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Wiadomości Lekarskie
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ORIGINAL ARTICLE

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Endometritis after hysteroscopic procedures in Ukraine: results a multicenter study

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ABSTRACT

Aim: To determine the current prevalence of endometritis after hysteroscopic procedures and antimicrobial resistance of responsible pathogens in Ukraine.

Materials and Methods: Multicenter prospective cohort study was conducted from January 2020 to December 2022 in fifteen hospitals from twelve regions of Ukraine. Definitions of endometritis were adapted from the Centers for Disease Control and Prevention's National Healthcare Safety Network. Antibiotic susceptibility was done by the disc diffusion test as recommended by EUCAST.

Results: Among 13,872 patients with hysteroscopic procedures, 1027 (7.4%) endometritis were observed. Of these cases, 0.4% were detected after diagnostic hysteroscopy, and 7.0% were detected after operative hysteroscopy. Of all endometritis cases, 64.2% were detected after hospital discharge. The most commonly reported bacterial species were *Escherichia coli* (24.3%), followed by *Enterobacter* spp. (12.7%), *Enterococcus* spp. (8.3%), *Pseudomonas aeruginosa* (8.1%), *Serratia marcescens* (6.8%), *Staphylococcus aureus* (5.9%), *Proteus mirabilis* (5.8%), *Klebsiella oxytoca* (5.1%), *Stenotrophomonas maltophilia* (4.5%), *Klebsiella pneumoniae* (4.1%). A significant proportion of patients were affected by endometritis caused by bacteria developed resistance to several antimicrobials, varying widely depending on the bacterial species, antimicrobial group, and geographical region of Ukraine.

Conclusions: Our data suggest a high prevalence of endometritis after hysteroscopic procedures. Risk for endometritis was higher after operative hysteroscopy compared with diagnostic hysteroscopy. Many most of patients were affected by endometritis caused by bacteria developed resistance to several antimicrobials. These data underscore the importance of tracking antimicrobial resistance of responsible pathogens of HAIs in hospitals.

KEY WORDS: hysteroscopic procedure, endometritis, responsible pathogens, antibiotic prophylaxis, antimicrobial resistance, Ukraine

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INTRODUCTION

Maternal morbidity are global socioeconomic and healthcare burdens, and healthcare-associated infections account for a significant, and often preventable, portion of that burden. Endometritis, primarily caused by bacterial pathogens, leading to poor reproductive performance [1]. Inflammation of the uterus can cause scarring, which prevents an embryo from implanting and developing normally within the uterine wall [2, 3]. In a prospective study, Kamiyama et al. [4] have demonstrated a negative biological effect of bacterial endotoxin in vitro fertilization – embryo transfer (IVF-ET) treatment, suggesting a link between endotoxin levels in menstrual effluent and pregnancy rate. Endotoxins are part of the outer membrane of the cell wall of Gram-negative pathogens such as *Escherichia coli*, *Salmonella, Shigella, Pseudomonas, Neisseria, Haemophilus influenza* [5]. Repeated implantation failure (RIF) and recurrent pregnancy loss (RPL) impose a heavy burden on women desiring children, especially when etiology is unclear [6]. Implantation failure has been identified by the European Society of Human Reproduction and Embryology as one of the main unresolved issues in reproductive medicine.

Endometritis is a condition involving the breakdown of the peaceful co-existence between microorganisms and the host immune system in the endometrium. Conventionally, the uterine cavity is assumed to be sterile, but in fact, microorganisms have been detected in the endometrial cavity of non-pregnant women. It has been

proposed that microorganisms ascending from the lower genital tract could colonize the uterine cavity; however, host mechanisms have been expected to restrict bacterial proliferation and invasion. These mechanisms involve the cervical mucus plug [7], the endometrial epithelium and its immune cellular components (neutrophils, macrophages, and natural killer cells), and elements of the innate immune system, including natural antimicrobial peptides present in the endometrium [8].

Infections that occur after hysteroscopic surgery can result in considerable ill health for the women. The prescription of antibiotics after an hysteroscopic surgery has become routine practice to overcome this situation in Ukraine. Faced with increasing antimicrobial resistance because of misuse and over-prescription of antibiotics, we need evidence about the effect of routine intake of antibiotics for preventing infections after hysteroscopic surgery. Currently, prevalence of endometritis after hysteroscopic surgery in women and the bacteria responsible for these infections have not been adequately studied.

AIM

The aim this study to determine the current prevalence of endometritis after hysteroscopic procedures in women and antimicrobial resistance and antimicrobial resistance of responsible pathogens in Ukraine.

MATERIALS AND METHODS

STUDY DESIGN, SETTING AND POPULATION

We performed a multicentre prospective cohort study was based on surveillance data for healthcare-associated infections (HAIs). The study population consisted of all women who had a hysteroscopic procedures from January, 2020, to December, 2022, and who received postoperative care in gynecological departments at fifteen general hospitals from twelve regions of Ukraine. All hospitals which are similar in terms of medical equipment, personnel, and laboratory facilities. Indications for the operative hysteroscopies included abnormal uterine bleeding, ultrasound or hysterographic findings indicative of intrauterine lesions, dysfunctional uterine bleeding. Exclusive criteria were pregnancy, cervical carcinoma, pelvic inflammatory disease and excessive bleeding. Hysteroscopies were performed in the above departments. First a diagnostic hysteroscopy was performed and afterwards the final diagnostic operative hysteroscopy was performed at the same time in the majority of the study population. The diagnostic hysteroscopies were performed using a standard 4-mm hysteroscope. Using a resectoscope submucous myomas and endometrial polyps were resected or a transcervical resection of endometrium (TCRE) was performed. In total TCRE the entire uterine cavity was treated together with the upper part of the endocervix.

