the candidate and their suitability for police work.

Thus, existing systems of professional psychophysiological selection differ between countries in terms of organizational and legal structure, medical examination procedures, and the presence of licensing bodies. At the same time, in all countries, the health status and work capacity of employees significantly depend on their psychophysiological characteristics, which confirms the relevance of further research in this area.

At present, in Ukraine, the only certified modern medical electronic system for conducting professional psychophysiological selection of domestic production, which meets all regulatory requirements for medical equipment and allows for the selection of candidates for high-risk jobs, is the PAK «Psycholot».

The relationship between psychophysiological qualities and the effectiveness of police officers' activities is a very important aspect of professional training and skills enhancement for this category of personnel. However, it is quite difficult to analyze and determine which specific psychophysiological qualities are professionally important for police officers, since this profession is characterized by a wide range of tasks and situations. In this regard, conducting a professiographic analysis of police officers' activities, taking into account psychophysiological characteristics, can help identify the most important qualities and properly organize professional training and qualification improvement for these employees [24].

Furthermore, the results of such an analysis are useful for improving the level of professional competence of police officers and ensuring the high-quality performance of their official duties. An adequate level of professionally important psychophysiological and psychological qualities determines not only a person's productivity but also ensures the proper functioning of systems that guarantee both personal safety and the safety of others [32].

A police officer's job description is a description of the requirements and characteristics of a police officer's professional activities, which are determined by their professional tasks, role functions, and place of work. Studying the job description allows us to identify the necessary qualifications and professional requirements for a police officer, as well as to determine their personal and psychological characteristics [33]. Such research is conducted by analyzing documents, talking

Table 1. Professionally important psychophysiological qualities in accordance with police work

Type of Police Activity	Professionally Important Psychophysiological Qualities
Special Police Units and Units of Special Purpose Police	Orientation in enclosed space, spatial orientation, memory, balance of nervous processes, psychomotor qualities, stress resistance, responsibility, risk propensity, attention (concentration, switching speed), functional mobility of nervous processes, spatio-temporal extrapolation, visual-motor coordination.
Criminal Police Units, Pre-Trial Investigation Bodies, and Security Police (except for personnel serving outdoors)	Spatial orientation, memory, balance of nervous processes, stress resistance, responsibility, attention (concentration, switching speed), functional mobility of nervous processes.
Drivers of Official Vehicles	Spatial orientation, memory, balance of nervous processes, psychomotor qualities, stress resistance, resistance to monotony, responsibility, risk propensity, attention (concentration, switching speed), functional mobility of nervous processes, spatio-temporal extrapolation, visual-motor coordination.
Patrol Police Units and Security Police Units Serving Outdoors	Memory, balance of nervous processes, psychomotor qualities, stress resistance, resistance to monotony, responsibility, attention (concentration, switching speed), visual-motor coordination.
Aviation Units	Orientation in enclosed space, spatial orientation, memory, balance of nervous processes, psychomotor qualities, stress resistance, responsibility, risk propensity, attention (concentration, switching speed), functional mobility of nervous processes, spatio-temporal extrapolation, visual-motor coordination.
Police Units Serving on Water Bodies	Orientation in enclosed space, memory, balance of nervous processes, psychomotor qualities, stress resistance, attention (concentration, switching speed), functional mobility of nervous processes.

Source: compiled by the authors based on [34-41]

to representatives of the profession, and studying the professional activities of police officers.

Without the appropriate qualifications and professional qualities, a police officer cannot effectively perform their duties and ensure the safety of citizens. Therefore, in the process of developing a profession profile, it is necessary to take into account not only the specific requirements of a particular specialization, but also the general requirements for police officers regarding their professional skills and character.

Currently, within the framework of professional psychophysiological selection, a widely recognized and common approach is to conduct psychodiagnostics of the following groups of individual characteristics of the examinee: cognitive properties (attention, memory, perception, spatial orientation, spatial-temporal extrapolation), basic properties of the nervous system (strength of the nervous system, functional mobility and balance of nervous processes), psychomotor qualities (sensory-motor reactions, visual-motor coordination), adaptive reserves of the organism (reserves of vegetative functions, resistance to stress; resistance to monotony), the general level of development and characteristics of thinking (operational thinking), personal qualities (aggressiveness, responsibility, risk-taking) and neuropsychic stability [34-41].

The table 1 below lists the types of high-risk work and professionally important qualities inherent in police work.

Assessing the psychophysiological qualities of police officers is a key element of professional selection, as it allows for the selection of the most suitable candidates and increases the reliability and safety of their work. This should be a continuous process aimed at maintaining the effectiveness of law enforcement agencies.

During testing, a psychophysiologist monitors task performance, records behavioral and vegetative reactions, emotional state, attitude to the procedure, and communication characteristics, providing clarification or additional instructions as needed. Observation and interviews are important methods for diagnosing cognitive and behavioral characteristics, as well as assessing the dynamics of emotional and functional states under stress.

The results are recorded in the Psychophysiological Examination Protocol, which, together with the informed consent form, is attached to the Medical Examination Report. Candidates who are deemed «suitable» are referred to further stages of medical selection, while a decision of «unsuitable» excludes the possibility of undergoing further examinations.

The effectiveness of the psychophysiological selection system is determined by the correspondence of the predicted assessment to actual professional performance and depends on the complexity of the profession: the higher it is, the more important the accuracy of the selection.

CONCLUSIONS

The results of the analysis confirm the key role of medical and psychophysiological indicators in determining the professional suitability of police officers and justify the need to integrate modern technologies into the personnel selection system. It has been established that the psychophysiological characteristics of the candidate – the stability of the nervous system, the speed of reaction, the ability to work under stressful conditions, sensorimotor coordination – are directly related to the type of future work and the level of its safety.

Medical screening remains one of the fundamental elements of professional selection, since somatic, neurological and mental conditions significantly affect the reliability and safety of work. Modern studies confirm the feasibility of using age standards and conducting regular medical assessments of both candidates and current police officers.

International experience shows the growing importance of cognitive testing, mental health monitoring, and automated response analysis systems. Such approaches, particularly in the British model, are integrated into long-term professional development programs and allow for the formation of a more accurate and stable profile of professional suitability.

The study showed that combining medical, cognitive, and psychophysiological criteria significantly improves the quality of professional performance prediction, reduces the risk of professional burnout, and contributes to the formation of effective human resources in law enforcement agencies.

The results obtained justify the need to modernize the system of professional psychophysiological selection of the National Police of Ukraine, in particular through the introduction of modern software and hardware complexes, standardization of procedures, expansion of the range of psychophysiological indicators, and adaptation of best international practices.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 02.12.2025
ACCEPTED: 10.06.2026

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REVIEW ARTICLE

Social exclusion, social isolation, and mental health: Understanding the Ukrainian context

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ABSTRACT

Aim: The paper aims to reveal the essence of social exclusion and social isolation, their impact on mental health, and consider the experiences of Ukrainians who may potentially fall under the definition of socially excluded groups.

Materials and Methods: The study is based on a transdisciplinary approach combining socio-psychological and philosophical analysis along with narrative interviews. The authors used interpretive research paradigm, integrative anthropological approach, system-analytical, discursive, hermeneutical, and comparative approaches. For narrative interviews, methods are reported in line with COREQ. The data collection was carried out using PubMed, Scopus, Web of Science, Google Scholar databases. Research papers were identified according to search terms: "social exclusion", "socially excluded groups", "social isolation", "mental health", "well-being", "discrimination", "poverty", "belonging", "depression", "anxiety", "anger", "hopelessness", "alienation", "loneliness", "communication". To understand problems faced by those who may belong to socially excluded groups, their symbolic systems of orientations, and their coping strategies for overcoming difficulties, the narrative interview was conducted. As recent studies show, nowadays, in the context of the war with its devastating consequences, analysis of narrative interviews acquires special significance, primarily from the standpoint of analyzing the mechanisms of individual adaptation to the tragedies of the war. The authors conducted five interviews with people who potentially fall under the definition of representatives of socially excluded groups. All participants were assigned pseudonyms, ensuring confidentiality and anonymity. Interviews took place online or in-person and lasted around two hours. The participants were interviewed between January and March 2026.

Conclusions: Being one of determinants of mental health, social exclusion has become increasingly widespread in Ukraine, and the ongoing war has given rise to new groups that are currently most susceptible to social exclusion. During narrative interviews aimed at uncovering the experiences of Ukrainians who may fall into these groups, it was found that participants do not consider themselves socially excluded, although everyone talks about voluntary or involuntary social isolation that negatively affects or may affect their mental health and well-being. The narratives illustrate not only experiences of social isolation, but also the ways in which participants propose to address the unmet needs of individuals suffering from social isolation.

KEY WORDS: social exclusion, socially excluded groups, social isolation, mental health, well-being, discrimination, poverty, belonging, depression, anxiety, anger, hopelessness, alienation, loneliness, communication

Wiad Lek. 2026;79(8):1940-1951. doi: 10.36740/WLek/235897 DOI

INTRODUCTION

One of the greatest minds of humanity, Aristotle, argued that "man is naturally a political animal, and that whosoever is naturally and not accidentally unfit for society, must be either inferior or superior to man". Indeed, from the dawn of human society, human beings have formed communities to survive as a group; and every newborn member of this group has required care and attention in order to survive as an individual. We are born with all possible genetic predispositions and potential, however, what exactly will be activated and developed depends on the impact of social environment. A human being is a complex biopsychosocial-spiritual phenomenon deeply rooted in each of these realms, which are critically important for him/her. The social component of human existence has played a vital role in shaping our identities, values, behaviors, and our destinies. We become "true" humans through interactions with other people. The need for social connections is so deeply ingrained in our nature that the fate of feral people seems terrible and even unrealistic to us. Striving for social connections, friendship, acceptance, affiliation, we are subconsciously afraid of being excluded from society. Therefore, it is no wonder that ostracism in ancient Athens was one of the terrible punishments. To this day, ignoring and exclusion – components of ostracism – make us suffer sometimes even more than overt physical violence. Recent studies have

convincingly demonstrated that "people have a need to belong and that threats to belonging have very real and very devastating consequences on the individual, both psychologically and physically" [1]. And although some people strive to disappear from the social scene preferring solitude, they still do not lose the feeling of belonging, which is "a fundamental requirement for security, reproductive success, and mental health" [2]. As Baumeister and Leary put it, the need to belong is a basic human motivation [3]. Accordingly, denial of acceptance and respect, rejection, and exclusion negatively impact the emotional and cognitive spheres, and overall well-being of those excluded.

Nowadays, much research has been devoted to the problem of social exclusion and the ways to overcome it. Impacting equality, social cohesion, and well-being, "social exclusion refers to the process by which individuals or groups are systematically marginalized and denied access to essential resources, opportunities, and social networks" [4]. With its far-reaching negative consequences, social exclusion dramatically affects human lives that undermines the entire global social organism. A happy future society with all civil liberties will remain an abstract concept unless it can be supported by people's chances to realize their potential and their own life projects. Both state institutions and a civil society share responsibility for progress towards human equality and inclusion that is the matter of our human existence.

The challenges of social exclusion do not bypass Ukraine. Despite ongoing research, characteristics and dynamics of social exclusion in the Ukrainian society leave room for exploration. Initially, the challenges of social exclusion were examined through the lens of economic status, low level of income and consumption, predominantly passive type of interaction with society, deep social polarization after the collapse of the USSR, downward social mobility, unemployment, the absence or rupture of vital social ties, the lack of necessary education that ultimately leads to poverty and, consequently, the lack of representation in society [5].

In fact, the concept of social exclusion is often used as a synonym for poverty and inequality. Sometimes the concepts of poverty and social exclusion go hand in hand acting as factors that hinder social integration. However, the concept of social exclusion encompasses a broader dimension of the social world and is associated with a specific understanding that varies depending on cultural norms, values, politics, national contexts, etc. Social exclusion is not only the result of the interaction of disadvantageous factors, but also a process by which individuals or groups become or remain systematically disadvantaged [6].

In the 2009 executive summary report "Social Protection and Social Inclusion in Ukraine", it was noted that despite progress towards reducing the absolute poverty, "the Ukrainian society does not address problems of some minorities, which face social exclusion. It concerns traditionally vulnerable population groups (disabled, ethnic minorities such as Roma, Crimean Tatar, etc.) as well as new groups that appeared rather recently – HIV/AIDS-infected, drug consumers (in particular injection users), and sex minorities. Generally, tolerant attitude to such people is combined with intolerance of staying in their neighborhood, leading to social isolation of these groups in all spheres of life… The main task of new strategy is determination of groups of social exclusion and development of measures on their integration in the society" [7].

Later, scholars were focused on the exacerbation of social tension, widening income gaps, increasing restrictions on access to resources and services for a significant portion of the population, the loss of part of Ukrainian territory (before large-scale military action), internally displaced persons, marginalization of certain groups, systemic corruption, hyperinflation, low wages, unemployment, the problems of remote communities, a decrease in the level of citizens motivation, deviant and delinquent behavior in society, etc. The researchers also emphasized such issues as poor health and physical limitations; gender, age, ethnic, religious, cultural and educational discrimination; restrictions on freedom of speech; limitations in satisfying cultural needs; decreased motivation for work; low participation in the political life; increased social instability, etc. [8]. One of the most important factors of social exclusion in Ukraine is unemployment, which entails informal employment, the expansion of the shadow economy, brain drain, and labor migration abroad.

Following the outbreak of a large-scale war unleashed by Russia in 2022, the situation became even more acute, adversely affecting Ukrainian citizens. Many of them have faced combined effects of the threatening physical consequences of the war, such as death, injury, disability, sexual violence, and emotional consequences, such as anxiety, depression, post-traumatic stress disorder, as well as indirect stressors, such as death or injury of the loved ones, economic hardships, or geographic displacement. Many Ukrainians joined the armed forces to fight against the enemy. Caught up in the tornado of the war, some Ukrainian citizens were forced to leave their homes being involved into the ongoing struggle for the future without any clear resolution. By 2026, over 4.6 million internally displaced persons (IDP) have been officially registered [9]. According to the Center for Economic Strategy, as of January 2026, 5.6 million Ukrainian refu-

gees remain abroad [10]. On the other hand, the Minister of Foreign Affairs of Ukraine, Andrii Sybiha, states that, according to the Ukrainian authorities, about 8 million citizens are forced to stay in the foreign countries [11]. As the result of the war, the number of people with disabilities is constantly growing in Ukraine. As of early 2026, over 3 million people in Ukraine have disabilities. In addition, the war increased sensitivity to Russian language and sometimes gave rise to a negative attitude towards its speakers. The qualitative research conducted by the analysts from the OPORA Civil Network in 2025 emphasizes that the representatives of the above-mentioned groups, namely, the Ukrainian people staying abroad, internally displaced persons, veterans and their families, people with disabilities, and the Russian-speaking Ukrainians, are the most susceptible to social exclusion at the present time [12]. The emergence of the new excluded groups in Ukrainian society creates an additional burden on the entire system of social functioning, including the healthcare system, since social exclusion is a trigger that initiates negative processes in health and well-being. According to WHO Europe, "being excluded from the life of society and treated as less that equal leads to worse health and greater risks of premature death" [13]. The process of social exclusion increases "the risks of divorce and separation, disability, illness, addiction and social isolation and vice versa, forming vicious circles that deepen the predicament people face" [13]. Actually, all of the above groups may fall into the realm of social exclusion. However, the question arises: do members of these groups truly experience the full depth of discrimination and social exclusion, and if so, how does it manifest itself?

AIM

The paper aims to reveal the essence of social exclusion and social isolation, their impact on mental health, and consider the experiences of Ukrainians who may potentially fall under the definition of socially excluded groups.

MATERIALS AND METHODS

The study is based on a transdisciplinary approach combining socio-psychological and philosophical analysis along with narrative interviews. The authors used interpretive research paradigm, integrative anthropological approach, system-analytical, discursive, hermeneutical, and comparative approaches. For narrative interviews, methods are reported in line with COREQ [14].

The data collection was carried out using PubMed, Scopus, Web of Science, Google Scholar databases. Research papers were identified according to search terms: "social exclusion", "socially excluded groups", "social isolation", "mental health", "well-being", "discrimination", "poverty", "belonging", "depression", "anxiety", "anger", "hopelessness", "alienation", "loneliness", "communication".

To understand the problems faced by those who may belong to socially excluded groups, their symbolic systems of orientations, and their coping strategies for overcoming difficulties, the narrative interview was conducted. As recent studies show, nowadays, in the context of the war with its devastating consequences, analysis of narrative interviews acquires special significance, primarily from the standpoint of analyzing the mechanisms of individual adaptation to the tragedies of the war [15].

The authors conducted five interviews with people who potentially fall under the definition of representatives of socially excluded groups. All participants were assigned pseudonyms, ensuring confidentiality and anonymity. Interviews took place online or in-person and lasted around two hours. The participants were interviewed between January and March 2026.

To reflect the participants' experiences and to understand whether respondents see themselves as socially excluded, three subthemes were developed: feelings of social exclusion before the war, during the war, and ways to overcome it (if any). The data were interpreted by the researchers in the context of the entire story.

ETHICS

The narrative study was approved by the Ethics Committee of the Taras Shevchenko National University of Kyiv within the framework of the project #26БФ041-01.

AI STATEMENT

The authors state that no AI tools were used in writing this article.

REVIEW AND DISCUSSION

SOCIAL HARMONY, MENTAL HEALTH AND WELL-BEING ARE INEXTRICABLY LINKED. SINCE THE ADOPTION OF THE SUSTAINABLE DEVELOPMENT GOALS IN 2015, THE PREVENTION AND TREATMENT OF NON-COMMUNICABLE DISEASES, INCLUDING BEHAVIORAL AND NEUROLOGICAL DISORDERS, HAVE BECOME A PRIORITY. Mental health is linked to almost all sustainable development goals, which are universal and cover all countries in the world. Although we cannot currently eliminate the biological causes of mental disorders, it is within our power to positively influence the social

determinants of mental health, which represent a modified set of intervention targets available to prevent the onset of mental health disorders and to promote positive mental health. Social determinants of mental health encompass a set of structural conditions that influence individuals' mental health outcomes and contribute to mental health inequalities across the lifespan [16]. Social determinants of mental health "are shaped by the distribution of money, power and resources at global, national and local levels, which are themselves influenced by policy choices" [17]. As Kirkbride at al. emphasize, they are not distributed randomly, but are determined by systems and institutions of power, which often generate and reproduce intergenerational inequalities in people's opportunities to realize safe, prosperous, and healthy lives [16]. Since the risks of developing any mental disorder are inextricably linked to people's living conditions, improving population mental health by developing effective strategies for preventing social risk factors becomes a central issue of social justice [18].

One of the most important social determinants of mental health is social exclusion. According to the latest estimates, between 2.33 and 2.43 billion people (roughly 32 per cent of the global population) are at high risk of social exclusion [19]. The situation becomes even more alarming when exclusion affects multiple identities, which often intersect and reinforce exclusion, and those who bear them are subject to increased negative attitudes and discrimination. This undermines the foundations of any society, negatively impacting both physical and mental health. An fMRI study of social exclusion shows that some of the same neural mechanisms that are involved in experiencing physical pain may also be involved in experiencing social pain associated with social exclusion and rejection, therefore, social pain is similar to physical pain in its neurocognitive function [20]. Painful feelings undermine the very foundation of well-being, which is the multidimensional construct [21]. They determine the quality of life of both an individual and society [22, 23]. Social exclusion can trigger a decline in emotional, psychological and social well-being and can lead to susceptibility to maladjustment and psychopathology [24].

Excluded groups tend to perceive prejudice against themselves in a wider range of contexts than members of privileged groups often reporting physical and mental health problems. They have higher rates of morbidity and mortality, high disability rates, shorter life expectancy, high level of infant mortality; demonstrate anxiety, depression, psychological distress, lower life satisfaction, post-traumatic stress disorder, hopelessness, feelings of worthlessness, resentment, fear and may be prone to excessive alcohol consumption or drug addiction [25 – 27].

Experience of prejudice and discrimination can reduce the sense of control over own lives trapping people in meaninglessness, which is one of the most dangerous "non-protocol" situations, in which the very existence of an individual becomes worthless, with all the ensuing negative outcomes. External threats, such as the war in Ukraine, further aggravate the situation. Being adversely affected by the war, all Ukrainians can develop the typical psychological profile of trauma, mistrust, suspicion, and a sense of hopelessness that can be even more pronounced among the members of excluded groups.

Despite a number of international and national programs aimed at maintaining and improving mental health of Ukrainians, the real situation leaves much to be desired. 83% of respondents experience high levels of stress, with 78% directly linking this to a full-scale Russian invasion. Financial difficulties worry 52% of the population, and the socio-political situation is a deep concern for 47%. 39% of respondents worry about the loss of a source of income. 58% of respondents experience anxiety and tension; 50% – poor sleep; 49% – exhaustion and bad mood; 45% – emotional instability; 44% – irritation and anger [28].

Ukrainian researchers stress that the most crucial factor that affects mental health of Ukrainians is the war with Russia; and social determinants closely related to the war are the political situation, the effectiveness of public administration, the level of democracy, social conflicts, social protection, inflationary processes, corruption, migration processes, crime, the health care system [29]. All these determinants are inextricably linked to social exclusion, which, as the overall situation worsens, can affect more and more people. Even after the war ends, the spread of mental disorders resulting from it will pose a serious problem for the Ukrainian society.

The deterioration of the environmental situation in Ukraine during the war has also negatively affected mental health and well-being of Ukrainians causing anxiety, panic, depression, insomnia, fear, and uncertainty [30]. Members of marginalized and excluded groups are particularly vulnerable to such adverse outcomes and often suffer disproportionately from mental health impacts of climate change, which can worsen existing mental health inequalities, particularly where health services are scarce or inadequate [31].

To reduce the burden of mental disorders in Ukraine, it is necessary to increase social and institutional support, which requires identifying potential interventions aimed at the social determinants of mental health,

including social exclusion with special tailoring for the representatives of excluded, underprivileged groups. The Ukrainian society must realize that social exclusion is the result of structural inequality in institutional systems, which is critically important for changing society's attitude towards financing social programs aimed at excluded groups [32]. This will facilitate prioritization of targeted psychological interventions by both decision-makers and representatives of excluded groups, as within the transdisciplinary paradigm, the voices of all stakeholders matter.

Given the unprecedented burden of mental health issues in Ukraine as a result of the large-scale invasion of Russian troops, it would be advisable to identify excluded groups for interventions, as well as to understand whether all potential members of these excluded groups are such in the classical sense, whether they feel excluded from life, and if so, what ways out of the situation they see for themselves.

To gain a deeper understanding of these issues, we conducted five narrative interviews with people who may potentially fall under the definition of socially excluded groups.

The participant *Ihor* is a 50-year-old injured military veteran who believes that social inclusion is activism and demand for justice. Based on his detailed story, Ihor was not very sociable even before the war, he felt a barrier between himself and other people.

"Groups in which there was a clear leader or several leaders were not for me. Everything, everything depends on them. And others, like me, introverts, for whom a common cauldron in hell is prepared, do not feel very comfortable there"

Nowadays, in Kyiv, he feels the same detachment, partly explaining this by the fact that Kyiv is a large city. Besides, seeing strong healthy men who live peaceful lives during the war, he does not understand them. Though Ihor does not demonstrate overt aggression, but condemnation, misunderstanding, and avoidance of contact with them are clearly expressed in his statements. All this distances him from the flow of social life in Kyiv.

"You feel like a stranger among these fit guys in the gym. The feeling that they are somehow not your type… Before, I used to be irritated. Now I feel more like an alienation. Well, they are not from my circle at all. Even if they are good guys… but when there is the war in Ukraine, they are strong, and they are in the gym, it is a little different. For people who voluntary went to fight in the first days, it is a completely different pole"

Ihor has always worked in graphic design sphere, even during his military service. Today, his job is related to this field. But he does not feel like a fully-fledged civilian, although he has no plans to return to the army like his friends.

"I am no longer a soldier; I have been discharged… And I do not really consider myself a civilian"

Striving for social communication and leading a rather active lifestyle (meetings, exhibitions, concerts, improvisations, master classes, sports), Ihor would like to be part of a community, for example, a veterans' one. However, when meeting other veterans, he remains detached from communication.

"I am often told that I lead a very active social life. But in reality, I feel that I have little contact with people. I am not involved in the activities of the veteran community. I can tell you that I am a passive consumer of the services provided by veteran organizations. I just use everything. But if it were not for this veteran activity – veteran sports, I would hardly go to the gym"

As Ihor put it, he needs communication at "a grassroots level" meaning family and close friends whom he lacks. His main circle of communication is at work, more often online, and social networks. As he explains:

"Sometimes I want to communicate with colleagues… It is interesting. Working moments. It is also important. It has meaning. And also, online communication, which is necessary… they are social media friends. Friends-acquaintances with whom, for example, you correspond several times a day. This is also important. But that is all… Family, friends, close circle are my failure"

Ihor attributes his lack of communication not to the fact that he is a veteran, but to his personal traits:

"This is probably not a veteran problem, but rather my personal one. Because, apparently, there is a barrier between me and another person in any way. And I need to cross it somehow. There are such barrier-free people, but not me"

In the case of Ihor, we cannot talk about social exclusion, since many organizations actually take care of him; he is not forcibly excluded from social life. While Ihor does not experience rejection as Other in real life, he nevertheless sees it on social media and believes that state bodies should address this issue at the institutional level. In his opinion, the veteran community should have certain privileges and recognition. Revealing his need for recognition, he says:

"Veterans should have a higher status, like a higher caste. And being next to them should also be a privilege. Unfortunately, it is probably not possible for everyone… Well, even one person said that she was proud to be next to me. I like it. I remember it. This is an important point"

As Ihor put it, the current situation can be improved by creation of permanent cultural centers that will provide a platform for joint events, entertainment, dating, etc. These centers should be intended for both veterans/

military and civilians, have convenient locations, and work schedules.

"I wonder why organizations involve male and female veterans only… however, people from the street, for example, women-teachers or someone else, are not involved. That is, those people who are ready to communicate, people of the opposite sex... Personally, I would be more interested in it"

The participant *Andrii* (in his 50s) is gay who serves in the Armed Forces of Ukraine. Before serving in the army, he had to go through the difficult path of an IDP, which led him to a state of depression and loneliness.

"I felt deep depression and loneliness during the war, because I was an IDP, I was forced to live with my parents, to take care of them, although before that they were independent, and because of the war their physical and emotional states deteriorated… and I was forced to move, to live somewhere not at home, but in tents, shelters"

Andrii felt he was thrown out of the flow of life. Having lost relationships and social connections, he actively looked for work in a new place. In the army this critical situation changed: the number of contacts increased, and the IDP's narrative of chaos was replaced by strict army discipline where everything is clearly laid out. He gradually developed an awareness that he could have a good time alone. While before this situation used to stress Andrii out, he now enjoys his time alone, though he is also happy to have company.

"Mostly, when I have a day off, I am alone. And if before it drove me into depression and sadness, now I get high from it. Well, I have no excessive expectations. When it happens that I cross paths with friends, acquaintances, or strangers, it makes me happy too"

Describing social exclusion as a process or state in which people cannot exercise their right to life, cannot satisfy their basic needs and pursue their own goals, Andrii, nevertheless, reduces the topic of social exclusion to his own experience stating that as a child he was an introvert and did not feel included in society or any group.

"Being an introvert, I was so shy and quiet. It was very difficult for me to start communicating with other people"

Although he tried to develop his communication skills, he failed to overcome his lack of self-confidence, which ultimately deepened his depression leading to alcohol abuse. However, as Andrii noted, this was caused not by external conditions, but by internal factors.

"I felt bad. I wanted to kill myself literally. It was such a difficult state: depression, despair, loneliness. But it was all on my individual level, regardless of any group or community"

As a gay person, Andrii did not feel any discrimination in his pre-war social circle, however, being in the army, he conceals this information, so it is difficult to say how Andrii's life in the army would have developed under different circumstances and whether he would have felt excluded.

"My situation is somewhat unique. On the one hand, I do not want to belong to any group or community, on the other, I definitely belong to the Armed Forces of Ukraine"

Andrii emphasizes that the most important thing now is not to focus on personal issues, but to win the war. And what he is doing now gives him a sense of pride and belonging to the Ukrainian nation.

"I feel I am a part of Ukrainian society. The most important thing is the fate of Ukraine. Serving in the army has been very beneficial to me psychologically, in terms of improving myself. I believe that I have not lived my life in vain. I have learned to value myself, my experience, and my achievements"

Andrii does not seem to feel like he is part of an excluded group. His depression was more likely caused by the intersection of his personality traits and his non-traditional sexual orientation, which he is now reluctant to discuss. Today, he says, he has learned to bring his depression under control.

"As soon as I see that I have something similar to depression, I try to cheer myself up, eat something tasty, do interesting things. You prioritize yourself…"

For Andrii, prevention and reduction of social exclusion (this concept for Andrii has an individual character) can be by creating cultural and artistic centers, in which people of different ages are involved.

"The participation of people of all ages is essential, because the older you are, the more isolated you become.... I think the more different people involved in these activities, the better"

Our third participant was *Mariia* – a 60-year-old Russian-speaking woman from Kyiv who is fluent in Ukrainian. Outwardly, no different from Ukrainian-speaking inhabitants of the city, she nevertheless does not associate herself with modern Kyiv, which has become alien to her.

"I feel like a stranger in Kyiv, where I was born. I have always been surrounded by people of different nationalities who understood and valued each other for their character and dignity, not for their language. Today I feel like I am not in the city or the country where I was born"

She perceives the neglect or prohibition of Russian culture as violence, although she is not Russian. For her, the so-called Russian culture we were talking about was associated with Kyiv.

"Probably, it was the common culture that united us here. It was local Kyiv culture; we had no associations with Russia. Growing up with foundational world literature and poetry shaped our personalities, and Pushkin, Lermontov,

Esenin were among them. I am offended that what was once dear and close to me has suddenly become hostile and harmful. I do not reject other cultures, so why am I being denied mine?"

She interprets the language confrontation as an artificially created situation, comparing it to a fight over a paper map as if it were a real territory and noting that a very high price is paid by those who have nothing to do with it at all, that is, ordinary Ukrainian- and Russian-speaking people. Taking the language problem into a wider realm, Mariia argues that this is not so much a problem of language per se, but rather a social, political, and cultural problem.

"I am outraged that they threw the baby out with the bathwater. And someone has earned financial and social capital... Although they may not believe in what they stand for. People are simply being butted heads; and behind the scenes, completely different games are being played. And those top players do not care that people die every day, the country is being destroyed, and that human life is worthless"

Mariia pursues her scholarly career, participates in humanitarian projects; she gives the impression of an open-minded and sociable person. According to her, she does not feel socially excluded and she personally has never been rejected or marginalized based on her mother tongue. Mariia has only observed such conflicts on social media. However, today she cut herself off from extensive communication.

"I do not feel socially excluded. On the contrary, I am involved in many groups. I just do not believe in anything anymore… From my perspective, normal interaction is when you can be yourself without playing any roles and meeting someone's expectations; and mutual acceptance is a must. There is less and less of this now, so I try to distance myself from unnecessary communication. It is my own choice, even though I am not a classic introvert. But I just get tired of people"

Despite her disappointment, Mariia believes that the situation can be changed. She states that many people have lost meaning in life now; and therefore, systemic changes are needed at all levels and in all social institutions, starting with the family.

"We need to revise all levels of education; change the academic world, media resource; develop social, economic, cultural life, etc. We need political will. And first and foremost, we have to realize that every person holds inherent value, every person is a small universe inseparably linked to the infinite universe. As for small steps, we need centers where people can freely express themselves, their positions and be heard. Where everyone can identify him/herself not as They, but as We. Different cultures that enrich each other should be represented there"

The threat of social exclusion was much more serious in a conversation with internally displaced persons. This time, our participants were *Nataliia* (58 y. o.) and *Oleh* (70 y. o.), a married couple who moved to Kyiv from the Donetsk region. Being well-respected members of the community well prepared for retirement, they suddenly lost everything they had worked for all their lives. Describing her situation, Nataliia emphasizes the attitude towards them before and after the loss:

"On top of everything else, you lose your social position. My husband was a media personality, and everyone knew him. We could turn to people anytime, and the attitude was completely different. Before the war, we were working hard, renovating our house, preparing for retirement. If we had known there would be the war, we certainly would not have done what we did. This war took everything away"

Deprived of everything, hoping for help and understanding, Nataliia and Oleh encountered rejection and downright rude treatment from social services in Kyiv that deeply hurt them and made them feel homeless. Undisguised bitterness and resentment are evident in Nataliia's words:

"They treat you like "What are you doing here?" We were, excuse me, going from one stop to the next like homeless people… And when we left the office, I was hysterical; I could not stop myself; I was just bursting with rage. And you really do feel like you are homeless"

Indeed, homelessness is a significant risk factor for social exclusion; it affects both people without a roof over their heads and those living in unstable conditions. Homelessness also represents the absence or weakening of the connections that bind people together in a network of interconnected social structures. This ultimately leads to marginalization, including housing and financial difficulties, as well as non-participation in social and political life [33]. Describing their difficult emotional state during the first year and a half, Nataliia and Oleh spoke about their ordeals associated with compensation for lost housing, which, as it turned out, was not provided for them. They are elderly people with health issues, so finding work was also very difficult. They truly found themselves disconnected from life, with little hope and no plans for the future.

"This exclusion from social life offends people. We need to rent an apartment; we simply need to survive. People have a problem; the state draws up regulations, but cannot solve it. We have nothing. My husband had spinal surgery, so physical work is not an option. We do not know what to do. I cannot predict the future, I do not know what will happen tomorrow, because we have no solid ground"

Despite depression, despair and hopelessness, the couple found donors, and Oleh began publishing a newspaper, which he did in his hometown. The newspa-

per serves a tool for communication within their home community. This activity is aimed at restoring lost connections that Nataliia and Oleh are so deeply distressed about, and it fosters their sense of belonging to their community and, more broadly, to the Ukrainian society.

"We do everything we can for our society. We want our community to be united. And the newspaper unites us as a connecting link between people"

The couple emphasizes that people, who fled the war but did not lose their homes, do not understand a total loss. Nataliia and Oleh are very vocal about creating organizations for internally displaced persons where their specific problems would be understood and aid would be provided.

"It is important to create centers and organizations for internally displaced persons. Everyone has suffered, and they do not have a roof over their heads. Financial assistance is desperately needed, especially for large families, the disabled, and pensioners. After all, the worst thing is that they do not have home"

The fifth participant was 45-year-old *Anna*, who left Ukraine after the start of the large-scale invasion and settled in Belgium with her two children. She met her husband there, and they had a child. Today, she is a mother of three and a French language student. In Ukraine, she felt a sense of belonging to various social groups; she was active and energetic. Relocation to another country radically changed her perception of the world and her habitual way of life. Anna says she never truly became part of a new society. Her only contacts are her children and her husband.

"When you have friends and regular meetings, you feel like you belong to a group. For example, in Ukraine, I was a member of a parents' committee; we did things together for our children and for our school. Today I feel isolated; I am in a foreign country with a different mindset. Apart from my child's father, I hardly know anyone in this country, and I miss social interactions. I do not understand how to fit into this Belgian society"

Anna occasionally meets with her husband's family, but her lack of language skills makes communication difficult, and she feels excluded from the communication process.

"My husband's family members speak French. Sometimes I understand a little, and sometimes I do not understand at all. I feel isolated. If I had different communication and a different family, it would not hurt so much"

Another disappointment for Anna was the way her husband's family treated her during her pregnancy. According to her, no one paid special attention to her poor health. It was such a shock, since, she says, in Ukrainian families everyone asks how you are doing, but there, it is not customary.

"Lately, I have realized it is not just a language issue, but also that people genuinely do not care. I was so disappointed that no one supported me. There were emotions, thoughts, even physical sensations... I realize they are not my family anymore"

There had also been an incident at her job before the birth of her child. Although Anna thought she had a relatively smooth relationship, the sudden dismissal was like a cold shower. Having high hopes, striving to understand a different mindset and become part of a team, Anna experienced deep disappointment which negatively impacted her self-esteem and trust in people.

"I was really, really upset… I could not believe this was happening to me. It really hurt me that I could not get the results I wanted. I wanted the contract… It affected my self-confidence. It affected my trust in people. You have to understand that any employer tries to exploit you. And no one wants to help you; it is every man for himself"

Despite caring for her family and three children, Anna feels very lonely. Communication with Ukrainians also failed. She feels quite comfortable communicating with her fellow students, but she understands that this communication will end with the end of her studies.

"I do not feel like I belong to any group. I have really lost myself"

Anna experiences the invisible losses of emigration, which are now common to millions of Ukrainians who found themselves abroad due to the war. The loss of a sense of security, social status, belonging, sociocultural and linguistic environment generates anxiety, stress and can lead to psychological problems. Though this state does not fall under the definition of social exclusion, it can lead to it, as these symbolic losses may result in isolation and marginalization.

Each of the presented stories is in a way unique. Certainly, all participants were impacted by the war that has changed their life, beliefs, values, and goals. However, just as not everyone experiences post-traumatic stress disorder, not all people who have undergone the above-described life changes fall within the definition of socially excluded. In some cases, it is appropriate to speak not of social exclusion, but of social isolation, which has key differences from social exclusion, although it can act as a precursor to social exclusion.

Though both social exclusion and social isolation refer to situations in which people are detached from society, "social isolation is conceptualized and operationalized as an individual-level characteristic of being detached from social contacts, whereas social exclusion emphasizes broader and multifaceted or multidimensional societal conditions that produce poverty and inequality which reduce people's abilities to participate in society"

[34]. "Sorting" according to social inclusion/exclusion is always a collective process.

In contrast to social exclusion, social isolation (individual exclusion) is an individual process that is an individual-level characteristic of being separated from the community and having unsatisfactory social relationships. This concept is still much less debated in political and social contexts than social exclusion [34], however, it is also a significant determinant of physical and mental health [35].

Social isolation is defined as "a state in which the individual lacks a sense of belonging socially, lacks engagement with others, has a minimal number of social contacts, and they are deficient in fulfilling and quality relationships" [36]. Unlike social exclusion, which is always involuntary, social isolation can be voluntary and involuntary. Some people choose to limit their social interactions due to their personality type, for personal reflection and inner growth, or rest. Being a deliberate choice, social isolation (solitude, "me time") can be beneficial because it connects us with ourselves; it provides emotional and mental recharge, personal development, stimulates creativity, improves decision-making [37].

However, more often than not, people find themselves isolated involuntarily, due to external circumstances, such as the loss of loved ones, injury, physical disabilities, displacement, systemic social conditions. In this case, a person wants social interaction but cannot get it. Sometimes involuntary isolation is caused by deeply rooted fears such as social anxiety, fear of negative evaluation, trauma, which makes communication painful [38]. Long-term involuntary isolation is widely recognized by psychologists as a major risk factor for deterioration of physical and mental well-being. Research demonstrates the negative impact of social isolation on the cardiovascular, immune, and neuroendocrine systems. Affecting mental health, social isolation causes depression, anxiety, suicidal thoughts, emotional distress, the development of dementia, premature death and poor health behaviors, sustained decreases in feelings of wellbeing [39; 40].

As can be seen from the participants' stories, all of them, to varying degrees, feel the negative impact of social isolation, but it cannot be said that any of them are systematically marginalized, subjected to systemic discrimination as members of a particular group, and forcibly deprived of access to necessary resources, opportunities, and social connections. While it is certainly true that a combination of social factors and their attitudes can determine exclusionary behavior and that characteristics specific to members of each of these groups may play a more important role in explaining the prevalence of these attitudes than individual traits, however it does not necessarily mean social exclusion. This is evidenced by the statements of participants:

Exclusion is probably not a veteran problem, but rather my personal one (Ihor)

In my case, exclusion is individual, when you somehow forcibly limit yourself, or are ashamed, or are in such a depressive state (Andrii)

I do not feel socially excluded. It is my own desire to be alone (Mariia)

We cannot predict the future, because we do not know what will happen, because we have no solid ground… But we feel, of course, part of society. We are part of the Ukrainian people (Nataliia i Oleh)

I miss social interaction. I have been excluded because I do not know the language and have a different mentality. I have not formed my own social circle yet (Anna)

Although the participants do not exhibit pronounced social exclusion as a result of their existential and social experiences of the war, they are still at risk and may ultimately form socially excluded groups. Therefore, today it is necessary to pay close attention to people experiencing social isolation to ensure that they do not join the ranks of socially excluded groups. To deal with this pressing issue, it is necessary to develop a multidimensional approach that is tailored to individual needs and that addresses both psychological and social aspects. It seems reasonable to take into account the ideas of the interview participants on how to improve the current situation (specialized centers that meet the needs of the groups).

LIMITATIONS AND FUTURE RESEARCH DIRECTIONS

Narrative interviews were conducted with only a few participants, who could potentially represent different socially excluded groups. Hence, caution should be taken with generalizing the findings. At the same time, this study may provide an avenue for more complex, transdisciplinary research at the intersection of mental health, psychology, sociology, public administration, political science, and philosophy.

CONCLUSIONS

Being one of determinants of mental health, social exclusion has become increasingly widespread in Ukraine, and the ongoing war has given rise to new groups that are currently most susceptible to social exclusion. During narrative interviews aimed at uncovering the experiences of Ukrainians who may fall into these groups, it was found that participants do not consider themselves socially excluded, although everyone talks about voluntary or

involuntary social isolation that negatively affects or may affect their mental health and well-being. The narratives illustrate not only experiences of social isolation, but also the ways in which participants propose to address the unmet needs of individuals suffering from social isolation.

Addressing social exclusion and social isolation requires a combination of systemic policies (anti-discrimination laws, economic reforms, inclusive public infrastructure) aimed at tackling social exclusion and impactful interventions (mental health support, relationship building, community groups, etc.) designed for confronting social isolation. Therefore, it is necessary to develop a long-term transdisciplinary strategy that would take into account both actual mechanisms operating in the context of social exclusion and intervention measures at the level of social isolation.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 18.03.2026
ACCEPTED: 29.07.2026

CREATIVE COMMONS 4.0

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REVIEW ARTICLE

Medication-related osteonecrosis of the jaw: Current concepts in epidemiology, pathophysiology, diagnosis, and management

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ABSTRACT

Aim: The aim of this review was to highlight the ongoing challenge of medication-related osteonecrosis of the jaw (MRONJ) in everyday clinical practice.
Materials and Methods: This review was conducted following a structured narrative approach, utilizing PubMed as the primary research database. The following keywords and their combinations with Boolean operators (AND, OR) were used: MRONJ, osteonecrosis, bisphosphonates, bone density conservation agents, denosumab. The literature search spanned publications from 2003 to April 2025, corresponding to the first description of bisphosphonate-related osteonecrosis of the jaw by Marx and subsequent evolution of the diagnostic and therapeutic concepts. The final set of 32 articles were reviewed and synthesized narratively.
Conclusions: Management strategies are examined across disease stages, from conservative measures and pharmacologic interventions to surgical resection and reconstruction. Emerging therapies, including teriparatide, hyperbaric oxygen, platelet-rich preparations, and cryosurgery, show promise as adjunctive treatments. Prevention remains paramount, emphasizing pre-treatment dental evaluation, patient education, and interprofessional collaboration.

KEY WORDS: bisphosphonates, osteonecrosis, denosumab, MRONJ, bone density conservation agents

Wiad Lek. 2026;79(8):1952-1959. doi: 10.36740/WLek/222500 DOI

INTRODUCTION

Medication-Related Osteonecrosis of the Jaw (MRONJ) is a severe and multifaceted adverse drug reaction that predominantly affects patients undergoing treatment with antiresorptive agents–such as BP (bisphosphonates) and denosumab–and, increasingly, antiangiogenic drugs used in oncologic and antineoplastic regimens [1,2]. The jawbone's unique anatomy, vascularization, and constant exposure to microtrauma and microbial flora make it particularly susceptible to the effects of these agents [3,4].

First identified by Marx in 2003, the condition was originally classified as Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ) [5] However, over time, reports of similar necrotic lesions associated with other agents prompted the American Association of Oral and Maxillofacial Surgeons (AAOMS) to adopt a more inclusive term–MRONJ–in its 2014 position paper. This term reflects a wider etiological scope and aligns with the evolving pharmacologic landscape of bone-modifying agents[6].

The AAOMS defines MRONJ by the following diagnostic criteria:

1. Current or previous treatment with antiresorptive or antiangiogenic agents;
2. Exposed bone or bone that can be probed through a fistula in the maxillofacial region persisting for more than eight weeks;
3. No history of radiation therapy to the jaws or metastatic disease involving the jawbones.

Under normal physiological conditions, mucosal healing following dental extraction or trauma is expected within approximately eight weeks. Persistence of bone exposure beyond this timeframe is therefore considered pathological [7].

The impact of MRONJ extends beyond localized bone necrosis. Patients frequently experience pain, impaired mastication, difficulties in speech, and compromised oral hygiene, all of which contribute to diminished quality of life [8,9]. In oncologic settings, the development of MRONJ may necessitate modification or discontinuation of essential systemic therapies, potentially affecting overall disease management.

Despite increasing awareness, MRONJ remains a diagnostic and therapeutic challenge. Its clinical course is often unpredictable, and management strategies vary depending on disease stage and patient-related factors. Early-stage disease may respond to conservative approaches, whereas advanced cases often require surgical intervention and long-term follow-up [10].

This review provides a comprehensive overview of MRONJ, focusing on epidemiology, risk factors, pathophysiology, clinical presentation, diagnostic modalities, and current treatment strategies, with particular emphasis on recent advances in imaging and adjunctive therapies.

AIM

The aim of this review was to highlight the ongoing challenge of medication-related osteonecrosis of the jaw (MRONJ) in everyday clinical practice. This remains an important issue for clinicians, as MRONJ is associated not only with bisphosphonates but also with denosumab, introduced in 2010 as a potentially safer alternative, which has likewise been linked to this condition. The review summarizes current knowledge on epidemiology, pathophysiology, diagnosis, and treatment, with a practical focus on prevention and on selecting appropriate management strategies based on disease severity in daily patient care.