DEFINITION

The criteria for endometritis after hysteroscopic surgery were adapted from the Centers for Disease Control and Prevention's (CDC) and National Healthcare Safety Network's (NHSN) case definitions. Endometritis must meet at least one of the following criteria: (a) patient has organism(s) identified from endometrial fluid or tissue by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment, for example, not Active Surveillance Culture/Testing (ASC/AST), (b) patient has suspected endometritis with at least two of the following signs or symptoms: fever (>38.0°C), pain or tenderness (uterine or abdominal) with no other recognized cause, or purulent drainage from uterus. Any bacterial isolate of the species under surveillance found in a sample taken from a normally sterile body fluid may be considered a pathogen.

DATA COLLECTION

Hospital staff participating in HAI surveillance underwent a training course that covered endometritis case definitions and diagnoses, and instructions for surveillance data collection and reporting. We developed a special questionnaire that collected data from medical records, including, age (years), discharges of patients, microbiological and radiographic investigations, hysteroscopic procedures, antibiotics usage, and culture and sensitivity of the clinical isolates. Follow-up of each patient was continued for one month after hysteroscopic procedures. The discharged patients were advised for ongoing follow-up care for a month after hysteroscopic procedures in the outpatient department. Information regarding the postoperative period following discharge was obtained from the outpatient records and from records documenting follow-up by referring gynecologists.

MICROBIOLOGICAL METHODS

In this study, pathogen strains were identified by an automated microbial identification system. The interpretation of antimicrobial susceptibility testing results was evaluated for strains with a correct species identification. The evaluation was performed according to the clinical breakpoints in the European Committee on Antimicrobial Susceptibility Testing (EUCAST) Clinical Breakpoints Tables v12.01, with the EUCAST categories

Table 1. Distribution of 1,027 endometritis cases in women after hysteroscopic procedures in Ukrainian hospitals, 2020-2022

Type of procedure	Number of patients	Endometritis		95% CI
		n	%	
Diagnostic hysteroscopy	8248	49	0.6	0.5 - 0.7
Operative hysteroscopy	5624	978	17.4	17.1 - 17.7
Total	13,872	1,027	7.4	7.2 - 7.6

Table 2. Distribution of pathogens isolated from patients with endometritis after hysteroscopic procedures in Ukraine, 2020-2022

Microorganisms	Number of isolates (n)	Percentage (%)
Gram-positive cocci	292	21.0
Enterococcus spp.	115	8.3
Streptococcus pneumoniae	41	2.9
Coagulase-negative staphylococci	54	3.9
Staphylococcus aureus	82	5.9
Gram-negative bacilli	1106	79.5
Escherichia coli	338	24.3
Klebsiella pneumoniae	57	4.1
Klebsiella oxytoca	71	5.1
Enterobacter spp.	177	12.7
Proteus mirabilis	81	5.8
Serratia marcescens	95	6.8
Stenotrophomonas maltophilia	62	4.5
Citrobacter spp.	52	3.7
Pseudomonas aeruginosa	113	8.1
Acinetobacter baumannii	45	3.2
Fungi	9	0.6
Candida albicans	9	0.6
Total	1392	100.0

"susceptible, standard dosing regimen" (S), "susceptible, increased exposure" (I), and "resistant" (R). An isolate is considered resistant to an antimicrobial agent when tested and interpreted as R in accordance with the clinical breakpoint criteria used by the local laboratory. Meticillin-resistant *Staphylococcus aureus* (MRSA) is based on AST results for cefoxitin or, if unavailable, oxacillin. AST results reported for cloxacillin, dicloxacillin, flucloxacillin or meticillin are accepted as a marker for oxacillin resistance if oxacillin is not reported.

ETHICS

All patients gave written consent before the procedure and the study was approved by the Institutional Research Ethics Committee of Shupyk National Healthcare University of Ukraine. All data from patients were anonymized prior to analysis.

STATISTICAL ANALYSIS

All clinical and microbiological data were entered in an Excel (Microsoft Corp., Redmond, WA, USA) database for statistical analysis. Results this study are expressed as median (range), mean ± standard deviation for continuous variables, and number and corresponding percentage for qualitative variables. Proportions of total endometritis cases meeting specific CDC/NHSN criteria were calculated, and characteristics of each category were compared by using Fisher's exact test. All statistical analyses were two-sided and significance was set at $P < 0.05$.

RESULTS

PREVALENCE OF ENDOMETRITIS

Of the 13,872 patients evaluated, 8,248 underwent a diagnostic hysteroscopy and 5,624 underwent an opera-

tive hysteroscopy. During the study period, 1027 (7.4%) of 13,872 patients after hysteroscopic procedures were found to have endometritis. Of the total endometritis cases, 64.2% were detected after hospital discharge. The prevalence of endometritis after hysteroscopic procedures

in Ukrainian hospitals was 7.4% (95% confidence interval [CI] 7.2-7.6), and the prevalence of endometritis in different types procedures was: after diagnostic hysteroscopy, 0.4% (95% CI 0.3-0.5), and after operative hysteroscopy, 7.0% (95% CI 6.9-7.3). The distribution of endometritis after hysteroscopic procedures in Ukrainian hospitals is shown in Table 1. The risk for endometritis was similar for endometrectomy, fibroma, or polyp resections.

RESPONSIBLE PATHOGENS

A total number of reported isolates from patients with endometritis after hysteroscopic procedures in 2020-2022 were 1392. The most commonly reported bacterial species in 2020-2022 were *Escherichia coli* (24.3%), followed by *Enterobacter* spp. (12.7%), *Enterococcus* spp. (8.3%), *Pseudomonas aeruginosa* (8.1%), *Serratia marcescens* (6.8%), *Staphylococcus aureus* (5.9%), *Proteus mirabilis* (5.8%), *Klebsiella oxytoca* (5.1%), *Stenotrophomonas maltophilia* (4.5%), *Klebsiella pneumoniae* (4.1%), Coagulase-negative staphylococci (3.9%), *Citrobacter* spp. (3.8%), *Acinetobacter baumannii* (3.2%), *Streptococcus pneumoniae* (2.9%). Distribution of pathogens isolated from patients with endometritis after hysteroscopic procedures are presented in Table 2.