MATERIALS AND METHODS

This review was conducted following a structured narrative approach, utilizing PubMed as the primary research database. The following keywords and their combinations with Boolean operators (AND, OR) were used: MRONJ, osteonecrosis, bisphosphonates, bone density conservation agents, denosumab. The literature search spanned publications from 2003 to April 2025, corresponding to the first description of bisphosphonate-related osteonecrosis of the jaw by Marx and subsequent evolution of the diagnostic and therapeutic concepts.The final set of 32 articles were reviewed and synthesized narratively.

ETHICS

All sources used in this literature review are publicly available.

AI STATEMENT

The author states that no AI tools were used in writing this article.

REVIEW AND DISCUSSION

EPIDEMIOLOGY

The true prevalence of MRONJ is difficult to determine due to variations in diagnostic criteria, underreporting, and heterogeneity among studies. A recent global scoping review by Clark and Glenny reported a pooled incidence rate of approximately 4.34%, though values ranged widely [11]. The incidence is markedly higher among cancer patients receiving high-potency intravenous bisphosphonates (such as zoledronic acid) or subcutaneous denosumab for skeletal metastases, with rates between 1% and 15%, and in some high-risk groups, even higher [12,13]. In contrast, MRONJ is less common in osteoporotic populations, with reported incidence typically between 0.01% and 0.3%. Nonetheless, given the vast number of patients treated for osteoporosis globally, the absolute number of MRONJ cases in this group remains clinically significant [14].

Risk factors include invasive dental procedures (particularly extractions), poor oral hygiene, use of corticosteroids, diabetes, smoking, and longer duration or higher cumulative doses of antiresorptive drugs. Females, especially postmenopausal women, appear more susceptible, likely due to the higher prevalence of osteoporosis and related treatments. MRONJ is more common in the mandible (up to 73% of cases) than in the maxilla, likely due to differences in vascularization and bone density. It is more frequently unilateral but may be bilateral in advanced cases or in patients with prolonged drug exposure [15,16].

PATHOPHYSIOLOGY

The pathogenesis of MRONJ is multifactorial and involves a combination of impaired bone remodeling, suppression of angiogenesis, microbial infection, immune dysregulation, and local trauma. Antiresorptive medications such as BP (bisphosphonates) bind avidly to hydroxyapatite and inhibit osteoclastic bone resorption, resulting in reduced turnover and accumulation of microdamage. Denosumab, a monoclonal antibody against RANKL, also suppresses osteoclast-mediated resorption but through a different mechanism [17].

The inhibition of bone turnover impairs the jaw's capacity to recover from physiological microtrauma and surgical insult. Antiangiogenic agents like bevacizumab further compromise vascular supply, leading to hypoxia and necrosis. Local infection, often by Actinomyces species, exacerbates tissue damage [18].

Table 1. Staging system for MRONJ based on „AAOMS American Association of Oral and Maxillofacial Surgeons' Position Paper on MRONJ–2022 Update

Stage	Bone condition	Infection/ inflammation	Symptoms	Anomalies
Stage 0	No clinical evidence of necrotic bone	-	tooth pain without an identifiable dental (odontogenic) origin dull, aching jawbone pain, potentially radiating to the temporomandibular joint (TMJ) area maxillary sinus discomfort, possibly accompanied by mucosal thickening and inflammation changes in neurosensory perception	alveolar bone loss or resorption not attributable to chronic periodontal disease. altered trabecular bone pattern, with sclerotic changes and absence of new bone formation in extraction sockets. osteosclerotic areas involving the alveolar and/or adjacent basal bone. thickening or obscuration of the periodontal ligament, including lamina dura sclerosis and narrowing of the periodontal ligament space
Stage 1	Exposed necrotic bone or bone probeable through a fistula	-	- symptom-free	radiographic changes characteristic of Stage 0 may also be observed, limited to the alveolar bone
Stage 2	Exposed necrotic bone	+	symptoms characteristic of Stage 0 may also be observed	radiographic changes characteristic of Stage 0 may also be observed, limited to the alveolar bone.
Stage 3	Exposed necrotic bone	+	one or a combination of: necrotic bone exposure beyond the alveolar region (e.g., mandibular border/ramus, maxillary sinus, zygoma) pathologic fracture extraoral fistula oral antral or oral/nasal communication osteolysis reaching the mandibular border or sinus floor	radiographic findings are more advanced

Source: compiled by the authors based on [7]

Contributing systemic factors include diabetes, corticosteroid therapy, malnutrition, and genetic predisposition. Recent evidence suggests that mucosal integrity may be compromised in MRONJ patients, facilitating bacterial invasion and promoting chronic inflammation. The cumulative effect is progressive bone necrosis with delayed or absent healing [19].

CLINICAL PRESENTATION AND STAGING

MRONJ presents with a broad spectrum of clinical manifestations, ranging from asymptomatic bone exposure to severe pain, swelling, purulent discharge, halitosis, trismus, fistula formation, and pathological fractures. Although often triggered by dental extraction or trauma, spontaneous cases are also observed.

The American Association of Oral and Maxillofacial Surgeons (AAOMS) has established a clinical staging system for MRONJ in American Association of Oral and Maxillofacial Surgeons' Position Paper on MRONJ–2022 Update encompassing Stages 0 through 3. This framework assists clinicians in assessing disease severity and provides standardized terminology for diagnosis and management. However, the treatment strategies associated with each stage require further evidence-based validation. This association identifies Stage 0 MRONJ as a potential precursor to more advanced stages of the disease in this Position paper, they emphasizes the importance of early identification and management of Stage 0 MRONJ to prevent progression (Table 1) [7].

IMAGING AND DIAGNOSTIC TOOLS

Accurate diagnosis relies on a combination of clinical examination and imaging. Panoramic radiography is commonly used as an initial assessment tool but lacks sensitivity for early disease.

Cone-beam computed tomography (CBCT) has become the preferred modality due to its ability to detect subtle osseous changes, including cortical disruption,

Table 2. Management strategies

Type of management	Indications	Menagement strategies
Conservative management	Stage 0 Stage 1 a selected cases	chlorhexidine rinses analgesics antimicrobial therapy (e.g., penicillin, clindamycin) routine follow-up emphasizes oral hygiene and non-surgical stabilization of dental conditions
Surgical management:	Stage 2 required for most Stage 3 cases	debridement of necrotic bone and surrounding granulation tissue sequestrectomy to remove loose necrotic fragments resection (marginal or segmental) in advanced cases reconstruction using local flaps (e.g., buccal fat pad), pedicled flaps, or vascularized free tissue transfer Perioperative antibiotics and sterile technique are vital to reduce recurrence. Adjunctive use of CBCT and intraoperative navigation improves precision.

Source: compiled by the authors based on [33]

sequestrum formation, and trabecular alterations. It is particularly valuable in early-stage disease.

Magnetic resonance imaging (MRI) provides superior soft tissue contrast and enables detection of bone marrow changes, often preceding visible bone exposure. T1-weighted images typically demonstrate hypointensity in necrotic regions, while T2-weighted sequences may reveal surrounding inflammation.

Additional modalities, such as bone scintigraphy, SPECT, and PET/CT, may be useful in selected cases but are limited by lower specificity.

The Composite Radiographic Index (CRIm) has emerged as a quantitative tool for assessing radiological severity and correlates with clinical staging, offering potential value in monitoring disease progression [21].

HISTOPATHOLOGY

Histopathological evaluation, though not mandatory in all cases, provides important confirmation of diagnosis and differentiation from other osseous pathologies such as malignancy, osteoradionecrosis, or chronic osteomyelitis.

Typical histopathological findings in MRONJ include:

· non-vital lamellar bone with empty osteocytic lacunae

· prominent cement lines and bacterial colonization on bone surfaces

· chronic inflammatory infiltrates composed of lymphocytes and plasma cells

· surface biofilms containing Actinomyces-like colonies

· surrounding fibrosis and granulation tissue encasing necrotic bone

These findings support the hypothesis that MRONJ lesions are typically initiated by aseptic osteonecrosis, which becomes secondarily colonized by bacteria. Immuno-histochemistry may occasionally be required to exclude neoplastic processes [22].

MANAGEMENT STRATEGIES

Management strategies presented in Table 2.

Repeat imaging and clinical examination are recommended at regular intervals. Healing can range from complete mucosal coverage to partial response or relapse requiring further intervention [23].

ADJUNCTIVE THERAPIES

Recent advances have highlighted the role of several adjunctive therapies in enhancing healing or reducing MRONJ progression.

• **Teriparatide** is an anabolic drug based on a fragment of parathyroid hormone (PTH 1–34) that helps the body build new bone by activating bone-forming cells (osteoblasts). It appears to work especially well in osteoporotic patients with early stages (Stage 1 or 2) of MRONJ. Studies show that treatment with teriparatide can improve bone density and reduce the size of bone lesions.

• **Hyperbaric oxygen therapy (HBOT)** involves breathing pure oxygen in a pressurized chamber, which increases the amount of oxygen reaching poorly supplied tissues. This helps stimulate the formation of new blood vessels and supports healing of soft tissues. It's often used before or after surgery, especially in more difficult or resistant cases. However, its use is limited because it requires many treatment sessions and access to specialized, often expensive equipment.

• **Low-level laser therapy (LLLT)** helps cells work more efficiently by boosting energy production in mitochondria and reducing inflammation. When combined with standard treatments, it can speed up healing of the mucosa and help relieve pain.

• **Cryosurgery** uses liquid nitrogen applied after surgical cleaning of the area to destroy dead (necrotic) tissue while leaving healthy bone intact. This helps clearly separate the damaged tissue from the healthy part and supports new bone formation. Early reports suggest that this method may lower the risk of recurrence and speed up healing.

Other investigational therapies have also emerged, including the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), both of which are aimed at enhancing local tissue regeneration. Ozone therapy has been explored for its antimicrobial and regenerative properties, while probiotic therapy is being studied for its ability to modulate the oral microbiota and reduce pathogenic colonization. Although these approaches are not yet incorporated into standardized clinical protocols, they represent promising directions for future MRONJ research and integrative care strategies

One substance that is worth mentioning is quercetin. It's a natural plant compound with anti-inflammatory and antioxidant effects that may support bone healing in MRONJ. It can influence osteoclasts and osteoblasts and reduce oxidative stress, but for now, the evidence comes mainly from lab and animal studies, with no strong clinical proof in patients yet [24-28].

PREVENTION

Prevention remains the cornerstone of MRONJ management. Pre-treatment dental evaluation is essential, particularly in oncology patients. Elimination of potential infection sources and completion of invasive procedures prior to therapy initiation significantly reduce risk. In patients already receiving antiresorptive treatment, invasive procedures should be minimized where possible. When unavoidable, careful surgical technique, antibiotic prophylaxis, and primary wound closure are recommended. The role of drug holidays remains controversial and should be considered on an individual basis, in collaboration with the prescribing physician. Effective prevention requires close interdisciplinary cooperation between dental and medical professionals [29,30].

DISCUSSION

MRONJ presents one of the most complex iatrogenic complications encountered in dental and medical practice, particularly due to its variable clinical course, multifactorial etiology, and challenges in early detection. As this review demonstrates, although substantial progress has been made in characterizing its pathophysiology and treatment options, gaps in knowledge continue to obstruct consensus in clinical practice [1,6,7,11,16].

A major point of concern remains the disparity in incidence data between osteoporotic and oncologic populations, and even within those subgroups depending on drug type, route of administration, and treatment duration. This variation complicates universal risk assessment and calls for stratified prevention protocols tailored to patient type. Moreover, inconsistent use of diagnostic criteria, particularly in borderline or Stage 0 cases, complicates both clinical interpretation and scientific comparison across studies [11,31].

Surgical and conservative treatments continue to evolve, with many clinicians advocating for minimally invasive protocols, particularly in early stages. However, surgical resection remains indispensable for advanced MRONJ. The integration of digital planning, 3D prototyping, and guided resection marks a significant improvement in surgical precision and postoperative outcomes. Adjunctive therapies such as teriparatide and cryosurgery offer exciting possibilities but require further validation through randomized controlled trials and long-term follow-up [7, 10, 32, 33].

Furthermore, the ethical and clinical dilemma of drug discontinuation continues to divide practitioners. While a drug holiday might mitigate MRONJ risk, especially in low-risk osteoporotic patients, it carries potential harm in cancer patients with skeletal metastases. [7] Prospective studies and clinical guidelines must better define the thresholds at which temporary cessation becomes more beneficial than harmful.

In terms of imaging, the increasing use of CBCT and the development of radiographic indices such as CRIm provide opportunities for earlier detection and better monitoring of treatment outcomes. Similarly, MRI's capability to detect bone marrow changes opens the door for preclinical identification of at-risk patients, though accessibility and cost remain barriers in many healthcare systems [21].

On a systemic level, there is a need for more robust educational efforts directed at both patients and non-dental healthcare providers. The oral manifestations of systemic medications are often underappreciated, leading to delayed referrals or inappropriate interventions. Interprofessional education and collaboration will be essential in improving outcomes [30].

Finally, the promise of personalized medicine–through genetic profiling, biochemical markers, and individualized imaging analytics–may revolutionize MRONJ risk prediction and therapy selection. Integration of such innovations into mainstream clinical practice will depend on multi-institutional collaboration and appropriate funding mechanisms. Until

then, meticulous preventive care, timely intervention, and coordinated management remain the bedrock of successful MRONJ care. The growing body of literature on MRONJ underscores the condition's complexity and the pressing need for evidence-based, multidisciplinary management. Despite increasing awareness, significant challenges remain regarding the timely identification of at-risk individuals, optimization of therapeutic strategies, and balancing the benefits of antiresorptive therapy with the risk of osteonecrosis [16,27,30].

The pathophysiology of MRONJ highlights the synergistic interplay between impaired bone remodeling, compromised vascularity, local trauma, and bacterial colonization. Understanding this interplay is critical for selecting the most appropriate interventions. For instance, early-stage MRONJ may benefit from conservative treatment, while advanced disease often necessitates surgical resection and reconstruction. However, the role of adjunctive therapies–ranging from teriparatide to hyperbaric oxygen–remains an active area of debate, with mixed outcomes reported in clinical trials [26,27,28].

Prevention is widely regarded as the cornerstone of MRONJ management. Yet, there is no consensus on the optimal strategy, particularly regarding drug holidays. This calls for more rigorous, prospective research to define risk-benefit thresholds. Similarly, variation in diagnostic criteria and staging systems hinders inter-study comparisons and evidence synthesis [7].

A shift toward personalized medicine, incorporating genetic, biochemical, and imaging markers, may enable risk-adapted therapy. Future guidelines should integrate these advances, offering dynamic, patient-specific protocols rather than static stage-based recommendations.

Ultimately, enhancing MRONJ outcomes will require better integration of dental and medical care. Dental professionals must be actively involved in treatment planning for patients prescribed antiresorptives, while physicians should be educated on oral health implications. Multidisciplinary collaboration and patient-centered care are pivotal in reducing the burden of MRONJ [29,30].

CONCLUSIONS

Medication-related osteonecrosis of the jaw is an increasingly recognized complication of antiresorptive and antiangiogenic therapies. Its multifactorial etiology, complex clinical course, and significant impact on patient quality of life make it a critical concern for both dental and medical professionals.

This review has outlined the current understanding of MRONJ, emphasizing the importance of early diagnosis, individualized treatment planning, and proactive prevention strategies. With innovations in imaging, surgical techniques, and adjunctive therapies, management outcomes are gradually improving.

Nonetheless, substantial gaps remain, particularly in identifying high-risk individuals, standardizing treatment protocols, and integrating care across disciplines. Addressing these gaps will require ongoing research, international cooperation, and continued investment in both clinical and translational science.

By fostering a multidisciplinary and evidence-driven approach, we can reduce the incidence of MRONJ, enhance therapeutic outcomes, and improve the overall well-being of patients undergoing vital skeletal therapies.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 18.03.2026
ACCEPTED: 26.05.2026

CREATIVE COMMONS 4.0

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REVIEW ARTICLE

Current aspects of the etiopathogenesis of antiphospholipid syndrome and its clinical manifestations

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ABSTRACT

Antiphospholipid syndrome is a systemic autoimmune disorder characterized by the persistent presence of antiphospholipid antibodies and a predisposition to arterial, venous, and microvascular thrombotic manifestations. In this article, the authors analyzed the available literature sources in the PubMed, Scopus, Web of Science, and Google Scholar databases for the period from 2019 to 2026, focusing on the epidemiological, gender-related, etiopathogenetic, clinical, and diagnostic aspects of antiphospholipid syndrome. Antiphospholipid syndrome emerges as a systemic immune-vascular nosological entity in which cerebrovascular and cardiovascular manifestations constitute the main clinical phenotype and determine the long-term prognosis of the disease. Understanding antiphospholipid syndrome as a unified immune-coagulation process is of fundamental importance for clinical practice, as it provides a basis for more accurate risk stratification, early identification of patients with a high probability of severe vascular complications, and the development of pathogenetically substantiated therapeutic methods targeting not only the coagulation cascade but also the immune and inflammatory components of the disease. Such an integrative approach is fundamental to optimizing treatment and improving the prognosis of patients with antiphospholipid syndrome.

KEY WORDS: antiphospholipid syndrome, literature data analysis, etiopathogenesis, clinical manifestations.

Wiad Lek. 2026;79(8):1960-1972. doi: 10.36740/WLek/235900 DOI

INTRODUCTION

Antiphospholipid syndrome is a systemic autoimmune pathology characterized by the persistent presence of antiphospholipid antibodies and a predisposition to arterial, venous, and microvascular thrombotic manifestations [1, 2]. Its pathogenesis extends beyond the classical concepts of thrombophilia and combines immune, coagulation, and inflammatory mechanisms, forming a systemic process [3]. The relevance of an in-depth study of antiphospholipid syndrome is determined by the high clinical significance of its vascular manifestations, primarily cerebrovascular, cardiovascular, and obstetric complications, which determine the prognosis, level of disability, and mortality of patients. Particular attention should be paid to the fact that severe thrombotic complications in antiphospholipid syndrome often occur at a young age and in the absence of traditional cardiovascular risk factors, which complicates their early diagnosis and prevention [4].

However, despite the substantial body of accumulated data on the immunopathogenesis of antiphospholipid syndrome, the scientific literature is still dominated by a fragmented analysis of individual clinical manifestations without sufficient emphasis on their pathogenetic unity. Current concepts of immunothrombosis allow cerebrovascular, cardiac, obstetric, and other organ lesions to be regarded as different manifestations of a single systemic process; however, such a perspective requires further generalization and conceptual understanding. The relevance of this study lies in the systematic analysis of antiphospholipid syndrome from the perspective of the unity of immunothrombotic mechanisms, with particular emphasis on obstetric manifestations as a distinct pathogenetic phenotype, as well as their relationship with cerebrovascular and cardiovascular lesions, which provides a basis for a more comprehensive assessment and improvement of current methods for the diagnosis, treatment, and prevention of antiphospholipid syndrome.

AIM

The aim of the study is to summarize current concepts of antiphospholipid syndrome as a systemic immune-vascular disorder, taking into account the pathogenetic unity of its manifestations, which constitute the main clinical manifestations and determine the prognosis of the disease.

MATERIALS AND METHODS

The study analyzed literature data published between 2019 and 2026 addressing the epidemiological, gender-related, etiopathogenetic, clinical, and diagnostic aspects of antiphospholipid syndrome. The literature search was conducted in the PubMed, Scopus, Web of Science, and Google Scholar databases.

REVIEW AND DISCUSSION

Antiphospholipid syndrome is a rare systemic autoimmune disease, the epidemiological study of which is complicated by a combination of clinical heterogeneity, variability in diagnostic criteria, and differences between the presence of antiphospholipid antibodies and clinically manifest syndrome [5, 6]. Review and population-based studies agree that the prevalence of antiphospholipid syndrome itself in the general population is low, whereas seropositivity for antiphospholipid antibodies is considerably more common and is not always accompanied by the development of clinical manifestations [5, 7].

According to a population-based registry study, the incidence of antiphospholipid syndrome is approximately several cases per 100,000 persons per year, while its prevalence is several dozen cases per 100 000 population, confirming the rare nature of this disease [8]. Similar rates were also obtained in a nationwide population-based study in South Korea, where the standardized incidence and prevalence of antiphospholipid syndrome remained consistently low throughout the observation period, despite increased awareness and improved diagnosis [9]. The synthesis of these data in recent reviews suggests that substantial differences between countries more often reflect methodological differences between studies rather than true epidemiological disparities [5].

Analysis of the age and gender distribution demonstrates a clear predominance of women among patients with antiphospholipid syndrome, which is consistent with the general patterns of autoimmune diseases [1, 7]. The highest frequency of diagnosis occurs in young and middle-aged individuals, with a particular concentration of cases among women of reproductive age, which is partly associated with the obstetric manifestations of the syndrome and more active screening in this population [10, 11]. At the same time, population-based data indicate that antiphospholipid syndrome may first manifest at any age, including old age, although the incidence of new cases is lower in older age groups [8].

Geographic variability in the prevalence and incidence of antiphospholipid syndrome remains a matter of debate, as studies conducted in Europe, North America, and Asia demonstrate generally comparable rates when standardized diagnostic criteria are applied [9]. At the same time, in regions with limited access to laboratory diagnostics and specialized medical care, the prevalence of the syndrome may be underestimated, as supported by individual regional reports, particularly those concerning pregnant women in African countries [12]. These data emphasize the influence of organizational and social factors on the detection of antiphospholipid syndrome, rather than solely true differences in its biological prevalence.

In modern medicine, antiphospholipid syndrome is regarded not as a collection of individual clinical manifestations but as an independent autoimmune nosological entity that develops at the intersection of immunological abnormalities and characteristic vascular and obstetric disorders [13]. The defining feature of the syndrome is not the isolated presence of thrombosis or other manifestations, but their combination with the persistent presence of antiphospholipid antibodies, which gives the clinical manifestations a systemic and recurrent character [14]. It is this conceptual unity of clinical and laboratory features that allows antiphospholipid syndrome to be regarded as a distinct pathological entity rather than as a complication of other diseases or a coincidental combination of symptoms.

Etiologically, antiphospholipid syndrome is a multifactorial disease, the development of which is determined by a combination of genetic predisposition, acquired immune abnormalities, and the effects of external triggering factors. At the current stage of understanding antiphospholipid syndrome, its etiology is not regarded as the result of the isolated influence of a single factor but is interpreted within a complex model that combines immunological determinants with the conditions for the development of a pathological response [15]. Thus, the central etiological link in the development of antiphospholipid syndrome is the formation of antiphospholipid antibodies, primarily antibodies against β2-glycoprotein I (β2GPI), which arise as a result of impaired immune tolerance to endogenous phospholipid-binding proteins. Structural changes in β2GPI caused by its binding to negatively charged phospholipids or by oxidative stress are believed to pro-

mote the exposure of immunodominant epitopes and the initiation of an autoimmune response [14]. Thus, autoantibody formation is not a random phenomenon but rather the result of specific molecular conditions that provide the basis for immune aggression.