ANTIMICROBIAL RESISTANCE

During study period the antimicrobial resistance (AMR) situation reported by Ukrainian hospitals varied widely, depending on the bacterial species, antimicrobial group and geographical region, as demonstrated by both varying AMR percentages and estimated incidences of endometritis with resistant bacteria. The reported AMR percentages and estimated incidences of endometritis with resistant bacteria varied widely among Ukrainian regions, often with a north-to-south and west-to-east gradient. In general, the lowest AMR percentages were reported by hospitals in the north of Ukraine and the highest by countries in the south and east of Ukraine.

In hospitals, more than half of the *E. coli* isolates reported, and almost a third of the *K. pneumoniae* isolates, were resistant to at least one antimicrobial group, and combined resistance to several antimicrobial groups was a frequent occurrence. With one notable exception (i.e. carbapenem resistance in *K. pneumoniae*), both *E. coli* and K. pneumoniae saw either decreasing trends in the Ukraine, or no trend. For third-generation cephalosporin-resistant *E. coli*, a decreasing trend in the estimated incidence of endometritis was also noted from 2020 to 2022 for the Ukraine with a 16.8% decrease in 2022 against the baseline year 2020. Among antimicrobial groups monitored for both species, mean AMR percentages were generally higher in *K. pneumoniae* than in *E. coli*.

Carbapenem resistance remained rare in *E. coli*, but almost one third of Ukrainian hospitals reported carbapenem resistance percentages above ≥10% in *K. pneumoniae*. There was a significantly increasing trend in the estimated incidence of endometritis with carbapenem-resistant *K. pneumoniae*, with a 19.5% increase in 2022 against the baseline year 2020. Carbapenem resistance was also common in *P. aeruginosa* and *A. baumannii*, with a higher mean percentage than in *K. pneumoniae*. For most gram-negative bacteria, increases in the Ukrainian hospitals mean AMR percentages between 2020 and 2022 were moderate, although AMR remained at high levels.

For *S. aureus*, a significantly decreasing trend in the hospitals mean percentage of meticillin-resistant *S. aureus* (MRSA) isolates (8.1%), and in the estimated incidence of endometritis with MRSA was reported during the period 2020–2022. In addition to the increase in the number of reported isolates in 2022 compared to 2020, the last five years have seen a significantly increasing trend for mean percentage of macrolide resistance and penicillin non-wild-type, including combined resistance in *S. pneumoniae*. One development of particular concern was that the significantly increasing trend in the mean percentage of vancomycin-resistant isolates of *Enterococcus* spp. rose further, from 10.2% in 2020 to 14.7% in 2022.

DISCUSSION

In the present study, to the best of our knowledge the largest prospective, controlled study to date, we evaluated the prevalence of endometritis after both diagnostic and operative hysteroscopy, and antimicrobial resistance of responsible pathogens. Our data suggest a high prevalence of endometritis after hysteroscopic procedures. Risk for endometritis was higher after operative hysteroscopy compared with diagnostic hysteroscopy. The present study found that a significant proportion of study population were affected by endometritis caused by bacteria developed resistance to several antimicrobials.

Hysteroscopy is a minimally invasive gynecological procedure and is considered the gold standard for the

treatment of intracavitary benign uterine pathology. This minimally invasive technique can be associated with serious complications that can lead to severe morbidity. As for any surgical intervention, there is a risk of infection after surgery. However, the rate and severity of such complications is poorly documented. Few authors have specifically evaluated the infectious risk according to the operative procedure. The epidemiology of HAIs after hysteroscopic procedures has not been well characterized. In part this is because of the limitations of surveillance systems, which usually monitor infections after hysteroscopic procedures that are recognized during hospitalization.

According to the literature, prevalence of endometritis after hysteroscopic procedures is estimated is between 0.01% [9] and 2.1% [10]. In our study, the prevalence of endometritis after hysteroscopic procedures in Ukrainian hospitals was 7.4% (95% CI 7.2-7.6%), and the prevalence of endometritis in different types procedures was: after diagnostic hysteroscopy, 0.4% (95% CI 0.3-0.5%), and after operative hysteroscopy, 7.1% (95% CI 6.9-7.3%). Of all endometritis cases, 64.2% were detected after hospital discharge. The risk for endometritis was similar for endometrectomy, fibroma, or polyp resections.

In this study a total, 1392 strains (Gram-negative and -positive bacteria, and fungi) were isolated from 1027 patients with endometritis after hysteroscopic procedures. The predominant endometritis pathogens were: *E. coli*, *Enterobacter* spp., *Enterococcus* spp., *P. aeruginosa*, *S. marcescens*, *S. aureus, P. mirabilis, Klebsiella oxytoca, S. maltophilia,* and *K. pneumoniae.* The antimicrobial resistance (AMR) situation reported by Ukrainian hospitals for 2020-2022 varied widely, depending on the bacterial species, antimicrobial group and geographical region, as demonstrated by both varying AMR percentages and estimated incidences of endometritis with resistant bacteria.

Previous studies found a high prevalence of HAI caused by multidrug-resistant organisms (MDROs), varying on geographical region of Ukraine. The majority of MDRO isolates carried b-lactamase genes [11-14]. These data underscore the importance of tracking antimicrobial resistance in hospitals.

Endometritis occurs as a result of an infection in the lining of the uterus, known as the endometrium. Such infections may develop due to abnormal bacteria, or bacteria usually found in the vagina. The cervix is the opening to the uterus, and it usually keeps bacteria out of the uterus. However, bacteria can get in when the cervix is open. This may happen for various reasons, such as during childbirth or surgery. Possible risk factors for endometritis include childbirth or pregnancy loss, cesarean delivery, sexually transmitted infections, bacteria in the uterus, pelvic inflammatory disease, and pelvic procedures [12, 13].

Recognizing these risk factors is crucial in identifying and addressing endometritis, as they can contribute to the development of this condition and guide preventive measures and treatment strategies. According to the literature, antibiotic treatment in case of endometritis in women with repeated implantation failure or recurrent pregnancy loss may increase the chances for live birth [1,6].

According to the literature clinical hysteroscopic procedures were mainly applied for diagnosis and therapy (such as diagnostic hysteroscopy, operative hysteroscopy and hystero resectoscopy). They may involve different operative processes, such as visually diagnostic checking, or with retrograde operations [15]. Thus far, infection after hysteroscopy is uncommon, but its prevalence is estimated at approximately around 1% of cases [16]. Thus antibiotic prophylaxis is not commonly considered to be a standard therapy, and its effects have not been specifically identified. However, postoperative infection complications are still a major concern in perioperative period because hysteroscopic procedures were performed in the relatively contaminated area, which has abundant bacterial flora, and the transcervical route may increase, per se, such a potential risk of local dysbacteriosis [17, 18]. In addition, hysteroscope insertion and removal may transfer vaginal and cervical flora into the uterine cavity. More importantly, a randomized controlled trial firstly reported by Bhattacharya claimed applying prophylactic antibiotics could significantly decrease the incidence of bacteremia for patients who underwent hysteroscopic surgery but revealed no clinical benefit for reducing essential infection rate [19]. Thus, so far, the clinical value of antibiotic prophylaxis for hysteroscopy is not well defined, and there is no relevant guideline for prophylactic antibiotic standardization. Currently, there are no randomised controlled trials that assess the effects of prophylactic antibiotics on infectious complications following transcervical intrauterine procedures. It is, therefore, not possible to draw any conclusions regarding the use of prophylactic antibiotics for the prevention of post-procedure transcervical intrauterine infections [20].

Meanwhile, the indiscriminate use of antibiotics has been associated with the development of antibiotic-resistant bacteria, and additional antibiotics may cost unnecessary medical expenses. Considering these drawbacks, we conclude that antibiotic prophylaxis is not recommended during hysteroscopic procedures as long as standardized aseptic procedures are performed.

However, faced with increasing antimicrobial resistance because of misuse and over-prescription of antibiotics, we need evidence about the effect of routine intake of antibiotics for preventing infections after hysteroscopic procedures. Given these findings, we concluded that antibiotic prophylaxis brought no clinical benefit for patients who underwent hysteroscopic procedures.

STRENGTHS AND LIMITATIONS

One strength of this study was that it was a prospective multi-centre observational cohort study, based on endometritis after hysteroscopic procedures surveillance data and using CDC/NHSN methodology. In the present study, to the best of our knowledge the largest prospective, controlled study to date, we evaluated the prevalence of endometritis after both diagnostic and operative hysteroscopy, and antimicrobial resistance of responsible pathogens. Also, this was the first study of phenotypic characterization of antibiotic resistance of responsible pathogens isolated from patients with endometritis after hysteroscopic procedures. Limitations of the study included that it was performed in fifteen hospitals only, and the prevalence of endometritis after hysteroscopic procedures and antimicrobial resistance and antimicrobial resistance of responsible pathogens in other hospitals was not investigated.

CONCLUSIONS

Our data suggest a high prevalence of endometritis after hysteroscopic procedures. The most of endometritis result from iatrogenic trauma to the uterine wall that occur during operative hysteroscopy, which allows for the introduction of bacteria into these normally sterile environments. Risk for endometritis was higher after operative hysteroscopy compared with diagnostic hysteroscopy. A significant proportion of patients were affected by endometritis caused by bacteria developed resistance to several antimicrobials, varying widely depending on the bacterial species, antimicrobial group, and geographical region of Ukraine. These data underscore the importance of tracking antimicrobial resistance of responsible pathogens of HAIs in hospitals. To reduce antimicrobial resistance of aetiologic agents of endometritis after hysteroscopic procedures, it is necessary to develop and implement advanced infection control measures based on HAI surveillance data. Lack of evidence on the effect of routine antibiotic prescription for prevention infections after hysteroscopic procedures and antimicrobial resistance calls for further research. Optimizing the antibiotic prophylaxis may reduce the burden of infection after hysteroscopic procedures, but prevention is the key element.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Comprehensive evaluation of efficiency to identify deficiencies in muscle activity in different modes in team sports

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ABSTRACT

Aim: To concern the scientific substantiation of a complex ergometer tests of aerobic and anaerobic character and quantitative criteria for assessing the condition of female handball players` respiratory and power supply systems in the maximum.

Materials and Methods: Descriptive analysis, correlation analysis, factor analysis. In order to solve those tasks within the framework there were measured the indicators of two hundred young female handball players at the pre-basic training stage.

Results: The outcomes of the research allow us to recommend the program for handball players` potential capabilities assessment that will help to characterize the state of power supply systems of the body under aerobic and anaerobic conditions. At the same time, the results of the testing can be used to identify strengths and weaknesses in the structure of handball players` special readiness indicators and to individualize the process of players' preparation at the subsequent stages.

Conclusions: As a result of experimental data, the quantitative criteria and the scale for the assessment of handball players' working capacity in ergometer maximum tests of aerobic-anaerobic character have been developed. On the basis of these tests, it is possible to analyze objectively the individual characteristics of children before making a final decision.

KEY WORDS: Handball, Female Players, Indicators' Performance, Ergometer Maximum Tests, Work Capacity

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INTRODUCTION

Many scientific studies for youth handball focuses on the result of sports performances and competitions [1, 2]. There should be research into the scientific aspects of the tests already validated and used for educational [3]. Sports selection is viewed as a social, economic and pedagogical concern for the society, basic concepts of which have been formulated in the works of many professionals [4]. Selection includes a number of organizational activities related to solving of the main tasks during the training of athletes at each stage [5, 6].

Several studies have been dedicated to mass observation and testing, aiming to determine children's potential in relation to the specific requirements in handball; selection of promising athletes to sport perfection teams and the formation of club teams; the selection of National teams [7]. Researches make it possible to obtain objective information regarding the most promising group of athletes from the total number of participants [8], reveal empirical and definitional flaws of the early specialization, deliberate play [9].