An important component of the etiology of antiphospholipid syndrome is genetic predisposition, which determines individual susceptibility to the formation of antiphospholipid antibodies and thrombotic complications. Although a specific «antiphospholipid syndrome gene» has not been identified, the role of genetic factors is supported by associations with certain HLA alleles, as well as with genes involved in the regulation of the immune response and hemostasis [16]. However, the genetic background is regarded not as a determining factor but as a modulating factor that increases the likelihood of the development of the pathological process in the presence of additional triggers.

Etiologically significant external factors include infectious agents, medications, and other conditions capable of inducing or temporarily increasing the production of antiphospholipid antibodies. The infection-induced presence of antiphospholipid antibodies is described as a consequence of molecular mimicry or nonspecific activation of the immune system; however, only in a proportion of cases does it progress to clinically significant antiphospholipid syndrome [17]. This observation emphasizes the fundamental difference between the transient presence of antiphospholipid antibodies and antiphospholipid syndrome itself as a nosological entity.

In this context, the «second hit» concept is of key etiological importance, according to which the presence of antiphospholipid antibodies creates only a potential predisposition to thrombotic manifestations, whereas their clinical development requires an additional triggering factor, such as inflammation, infection, hormonal changes, surgical interventions, or vascular injury [18]. This model explains the variability in the clinical course of antiphospholipid syndrome and the intermittent nature of thrombotic complications.

Currently, primary and secondary antiphospholipid syndromes are traditionally distinguished. Primary antiphospholipid syndrome is diagnosed in the absence of another systemic autoimmune disease, whereas secondary antiphospholipid syndrome develops in the setting of systemic lupus erythematosus or other immune-inflammatory conditions. This distinction has not only formal but also pathophysiological and clinical significance, as secondary antiphospholipid syndrome is more often associated with a broader spectrum of immune abnormalities and a more complex clinical course [1]. At the same time, recent reviews emphasize that, in terms of the mechanisms of thrombosis and immune activation, primary and secondary forms of the syndrome share many common features, which calls into question their strict distinction as separate diseases [19, 20].

A significant methodological challenge remains the relationship between so-called «classical» antiphospholipid syndrome, which meets the current classification criteria, and the spectrum of non-criteria manifestations that fall outside the formal diagnostic framework [14].

The classification criteria were developed primarily to standardize research and do not encompass all possible clinical phenotypes of the syndrome, as confirmed by data from multinational cohort studies [21]. In this context, the concept of «non-criteria» antiphospholipid syndrome is increasingly used to reflect clinical reality but requires cautious application to avoid unjustified expansion of the diagnostic criteria. Current expert publications emphasize that non-criteria manifestations may have prognostic significance; however, they should not, by themselves, be automatically interpreted as confirmation of the presence of the syndrome [23].

Also important for understanding antiphospholipid syndrome is a clear distinction between the isolated presence of antiphospholipid antibodies and clinically manifest syndrome. Population-based studies and recent reviews consistently indicate that the presence of antiphospholipid antibodies in blood serum is considerably more prevalent than the syndrome itself, and most antiphospholipid antibodies-positive individuals never develop clinical manifestations characteristic of antiphospholipid syndrome [1]. This distinction is of fundamental importance for both epidemiological assessment and clinical practice, since equating antibody positivity with the syndrome leads to an overestimation of prevalence rates and potential overdiagnosis [23]. Therefore, in current conceptual studies, antiphospholipid syndrome is defined as the result of the interaction between immunological predisposition and additional triggering factors, rather than as an inevitable consequence of the presence of antiphospholipid antibodies [24].

Current diagnosis of antiphospholipid syndrome is based on a comprehensive assessment of clinical manifestations and laboratory findings. In 2023, the American College of Rheumatology and the European Alliance of Associations for Rheumatology proposed new classification criteria requiring the presence of at least one clinical manifestation of antiphospholipid syndrome and one positive antiphospholipid antibody test performed within three years of the onset of clinical manifestations [6]. Further assessment is performed using a scoring system that takes into account clinical features (venous and arterial thrombosis, microvascular and obstetric manifestations, heart valve involvement,

and hematological abnormalities) and laboratory parameters (lupus anticoagulant, anticardiolipin antibodies, and anti-β2GPI antibodies) [25]. To establish antiphospholipid syndrome, at least three points must be obtained separately for the clinical and laboratory criteria. Another general diagnostic algorithm for antiphospholipid syndrome involves the assessment of clinical manifestations, laboratory testing for the main antiphospholipid antibodies, and repeat testing after 12 weeks to confirm their persistence [23]. Particular attention is also paid to risk stratification, as the most unfavorable prognosis is more characteristic of patients with lupus anticoagulant and high titers of anticardiolipin and anti-β2GPI antibodies [1].

Cerebrovascular and cardiovascular manifestations of antiphospholipid syndrome result from an integrated immune-coagulation process in which autoantibodies, blood cells, the endothelium, complement, and inflammation act as a mutually reinforcing system that stabilizes the prothrombotic state. This pathogenetic chain should be regarded not as a sum of isolated abnormalities but as a form of so-called immunothrombosis, in which thrombus formation becomes the effector phase of chronic immune activation [26].

The formation and functional activity of anti-β2GPI antibodies are considered the key immunopathogenetic link, conferring specificity on antiphospholipid syndrome and explaining its systemic thrombotic potential [27]. According to current concepts, β2GPI acts as a central cofactor that ensures the binding of immune complexes to cell surfaces and the translation of the autoimmune signal into a procoagulant response [28]. Anti-β2GPI antibodies increase tissue factor expression in endothelial cells and monocytes, thereby promoting activation of the coagulation cascade, enhancing thrombin generation, and facilitating coagulation [19].

For cerebral and cardiac vessels, the key factor is that, in response to antiphospholipid antibodies, the endothelium shifts from a vasoprotective state to an activated, prothrombotic phenotype [3]. This activation is accompanied by increased expression of adhesion molecules, enhanced interactions with leukocytes and platelets, and alterations in the local regulation of hemostasis, which promote the adhesion of cellular aggregates and the formation of a thrombotic substrate. Importantly, antiphospholipid antibodies are capable of inducing proinflammatory and procoagulant signals in the endothelium, causing the vascular wall itself to actively support thrombogenesis [18, 20]. In this sense, endothelial dysfunction is not merely a «background» condition but a central link that directly connects the systemic autoimmune trigger with local cerebrovascular and coronary manifestations.

In parallel with the endothelium, platelet activation is an important factor contributing to the predisposition to thrombosis; in antiphospholipid syndrome, it exhibits features of persistent hyperreactivity and may be regarded as one of the mechanisms maintaining the risk of arterial manifestations and complications. In patients with primary antiphospholipid syndrome, markers of increased platelet activation are detected, which is consistent with the concept of enhanced aggregation and increased propensity for thrombus formation [30]. Platelet activation is pathogenetically significant not only because of aggregation but also because of the involvement of platelets in intercellular communication, particularly in their interactions with the endothelium and leukocytes and in the maintenance of local inflammation [26].

A link that amplifies and «consolidates» vascular injury is activation of the complement system, which in antiphospholipid syndrome is regarded as a universal mechanism for amplifying the immune signal and coagulation response. Complement can exacerbate endothelial dysfunction, increase the expression of tissue factor (TF, CD142), and thereby integrate immune reactions with the blood coagulation cascade [31]. In current models of pathogenesis, complement is regarded not as a peripheral component but as a fully integrated link that mediates the transition from antibody-mediated activation to clinically significant thrombosis, including microvascular lesions [32].

Inflammation in antiphospholipid syndrome is not merely a secondary response to thrombosis but is a component of the aforementioned conceptual pathogenetic chain of «immune activation + endothelial dysfunction + coagulation». The concept of immunothrombosis emphasizes that elements of innate immunity, proinflammatory mediators, and cellular effectors form a microenvironment in which thrombus formation becomes a physiologically «supported» response [33]. In this context, antiphospholipid syndrome is regarded as a condition in which the immune response and hemostasis function as a unified system, while its vascular manifestations represent a predictable final manifestation of systemic imbalance [1].

The clinical and pathogenetic reality of the systemic risk of thrombotic manifestations and complications is confirmed by data indicating a high risk of their recurrence in patients with antiphospholipid syndrome, particularly in high-risk groups, which indicates the persistence of pathogenetic imbalance even during treatment. This predisposition to recurrent complications is consistent with the concept of sustained endothelial activation maintained by autoantibodies and inflammatory mechanisms [23].

The mechanistic unity of arterial, venous, and microvascular thrombosis in antiphospholipid syndrome requires particular attention, as it allows for an understanding of the systemic nature of the vascular manifestations of the disease and explains their occurrence in different vascular beds in the presence of a common immunological background. Unlike classical thrombotic conditions, in which the localization of thrombosis is often determined predominantly by hemodynamic factors or structural characteristics of the vascular wall, in antiphospholipid syndrome the decisive role is played by systemic immunopathogenetic activation, which creates a universal prothrombotic environment regardless of vessel type [26, 34]. Despite substantial differences between arterial, venous, and microvascular circulation, particularly in terms of flow velocity, pressure, and other parameters, a common pathogenetic mechanism is reproduced in all these vessels in antiphospholipid syndrome. Its main components include the persistent effects of antiphospholipid antibodies, activation of vascular wall cells and blood cells, development of endothelial dysfunction, involvement of platelets and the complement system, as well as the formation of a local proinflammatory microenvironment that maintains and enhances thrombus formation [19]. The recurrence of this set of mechanisms across different vascular beds indicates that thrombosis in antiphospholipid syndrome is a consequence not of local injury but of a systemic immune-coagulation imbalance. Therefore, this approach allows arterial, venous, and microvascular thrombosis to be regarded not as separate phenotypes but as different clinical manifestations of a single pathogenetic process modified by local vascular conditions [35]. In this context, antiphospholipid syndrome fundamentally differs from «classical» inherited or acquired thrombophilias, which are characterized by the predominance of defects in the coagulation cascade in the absence of a pronounced immune component.

Thus, the pathogenetic mechanisms of antiphospholipid syndrome discussed above form a universal immune-dependent basis for the development of vascular lesions in various organs and tissues. At the same time, the clinical significance of these mechanisms is most clearly manifested in the cerebral vasculature, where even minor thrombotic or microcirculatory changes lead to severe and often irreversible consequences. Therefore, the following discussion focuses on cerebrovascular and cardiovascular disorders in antiphospholipid syndrome, which represent one of the leading clinical phenotypes of the disease, determine patient prognosis, and at the same time reflect the key pathogenetic principles characteristic of systemic vascular pathology in antiphospholipid syndrome.

Ischemic stroke is one of the most common and clinically significant arterial manifestations of antiphospholipid syndrome and occupies a leading position in the spectrum of its cerebrovascular complications [36]. According to large prospective and multicenter studies, stroke accounts for a substantial proportion of arterial thromboses in antiphospholipid syndrome and is often the first manifestation of the disease, which determines its high diagnostic and prognostic significance. Particular attention is drawn to the association of antiphospholipid syndrome with ischemic stroke at a young age, when traditional vascular risk factors are often absent or minimally expressed [4]. A systematic review examining the prevalence of antiphospholipid antibodies in young adults with cerebrovascular disorders showed that antiphospholipid antibodies are detected in a substantial proportion of patients with ischemic stroke or transient ischemic attacks, at rates significantly higher than those observed in the general population [37], which confirms the role of antiphospholipid syndrome as one of the leading non-traditional risk factors for stroke in young individuals.

The association between antiphospholipid antibodies and ischemic stroke in young patients has been demonstrated in classical neuroepidemiological studies, in which the presence of antiphospholipid and/or anticardiolipin antibodies correlated with an increased risk of cerebral ischemia [38]. Moreover, this association is independent of traditional vascular risk factors, which emphasizes the pathogenetic specificity of antiphospholipid syndrome [36].

A distinct characteristic of the cerebrovascular manifestations of antiphospholipid syndrome is the tendency toward recurrent ischemic stroke. Prospective observations and analyses of risk factors for recurrent thrombosis indicate that in patients with antiphospholipid syndrome, the risk of recurrent arterial thrombotic complications remains elevated even during standard antithrombotic therapy [39]. This is consistent with the concept of a persistent immunopathogenetic imbalance that is not completely eliminated even when the coagulation cascade is controlled.

An important aspect of stroke risk in antiphospholipid syndrome is the patients' serological profile. Studies have shown that the presence of antiphospholipid antibodies, as well as positivity for multiple types of these antibodies, correlates with a higher likelihood of arterial thrombotic complications, including ischemic stroke [40]. High-risk serological profiles are considered a tool for the stratification of patients with cerebrovascular manifestations of antiphospholipid syndrome.

Transient ischemic attacks are also an important, although often underestimated, component of the

spectrum of cerebrovascular manifestations of antiphospholipid syndrome and are regarded as one of the forms of its arterial manifestation. In clinical series and review articles, transient ischemic attacks are described as a common initial manifestation of cerebrovascular involvement in antiphospholipid syndrome, preceding the development of a full-blown ischemic stroke [24].

Available data indicate that transient ischemic attacks in antiphospholipid syndrome are not incidental but reflect the same immune-thrombotic mechanism that underlies ischemic stroke. In a systematic review examining the prevalence of antiphospholipid antibodies in young patients with cerebrovascular manifestations, transient ischemic attacks were considered together with ischemic stroke as part of a single pathological continuum, confirming their common pathogenetic basis [41].

The particular significance of transient ischemic attacks in antiphospholipid syndrome lies in their prognostic role. Accumulated data indicate that transient ischemic attacks in patients with antiphospholipid syndrome may serve as predictors of subsequent cerebrovascular manifestations, particularly ischemic stroke [1, 4, 34]. Such a sequence of events is consistent with the concept of persistent vascular activation and chronic immune-coagulation imbalance characteristic of antiphospholipid syndrome.

From a pathogenetic perspective, transient ischemic attacks in antiphospholipid syndrome should not be regarded as a «mild» or clinically insignificant form of cerebrovascular pathology. On the contrary, their occurrence reflects temporary but recurrent ischemia caused by activation of the endothelium, platelets, and the coagulation cascade involving antiphospholipid antibodies. Thus, transient ischemic attacks are a manifestation of the same systemic process that, if it progresses further or is inadequately controlled, may lead to irreversible ischemic damage to brain tissue.

Thus, cerebrovascular disorders in antiphospholipid syndrome should be regarded not as an isolated chain of thrombotic manifestations but as one of the clinical manifestations of a systemic immune-thrombotic process that develops against the background of the persistent effects of antiphospholipid antibodies [44]. In the presence of a common immunological background, the brain represents a particularly vulnerable target due to the combination of its high metabolic sensitivity, the complex organization of the microcirculatory bed, and the limited compensatory capacity of the cerebral circulation.

Importantly, the development of cerebrovascular disorders in antiphospholipid syndrome is not limited to a single pathogenetic mechanism. Within a unified systemic process, both arterial thrombotic manifestations in the cerebral vascular bed and cardioembolic mechanisms associated with valvular involvement or intracardiac thrombus formation, as well as microvascular forms of brain injury, may develop [40]. The described variability in the pathways of ischemia does not contradict the thrombotic nature of antiphospholipid syndrome but, on the contrary, emphasizes its multifocal and systemic nature.

Particular attention in this context should be paid to the microvascular component, which reflects the ability of antiphospholipid syndrome to manifest at the level of the cerebral microcirculation even in the absence of large-vessel occlusion. Thus, microcirculatory and microperfusion disturbances are regarded as a functional continuation of systemic immune-endothelial activation and may determine both subclinical and clinically significant manifestations of cerebrovascular dysfunction [45, 46].

Cerebrovascular disorders in antiphospholipid syndrome should be regarded not as localized involvement of an individual vascular bed but as one of the clinical manifestations of systemic vascular pathology caused by the persistent effects of antiphospholipid antibodies. Arterial thrombosis, microvascular lesions, and cardioembolic mechanisms underlying stroke and transient ischemic attacks are simultaneously involved in the development of cardiac and pulmonary vascular complications. In this context, the analysis of cardiovascular manifestations of antiphospholipid syndrome is essential for a comprehensive understanding of the systemic nature of the syndrome and the relationship between cerebral and cardiac vascular complications.

Antiphospholipid syndrome is associated with a broad spectrum of cardiovascular lesions involving both arterial and venous vascular beds, as well as cardiac structures. Cardiovascular manifestations of antiphospholipid syndrome are not limited exclusively to the consequences of classical thrombus formation but develop as a result of the aforementioned combination of immune-mediated endothelial activation, a prothrombotic state, and chronic vascular inflammation, leading to involvement of the coronary arteries, valvular apparatus, pulmonary vasculature, and intracardiac structures [47, 48].

Arterial thromboses are among the cardiovascular manifestations of antiphospholipid syndrome. They predominantly include coronary artery involvement with the development of ischemic heart disease. Coronary manifestations in antiphospholipid syndrome often occur in patients without classical risk factors for atherosclerosis, which emphasizes the independent role of immune mechanisms in the pathogenesis of coronary vascular involvement [49, 50]. In such cases,

coronary artery thrombosis may occur in the presence of minimal or even absent atherosclerotic changes, which distinguishes antiphospholipid syndrome from classical atherothrombotic ischemic heart disease [51].

Myocardial infarction is another clinically significant, although relatively rare, manifestation of antiphospholipid syndrome and is of particular importance in young patients. Data from the RATIO study convincingly demonstrated that the presence of antiphospholipid antibodies is significantly associated with an increased risk of myocardial infarction in young women, independently of traditional cardiovascular risk factors [52]. In the large prospective Euro-Phospholipid Project, myocardial infarction was documented as one of the major arterial manifestations in patients with confirmed antiphospholipid syndrome and was associated with increased mortality [2].

Venous thromboses are the most common form of vascular involvement in antiphospholipid syndrome and include deep vein thrombosis and pulmonary embolism. Venous thrombus formation in antiphospholipid syndrome is caused by a combination of a hypercoagulable state, endothelial and platelet activation, and impaired fibrinolysis, which distinguishes this syndrome from isolated inherited thrombophilias [53]. In turn, pulmonary embolism may be either a primary manifestation of antiphospholipid syndrome or a consequence of recurrent venous thrombosis, providing a basis for the subsequent development of pulmonary vascular complications [54].

Pulmonary hypertension occupies a special place among the cardiovascular manifestations of antiphospholipid syndrome and may develop as a result of chronic thromboembolic obstruction of the pulmonary arteries or microvascular thrombotic lesions of the pulmonary vascular bed [55]. Systematic reviews indicate that pulmonary hypertension in antiphospholipid syndrome is an underestimated complication and often has a progressive course, which significantly worsens patient prognosis [56, 57]. Importantly, antiphospholipid antibodies may serve as an independent risk marker for the development of pulmonary hypertension even in the absence of clinically apparent episodes of acute pulmonary embolism.

Valvular heart lesions are a characteristic, although often subclinical, feature of antiphospholipid syndrome. The most typical morphological variant is nonbacterial thrombotic endocarditis (Libman-Sacks endocarditis), which manifests as leaflet thickening, vegetations, and varying degrees of regurgitation [58, 59] Such lesions are associated with the persistent presence of antiphospholipid antibodies and may serve as a source of cardioembolic complications, including cerebral ones. Thus, echocardiographic studies indicate that valvular changes in antiphospholipid syndrome often progress over time, even in the absence of an infectious process [60].

At the same time, current research increasingly emphasizes the reconsideration of the reproductive manifestations of antiphospholipid syndrome as a distinct clinical and pathogenetic phenotype that reflects the systemic nature of immunothrombosis and determines the course of pregnancy and perinatal outcomes [11]. Reproductive manifestations of antiphospholipid syndrome have independent clinical significance and at the same time reflect the systemic nature of the disease. They occur in women of reproductive age, form a significant proportion of perinatal complications and losses and form a significant medical and social burden due to miscarriage, preeclampsia, fetal growth retardation and premature birth [6] Epidemiologically, placental-mediated complications predominate among the obstetric manifestations of antiphospholipid syndrome [5]. Thus, according to the EUROAPS registry, among 1 000 cases of antiphospholipid syndrome in pregnant women, the rate of miscarriage was approximately 38.6%, early preeclampsia 18.1%, and early fetal growth restriction 16.1%. Placental dysfunction is the pathophysiological basis of these manifestations [61]. At the same time, clinical data on the insufficient efficacy of standard antithrombotic prophylaxis (low-dose acetylsalicylic acid in combination with low-molecular-weight heparin) indicate that perinatal complications in antiphospholipid syndrome «are not limited to «classical» thrombosis but develop through a more complex cascade of immune-inflammatory-coagulation reactions» [62, 63].

In current studies of pathogenesis, the concept of «placental immunothrombosis» is gaining increasing support, defining the reproductive manifestations of antiphospholipid syndrome as a tissue-specific phenotype of systemic immunothrombosis. In this model, the placenta is regarded as a target organ characterized by unique processes of trophoblast invasion, spiral artery remodeling, and the need to maintain a delicate immune tolerance within the «mother-placenta-fetus» system [26, 64]. The initial trigger is the interaction of antiphospholipid antibodies, primarily anti-β2GPI antibodies, with the trophoblast and endothelium, which initiates cellular activation, impairs the invasive and differentiation potential of the trophoblast, and contributes to impaired placental development even before the establishment of mature placental perfusion [30]. Placental dysfunction and its associated clinical manifestations (early or severe preeclampsia, fetal growth restriction, and preterm birth) are not «late» consequences of incidental thrombosis but

rather expected outcomes of early placentation failure, exacerbated by a local thrombo-inflammatory microenvironment [65]. Subsequently, the link between autoimmune activation and coagulation within the placenta is mediated by the complement system. In antiphospholipid syndrome, complement is not merely a marker but an effector of injury and the C5a fragment is capable of inducing the recruitment and activation of innate immune cells and enhancing tissue factor expression, thereby shifting the balance toward a procoagulant state [31, 66]. In parallel, neutrophil activation occurs with the formation of «neutrophil extracellular traps» (NETs), which link inflammatory and coagulation mechanisms by damaging the trophoblast and promoting microthrombosis. These structures consist of networks of extracellular DNA associated with proteases, are formed by activated neutrophils, damage the endothelium and trophoblast, and provide a matrix for microthrombus formation, thereby linking inflammatory and coagulation mechanisms within the placental circulation [67]. Collectively, these processes sustain endothelial dysfunction, microvascular perfusion disturbances, and microthrombosis, which are of particular clinical significance in the placenta, since even moderate changes in microcirculation may result in significant hypoxia and fetoplacental insufficiency [26]. Thus, individual clinical manifestations of the obstetric phenotype of antiphospholipid syndrome reflect different aspects of a unified immunothrombotic cascade. Early reproductive complications are associated primarily with impaired implantation and trophoblast invasion, preeclampsia with endothelial dysfunction and complement-mediated inflammation, while fetal growth restriction and preterm birth result from chronic placental insufficiency caused by microthrombosis and impaired placental perfusion. Epidemiological data are additionally consistent with this model: positivity for antiphospholipid antibodies is associated with an increased risk of fetal growth restriction, reflecting the placenta-mediated nature of a substantial proportion of perinatal complications [68].

The described concept most consistently explains the limitations of antithrombotic prophylaxis. If primary trophoblast injury, complement-dependent inflammation, and cytotoxicity associated with the formation of NETs develop during the early stages of placentation, then anticoagulation, while reducing the risk of thrombosis, is not always capable of neutralizing the immune-inflammatory mechanisms underlying impaired placentation and subsequent placental insufficiency [26, 63]. Clinical data indicate that even with standard prophylactic therapy, the risk of complications remains elevated in patients with an unfavorable antiphospholipid antibody profile, particularly in the presence of lupus anticoagulant, anticardiolipin antibodies, and anti-β2GPI antibodies. According to the results of the PREGNANTS study, this group showed a reduced live birth rate (to approximately 30%) and increased rates of preeclampsia, fetal growth restriction, and stillbirth [69]. In this case, targeted modulation of the effector mechanisms of immunothrombosis appears promising. For example, experimental data demonstrate that hydroxychloroquine may prevent complement-dependent placental and fetal injury by reducing C5a levels without altering antibody titers. This study supports the hypothesis that a combined effect on coagulation and immune-inflammatory mechanisms is necessary [70].

Clinically, these mechanisms manifest as characteristic complications reflecting different stages and components of impaired placental function. In particular, individual clinical manifestations develop as a consequence of the predominance of specific components of the immunothrombotic cascade. Thus, early pregnancy loss in antiphospholipid syndrome results from impaired implantation and early placentation caused by the interaction of antiphospholipid antibodies with the trophoblast. Anti-β2GPI antibodies inhibit the invasive capacity of the trophoblast, impair its proliferation and differentiation, and promote local complement activation, leading to cellular injury during the early stages of placental development [11]. As a result, adequate implantation and early uteroplacental blood flow fail to develop, clinically manifesting as recurrent miscarriages [65].

Preeclampsia in antiphospholipid syndrome results from systemic and local endothelial dysfunction that develops under the influence of complement-dependent inflammation and immunothrombosis. Complement activation, particularly the generation of C5a, induces the expression of tissue factor CD142, endothelial activation, and neutrophil recruitment, thereby promoting the activation of inflammatory and coagulation mechanisms [64, 71]. Impaired spiral artery remodeling and reduced placental perfusion, in turn, lead to the development of hypoxia, the release of antiangiogenic factors, and the development of the clinical picture of preeclampsia, which is often early-onset and severe [3, 72].

Fetal growth restriction in antiphospholipid syndrome is a direct consequence of chronic placental dysfunction that develops in the setting of impaired blood flow in small vessels and immunothrombotic processes within the placenta. As a result, microthrombosis, cellular injury, and endothelial dysfunction reduce the efficiency of oxygen and nutrient transport, leading to chronic fetal hypoxia. At the same time, defective trans-

formation of the spiral arteries reduces the adaptive capacity of placental blood flow, clinically manifesting as fetal growth restriction [73].

Preterm birth is also mentioned among the complications; however, it is predominantly iatrogenic and results from severe placenta-mediated complications, particularly preeclampsia or fetal growth restriction. Progressive placental insufficiency, inflammatory-coagulation activation, and deterioration of fetal condition necessitate early delivery to reduce the risk of perinatal complications. In some cases, local inflammation and activation of innate immunity play an additional role and may contribute to the premature onset of labor [74].

Stillbirth in antiphospholipid syndrome is also associated with severe placental insufficiency, extensive microthrombosis, and impaired fetoplacental circulation. Complement-mediated injury, activation of NETs, and persistent placental hypoperfusion play a major role in the pathogenesis, leading to fetal hypoxia [69, 75]. These processes reflect the most severe degree of placental dysfunction in antiphospholipid syndrome. Thus, as mentioned above, the reproductive manifestations of antiphospholipid syndrome represent a tissue-specific manifestation of systemic immunothrombosis at the placental level, where the interaction of immune, inflammatory, and coagulation mechanisms leads to the development of placental dysfunction and associated perinatal complications.

Isolated cases of antiphospholipid syndrome associated with peripartum cardiomyopathy have also been described in the literature [76]. It has been suggested that endothelial dysfunction, microvascular thrombosis, and the hypercoagulable state characteristic of antiphospholipid syndrome may contribute to the development of myocardial dysfunction in the postpartum period.

Of fundamental importance for a comprehensive understanding of antiphospholipid syndrome is the recognition of the common vascular mechanisms underlying lesions of the brain, heart, and placenta. In all these vascular beds, a universal pathogenetic scenario is repeated: the effects of antiphospholipid antibodies, endothelial activation, involvement of platelets and complement, formation of a proinflammatory microenvironment, and development of thrombotic and microcirculatory disturbances. At the same time, the differences between cerebrovascular, cardiac, and obstetric manifestations of antiphospholipid syndrome are determined not so much by differences in the nature of the pathological process as by the characteristics of the local vascular bed and organ-specific susceptibility to ischemia [76].

However, it should once again be emphasized that antiphospholipid syndrome is a systemic vascular-immune nosological entity in which clinical manifestations are not limited to large arterial or venous thromboses. Along with cerebrovascular, cardiac, and obstetric disorders, a broad spectrum of other systemic manifestations is observed in antiphospholipid syndrome, reflecting the generalized nature of endothelial dysfunction, microvascular thrombus formation, and chronic inflammation [77].

For example, neurological complications in antiphospholipid syndrome extend beyond ischemic stroke and transient ischemic attacks and may also include cognitive impairment, headache, epileptic seizures, and other manifestations of central nervous system dysfunction resulting from a combination of recurrent microischemic events, chronic disturbances of cerebral microcirculation, and the direct immune-mediated effects of antiphospholipid antibodies on cerebral microcirculation [44, 78]. The presence of such manifestations is associated with a more severe course of the disease and an increased risk of future thrombotic complications.

Renal involvement in antiphospholipid syndrome, collectively referred to as antiphospholipid nephropathy, is a characteristic example of organ-specific microvascular pathology. It includes thrombotic lesions of intrarenal arterioles and capillaries, leading to arterial hypertension, proteinuria, and progressive decline in renal function [79]. Antiphospholipid nephropathy is regarded as a marker of systemic microangiopathy and correlates with high cardiovascular risk, particularly with the incidence of arterial thrombosis [80, 81].

Cutaneous manifestations, such as livedo reticularis, livedo racemosa, ulcerative lesions, and necrosis, are among the earliest and most visually apparent signs of systemic vascular involvement in antiphospholipid syndrome. They reflect impaired microcirculation and thrombosis of small cutaneous vessels and are often associated with central nervous system or renal involvement, underscoring their prognostic value [1].

Hematological manifestations, primarily thrombocytopenia, are a common finding in antiphospholipid syndrome and have a complex pathogenetic basis. Despite the reduced platelet count, thrombocytopenia in antiphospholipid syndrome does not reduce the risk of thrombosis but, on the contrary, is often associated with an increased thrombotic risk, reflecting the paradoxical combination of immune-mediated platelet destruction and platelet activation [82]. The presence of hematological abnormalities is regarded as an additional marker of systemic disease activity.

An important conceptual aspect is the relationship between these systemic lesions and the risk of cardio-

vascular complications. Neurological, renal, cutaneous, and hematological manifestations are not isolated phenomena but develop against a common immunopathogenetic background with arterial and venous thromboses. Their presence indicates generalized involvement of the vascular endothelium and microcirculation and should be regarded as a factor associated with an unfavorable prognosis for the development of severe cardiovascular complications.

CONCLUSIONS

Antiphospholipid syndrome emerges as a systemic immune-vascular nosological entity in which cerebrovascular and cardiovascular manifestations constitute the main clinical phenotype and determine the long-term prognosis of the disease. Understanding antiphospholipid syndrome as a unified immune-coagulation process is of fundamental importance for clinical practice, as it provides a basis for more accurate risk stratification, early identification of patients with a high probability of severe vascular complications, and the development of pathogenetically substantiated therapeutic methods targeting not only the coagulation cascade but also the immune and inflammatory components of the disease. Such an integrative approach is fundamental to optimizing treatment and improving the prognosis of patients with antiphospholipid syndrome.

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CONFLICT OF INTERESTS

The Authors declare no conflict of interest

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RECEIVED: 08.03.2026
ACCEPTED: 27.07.2026

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REVIEW ARTICLE

Investigating the association between genetic factors and the mechanisms underlying post-traumatic stress disorder development

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ABSTRACT

Aim: To investigate the association between the main mechanisms underlying the post-traumatic stress disorder development and polymorphisms in genes encoding regulatory proteins, their receptors, and those regulating the functioning of dopaminergic, serotonergic and other neurobiological systems.

Materials and Methods: As part of the preparation of this review, a search for publications was conducted in the PubMed, Scopus and ResearchGate databases. Keywords relating to the genetic aspects of post-traumatic stress disorder and the functioning of dopaminergic, serotonergic and other neurobiological systems were used to select the relevant literature. The analysis included studies from the last decade that examined single-nucleotide polymorphisms and their impact on the pathophysiological mechanisms that may lead to post-traumatic stress disorder.

Conclusions: The study of polymorphisms in genes associated with the regulation of metabolic changes not only deepens our understanding of the pathogenesis of the disorder but also opens up new avenues for research aimed at identifying risk biomarkers and clarifying the mechanisms of stress reactivity. Further work in this area has the potential to lay the foundations for more accurate predictive models and the development of innovative therapeutic strategies.

KEY WORDS: post-traumatic stress disorder, pathogenesis of PTSD, serotonergic systems, dopaminergic systems, risk biomarkers, personalised approaches

Wiad Lek. 2026;79(8):1973-1981. doi: 10.36740/WLek/235901 DOI

INTRODUCTION

Post-traumatic stress disorder (PTSD) is one of the most serious problems in modern psychiatry and public health, as its development is linked to exposure of traumatic events, which can occur both in armed conflicts and in civilian life. PTSD is characterised by a range of symptoms that significantly reduce quality of life and affect a person's social functioning and work capacity. According to the DSM-5, the clinical manifestations of this disorder include intrusive memories, sleep disturbances, anxiety, emotional instability and avoidance of activities associated with the traumatic experience [1]. The persistence of symptoms for at least one month is a diagnostic criterion for PTSD, and the clinically administered CAPS-5 scale is used to assess their severity [2]. Research into this disorder is of not only medical but also social significance, as PTSD affects an individual's ability to adapt to society, their capacity for professional activity and their interpersonal relationships.

A nationwide cross-sectional study was recently carried out, involving over three thousand people. Its aim was to investigate the prevalence of stress, anxiety and symptoms of post-traumatic stress disorder amongst Ukrainians as a result of the full-scale russian invasion. The participants were divided into three groups: those who had not changed their place of residence; internally displaced persons; and a third group – those who had moved abroad. According to the results obtained, it was found that 50.8% of those who had not changed their place of residence met the DSM-5 criteria used to diagnose PTSD. For groups of internally displaced persons and those who have left Ukraine, this figure stands at 55.4% and 62.2% respectively. Only 7.2% of those surveyed reported no stress or anxiety, or low levels of either [3]. According to the National Health Service of Ukraine, the number of registered cases of PTSD in the first two months of 2024 was almost equal to the figures for the whole of 2021. In 2023, the incidence rate was more than four times higher than in 2021.

Post-traumatic stress disorder is a complex, multifactorial condition involving various pathogenetic mechanisms and the body's regulatory systems. Dysfunction of the serotonergic and dopaminergic systems, as well as other interrelated neurobiological mechanisms, plays an important role in its development. Serotonin regulates emotional state, sleep and the response to stress, and disturbances in the function of this neurotransmitter's transporters and receptors are associated with increased anxiety and reduced stress resilience. Dopamine, in turn, plays a key role in motivational processes, cognitive control and emotional regulation. An imbalance in its signalling pathways leads to disruption of the reward system and emotional stability, which are characteristic features of PTSD [4, 5]. This is precisely why genetic variants that influence the functioning of these neurobiological systems are regarded as important factors in an individual's vulnerability to developing the disorder.

AIM

The aim of this study was to perform a systematic review of the role of polymorphisms in genes that regulate the functioning of serotonergic, dopaminergic and other neurobiological systems in the development of a genetic predisposition to post-traumatic stress disorder. The main focus was on summarising current data on the relationship between genetic variants and patterns of stress reactivity, determining their contribution to the pathogenesis of PTSD, as well as outlining promising areas for further molecular-genetic research directed at identifying risk biomarkers and developing personalised approaches to prevention and treatment.

MATERIALS AND METHODS

Within the framework of this review, a comprehensive search was carried out for scientific publications in leading international databases – Scopus, PubMed and ResearchGate – which are widely used for medical and biological research. The search strategy was based on the use of key terms related to the genetic factors underlying the development of post-traumatic stress disorder, in particular single-nucleotide polymorphisms (SNPs) in genes that regulate the functioning of serotonergic, dopaminergic and other neurobiological systems. To ensure the analysis remained up to date, the focus was on articles published over the last decade. The review included studies examining the molecular and genetic basis of PTSD, the role of genetic variations in shaping individual susceptibility to stressors, and their impact on hormonal regulation.

This study is in line with the UN Sustainable Development Goals, in particular Goal 3 –'Good Health and Well-being'. Its significance lies in helping to create a society where everyone has access to high-quality healthcare, can maintain their physical and mental health, and has the means to lead a long and active life [6].

ETHICS

All sources used in this literature review are publicly available.

REVIEW AND DISCUSSION

Recent research has confirmed that post-traumatic stress disorder is a complex psychoneurobiological condition involving numerous regulatory systems within the body. The genetic variants that have been studied most extensively are those relating to the functioning of the, dopaminergic and serotonergic systems. The following sections provide an overview of the main findings from studies investigating associations between single-nucleotide polymorphisms of these systems and the risk of developing PTSD.

SEROTONERGIC SYSTEM

Serotonin (5-HT) is one of the key neurotransmitters in the central nervous system, playing a role in regulating a wide range of physiological and psychological processes. Its functional role includes controlling mood, sleep cycles and eating behaviour, as well as modulating responses to stress. Increased serotonin availability in the synaptic space is associated with an improvement in emotional state and a reduction in anxiety levels, which has formed the basis for the development of pharmacological agents that block its reuptake. It is precisely these mechanisms that underlie the action of most modern antidepressants. At the same time, reduced expression of the serotonin transporter (5-HTT) is regarded as one of the key factors in the development of stress-related psychopathological conditions, including post-traumatic stress disorder [7]. Variability in the structure of the genes that regulate the functioning of this system is the subject of active scientific research and may account for individual differences in susceptibility to stress-related psychopathology.

One of the most promising genes in the serotonergic system, which has attracted the attention of researchers, is *SLC6A4*, which encodes the serotonin transporter (5-HTT). This protein is responsible for the reuptake of serotonin from the synaptic space, thereby regulating its concentration and duration of action on postsynaptic

receptors. Disruptions in the functioning of the transporter may lead to an imbalance in serotonergic transmission, which is associated with increased vulnerability to anxiety and depression.

Particular attention is being paid to the study of single nucleotide polymorphisms in the *SLC6A4* gene, which may change the transporter's expression level or functional activity. For example, variations in the promoter region of this gene can influence the amount of protein synthesised and, consequently, the effectiveness of serotonin signalling regulation. Such genetic differences are regarded as potential biomarkers of an individual's susceptibility to developing post-traumatic stress disorder, as they may determine varying levels of stress resilience and emotional regulation. Therefore, research focusing on SNPs of the *SLC6A4* gene offers the prospect of a deeper understanding of the molecular mechanisms underlying PTSD and the development of personalised approaches to its prevention and treatment. A polymorphic region (5-HTTLPR) has been identified, located in the promoter region of the *SLC6A4* gene, with short (S) and long (L) repeats. Carriage of the S allele is associated with reduced expression of 5-HTT compared with the L allele [8, 9]. According to the results of a meta-analysis, it has been established that individuals who are carriers of the S allele show an association with increased sensitivity to stress [10]. Carriers of the S allele were found to have an increased susceptibility to developing anxiety and depressive symptoms, panic disorders and aggressive behaviour [11]. Other studies have also investigated the effect of promoter polymorphisms on serotonin transporter levels. In addition, the role of the rs25531 polymorphism (A/G, LG alleles) in regulating 5-HTT expression levels was also investigated. It turned out that carriers of the S allele exhibited a similar level of 5-HTT expression to that seen in carriers of the L and LG alleles. The studies concluded that impaired regulation of the 5-HTTLPR, and consequently impaired maintenance of extracellular serotonin levels, among individuals who are carriers of the LG and S alleles contributes to an increased risk of stress-related disorders, and in particular PTSD [12, 13]. Some researchers highlight the mediating role of 5-HTTLPR in the interaction between genotype and environment, particularly given that this gene undergoes significant epigenetic changes [14, 15]. *Wankerl et al.* found that individuals who combine two risk factors—the presence of the S allele and adverse prenatal or early childhood influences—exhibit significantly lower levels of serotonin transporter mRNA expression compared with those who do not have these factors. These molecular changes thus form the basis for an increased susceptibility to developing PTSD in the presence of adverse environmental factors. In particular, in cases of child abuse, the risk of developing PTSD increased by 56.3% [16]. The presence of variants in the promoter region of the serotonin transporter gene, defined as an 'unfavourable genotype', is not an independent factor determining the development of post-traumatic stress disorder. However, the combination of this genotype with traumatic events in childhood or adulthood increases the probability of its occurrence. It has been confirmed that the highest risk of developing PTSD is found in individuals carrying the 5-HTTLPR polymorphism who have also experienced trauma during their lifetime [17].

Serotonin exerts its effects by interacting with specific receptors, consequently, the role of polymorphisms in the genes encoding these receptors is also being actively studied. *Donaldson et al.* investigated the effect of the rs6295 polymorphism of the serotonin 1A receptor (*HTR1A*) gene on the development of depression and PTSD. This polymorphism has been the subject of research as it may influence the regulation of *HTR1A* gene expression. It is located at position -1019 relative to the basal promoter region and is known as the C(-1019)G variant, which is common among population genetic variations. The results showed that carrying the G allele is associated with an increased risk of substance dependence, more frequent psychiatric hospitalisations and suicide attempts [18]. It has also been confirmed that elevated expression of serotonin 1A (5-HT1A) receptors among individuals carrying the G allele of the C(-1019)G polymorphism may lead to an increased risk of developing depressive disorders and a reduced therapeutic response. This effect is most intensely manifested in cases where a person has experienced significant stressful life events [19]. The results of another study also demonstrated a link between the rs6295 polymorphism of the *HTR1A* gene and conditions such as major depressive disorder and bipolar disorder [20]. The results of the meta-analysis revealed a significant association between the C(-1019) G (rs6295) polymorphic locus of the *HTR1A* gene and the development of panic disorder [21]. Other types of serotonin receptors and their genes, particularly 2A and 1B (*HTR2A* and *HTR1B*), were investigated to determine their influence on the development of aggressive behaviour and PTSD symptoms. The results showed that two polymorphisms of the *HTR2A* gene (rs7322347 and rs977003) are associated with the development of post-traumatic stress disorder. Furthermore, the association between the rs7322347 polymorphism and changes in behaviour and the development of aggression was confirmed [5]. Another polymorphism of the serotonergic system, G861C, located in the

serotonin 1B receptor gene (*HTR1B*), was investigated. A significant association of this polymorphic site was found in individuals with major depressive disorder. This is associated with the inhibition of serotonin release in the basal ganglia, which is explained by the activation of second messengers that reduce adenylate cyclase activity and regulate neurotransmitter secretion [22]. Other researchers have investigated the role of the rs6311 (-1438A/G) polymorphism in the promoter region of the *HTR2A* gene in increasing the risk of developing depressive disorders. This association has been confirmed, and the rs6311 polymorphism has been recognised as an important factor contributing to susceptibility to depression [20, 23].

DOPAMINERGIC SYSTEM

Dopamine is one of the key neurotransmitters in the central nervous system, playing a role in regulating motivational processes, emotional reactivity, and cognitive functions. It is synthesised in dopaminergic neurons of the midbrain, particularly in the ventral tegmental area and the substantia nigra, and is transmitted to various brain structures via the activation of specific receptors. There are five main types of dopamine receptors (D1–D5), which belong to two functional families: D1-like (D1, D5) and D2-like (D2, D3, D4). The first activate adenylate cyclase and enhance intracellular signalling, whilst the second inhibit it, maintaining a balance between excitation and inhibition in neural networks. This diversity of receptors enables dopamine to modulate a wide range of mental and behavioural processes. The dopaminergic system functions via several main pathways: the mesolimbic, mesocortical, nigrostriatal and tuberoinfundibular pathways. The mesolimbic pathway is responsible for the formation of motivation and emotional strengthening, the mesocortical pathway for cognitive control and emotional regulation, the nigrostriatal pathway for motor activity, and the tuberoinfundibular pathway for hormonal regulation. The coordinated functioning of these pathways ensures the body's adaptive response to stressors and maintains mental balance. Disruptions in the functioning of the dopaminergic system, particularly an imbalance in the activity of dopamine receptors or transporters, can lead to pathological changes in memory processes and emotional regulation, which is of direct relevance to the development of post-traumatic stress disorder [24].

Disruptions in the regulation of the dopaminergic system are considered to be one of the key mechanisms underlying the pathogenesis of post-traumatic stress disorder. Imbalances in neurotransmitter systems can lead to emotional instability and alter reward processing, which are characteristic features of PTSD. Particular importance is attached to the mesolimbic dopaminergic pathway, which underpins motivational processes and reward processing. Findings from neurobiological studies indicate that patients with PTSD exhibit reduced responsiveness in the reward system compared with a control group, suggesting that it is dysfunctioning. Such dopaminergic dysregulation may be a critical factor in the development of the disorder's symptoms, highlighting the importance of studying changes in dopamine signalling pathways to understand the pathophysiology of PTSD [25]. Because of this, the dopamine D2 receptor gene (*DRD2*) was the subject of the study. It is known that the D2 receptor is involved in the transmission of dopamine signals in presynaptic and postsynaptic neurons; its function is linked to G-protein-coupled receptors (GPCR) and is also associated with the development of PTSD [*26*]. Genetic variations of the *DRD2* gene are considered to be a factor that may influence an individual's susceptibility to developing post-traumatic stress disorder [*27*]. Studies show that this gene is associated with a range of psychopathological symptoms, including irritability and schizophrenia [28]. It is suggested that polymorphisms in the *DRD2* gene may alter the typical response to stressful stimuli by influencing cognitive information processing and increasing the risk of developing PTSD and aggressive behaviour [29]. *Niu et al.* investigated the effect of the rs1800497 polymorphism of the *DRD2* gene on susceptibility to PTSD. Two alleles, T (A1) and C (A2), were identified at this polymorphic site. This DRD2/ANKK1-Taq1A polymorphic site (rs1800497) is located on chromosome 11 within the ANKK1 gene and in close proximity to the *DRD2* gene. The rs1800497 polymorphism is associated with impaired regulation of dopamine synthesis and reduced expression of D2 receptors in the brain, creating the neurobiological conditions for the manifestation of post-traumatic stress disorder symptoms. The available data suggest that this genotype variant may intensify the severity of clinical manifestations of PTSD, and carriers of the A1 allele show an increased susceptibility to developing the disorder following a traumatic event [30].