An important link in the overall chain of events for the selection of talented children and adolescents is the substantiation of complex testing programs, standardization and unification of athletes` capacity evaluation criteria. At the same time, researchers focus their attention on the specific requirements and objectives of the preparation stages [10]. Therefore, it is fundamentally important to study the age characteristics of physical development of children by conventional motor tests of team sports [11], as well as by motor tests adapted to the specific characteristics of handball [12]. Taking into account the general trend of handball development towards the game activity intensification, we anticipate a significant increase in requirements for the special physical preparedness. This includes those systems of the body which limit the anaerobic, aerobic-anaerobic and aerobic work capacity. Thus, filling this gap can help both in selecting and developing female handball players in future.

AIM

Aim of the study: to concern the scientific substantiation of a complex ergometer tests of aerobic and anaerobic character and quantitative criteria for assessing the condition of female handball players` respiratory and power supply systems in the maximum.

MATERIALS AND METHODS

The participants of the study consisted of two hundred young female handball players of Ukrainian Children's Youth Sports School at the pre-basic training stage (age=10-11 years). All athletes volunteered to participate in the research. Prior to the testing, the procedures were explained to all of them, including possible risks involvement, and, after the explanation, an informed consent form was signed. The athletes were free from any injuries or neuromuscular disorders.

The research was approved by the Institutional Ethics Committee, complied with all relevant national regulations and institutional policies, followed the tenets of the Declaration of Helsinki, and has been approved by the authors' institutional review committee. Exclusion criteria were a history of injury or disease that would prevent participants from safely performing the research protocol. All participants were asked to refrain from alcohol and physical exercises 24 hours prior to participation and abstain from food intake and beverages that contain caffeine, for 2 h prior to participation.

A systematic science review was applied in accordance with the Preferred Reporting Items for systematic reviews and meta-analyses. Electronic databases: Scopus, Web of Science, PubMed – were searched for relevant publications. The publications included met the following criteria and principles: included handball players; contained relevant data concerning in handball; were written in English, Poland, Ukraine.

RESEARCH METHODS

THEORETICAL METHODS

Method of analysis and systematization of domestic and foreign experience was used to study the degree of scientific research and determine the to concerned the scientific substantiation of a complex of the most informative, not difficult in the daily implementation, available to coaches control tests and quantitative criteria.

PRACTICAL METHODS

Method of practical testing at stage of preparation will allow coaches to draw conclusions regarding the advisability of continuing sports perfection, or to determine the main directions of preparation, taking into consideration the individual characteristics of young handball players.

Predominantly, the methodology of the research corresponded to the recommendations of the leading experts in the field of sports physiology. Regarding the abovementioned trends in the handball development, it is necessary to use breathing performance and energy supply indicators in the common system of tests which has already been widely used for the players` motor functions monitoring. As shown in Table 1, registered indicators of handball players in their age groups met the requirements of a regular statistical distribution.

That allowed to utilize the method of correlation analysis in order to determine a quantitative measure of the correlations between the registered performance indicators in three ergometer tests:

1. Power in 15, 60 and 240-s tests (W/kg);
2. Overall work in 15, 60 and 240-s tests (J/kg);
3. Holding time Pmax, in 16 and 60-s tests: 16 and 60 s.

The only requirement for the application of temporal criteria for the tests batching is their standardization and application under determined conditions of the athletes' preparation. Based on this factor, particular test loads were bonded to the necessity of realization of maximum intensity (depending on the time of the test task) and execution of the workload in certain time.

Tests were performed on an oval running track at a stadium in the morning, after the standard warm-up and under condition that the restoration of athletes' bodies after previous trainings with heavier workloads had been completed. Therefore, quantitative performance criteria included quantitative characteristics of distance registered during the process of performing tests.

Modern systems, the Global Position System (GPS) made it possible to establish the proportion of working time and quantitative distance lengths. During the formation of the correlation matrix, we proceeded from considerations that it was inappropriate to calculate the correlation coefficients between the derived parameters, for instance, indicators of the overall work in absolute terms – kilojoules (KJ) and relative values (J/kg); maximum and relative power in the test (W and W/kg); oxygen uptake (VO_2, $l \cdot min^{-1}$ and VO_2, $ml \cdot kg^{-1} \cdot min^{-1}$).

The statistical analysis of the actual research data was conducted using several methods. The analysis of experimental data was performed using integrated statistical and graphics packages MS Excel-7, Statistica-7. Descriptive analysis methods were used, comprising tabular representation of individual variables and calculating the arithmetic mean values – X, and standard

deviation – S. To separate the leading components of functional readiness structure, the factorial analysis was provided [13].

Thus, in order to substantiate the minimum complex of the most informative indicators which allow objectively and highly informatively characterize the state of main components of female handball players' motor function, correlation analysis method was used. Utilizing a large number of tests for female handball players, correlation analysis was applied to study the results of primary examinations. Then, the correlation matrices were processed by methods of factor analysis which allowed to study the players` physical readiness factor structure, select tests and certain indicators that were highly informative and, as a result, recommend the optimal content control. Correlation analyses of players` achievements in these tests were conducted for each age group separately in accordance with metrological requirements. One must not forget the importance of creating a harmonious environment, to have a correct reliability of the results.

In order to achieve the goal and the objectives of this research and to update the informative tests, the correlation between the results of different general and specific test exercises of female handball players were studied. Furthermore, the correlations between the control parameters for quantification of the linear dependence between different parameters were shown when the Pearson correlation coefficient was calculated. Preliminarily, the regular distribution of the registered indicators for the athletes had been conducted. Therefore, we decided to limit ourselves to the study of the distribution character by the rule of three sigmas.