The potential influence of polymorphisms in other dopamine receptor genes on the development of PTSD has also been studied intensively. Four polymorphisms of the dopamine D3 receptor (*DRD3*) gene were investigated: rs2134655, rs201252087, rs4646996 and rs9868039. An association between these polymorphic loci and a reduced risk of developing PTSD has been confirmed. Individuals who were carriers of the minor allele for the polymorphisms under investigation showed a statistically significant reduction in the risk

of developing PTSD [25]. Another genetic variant that may be linked to the mechanisms underlying mental disorders such as PTSD is a polymorphism of the dopamine D4 receptor gene (*DRD4*). This gene is characterised by the presence of a variable number of tandem repeats (VNTR), which can range from 2 to 10 copies, with alleles containing 4 and 7 repeats being the most common. A statistically significant association has been identified between this polymorphic site of the DRD4 gene and PTSD: carriers of the 7-repeat allele have an increased risk of developing this disorder compared with non-carriers. These findings highlight the role of genetic factors in determining vulnerability to PTSD [5]. The dopamine transporter (DAT), which is responsible for dopamine reuptake and maintaining the balance of extracellular dopamine concentrations, is of interest in studies investigating the role of polymorphisms in the gene encoding it (*SLC6A3*) in dopamine metabolism and PTSD development. One of the most extensively studied polymorphisms is the VNTR located in the 3' UTR region of the *SLC6A3* gene. This genetic polymorphism is characterised by the presence of alleles with 9 repeats (9R) and 10 repeats (10R). The presence of the 9R allele in the genotype is associated with reduced DAT expression and increased dopamine levels in the synaptic space. As for carriers of the 10R allele, an increase in affinity for the dopamine transporter and in the efficiency of dopamine reuptake has been observed [31]. Such changes in dopamine metabolism may alter the neuronal response to stressful and traumatic stimulations, thereby impairing the effectiveness of adaptive mechanisms. Dysregulation of this system creates conditions that reduce stress resilience and increases the probability of developing post-traumatic stress disorder, forming the neurobiological basis for its clinical manifestations.

Given the metabolic changes associated with PTSD, researchers have turned their attention to an enzyme known as catechol-O-methyltransferase (COMT), whose function is to inactivate neurotransmitters such as noradrenaline and dopamine in the prefrontal cortex. This enzyme is encoded by the *COMT* gene and is located on chromosome 22q11.21. The rs4680 (Val158Met) polymorphic site of the *COMT* gene is one of the most extensively studied single-nucleotide variants of this gene. It has attracted considerable attention from researchers analysing the neurobiological mechanisms of psychiatric disorders, including post-traumatic stress disorder, obsessive-compulsive disorder and schizophrenia [32]. As a result of the rs4680 single-nucleotide polymorphism, located in exon 4 of the *COMT* gene, an amino acid substitution from valine (Val) to methionine (Met) occurs at codon 158 (Val158Met). Such changes in amino acid composition result in a four-fold reduction in the activity of the enzyme catechol-O-methyltransferase among individuals who are carriers of the minor allele, compared with homozygotes for the major allele [33]. Such a reduction in enzyme activity leads to changes in neurotransmitter metabolism and, in particular, to an increase in the bioavailability of dopamine, which may have a significant impact on the neurobiological mechanisms governing emotions and stress responses. As a result, carriers of the minor allele show an increased susceptibility to psychiatric disorders, including post-traumatic stress disorder. A research team headed by *Mestrovic H.A.* conducted a study involving military veterans of combat operations with a confirmed diagnosis of PTSD and members of a control group without mental disorders. The aim of this study was to investigate the effect of the Val158Met polymorphism on the activity of catechol-O-methyltransferase and dopamine availability, which are associated with cognitive impairment. An association between this polymorphic variant of the *COMT* gene and the development of PTSD was confirmed; it was also found that cognitive function scores, as assessed using specialised tests (ROCF), were significantly higher among individuals in the control group compared with the group of veterans. For individuals with PTSD who are carriers of the Met allele, the results of cognitive tests were higher than those of Val/Val homozygotes. Thus, the presence of one or two Met alleles of the *COMT* gene at the rs4680 polymorphism exerts a protective effect on working memory mechanisms and cognitive functions in military personnel who have experienced trauma during combat operations and have been diagnosed with PTSD. [34]. *Deslauriers et al.* conducted a study into the role of the Val158Met polymorphism of the *COMT* gene in the development of PTSD among marines and navy personnel of European-American descent. The service personnel were assessed prior to deployment on combat missions in Afghanistan and 4–6 months thereafter; the study evaluated the presence and resolution of fear-potentiated startle, combat experiences and childhood trauma, as well as symptoms of post-traumatic stress disorder. Studies investigating the association between the *COMT* genotype and fear extinction in healthy, non-traumatised individuals found no such association. However, among military personnel who were Met/Met carriers, a statistically significant association was found between combat trauma and reduced fear extinction, compared with Val/Val carriers [35].

OTHER POLYMORPHIC SITES

In addition to the most extensively studied genetic mechanisms related to key neurobiological systems,

the current literature describes the role of a broader spectrum of polymorphisms that may be involved in the mechanisms underlying vulnerability to post-traumatic stress disorder. Such polymorphisms may be associated with social behavior, hormonal regulation, and emotional reactivity, and may play an important role in individual differences in response to traumatic events. Since, despite numerous studies of the complex pathogenic mechanisms underlying the development of PTSD and the role of genetic factors in these mechanisms, no gene has been identified whose structural changes could unequivocally be the cause of PTSD, scientists continue to expand the scope of their research.

One of the genetic factors that may be involved in the development of clinical manifestations of PTSD is polymorphisms in the oxytocin receptor (*OXTR*) gene. A significant association has been identified between the rs53576 polymorphic site of the *OXTR* gene and the pathogenic mechanisms underlying the development of PTSD throughout life [36]. *Zhang et al.* analyzed the effect of polymorphisms in the dopaminergic and oxytocinergic systems on the development of PTSD among a Chinese population that had experienced trauma as a result of an earthquake. This study examined the rs2268498 polymorphism of the *OXTR* gene and the rs1801028 polymorphism of the *DRD2* gene. An increased risk of developing PTSD was found in the presence of the combined effect of the rs2268498×rs1801028 polymorphisms of the genes under study ($P = 0.043$). Thus, this study confirmed the significant role of the interaction between the dopaminergic and oxytocinergic systems in the development of PTSD [37].

It is known that the activity of the monoamine oxidase A enzyme, which breaks down neurotransmitters such as serotonin, dopamine, and epinephrine, may influence the development of aggressive behaviors and PTSD. Four polymorphic sites of the monoamine oxidase A (*MAOA*) gene (rs5906893, rs5906957, rs2283725, rs2072744, and rs979605) were studied, and an association with the onset of antisocial personality disorder was established. [5]. Monoamine oxidase B also plays a role in the breakdown of neurotransmitters. A significant association has been found between the rs1799836 polymorphism of the monoamine oxidase B (*MAOB*) gene and the development of depressive states and the presence of negative emotional personality traits. In addition, an association has been confirmed between this polymorphic locus of the *MAOB* gene and the severity of PTSD in male military personnel and combat veterans [25].

Another factor considered to potentially increase the probability of developing anxiety disorders, particularly post-traumatic stress disorder, is the neuropeptide Y (*NPY*) gene. The study results showed that individuals who are carriers of the minor allele at the rs16147 polymorphism of the *NPY* gene exhibited an increased susceptibility to developing PTSD [38].

The ADCYAP type I receptor gene (*ADCYAP1R1*) encodes a G-protein-coupled receptor that interacts with the neuropeptide PACAP (pituitary adenylate cyclase-activating peptide) and plays a role in regulating a number of physiological processes, including the body's response to stress. The results of the meta-analysis showed that carrying the C allele at the rs2267735 polymorphism of the *ADCYAP1R1* gene is associated with an increased risk of developing PTSD in the overall study sample and among women and girls, whereas no such association was found among men and boys. The findings suggest a possible role for the *ADCYAP1R1* gene in the development of PTSD, and this effect may differ depending on gender [39].

According to some scientists, inflammatory changes play an important role in the pathogenic mechanisms underlying the development of PTSD. For this reason, the influence of polymorphisms in genes of the inflammatory system was also investigated. Polymorphisms in the promoter region of the *TNFα* gene, which encodes the key pro-inflammatory cytokine tumor necrosis factor α, are associated with an increased susceptibility to post-traumatic stress disorder. In particular, the SNP rs1800629 was found to be significant in terms of the severity of PTSD symptoms, with the GG genotype identified as a risk variant for mental disorders. In addition, significant differences in serum TNFα levels were found between patients with PTSD and the control group, and correlations were identified between elevated expression of this cytokine and a more severe clinical course of PTSD. These findings highlight the potential role of TNFα as a genetic risk factor and a biomarker of functional changes that contribute to the pathogenesis of the disorder [40]. The *IL1B* gene, which encodes the pro-inflammatory cytokine interleukin-1 beta and regulates immune mechanisms, was studied in the context of its association with the development of PTSD. The analysis showed that the minor alleles of SNPs rs1143633C and rs16944A were significantly less common among individuals with PTSD compared to the control group. This association suggests a potential protective effect of these alleles against the development of PTSD, which, in turn, indicates a possible involvement of the IL1B gene in the pathogenic mechanisms of the disorder [41].

CONCLUSIONS

Post-traumatic stress disorder is a complex, multifactorial condition that develops as a result of the interaction

of numerous neurobiological and psychosocial mechanisms. Research confirms that imbalances in key neurotransmitter systems, disruptions in hormonal regulation and changes in the functioning of neural networks create conditions that reduce stress resilience and increase vulnerability to the development of PTSD. Importantly, genetic variations do not act in isolation – their impact is amplified when combined with adverse environmental factors, such as childhood trauma or combat experience.

Therefore, PTSD should be regarded as the result of a complex interplay of genetic, biological and social factors. Further research should focus on integrating molecular-genetic data with clinical and psychosocial indicators, which will enable the development of more accurate risk prediction models. A promising area of research is the search for biomarkers that could form the basis for personalised diagnosis and treatment, as well as the development of individualised prevention and treatment strategies that take into account patients' genetic characteristics and life experiences.

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This paper was supported by the grants from the Ministry of Education and Science of Ukraine: "Investigation of Genetic Predictors of Post-Traumatic Stress Disorder Development and Their Prognostic Value" (State Registration No. 0126U000871) and "Medico-Social Substantiation of the Optimization of the Healthcare Model for Patients with Post-Traumatic Stress Disorder Considering Molecular Genetic Risk Factors" (State Registration No. 0126U000873).

CONFLICT OF INTEREST
The Authors declare no conflict of interest

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RECEIVED: 10.03.2026
ACCEPTED: 27.07.2026

CREATIVE COMMONS 4.0

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REVIEW ARTICLE

Effects of hyperbaric oxygen therapy in the treatment of selected diseases of the nervous system

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ABSTRACT

Hyperbaric Oxygen Therapy (HBOT) has attracted increasing interest as a potential supportive intervention in neurological disorders. By increasing the amount of oxygen dissolved in blood plasma, HBOT enhances oxygen delivery to hypoxic tissues and may influence mechanisms involved in neuroplasticity, inflammation, and tissue repair. Experimental and clinical studies suggest that HBOT may support neurological recovery in selected conditions, particularly following ischemic or traumatic brain injury. However, the effectiveness of HBOT varies depending on the underlying disease, and further high-quality clinical studies are needed to establish its role in neurological rehabilitation.

The article was based on an analysis of data from Google Scholar and PubMed regarding the effects of hyperbaric therapy.

KEY WORDS: Alzheimer's disease, Parkinson's disease, stroke, hyperbaric oxygen therapy

Wiad Lek. 2026;79(8):1982-1988. doi: 10.36740/WLek/226613 DOI

INTRODUCTION

Hyperbaric oxygen therapy (HBOT) is an established treatment modality that involves breathing 100% oxygen under increased atmospheric pressure, typically between 2.0 and 3.0 ATA. Initially developed for the management of decompression sickness, HBOT is currently used in several approved clinical indications, including carbon monoxide poisoning, chronic wound healing, radiation-induced tissue injury, and selected ischemic conditions [1].

The therapeutic effects of HBOT result from increased oxygen dissolution in blood plasma, which enhances oxygen delivery to hypoxic tissues independently of hemoglobin, in accordance with Henry's law. Elevated tissue oxygen tension stimulates angiogenesis, collagen synthesis, fibroblast proliferation, leukocyte antimicrobial activity, and stem cell mobilization while reducing tissue edema through vasoconstriction without compromising oxygen supply [2,3]. These mechanisms have generated increasing interest in the potential application of HBOT in regenerative and neurological medicine.

The brain is highly dependent on aerobic metabolism, consuming approximately 20% of the body's oxygen despite representing only about 2% of total body mass. Adequate oxygen availability is essential for mitochondrial ATP production, neuronal signaling, and maintenance of redox homeostasis. Cerebral hypoxia and impaired perfusion contribute to oxidative stress, neuroinflammation, and neuronal dysfunction, which are common features of stroke, traumatic brain injury, vascular cognitive impairment, and other neurological disorders [4–8]. Experimental and clinical studies suggest that HBOT may improve tissue oxygenation and modulate cellular pathways involved in neuroplasticity and neurorepair, although the clinical evidence remains heterogeneous and requires further investigation.

Therefore, HBOT has emerged as a promising adjunctive therapy in neurological rehabilitation, warranting continued evaluation of its mechanisms of action and clinical effectiveness.

MATERIALS AND METHODS

The article was developed based on an analysis of data from Google Scholar and PubMed regarding the effects of hyperbaric therapy.

REVIEW AND DISCUSSION

THE STATE OF KNOWLEDGE

Hyperbaric oxygen therapy (HBOT) exerts its effects on the central nervous system by increasing both ambient pressure (typically 1.5–3.0 ATA) and oxygen concentration, thereby markedly enhancing oxygen solubility in blood plasma. This facilitates oxygen diffusion to hypoxic neural tissues independently of hemoglobin and improves tissue oxygenation in regions with impaired perfusion [9].

The neuroprotective effects of HBOT are mediated through several complementary mechanisms. Increased tissue oxygenation promotes cerebral vasoconstriction while maintaining adequate oxygen delivery, contributing to a reduction in intracranial pressure and cerebral edema. At the cellular level, HBOT supports mitochondrial respiration, enhances ATP synthesis, and limits excessive production of reactive oxygen species, thereby reducing neuronal apoptosis and necrosis following hypoxic or ischemic injury. In addition, hyperoxia activates signaling pathways involved in neurogenesis and angiogenesis, including the HIF-1α/VEGF axis, and increases the expression of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF), which are essential for neuronal survival and synaptic remodeling [9].

HBOT has also been shown to modulate neuroinflammatory processes by suppressing microglial activation and decreasing the production of pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β). Furthermore, experimental studies suggest that hyperbaric oxygen may promote autophagy, facilitating the clearance of pathological protein aggregates and supporting synaptic plasticity [9,10].

Clinical and neuroimaging studies have demonstrated that HBOT may improve cerebral perfusion and functional recovery following traumatic brain injury, ischemic stroke, and selected neurodegenerative disorders. Improvements in cognitive performance and motor function have been reported after repeated treatment sessions; however, the magnitude of these effects varies across patient populations, and further well-designed randomized controlled trials are required to establish the long-term efficacy of HBOT in neurological rehabilitation [9,10].

INNOVATIVE APPROACHES TO HYPERBARIC OXYGEN THERAPY IN SELECTED MEDICAL CONDITIONS

ALZHEIMER'S DISEASE (AD)

Alzheimer's disease (AD) is the most common neurodegenerative disorder, characterized by progressive cognitive decline associated with extracellular accumulation of β-amyloid (Aβ) plaques, intracellular neurofibrillary tangles composed of hyperphosphorylated tau protein, synaptic loss, neuronal degeneration, and gliosis [11]. Despite significant advances in understanding its pathophysiology, no curative treatment is currently available, and therapeutic strategies remain primarily symptomatic.

Hyperbaric oxygen therapy (HBOT) has been proposed as an adjunctive intervention in AD, aiming to improve cerebral oxygenation, reduce hypoxic injury, and modulate neurodegenerative processes. Standard therapeutic protocols typically include 40–60 sessions lasting 60–90 minutes at pressures ranging from 1.5 to 2.0 ATA. Under these conditions, increased plasma-dissolved oxygen enables enhanced delivery to metabolically compromised brain regions, particularly the hippocampus and cerebral cortex, which are critically affected in AD.

Experimental and clinical data suggest that HBOT may exert multifactorial effects, including modulation of neuroinflammation, reduction of oxidative stress, and activation of pathways associated with neuroplasticity, such as BDNF and VEGF signaling. Additionally, HBOT has been associated with enhanced autophagic processes potentially involved in the clearance of pathological protein aggregates, including β-amyloid and tau.

Clinical studies have reported potential cognitive and functional benefits in patients with mild to moderate AD. In a randomized controlled trial by Harch et al. (2012), 40 HBOT sessions (1.5 ATA, 90 minutes) resulted in significant improvements in Mini-Mental State Examination (MMSE) and Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog), accompanied by increased cerebral glucose metabolism in frontal brain regions assessed by PET imaging. Similarly, Shapira et al. (2020) observed cognitive improvement and reduced amyloid burden in patients undergoing HBOT, with corresponding neuroimaging changes.

Meta-analytical data from randomized controlled trials further indicate that HBOT may improve cognitive performance and activities of daily living in patients with AD and mixed dementia, with the most pronounced effects observed in protocols involving at least 40 sessions at 2.0 ATA. Reported adverse events are generally mild and primarily related to barotrauma of the middle ear, without evidence of severe oxygen toxicity in analyzed studies. However, heterogeneity of study designs and limited long-term follow-up necessitate cautious interpretation of results [12].

Overall, current evidence suggests that HBOT may represent a promising adjunctive therapy in Alzheimer's disease, potentially improving cognitive function and metabolic brain activity. Nevertheless, it should be

Table 1. Meta-analysis of the effects of hyperbaric oxygen therapy on cognitive function, motor symptoms, and sleep parameters in Parkinson's disease

Scala/Parametr	Change in the group HBOT (MD/SMD, 95% CI)	p- value	Heterogeneity (I^2)
MoCA (cognitive functions)	MD=2,45(1,23-3,67)	<0,001	28%
MMSE	SMD=0,68(0,15-1,21)	0,012	42%
PDSS (sleep quality)	MD=4,72(2,10-7,34)	<0,001	15%
PSQI	MD=-2,18(-3,45 to-0,91)	0,001	35%
Kubota swallowing test	SMD=0,82(0,29-1,35)	0,002	22%
UPDRS III (Motor Symptoms)	MD=-5,63(-8,92 to-2,34)	<0,001	51%
Total sleep time	MD=45 min(22-68 min)	<0,001	18%
Sleep efficiency	MD=8,2%(4,1-12,3%)	<0,001	29%

considered experimental in this indication, and further large-scale randomized controlled trials are required to determine optimal treatment parameters and long-term efficacy [12,13].

PARKINSON'S DISEASE (PD)

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized primarily by the degeneration of dopaminergic neurons in the substantia nigra, associated with motor and non-motor symptoms. Key pathogenic mechanisms include oxidative stress, mitochondrial dysfunction, neuroinflammation, and abnormal accumulation of α-synuclein, which contributes to neuronal dysfunction and loss.

Hyperbaric oxygen therapy (HBOT) has been proposed as a supportive intervention in PD, with the aim of reducing oxidative damage, improving mitochondrial function, and modulating neuroinflammatory processes. Experimental data suggest that increased tissue oxygenation may support the survival of dopaminergic neurons, reduce glial activation, and attenuate the production of pro-inflammatory cytokines involved in disease progression. In addition, HBOT may influence autophagic pathways, potentially facilitating the clearance of misfolded proteins such as α-synuclein, which plays a central role in PD pathophysiology.

Clinical evidence regarding the efficacy of HBOT in Parkinson's disease remains limited but emerging. A meta-analysis by Pan et al. (2025), published in *Clinical Rehabilitation*, included four randomized controlled trials (n=152 patients) evaluating HBOT in PD, primarily focusing on non-motor symptoms. The pooled results indicated statistically significant improvements in clinical outcomes, with moderate to large effect sizes (SMD > 0.5). No significant differences in safety outcomes were observed between HBOT and control groups (RR = 1.12; 95% CI 0.78–1.61; p = 0.54).

However, considerable heterogeneity was noted across included studies, particularly in treatment protocols (pressure ranging from 1.5 to 2.4 ATA and 30–40 treatment sessions), which limits direct comparability of results. The overall quality of evidence was rated as moderate according to GRADE criteria. Despite promising findings, HBOT is not currently included in standard clinical guidelines for Parkinson's disease (e.g., ECHM/ECGP recommendations), and its use remains experimental in this indication.

In summary, HBOT shows potential as an adjunctive therapy in Parkinson's disease, particularly in relation to non-motor symptoms, through mechanisms involving neuroprotection, angiogenesis, and neuroplasticity. Nevertheless, due to limited high-quality evidence and lack of protocol standardization, further large-scale randomized controlled trials are required to confirm its clinical utility [14].

THE EFFECT OF HYPERBARIC OXYGEN THERAPY ON STROKE OUTCOMES

Clinical analyses of hyperbaric oxygen therapy (HBOT) indicate its considerable therapeutic potential in promoting neuroplasticity and functional recovery in patients with chronic neurological deficits following ischemic stroke and traumatic brain injury (TBI). Intensive HBOT protocols, most commonly consisting of 40–60 sessions at pressures ranging from 1.5 to 2.0 ATA, have been associated with statistically significant improvements in cognitive performance, motor function, and health-related quality of life, even in the late stages of neurological impairment traditionally regarded as stable and resistant to further recovery.

The proposed mechanisms underlying the regenerative effects of HBOT are primarily related to the concept of the "hyperoxic–hypoxic paradox". Repeated exposure to elevated oxygen concentrations followed by normox-

ic conditions activates adaptive molecular pathways responsible for angiogenesis, endogenous stem cell mobilization, mitochondrial function enhancement, and attenuation of chronic neuroinflammation within ischemic penumbra regions. HBOT-mediated stimulation of hypoxia-inducible factors (HIFs) promotes the expression of genes involved in tissue repair and neuroplasticity. Furthermore, neuroimaging studies using single-photon emission computed tomography (SPECT) and perfusion magnetic resonance imaging (MRI) have demonstrated increased cerebral metabolism and blood flow in previously impaired cortical regions, supporting the hypothesis that HBOT may reactivate metabolically compromised but viable neurons and facilitate functional reorganization of neural networks [15][16].

A systematic review by Marcinkowska et al. (PMC8888529) analyzed data from multiple clinical studies, including randomized controlled trials involving patients with chronic neurological deficits after cerebral injury and ischemic stroke. The reviewed evidence demonstrated significant improvements in neuropsychological outcomes, particularly in verbal and visual memory, sustained attention, and executive functions. Improvements were reported in standardized assessments such as the Rey Auditory Verbal Learning Test, Trail Making Test, and Stroop Test. These effects have been attributed to enhanced tissue oxygenation, stimulation of angiogenic pathways involving vascular endothelial growth factor (VEGF), improved cerebral perfusion, and reduction of ischemic tissue edema [15][16][17].

The study identified by PMID 31985478 evaluated the effects of an intensive HBOT protocol consisting of 40 sessions at 2.0–2.5 ATA in patients with chronic cognitive impairment following cerebral hypoxic injury. The intervention resulted in measurable improvements in global cognitive function, including increases in Mini-Mental State Examination (MMSE) scores and improvements in episodic memory and spatial orientation. The persistence of these effects during follow-up suggests that HBOT may induce long-term neuroplastic changes through mechanisms involving enhanced brain-derived neurotrophic factor (BDNF) activity, synaptic remodeling, and reduced neuronal apoptosis [16].

Further evidence was provided by the study reported in PMID 35821512, which investigated 63 patients in the chronic phase following ischemic stroke (>6 months after the acute event). After completion of 40 HBOT sessions, patients demonstrated approximately 20% improvement in global neurocognitive performance measured by the Neuropsychological Assessment Battery, including domains such as information processing speed and verbal fluency. Improvements in quality of life assessed using the SF-36 questionnaire were also observed. The treatment was generally well tolerated, with mild barotrauma reported in approximately 5% of participants [17].

The molecular and physiological mechanisms of HBOT were further examined in the study associated with PMID 33847854. Treatment protocols involving exposure to 2.4 ATA for 90 minutes per session were shown to reduce inflammatory biomarkers, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), while improving cerebral perfusion parameters assessed by MRI. Reported increases in cerebral blood flow (CBF) of approximately 12–18% were associated with improved performance in executive function tests among patients recovering from both ischemic and hemorrhagic stroke [16].

Overall, current evidence suggests that HBOT may represent a valuable non-invasive adjunctive therapy in post-stroke rehabilitation, particularly for patients with persistent cognitive and functional deficits. The beneficial effects appear to result from a combination of increased oxygen availability, stimulation of angiogenesis and neurogenesis, modulation of inflammatory processes, and enhancement of neural network plasticity.

However, interpretation of existing findings requires caution due to several methodological limitations, including relatively small study populations (frequently fewer than 100 participants), limited availability of blinded randomized controlled trials, and significant heterogeneity in treatment protocols, including variations in pressure parameters (2.0–2.5 ATA), session duration, and total number of treatments (40–60 sessions). Therefore, large-scale multicenter randomized controlled trials with extended follow-up periods exceeding 12 months are required to determine optimal HBOT protocols and confirm the long-term sustainability of clinical benefits.

THE INFLUENCE OF HYPERBARIC OXYGEN THERAPY ON COGNITIVE FUNCTIONS IN HEALTHY ELDERLY INDIVIDUALS

Hyperbaric oxygen therapy (HBOT) has demonstrated potential as a non-pharmacological intervention capable of enhancing neuroplasticity and improving cognitive performance not only in patients with neurological disorders but also in healthy older adults experiencing age-related cognitive decline. Recent evidence suggests that repeated exposure to hyperbaric oxygen may optimize cerebral metabolism, improve vascular function, and stimulate adaptive mechanisms associated with brain aging.

In a randomized controlled trial involving 63 healthy adults over 64 years of age without a history of stroke or major neurological disease, a protocol consisting of 60 HBOT sessions (100% oxygen at 2 ATA for 90 minutes, five sessions per week, with intermittent air breaks) resulted in statistically significant improvements in global cognitive performance. The most pronounced effects were observed in domains associated with attention, information processing speed, and executive functions. The reported net effect sizes were 0.745 for attention and 0.788 for information processing speed, indicating a clinically meaningful improvement following the intervention [18].

Neuroimaging analysis using magnetic resonance imaging (MRI) and perfusion-based methods demonstrated significant increases in cerebral blood flow (CBF) following HBOT, particularly within regions involved in higher cognitive processing, including the middle and superior frontal gyri, prefrontal cortex, parietal cortex, and motor-related cortical areas. These findings suggest that cognitive enhancement following HBOT is associated with improved cerebral perfusion and metabolic activation of brain regions vulnerable to age-related functional decline.

The observed effects may be explained by several biological mechanisms, including stimulation of angiogenesis, improved mitochondrial efficiency, increased oxygen availability to neural tissue, and activation of pathways associated with neuroplasticity. Similar to the mechanisms described in neurological rehabilitation, the "hyperoxic–hypoxic paradox" induced by repeated oxygen fluctuations may activate hypoxia-inducible factors (HIFs), promote vascular remodeling, and support neuronal adaptation.

Importantly, the magnitude of cognitive improvement reported in this study suggests that HBOT may provide benefits beyond conventional lifestyle interventions, including physical exercise-based approaches, although direct comparisons between HBOT and aerobic training require further investigation. These findings indicate that HBOT may represent a promising therapeutic strategy for maintaining cognitive function and delaying age-associated neurological decline in healthy elderly populations.

Nevertheless, further large-scale, multicenter randomized controlled trials are required to confirm the reproducibility of these findings, establish optimal treatment protocols, and determine the long-term clinical relevance of HBOT-induced cognitive enhancement in aging populations [18].

CLINICAL CASE REPORTS DEMONSTRATING THE EFFECTS OF HYPERBARIC OXYGEN THERAPY AFTER STROKE

Several clinical case reports published in the available literature describe functional and neurophysiological improvements following hyperbaric oxygen therapy (HBOT) in patients with chronic neurological deficits after stroke. Although individual case reports cannot provide definitive evidence of treatment efficacy, they offer valuable insights into possible mechanisms of recovery and highlight the potential role of HBOT as an adjunctive intervention in long-term neurorehabilitation.

One reported case involved a 45-year-old Arabic male who developed a left-sided hemorrhagic stroke resulting in persistent neurological impairment 15 months after the acute event. At baseline evaluation, the patient presented with right-sided hemiparesis, severe gait impairment requiring wheelchair mobility, and cognitive deficits. The patient received 83 HBOT sessions over a period of 16 weeks using a protocol of 2.0 ATA for 90 minutes per session with intermittent air breaks. Clinical assessment included neurological and cognitive evaluation, while structural and functional brain changes were examined using diffusion tensor imaging (DTI) and single-photon emission computed tomography (SPECT).

Following completion of the HBOT protocol, substantial functional improvements were observed. The patient demonstrated increased muscle strength, reduced spasticity, improved postural balance, and progression from wheelchair dependence to independent ambulation with the assistance of a quadruped cane. Cognitive assessment revealed improvements in attention, verbal memory, and information processing speed. Neuroimaging findings supported these clinical changes: DTI demonstrated increased fractional anisotropy within major white matter tracts, suggesting improved structural connectivity, while SPECT revealed significant increases in cerebral perfusion within the right motor cortex (+15.83%) and right frontal lobe (+15.92%) [19].

Another case described a 73-year-old Romanian female with a medical history of hypertension, atrial fibrillation, and cerebellar ischemic stroke occurring on December 25, 2019. The patient was evaluated approximately one year after stroke onset. Perfusion MRI demonstrated reduced cerebral blood flow in the region of the left cerebellar lesion and surrounding cerebral tissue. Clinically, the patient exhibited severe balance impairment affecting activities of daily living, requiring caregiver assistance for indoor mobility and wheelchair use outdoors. Neurological examination revealed left-sided muscle strength of 4/5, preserved range of motion in all extremities, a motor Functional Independence Measure (FIM) score of 13/21, and a positive Romberg test. Before treatment, the patient was unable to independently perform sit-to-stand (STS), 10-meter walking, dual-task walking, or the Timed Up and Go (TUG) test.

Following HBOT, the patient demonstrated clinically meaningful improvements in balance, mobility, and functional independence. She progressed from wheelchair dependence to assisted walker ambulation indoors and improved her ability to perform previously impossible functional assessments, including STS repetitions, Romberg balance maintenance for 30 seconds under supervision, 10-meter walking, dual-task walking, and the TUG test. Follow-up perfusion MRI demonstrated increased cerebral blood flow in both cerebellar hemispheres, while the core of the previous lesion remained unchanged, suggesting functional recovery through improved perfusion and activation of surrounding neural networks rather than structural regeneration of the infarcted tissue [20].

These case reports support the hypothesis that HBOT may promote recovery in chronic post-stroke conditions through mechanisms involving enhanced cerebral perfusion, improved white matter integrity, modulation of neuroplastic processes, and functional reorganization of remaining neural circuits. However, due to the observational nature and limited number of reported cases, these findings should be interpreted as preliminary evidence requiring confirmation in larger controlled clinical trials.

CONCLUSIONS

Hyperbaric oxygen therapy (HBOT) represents a promising supportive approach for modulating nervous system function through mechanisms associated with enhanced tissue oxygenation, improved neuronal metabolism, and stimulation of neuroplasticity. Available experimental and clinical evidence suggests that exposure to elevated oxygen concentrations under hyperbaric conditions may promote adaptive changes within the central nervous system, including improved mitochondrial activity, regulation of inflammatory responses, reduction of oxidative stress, and activation of pathways involved in neuronal survival and repair.

The clinical effects reported in the literature indicate that HBOT may contribute to improvements in selected neurological outcomes, including cognitive performance, attention, information processing, sleep quality, and reduction of neuropsychiatric symptoms. In patients with chronic neurological deficits following stroke or traumatic brain injury, HBOT has been associated with functional recovery, improved cerebral perfusion, and enhanced neurocognitive performance, suggesting a potential role in long-term neurorehabilitation. Furthermore, preclinical studies provide evidence that HBOT may exert neuroprotective effects by regulating mitochondrial function, reducing apoptosis, and supporting the preservation of vulnerable neuronal structures.

Despite these encouraging findings, the current evidence base remains limited by methodological challenges, including variability in treatment protocols, differences in patient populations, relatively small sample sizes, and an insufficient number of large-scale randomized controlled trials. Therefore, further multicenter studies with standardized HBOT protocols and long-term follow-up are required to establish optimal therapeutic parameters and define the populations most likely to benefit.

Overall, the available evidence supports the potential value of HBOT as an adjunctive therapy in neurological rehabilitation and disorders associated with cognitive decline. When integrated with established treatment strategies, HBOT may represent a valuable therapeutic modality for enhancing nervous system recovery and maintaining neurological function, particularly in conditions characterized by impaired neuroplasticity and progressive cognitive dysfunction.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 11.03.2026
ACCEPTED: 28.07.2026

CREATIVE COMMONS 4.0

CASE STUDY

Diagnosis and treatment of Crohn's disease with strong activity and rapid progression in the general surgery department

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ABSTRACT

Female patient was urgently admitted to the surgical department. The patient underwent a general clinical examination, abdominal and chest radiography, endoscopy, CT of the abdominal organs, consultations with related specialists. To establish a definitive diagnosis and determine the course of treatment, a laparotomy was performed, involving debridement and drainage of the abdominal cavity. As the condition continued to progress, a subtotal colectomy with colostomy was performed.

X-ray of the chest, abdominal organs, and fibrogastroduodenoscopy revealed no pathology. CT scan revealed signs of bilateral pneumonia and ascites. During fibrocolonoscopy, a diagnosis was made: Crohn's disease of the sigmoid colon. Due to the development of peritonitis, laparotomy, sanitation and drainage of the abdominal cavity were performed. The condition was worsening. Relaparotomy, subtotal colectomy, and colostomy were performed. On the third day after relaparotomy, the condition sharply worsened and death occurred.

The case we studied emphasizes that when assessing the nature of acute surgical pathology of the abdominal cavity, it is necessary to remember Crohn's disease, especially when combined with damage to other systems. When diagnosing this disease, it is necessary to use all possibilities, but the determining factor for making a diagnosis is histological examination. Surgical treatment of Crohn's disease should include all drugs in accordance with clinical protocols, with the use of surgical treatment if complications develop.

KEY WORDS: Crohn's disease, rapid progression, diagnostics, treatment

Wiad Lek. 2026;79(8):1989-1996. doi: 10.36740/WLek/235894 DOI

INTRODUCTION

Crohn's disease (CD) is a chronic relapsing disease with granulomatous inflammation and segmental lesions of the gastrointestinal tract [1, 2]. This disease is more common in developed countries, especially North America and Western Europe. Thus, in the United States, the incidence of CD is up to 20 cases per year per 100 thousand population [3, 4]. A third of patients with CD have various complications already at diagnosis, and more than 10% of people with CD become disabled [4, 5]. About 20% of patients with CD are hospitalized each year, and the risk of surgery after 10 years of disease is more than 40%. Approximately half of all patients develop intestinal complications such as fistulas, cellulitis, strictures and abscesses within 20 years of diagnosis [6, 7].

As a rule, the disease develops gradually. Initially, patients with CD exhibit nonspecific symptoms, then gastrointestinal manifestations are more common, and damage to other organs may occur. Common symptoms are diarrhea, abdominal pain, nausea or vomiting. Weight loss and fever are systemic manifestations of this disease [1, 6]. CD can affect any part of the digestive tract and manifests itself in the ileum or colon in a third of cases [2, 8]. Such a wide range of clinical manifestations leads to diagnostic difficulties and delays in treatment of this disease.

The diagnosis of CD is based on a combination of clinical presentation and endoscopic, radiological, histological and pathological findings, which demonstrate granulomatous inflammation of the gastrointestinal tract [8, 9]. Laboratory testing is optional, and there is no laboratory test that can definitively diagnose CD [2, 10].

Knowledge of the clinical course of CD, potential complications, and medications for its treatment is critical to optimizing medical care for patients with CD. Many issues in the treatment of CD remain controversial even in specialized clinics, especially with regard to severe and atypical forms of the disease [11, 12].

In recent years, the development of CD treatments has focused on patients with early stages of the disease [2, 10, 12], rather than on its complications, when medical care may be delayed, especially in active forms of CD with rapid progression. The choice of indications and volume of surgical intervention in these patients is also difficult [10, 11]. In addition, often such patients are treated not in specialized clinics, but in a general surgical hospital, where the possibilities for their examination and treatment are limited, which complicates the situation.

Thus, despite the development of science, the issues of timely diagnosis and treatment of CD remain relevant. Considering the high incidence of morbidity and mortality in such patients [3, 4, 5], the problem of rational treatment of CD is of great social and medical importance.

FRAMEWORK

The paper is written within the research study entitled "Development of modern scientifically based principles of stratification, monitoring and forecasting of the course of surgical diseases and injuries" (State Registration No. 0120U101176).

CASE REPORT

This case report discusses an atypical presentation of CD in a seventy-seven-year-old woman. Female patient S., born in 1947, was urgently admitted to the surgical department of the Third City Clinical Hospital of Poltava, Ukraine, in 2025. The patient underwent a general clinical examination, plain abdominal radiography, chest radiography, fibrogastroduodenoscopy, colonoscopy, and ultrasound of the abdominal organs, CT of the abdominal organs, consultation with an infectious disease specialist, therapist, and endocrinologist. To establish a final diagnosis and treatment, laparotomy with sanitation and drainage of the abdominal cavity was performed, and in case of disease progression – subtotal colectomy with colostomy. This case report serves as a reminder to clinicians to consider CD in patients presenting with acute surgical pathology, even if they have no previous history of the disease and no family history.

Upon admission to the surgical department, the patient complained of pain in the upper abdomen, dry mouth, and diarrhea for 5 days. She suffers from type 2 diabetes mellitus, insulin-dependent, diabetic nephropathy, chronic pyelonephritis. The family history is not burdened; there were no previous chronic diseases of the gastrointestinal tract. She was examined by an infectious disease specialist, and the conclusion was that there was no evidence of acute infectious pathology.

Upon admission to the hospital, the general condition was of moderate severity. Consciousness is clear. The skin and mucous membranes are of normal color. Blood pressure was 120/80 mmHg, pulse – 76 beats per minute. The abdomen is swollen, symmetrical, increased in size due to subcutaneous tissue, and is involved in breathing. The abdomen is soft, painful in the epigastrium and right hypochondrium. There are no symptoms of peritoneal irritation. Peristalsis is active. The tone of the rectal sphincter was preserved; no additional formations were identified. The stool is loose, daily, and of normal color. Diagnosis has been made: chronic pancreatitis in the acute stage.

The patient was examined. General blood test: leukocytes – 16.7×10^{9}/l, Hb – 124 g/l, erythrocytes – 3.64×10^{12}/l, ESR – 10 mm/h, band neutrophils – 15%, segmented cells – 71%, lymphocytes – 10%. Biochemistry: total protein –71.5 g/l, bilirubin – 8.47 µmol/l, creatinine – 74.9 µmol/l, amylase 34.6 U/l, glucose – 6.3 mmol/l. Chest X-ray is within normal limits. Fibrogastroduodenoscopy revealed no pathology. Plain abdominal X-ray: no free gas and liquid are noted. Kloiber's cup has not been identified, there is no hyperpneumatosis.

The patient was consulted by a therapist. A diagnosis was made: chronic pancreatitis, acute stage, coronary heart disease, supraventricular extrasystole. Treatment was carried out: ezozol, drotaverine, anapirone, infusion, detoxification therapy.

The next day the patient's condition worsened. There were complaints of pain in the lower abdomen, diarrhea, fever up to 39 °C, weakness, dry mouth. A consultation of doctors was held. A CT scan, an ultrasound scan of the abdominal cavity, and a plain radiography of the abdominal cavity were prescribed. Plain abdominal X-ray: no free gas and liquid were detected. Kloiber's bowls have not been identified, there is no hyperpneumatosis. Ultrasound and CT scan of the abdominal cavity revealed: signs of a left kidney cyst, hepatosteatosis, pancreatic lipomatosis.

When examining the patient, the skin is pale. The abdomen is uniformly swollen, has limited participation in breathing, and is painful in the lower sections. Blumberg's symptom is positive. Peristalsis is single. Conclusion: the patient has peritonitis. Surgical intervention is indicated, consent for surgery has been obtained. An operation was performed: laparotomy, sanitation and drainage of the abdominal cavity. Diagnosis after surgery: CD with damage to the sigmoid colon, serous-fibrinous pelvic peritonitis.

Further treatment of the patient was carried out in the intensive care unit. The following drugs were

Fig. 1. Subtotal damage to the colon. The wall of the colon is sharply swollen, infiltrated, the mesentery is swollen, the cecum is enlarged in size, and there are signs of intestinal obstruction.
Picture taken by the authors

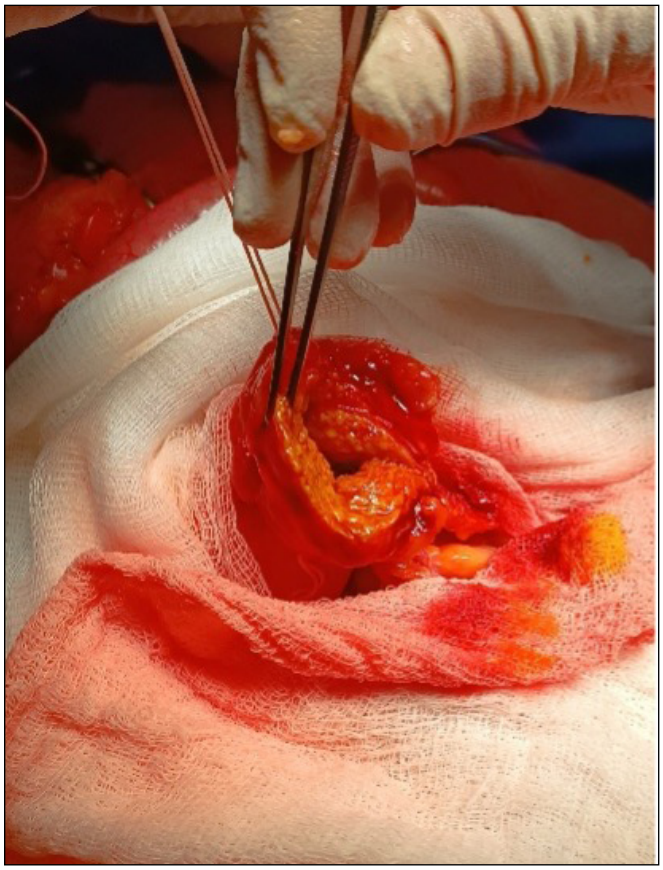

Fig. 2. Subtotal colectomy. Colostomy
Picture taken by the authors

prescribed: esozol, dexamethasone, magnesia, anapirone, analgesics, metronidazole, cefotrin, heparin, insulin therapy, and detoxification, infusion therapy. The general condition is serious, complaints of pain in the area of postoperative wounds. Consciousness is clear. The skin is pale. Body temperature was 37.3° C, pulse – 82 per minute, blood pressure – 137/80 mmHg. The abdomen is soft, painful in the area of postoperative wounds. Bloomberg's symptom is negative. Peristalsis is sluggish. Urine is removed by a catheter. There was up to 450 ml of serous-hemorrhagic contents per day through drainage from the abdominal cavity. An increase in temperature to 38.4 °C was observed during the first to third days after surgery. Biochemical blood test revealed hypoproteinemia, hyperglycemia. General urine analysis: picture of toxic kidney syndrome.

On the third day after surgery, the patient was again consulted by an infectious disease specialist. Diagnosis: chronic pancreatitis, acute stage, chronic calculous cholecystitis, enterocolitis, nonspecific ulcerative colitis, CD? A coprogram and stool culture for pathogenic flora was recommended. The patient was consulted by an endocrinologist. Diagnosis has been made: diabetes mellitus type 2, insulin dependent, moderate severity. Insulin therapy was adjusted.

The following treatment was administered: omeprazole, corticosteroids, diuretics, anapyrone, analgesics, metronidazole, cefotrine, nifuroxazide, salofalk, metoclopramide, fluconazole, haloperidol, chlorpromazine, heparin, insulin therapy, detoxification, infusion therapy.

A general blood test revealed: leukocytes – 37.3×10^{9}/l, Hb – 140 g/l, erythrocytes – 4.1×10^{12}/l, ESR – 32 mm/h, band neutrophils – 60%, lymphocytes – 1%. Examination of the fluid from the abdominal cavity revealed: protein – 31.3 g/l, Rivalta test positive, leukocytes 3-6 in the field of view, red blood cells in the entire field of view, unchanged, and amylase – 45.2 U/l.