The analysis of the correlations of indicators was as follows. During the first cycle of statistical operations it was registered that the athletes` control indicators corresponded to the normal, regular character and Gaussian distribution. In the case of normal distribution of the experimental data, the subsequent statistical operations – correlation and factor analysis were applied. Average values and standard deviations of the control indicators were used as criteria for normal statistical distribution. This made it possible to characterize the frequency distribution of all the variants that fall within the range of $\pm 3\sigma$ – $\pm 1\sigma$. The method is recommended for solving similar problems in the science of sport which emphasizes that the regular distribution registered during the athletes' motor functions analyses is very common. Generalized estimate of working capacity can be calculated by summing the estimates in points obtained in each control test, using the following formula:

$$WCC = (I1 + R10 + I2 + \dots (I7 + R7),$$

where WCC – generalized working capacity criteria; I1…I7 – number of points for each indicator; R1 …R7 – ratios in connection with the value of the indicator.

The use of a single scale for players of a different age required an application of the differentiated approach in order to formulate the qualitative characteristics of the working capacity on the basis of the test outcomes. We determined the levels: low – lower than 14 points; average – 15-19 points; above the average – 20-24 points; high – 25 points or more. In order to get an opinion on one or another level of working capacity, 10-11-year-old athletes need to score a certain amount of points. Therefore, players aged 10 or 11 years need to earn 25 points to prove a very high level of working capacity. For the players of older age groups these requirements are higher.

RESULTS

The standardization of the control programs and the unification of athletes` assessment criteria should proceed in accordance with specific requirements of the team sports and preparation stages' tasks [14]. Therefore, as a result of several experiments, analysis of empirical experience from scientists and specialized literature data, the algorithm of sports system principles` implementation, as well as specific scientific and methodical bases for handball players training process organization have been generated [15, 16].

The results of the statistical distribution analysis are shown in Table 1. In our research, practical significance is given to the information about the correlations of working capacity indicators that were registered in three tests, due to different mechanisms of athletes` power supply.

Handball is a dynamic team game, characterized by high-intensity movements with passes, sprints, jumps, changes of direction, stops, throws on goal, and body tackles, interspersed with walking and standing, when relative workload – 75–85% of the maximal oxygen uptake (VO_2max) [17]. Handball highly taxes the neuromuscular and cardiovascular systems, stimulates adaptations oxygen utilization and skeletal muscle capacities. The presence or absence of the correlation between the working capacity indicators in anaerobic, aerobic-anaerobic and aerobic modes have fundamental importance for the formation of a complex of control tests for assessment of specific working capacity of female handball players. The results of the analysis are presented in Table 2.

It should be noted that the correlation matrix contains common regularities (the calculation was based on the female handball players` data). Working capacity indicators in relative terms in 15, 60 and 240-s tests

Table 1. Characteristics of the Statistical Distribution of Indicators for the Players Performance in Maximum Ergo-Metric Tests

Indicators	Characteristics of the statistical distribution of the data in the range of three sigma, %			
	±1δ	±2δ	±3δ	Σ
Work (J/kg), 15-s test	63.5	23.7	5.1	92.3
Work (J/kg), 60-s test	71.8	21.2	3.1	96.1
Work (J/kg), 240-s test	63.9	30.1	4.5	98.5
Power (W/kg), 15-s test	62.7	27.3	6.2	96.2
Power (W/kg), 60-s test	64.6	26.2	5.2	96.0
Retention time Pmax, 15-s test	60.9	26.7	6.8	94.4
Retention time Pmax, 60-s test	64.7	24.3	5.7	94.7
VO_2 1·min·^{1} /KJ/kg, 240-s test	62.9	25.2	5.6	93.7
VO_2 1·kg·^{1}·min·^{1}, 240-s test	66.5	25.4	4.8	96.7
Pulmonary ventilation, 1·min·^{1}	64.8	23.3	5.8	93.9

Table 2. The Outcomes of Correlation Analysis of Indicators' Performance of Handball Players to Maximum Ergo-Metric Tests (n=200)

№	Indicators	1	2	3	4	5	6	7	8	9	10
1	Work (J/kg), 15-s test	x	893	715	899	411	573	217	315	118	530
2	Work (J/kg), 60-s test		x	700	600	891	799	613	603	717	611
3	Work (J/kg), 240-s test			x	215	593	11	702	910	877	899
4	Power (W/kg), 15-s test				x	600	713	210	411	393	517
5	Power (W/kg), 60-s test					x	017	503	619	010	714
6	Retention time Pmax, 15-s test						x	270	511	417	273
7	Retention time Pmax, 60-s test							x	853	814	902
8	VO_2 1·min·^{1} /KJ/kg, 240-s test								x	849	814
9	VO_2 1·kg·^{1}·min·^{1}, 240-s test									x	900
10	Pulmonary ventilation, 1·min·^{1}										x

NB: For convenience, all the coefficients are multiplied by 1000.

Table 3. Optimal Quantitative Criteria of Readiness for Handball Players of 10-11 Years Old the Maximum Ergo-Metric Tests

Indicators and measurement units	M	min	max
Work (J/kg), 15-s test	108	0,97	120
Work (J/kg), 60-s test	313	296	360
Work (J/kg), 240-s test	134.2	115	153
Power (W/kg), 15-s test	8.41	7.78	9.26
Power (W/kg), 60-s test	6.21	5.35	8.04
Retention time (Pmax, s), 15-s test	4.78	1.57	7.41
Retention time (Pmax, s), 60-s test	10.21	4.17	16.50

Table 4. The Expression Method in Points of Handball Players Achievement in Maximum Ergo-Metric Tests

Indicators	K	Absolute values and points									
		1	2	3	4	5	6	7	8	9	10
R1 Work (J/kg), 15-s test	1.2	0.97	102	107	112	120	130	140	150	160	168
R2 Work (J /kg), 60-s test		285	300	310	320	330	340	350	360	370	380
R3 Work (J/kg), 240-s test		50	70	80	90	100	115	130	140	150	160
R4 Power (W/kg), 15-s test		7.8	8.2	8.6	9.0	9.4	9.8	10.2	10.6	11.2	12..0
R5 Power (W/kg), 60-s test	1.3	5.2	6.0	6.4	6.8	7,0	7.2	7.4	7.8	8.2	8.6
R6 Retention Time(Pmax, s), 15-s test		1.5	2.5	3.5	4.0	4,5	5.0	5.5	6.0	7.0	8.0
R7 Retention time (Pmax,s), 60-s test	1.5	1.7	3.5	5.0	6.5	8.0	9.5	11.0	12.5	15.0	17.0

Note. R1-7: according to the formula, symbols for calculating the generalized estimation.

showed a high correlation (r – 0.715-0.899), reflecting the general level of physical condition of participants. High correlation coefficients of 0.899 and 0.891 were found in ergometer tests (15 and 60 s), between indicators of work in relative units of J/kg and the relative value of the maximum power W/kg.

The character of such distinctive features was affirmed in specialized literature data. However, the ability, as the duration of the maintenance of the maximum power Pmax in these tests, doesn't depend on the absolute values of work and indicators of the maximum power. The correlation coefficients between these parameters were statistically less significant and ranged between 0.573-0.613.

The high correlation was detected between the indicators of work in ergometer test for 240 s, and the ability of female handball players to maintain high efficiency for a long time Pmax at 60-s test (r-0.70). It could be assumed that this ability appeared mostly due to the same physiological mechanisms that determined the high level of working capacity in the aerobic test at the duration of 240 s. The high correlation paired coefficients between indicators of oxygen consumption, the pulmonary ventilation and work in the aerobic mode 0.814-0.902 can be taken as evidence of it.

Some scientists have developed the concept of an individual anaerobic threshold, but experimental evidence is lacking [18]. The effect of aerobic capacity on the validity of the anaerobic intensity threshold can only be assessed using constant exercise tests. As a result of statistical analysis of experimental data, the quantitative criteria and the scale for assessing working capacity of female handball players during ergometer maximal tests of aerobic-anaerobic nature have been presented (Tables III and IV). Therefore, we have transferred the results of the players' examination which were expressed in different units of measurement – joules, watts and seconds, into a single rating system – in points.

Relevant information can be used in the system of a long-term players' preparation for the purpose of individualization in the training process. An integral assessment of working capacity in each of the three tests can help to identify specific flaws in an athlete's muscle activity in different modes.

DISCUSSION

Modern scientists pay special attention to analyzing the structure and effectiveness of the pre-basic training stage. It is crucial to note that at this stage of sports preparation coaches and sports specialists are trying to increase the level of functionality and sports achievements in the process of participation in the national handball championship among youth teams.

The challenge lies in determining the quantitative and qualitative characteristics of the training structure, when the handball players are able to use skills and methods of their training, which provide growth of capabilities while maintaining the positive dynamics of the technical and tactical improvements [19].

Our research presents the technology and specific criteria that can help to select promising female handball players during the formation of groups in sports organizations for children. We considered it appropriate to focus on the creation of the complex of control indicators that allows to assess the status of the main components of motor function which provide high performance of players in the specific conditions of the game activity.

This approach to preparedness evaluation meets the modern requirements of management and control organization in sport games. Because of the objective organizational difficulties, research data from handball players of various ages were processed together in a unified correlation matrix. For this reason, there arose a necessity to study the physiological mechanisms and performance profiles become relevant at the early stages of female handball players identification and selection as well as for physical development programs at future stages.

However, the ensuing discussion of energy ensuring indicators in ergometer tests was conducted strictly in accordance with the age characteristics of involved athletes, as evidenced by the data in Tables 3 and 4. Such correlations were understandable from the standpoint of well-known physiological mechanisms and additional statistical calculation was not needed. In order to improve the control methodology of special physical preparedness, the testing results of handball players were expressed in metric values and the proper scale was used. It was necessary to represent the athletes' achievements in different tests (expressed in different, not comparable with each other measurement units), in a united system in the form of points. In order to solve that problem, we decided to use the percentile scale, the most suitable for the evaluation of results of large groups of athletes in tests. In this case, information regarding the nature of the statistical distribution of the primary control materials obtained during the examination of a large number of handball players of different age was used.

According to the most control indicators, the distribution corresponded or was very close to the normal requirements. On the scale, the high and low results

in the control tests were placed on the left and on the right sides, and the average results, which were shown by the most athletes – in its middle part. The utilization of this kind of scale allowed to present the female handball players` achievements in various tests in generalized evaluation in points. The distribution of the points for the quantitative indicators, placed on the scale of a normal distribution, was considered as equable. Nevertheless, to model the scales, we had to use generally accepted guidelines [20].

Each control indicator was assigned a so-called premium rank coefficient which corresponded to its factorial validity. The concurrent use of the quantitative and qualitative criteria for the assessment of the female handball players` readiness opens new, additional opportunities to increase the objectivity of administrative decisions not only at the pre-basic training stage during the selection of talented children to practice handball, but also at the subsequent stages of long-term preparation.

CONCLUSIONS

Statistical analysis of the experimental data allowed us to substantiate the minimum testing program on the basis of the most informative indicators concerning the age peculiarities of involved players and specific requirements of the game. Additionally, we developed quantitative criteria and the scales for evaluating the anaerobic-aerobic productivity of an organism in the maximum duration of ergometer tests at 15, 60 and 240 s.

The results of our research allow to characterize the structure of the special readiness of female handball players, which offers opportunities to improve the training methodology at the level of analytical and synthetic approaches. In other words, relying on the knowledge of the structure of female handball players preparedness, there is an opportunity to selectively influence the improvement of its individual components and to optimize training loads by aligning them with the requirements of competitive activity, as well as to take into the account some features of the basic systems of vitality in the bodies of female handball players caused by genetic factors.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Association of the key immunological and hemodynamic determinants with cervix ripening in pregnant women

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ABSTRACT

Aim: To investigate a correlation between cervical ripening, the immunological features and the hemodynamic characteristics of the cervix during the preparation for vaginal labor.

Materials and Methods: We examined 75 pregnant women at different gestational age. General clinical and immunological studies were conducted in order to check serum concentration of cytokines IL-6, IL-1β, and TNF-α. Ultrasound and Doppler study were used to determine resistance index and systolic-diastolic ratio of blood flow in the common uterine artery as well as the descending and ascending parts and cervical stromal arteries.