On the fourth day after surgery, the patient's general condition was serious; the level of consciousness is stupor. She had pale skin, swelling of the extremities. The patient is oxygen dependent; oxygen saturation is 96% with oxygen inhalation. Pulse 75 beats per minute, blood pressure 120/70 mmHg. The abdomen is soft, painful more in the area of surgical wounds. Bloomberg's symptom is negative. Peristalsis is sluggish, gases escape with the release of liquid. Urine is excreted by catheter, 500.0 ml per day. Laboratory examination revealed: leukocytes – 41.0×10^{9}/l, Hb – 147 g/l, erythrocytes – 4.21×10^{12}/l, ESR – 33 mm/h, band neutrophils – 44%, lymphocytes – 2%. In the biochemical blood test: total protein – 47.0 g/l,

Fig. 3. A removed section of the colon with inflammatory infiltration of the mucous membrane, mucosal necrosis and fibrinous-purulent coating
Picture taken by the authors

Fig. 4. A removed section of the colon with infiltration of the mucous membrane, necrosis of the mucosa and submucosal layer and fibrinous-purulent coating
Picture taken by the authors

bilirubin – 3.07 µmol/l, creatinine – 249.7 µmol/l, glucose – 16.7 mmol/l, calcium – 1.13 mmol/l.

A fibrocolonoscopy was performed: CD of the rectum and sigmoid colon. Repeated CT examination revealed signs of bilateral pneumonia, slight bilateral hydrothorax, hepatosteatosis, ascites, and pancreatic lipomatosis, a small amount of fluid in the abdominal cavity.

A medical consultation was held. Due to increasing intoxication and the development of multiple organ failure, a decision was made to perform relaparotomy. The operation was performed (Fig. 1).

A medical consultation was also held in the operating room. A diagnosis was made: acute necrotizing colitis, CD, peritonitis. Name of operation: laparotomy, subtotal colectomy, colostomy, sanitation and drainage of the abdominal cavity (Fig. 2).

An intraoperative pathohistological examination was performed (Fig. 3 - 5). Conclusion: Intestinal walls with edema, diffuse lympho-leukocyte infiltration, areas of necrosis of the mucosa and submucosal layer. Signs of reactive hyperemia were revealed in the lymph nodes of the mesentery. Final diagnosis: CD.

The day after relaparotomy, the general condition was serious, level of consciousness – stupor-stupor. Oxygen saturation was 94%, oxygen dependence. Pulse – 107 beats per minute, blood pressure was 135/75 mmHg. There was swelling of the trunk and limbs. The abdomen is not swollen, participates in breathing, is soft, and responds to palpation in the area of surgical wounds. Peristalsis is sluggish. The stoma is functioning and viable. Urine is excreted by catheter, 100.0 ml. Wounds were without signs of inflammation. Conservative therapy was continued in the intensive care unit. The blood test revealed pronounced leukocytosis, a shift in the leukocyte formula to the left, hypoproteinemia, azotemia, and hyperglycemia.

Fig. 5. Swelling of the intestinal wall, infiltration, areas of necrosis of the mucosa and submucosal layer
Picture taken by the authors

The patient was subsequently treated in the intensive care unit. The condition progressively worsened, extremely serious, consciousness is stupor. On a ventilator. There were swellings of the upper and lower extremities, phenomena of multiple organ failure, oliguria. There is no peristalsis. An increase in temperature to 38.0 °C was observed.

The patient had increasing signs of intoxication and multiple organ failure: anuria, signs of cardiovascular, pulmonary and liver failure, protein metabolism disorders.

On the third day after relaparotomy, the patient's condition sharply worsened. Level of consciousness is coma II, blood pressure 70/30 mmHg. Blood pressure is maintained by administering vasopressors. Despite the therapy, the patient's condition worsened, agony and clinical death occurred, resuscitation measures were carried out, and biological death was diagnosed.

A diagnosis was made: CD. Diffuse serous peritonitis. Intoxication. Multiple organ failure. Ischemic heart disease. Diffuse cardiosclerosis. Heart failure II. Diabetes mellitus type II, moderate severity, stage of decompensation with multiple complications. Hypertension II degree. Obesity III degree.

DISCUSSION

With all the polymorphism of CD, there are certain patterns of development and clinical picture of this disease. On average, the disease begins at the age of about 30 years [1, 2, 3]. The clinical course with gradual progression has two peaks of activation, first from 20 to 30 years, and then the peak is observed at the age of about 50 years [1, 3, 4]. Features of the clinical course for each patient are difficult to predict, but the constant progression of the disease ultimately leads to the development of complications. About 75% of patients with CD undergo surgery due to complications of the disease [4, 5].

In the case we examined in the patient, CD appeared suddenly and actively at the age of 77 years; before that, the patient and her relatives had no signs of the disease.

The clinical picture of CD is usually characterized by an alternation of lesions over a large area and unchanged areas between them [1, 2]. Most often, CD involves damage to the terminal ileum [1, 2, 3]. When the disease is localized in the colon, in contrast to the upper gastrointestinal tract, an aggressive course of the disease, the development of complications and the need for surgical intervention are much less likely to be observed [2, 6].

In the case we studied, there was subtotal damage to the colon with massive damage to the mucosa and submucosal layer without unchanged areas. Here, apparently, toxic colitis took place – a rare complication of CD, which occurs in less than 10% of patients with a severe, fulminant course of the inflammatory process [1, 2, 10]. Unlike ulcerative colitis, which affects only the mucous membrane, CD affects all layers of the intestinal wall. At the same time, the colon expands, intestinal obstruction occurs and peritonitis develops [2, 10].

Ileocolonoscopy with targeted biopsy and CT examination for CD are the procedure of choice [2, 8]. The accuracy of CT for CD is more than 90% [8, 9]. Macroscopically, in CD, confluent deep linear ulcers and fissures, segmental disease, nodular compaction of the mucous membrane and thickening of the intestinal wall are observed. Upper endoscopy is performed only in patients with signs of damage to the upper gastrointestinal tract. [1, 2, 13].

In addition to different types of CD, there are also different patterns of disease progression [13, 14, 15]. Thus, with the luminal form of CD, changes in the intestinal mucosa due to inflammation are observed. Fibrostenotic CD involves the presence of intestinal strictures. The penetrating form of CD leads to the formation of fistulas between the inflamed intestine and other parts

of the body. In the clinical case we reviewed, there was a luminal form of CD.

In clinical trials and when choosing treatment, the CD Activity Index (CDAI) is used [2, 10, 16]. This takes into account: age, gender, body mass index, hematocrit, the presence of a mass in the abdominal cavity, as well as symptoms over the last 7 days and general well-being. A score of less than 150 points indicates clinical remission, 150-220 points – low disease activity, 220-450 – moderate activity, and more than 450 points means high activity [1, 2]. According to this scale, this patient had a score of more than 450 points, that is, she had CD of strong activity and rapid progression.

Selecting optimal drug therapy for moderate to severe CD is challenging, with limited applicable recommendations on the effectiveness and safety of various treatments, leading to significant variability in practice [11, 17, 18].

Optimal management of patients with severe luminal CD often requires the use of glucocorticosteroids, immunomodulators (thiopurines, methotrexate) or tumor necrosis factor-α (TNF-α) inhibitors [2, 10, 12]. Oral mesalazine has not been shown to be effective in inducing remission in patients with active CD. Patients with severe CD are advised to avoid the use of 5-aminosalicylates to induce remission [2, 10, 14]. For the treatment of severe or fulminant CD, the use of intravenous corticosteroids is recommended, as was the case in this clinical case. At the same time, preoperative use of steroids leads to an increased risk of postoperative complications (anastomotic leakage, intra-abdominal abscess) [10, 19, 20]. Azathioprine and 6-mercaptopurine are not recommended for patients with severe forms. In such patients, it is proposed to use methotrexate monotherapy [10, 11, 19]. TNF-α inhibitors should be used to treat CD that is resistant to corticosteroid treatment, as well as in the case of severe active and fulminant forms [10, 17, 18].

The patient underwent all examinations available in a general surgical hospital, as provided for by modern clinical practice guidelines for the treatment of moderate and severe CD [2, 10]. The patient also received conservative therapy in accordance with the approved current clinical protocols and recommendations for the treatment of CD [14, 15, 18]. Anti-TNF drugs were not used in treatment due to the fulminant course of the disease. The severe manifestation of the disease in the patient, the presence of SIRS, and multiple organ failure required combined empirical de-escalation antibacterial therapy with drugs with a broad spectrum of action.

According to leading experts [2, 10, 21], terminal ileitis and inflammatory changes in the colon in CD, discovered incidentally during laparotomy, should not be subject to mandatory resection. Surgery is indicated for the development of complications (acute toxic dilatation of the colon, wall perforation, pericolar abscess, peritonitis) [21, 22]. Moreover, resection of the affected area of the intestine is the most common operation for CD, which is used in patients even in critical condition [2, 21, 22]. This is exactly the volume of surgical interventions performed on this patient.

Unfortunately, the patient sought medical help with a long delay – five days after the onset of the disease, which led to progression of the disease, multiple organ failure and significant difficulties in diagnosing the disease. The outcome of the patient's treatment was also, of course, influenced by the presence of immunosuppression against the background of long-standing diabetes mellitus, chronic pyelonephritis and nephropathy, as well as other concomitant pathologies.

CONCLUSSIONS

The case we studied emphasizes that when assessing the nature of acute surgical pathology of the abdominal cavity, it is necessary to remember CD, especially when combined with damage to other organs and systems, even in the absence of a family history and previous manifestations in the patient.

When diagnosing this disease in a general surgical department, it is necessary to use all available possibilities, but the determining factor for making a diagnosis is histological examination.]

Surgical treatment of CD with severe activity and rapid progression should include all drugs in accordance with clinical protocols, with the use of surgical treatment if complications develop.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 11.03.2026
ACCEPTED: 29.07.2026

CREATIVE COMMONS 4.0

CASE STUDY

Pulmonary artery thromboembolism and its recurrence in penetrating injuries of the lower extremities (analysis of clinical cases)

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ABSTRACT
Two clinical cases of the onset and recurrence of pulmonary embolism (PE) in military personnel with penetrating wounds of the lower extremities are presented. Both patients were taking a prophylactic dose of anticoagulants.
In the first case, high-risk PE developed with recurrent hypertension and few symptoms, which contributed to late diagnosis and sudden death. In the second case, PE recurred in a patient receiving a full dose of anticoagulants for no apparent reason.
Therefore, attention should be paid to this category of patients with penetrating injuries of the lower extremities, their risk of VTE should be stratified in more detail, and the possibility of PE recurrence should be considered, even against the background of anticoagulant therapy.It is promising that risk scales should be reviewed and new criteria for the diagnosis and possibility of recurrence of PE should be developed for this category of patients, which will take into account a greater number of risk factors, develop algorithms for the diagnosis of PE with the possibility of more frequent detailed examinations, and adjust the prophylactic doses of anticoagulants, taking into account the inability to wear elastic stockings due to wounds on the lower extremities.

KEY WORDS: pulmonary embolism, penetrating injury of the lower extremities, clinical cases

Wiad Lek. 2026;79(8):1997-2002. doi: 10.36740/WLek/222259 DOI

INTRODUCTION

Since the start of the war in Ukraine, there's been a big jump in the number of patients with injuries, including penetrating injuries to the lower limbs, which is dangerous because of damage to blood vessels, nerves, and muscles, and the development of infectious complications that are resistant to antibiotic treatment. However, such injuries have another complication that often goes unrecognised in time and can lead to death, as there is often an mildly symptomatic clinical condition that ends in sudden death [1]. This complication is pulmonary embolism (PE), which is recognised by the WHO as one of the most common cardiovascular diseases and is the third leading cause of sudden death after ischaemic heart disease and acute cerebrovascular accident, even in peacetime [2]. The incidence of PE in peacetime mechanical injuries ranges from 1% to 3%, and in mine-blast injuries and gunshot wounds, it is 3–5% of cases, with predominant development on the 2nd–4th day, but most often observed within 5–7 days after the injury, with a high risk of recurrence in the following 4–6 weeks [3]. Patients with multiple and combined chest injuries, accounting for up to 15% of medical losses, are most alert to the occurrence of PE, which has led to significant adjustments in the understanding of the etiology, pathogenesis, clinical course and treatment, including in the cohort of patients with multiple injuries [2]. However, patients with penetrating wounds of the lower extremities require no less attention in terms of vigilance for the occurrence of PE, as they may have an atypical clinical picture of PE and, due to limited mobility, may not notice pathognomonic symptoms. An equally important factor that significantly increases the risk of VTE is the development of traumatic shock in combat trauma, including penetrating wounds of the lower extremities, which is diagnosed in 8-10% of individuals [2]. During traumatic shock, haemodynamic disorders occur in the pulmonary circulation, contributing to the development of microthrombi and surfactant microatelectasis. As a result of fractures of long and tubular bones, the dispersibility of neutral blood plasma fat is disrupted, which provokes the development of fat

embolism, including in the vessels of the small circle, against the background of microthrombi. An additional component that significantly increases the risk of thrombosis is massive blood loss and the development of microcirculation disorders [2]. Another important factor is the type of vessel that was damaged during the injury. The Pennsylvania Trauma Outcome Study registry showed that the incidence of VTE fluctuates around 13.2% in penetrating injuries of the femoral and popliteal arteries, while in isolated arterial injuries it is only 3.1%. Open surgical interventions significantly increase the risk of deep vein thrombosis, which in turn increases the risk of PE [4].

An important component of the treatment of penetrating injuries of the lower extremities is the prophylactic use of anticoagulants. Pharmacological prevention of VTE is a critically important component of optimal trauma care, significantly reducing the risk of VTE [5]. The D-dimer Age Sex Hormones (DASH) scale has been proposed to assess the likelihood of recurrence after a first episode of VTE [6]. The basis is the level of D-dimer concentration 30 days after the end of anticoagulant prophylaxis. The incidence of VTE is the same in patients with blunt or penetrating trauma, but independent risk factors for VTE differ depending on the mechanism of injury, the severity of the patient's condition, and the need for oxygen support, which is crucial when considering a thromboprophylaxis strategy. Factors that increase the risk of VTE in patients with blunt trauma include blood transfusion, deterioration of neurological status, and pelvic fracture. Factors that increase the risk in patients with penetrating trauma include vascular injury, severe abdominal trauma, and age between 40 and 59 years. Taking these characteristics into account, it is possible to predict the risk of VTE, which depends on the mechanism of injury. There are studies whose authors argue that by examining APACHE II scores in surgical patients, it is possible to detect VTE even in patients with a low risk of VTE, which will allow preventive measures to be taken in a timely manner. However, this approach is most appropriate for patients with severe trauma who are in the intensive care unit undergoing various types of oxygenation and blood gas correction [7]. Elevated D-dimer levels detected after discontinuation of anticoagulant therapy have high negative predictive value for VTE recurrence. Even when D-dimer levels are within reference ranges, other factors such as age, gender, and other factors that may contribute to VTE are important [8]. For example, VTE is more common in men than in women. The risk of VTE also increases with age, especially in the presence of additional risk factors [8].

CASE REPORT

Two clinical cases of the onset and recurrence of PE in military personnel with penetrating wounds of the lower extremities are presented. The patients were over 40 years of age. Both patients were taking a prophylactic dose of anticoagulants. Both patients had no history of traumatic shock, major blood loss, injury to the femoral and popliteal arteries, pelvic fractures, or severe injuries to the chest and abdominal organs. Prior to the episode, the patients were somatically stable and did not require resuscitation measures.

CLINICAL CASE 1

A 44-year-old soldier, V., was admitted to the surgical department with a penetrating wound to his right lower limb. He underwent surgery the next day. Due to severe pain, he was practically bedridden for 5 days. On the evening of the fifth day after the operation, he went to the hospital restroom on his own, where he briefly lost consciousness. When he came to, he returned to his ward. He complained only of slight dizziness. His blood pressure was measured at 85/45 mm Hg, but an hour later it was 110/70 mm Hg, and the dizziness had disappeared. He noted slight general weakness. The patient refused further examination on that day, arguing that he had recovered satisfactorily and was feeling better. The next day, on Monday, the risk of PE in this patient was stratified using the Caprini scale. The patient scored 12 points, indicating an extremely high risk of VTE. Accordingly, compression ultrasonography of the lower extremities was performed, revealing an enlarged inferior vena cava that did not collapse on inspiration and thrombotic masses in the deep veins. The results obtained indirectly indicate right ventricular dysfunction, which is probably caused by the development of acute pulmonary heart disease. An ECG was performed, which showed no rightward shift of the electrical axis, partial blockage of the right bundle branch, minor repolarisation abnormalities in the form of flattened T waves and slight inversion in the right chest leads. PE was suspected, although the patient did not complain of shortness of breath. However, an objective examination revealed a decrease in saturation to 92%. A transthoracic echocardiogram was performed, which revealed significant enlargement of the left ventricle with signs of hypokinesis, tricuspid regurgitation of the II degree, prolapse of the mitral valve into the left ventricle, enlarged pulmonary artery valve that does not close during inspiration, grade II pulmonary hypertension, and a floating thrombus in the right atrium. The patient was diagnosed with PE, which causes haemodynamic disturbances and right ventricular dysfunction.

Auscultation of the lungs revealed weakened vesicular breathing on the right above the upper lobe, indicating the development of infarct pneumonia. A contrast-enhanced computed tomography (CT) scan of the chest was performed: thrombotic masses in the pulmonary artery trunk with 90% occlusion, increased diameter of the pulmonary artery, symptom of 'amputation' of the branches of the right upper lobar artery. Infiltrative changes in the right upper lobe of the lung. Given the presence of persistent hypotension and right ventricular dysfunction, the patient was diagnosed with high-risk PE and the following diagnosis was made: Penetrating injury of the right lower extremity, condition after surgery. High-risk PE, grade II cardiopulmonary shock. Right upper lobe infarction-pneumonia. Grade I respiratory failure ($Sa\ O2$ 92%).

When analysing this clinical case, it should be noted that the patient did not have typical clinical symptoms of PE, which would manifest as sudden shortness of breath, coughing, and chest pain. The presence of persistent hypotension, which was recorded, indicated the development of a catastrophic situation, but the patient's general condition did not correspond to the severity of the developing pathology. Even his heart rate was within the range of 85-92 beats per minute. Only the next day (Tuesday) did the patient begin to notice slight difficulty breathing and palpitations. The patient was examined only with regard to the risk factors for PE, rather than the presence of a typical clinical situation, although there was thrombosis of 90% of the pulmonary artery trunk, which may indicate a subacute course of PE. The laboratory test results corresponded to the severity of the injury: moderate leukocytosis, haemoglobin 120 g/l, transaminases elevated 1.2 times, so they were not interpreted as changes in PE. Another important point was that the patient received a prophylactic dose of anticoagulants (enoxaparin 0.4 ml twice daily), but there was no complete prevention of thrombus formation. Complete mechanical prevention with elastic bandages was impossible due to surgery on the lower leg. The patient was consulted by vascular surgeons and a decision was made to perform surgery – thromboectomy. However, the patient died during the operation.

CLINICAL CASE 2

A 46-year-old soldier, S., was brought to the hospital by an ambulance team after suddenly experiencing shortness of breath at rest. He also complained of pain in his left lower leg, which disappeared after taking painkillers. The medical history shows that he had an explosive-fragment blind wound of the soft tissues of the right lower leg and lower third of the left lower leg, with an open comminuted fracture of the tibia and fibula. A week after the injury, surgery was performed to install an external fixation device, and another week later, autodermoplasty of the left lower leg wound was performed. One and a half months after the last operation, PE of the right lobar branches and segmental branches of both pulmonary arteries was diagnosed. The patient was treated and received rivaroxaban 20 mg/day to prevent recurrence. Recent contrast-enhanced CT scans showed no fresh thromboembolic masses, only a small number of thrombi with complete recanalisation. On objective examination, the general condition is moderate, blood pressure is 140/100 mm Hg, pulse is 75 beats per minute, breathing is vesicular, weakened in the lower sections, respiratory rate is 17 per minute, stage I obesity (body mass index 33.95 kg/m^2), edema of the lower legs, more pronounced on the left side. The patient was assessed using the Caprini scale (verification of the risk of VTE in surgical patients), on which he scored more than 5 points, indicating an extremely high risk of VTE. Based on clinical data, a recurrence of PE is suspected, as the patient has been ruled out for heart disease and other comorbidities that would cause such a clinical picture. Given the stability of haemodynamics, the patient immediately underwent a CT scan of the chest, which revealed thromboembolism of the right lobe and branches of both pulmonary arteries, chronic bronchitis, pulmonary pneumofibrosis in D5 as a result of resolution of infarction pneumonia, signs of pulmonary hypertension, recanalisation of thrombotic masses in segmental branches. Congestive phenomena of the small circle of blood circulation. Analysing the clinical course in the first case, a distinctive feature was that, despite prophylactic doses of anticoagulants, a combination of risk factors, such as major surgery, prolonged immobilisation and, possibly, the use of painkillers, significantly influenced the development of VTE, although there were no significant risk factors such as traumatic shock, severe blood loss, or injury to large arteries. An important feature was that, in the case of high-risk PE, there was no corresponding pathognomonic shortness of breath, palpitations, or heart pain, despite the presence of recurrent hypotension, which indicated a subacute course of PE development. However, this contributed to a later diagnosis of the disease and subsequent fatal outcome.

In the second case, the patient had a recurrence of PE with pathognomonic symptoms while taking a sufficient dose of anticoagulants. It was too early to stratify such a patient according to the DASH risk probability scale, which primarily includes D-dimer indicators. His first episode of PE occurred 1.5 months

after the injury and the last surgery, and the second episode of PE occurred 1.5 months after the first episode. No apparent reasons for the recurrence of TEA were identified.

A distinctive feature of the first case is the asymptomatic course of PE, which can be explained by the patient's significantly reduced physical activity after surgery and the presence of pain symptoms, which masked shortness of breath and palpitations. There is insufficient literature on this topic, but there are studies explaining the asymptomatic course of PE in cancer patients, although there is insufficient information about wounded patients, especially those with specific wound locations.

Recurrence of PE has a marked tendency to occur after the first episode of PE, which occurs in 4% of patients after VTE, even with adequate anticoagulant therapy [9]. The occurrence of PE contributes to the development of pulmonary hypertension, which in turn increases the formation of microthrombi and contributes to the recurrence of PE. At the same time, the frequency of recurrence increases significantly in patients who discontinue anticoagulant therapy. The highest risk of recurrence occurs in the first 6-12 months, but never decreases to zero, which is why some scientists believe that VTE is a chronic disease with episodic recurrences [9]. The risk of recurrence is significantly lower in distal vessels than in proximal vessels, which makes the presented clinical case noteworthy. Both relapses and the initial onset of PE can be caused by thrombophilia, which is not determined in the general population and was not determined in the patients presented, although in the second case, the patient was recommended to determine his genetic predisposition to thrombophilia.

CONCLUSIONS

Therefore, attention should be paid to this category of patients with penetrating injuries of the lower extremities, their risk of VTE should be stratified in more detail, and the possibility of PE recurrence should be considered, even against the background of anticoagulant therapy. It is promising that risk scales should be reviewed and new criteria for the diagnosis and possibility of recurrence of PE should be developed for this category of patients, which will take into account a greater number of risk factors, develop algorithms for the diagnosis of PE with the possibility of more frequent detailed examinations, and adjust the prophylactic doses of anticoagulants, taking into account the inability to wear elastic stockings due to wounds on the lower extremities.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 24.11.2025
ACCEPTED: 20.05.2026

CREATIVE COMMONS 4.0