Results: Pregnant women with high cervical ripening score had high concentrations of the major proinflammatory cytokines (IL-1β, IL-6, and TNF-α). Analysis of the of the cervical blood flow indicators of the studied groups showed significant differences in the indices of vascular resistance in the vessels that feed the cervix. Our data showed a significant correlation between the cervix ripening and both the serum levels of the studied cytokines and the level of peripheral vascular resistance indices in the common uterine arteries of the cervix, and the blood flow indices in the cervical stromal vessels.

Conclusions: Our study shows that the process of preparing the woman's body for labor is associated with immunological adjustment and increased hemodynamics of the cervix. We report that cervical ripening is associated with the immunological components and hemodynamic parameters of the cervix at late-stage pregnancy. Measuring cervix ripening and the accompanied changes in cytokine levels and hemodynamic parameters will form a more accurate assessment of birth preparedness and labor complications.

KEY WORDS: cytokines, cervical ripening, vaginal labor, cervical blood flow

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INTRODUCTION

To date one of the most important ways to reduce perinatal morbidity in Ukraine and in the world is the concept of safe motherhood and this is primarily due to improved methods of reliable prediction of labor and complications of labor for mother and fetus [1, 2]. Determining the birth preparedness is one of the most difficult and relevant issues in modern obstetrics. Additionally, the effective monitoring of the cervix during preparation to pre-induction of labor is also important. Timely assessment of the state of cervix ripening is critical in determining the prognosis of labor, especially when it comes to choosing the method of induction. Therefore, characterizing the mechanisms and factors contributing to spontaneous labor is key in establishing the steps for safe childbirth [3].

According to the literature, pre-induction of cervical ripening before spontaneous vaginal labor depends on the interaction of complex multilevel mechanisms that result in changes in morphological and biochemical state of the cervix. Of note many studies have focused on the immunological aspects of cervical ripening due to the observed local inflammatory reaction in the cervix during the process [4-6]. Before the onset of labor, the inflammatory process is accompanied by cervix infiltration with leukocytes, synthesis of a wide range of mediators as well as changes in the physical state of collagen and extracellular matrix [7].

Immunohistochemical analysis revealed that leukocytes infiltrating the cervix before vaginal labor are the main source of increasing synthesis of proinflammatory cytokines, which along with prostaglandins are involved in the inflammatory reaction associated with cervix remodeling before labor [8-10]. The physiological course of labor plays an important role in the balance of proinflammatory cytokines. Interleukins (IL) such as IL-1β, IL-6 and TNF-α, which have previously been shown to trigger abortion, are central mediators of local and systemic inflammatory reactions [11, 12]. Furthermore, these cytokines activate the neutrophil migration to the peripheral tissue and increase the production of matrix metalloproteinases that affect the conversion of collagen in the cervix.

It has previously been shown that local and systemic cytokine profiling at different stages of pregnancy can allow to identify risk groups for gestational complica-

tions such as preterm labor, intrauterine infection and others [13-15].

Cervix preparedness for labor depends on a number of parameters. Previous studies focused largely on prenatal biometric indicators of the cervix preparedness for labor including length, width, thickness of the cervix, diameter of the inner eye and location of the cervix in the pelvic cavity [16]. There is evidence in the literature that the ultrasound Doppler assessment of the cervix hemodynamic parameters can also be used to predict the course of labor. Interestingly, a number of recent studies have demonstrated the initial role of immunostimulation in the processes of neovascularization and blood supply during pregnancy [17, 18]. Despite a number of studies focusing on the regulation of initiation mechanism of women's spontaneous parturition, the ambiguity in the field persists and further research is needed to define and optimize the reliable markers and indicators that can effectively be used to assess the preparedness for labor for a mother and a fetus.

Taking into account that before labor cervix is undergoing both immunological and hemodynamic changes, we aimed to investigate whether there is a link between immunological signalling and cervical blood flow parameters before the induction of labor. Our results demonstrate that cervix ripening is associated with both the uterine blood flow parameters and the major pro-inflammatory cytokines indicating that blood flow and cytokine levels can be used together as a screening tool to assess the course of labor.

AIM

The aim of the study is to investigate if there is a link between the state of the cervix ripening, the immunological features and the hemodynamic characteristics of the cervix during the preparation for vaginal labor.

MATERIALS AND METHODS

75 pregnant women at a gestational age of 38-40 weeks were examined in the Kharkiv Regional Perinatal Clinical Hospital, Kharkiv, Ukraine. The study groups included primiparous women without severe extragenital and obstetric pathology. The study did not include women with repeated pregnancies and births, pregnant women admitted for planned cesarean section, or women with exacerbations of chronic extragenital diseases, fever, and severe preeclampsia. The study was conducted in compliance with the standards of the Declaration of Helsinki and approved by the independent ethics committee of the Kharkiv National Medical University protocol No. 32 of 01/03/2023). All patients gave their written in- formed consent to participate in the study.

The examined women were divided into two clinical groups on admission to the hospital, depending on the degree of cervical ripening. The degree of cervical ripening was assessed with the help of Bishop (1964) score. Group 1 consisted of 29 patients with high cervical ripening score (9-13 points), group 2 included 31 pregnant women with low cervical ripening score (6-8 points). The control group consisted of 15 primiparous women with a gestational age of 35-36 weeks before the start of physiological processes of cervical remodeling. These women had no signs of emergency preterm birth according to somatic status or medical records.

All pregnant women underwent complete clinical and laboratory examination, regulated by the Order of the Ministry of Health of Ukraine. Their fetuses were studied using ultrasound and cardiotocography.

Immunological studies were performed once upon admission to the hospital. The serum concentration of cytokines IL-6, IL-1β and TNF-α was determined by solid-phase enzyme-linked immunosorbent assay using commercial kits (CJSC "Vector Best").

Ultrasound and Doppler examination was performed using ultrasonic diagnostic device Aloka SSD – 3500 SV (Japan) with color Doppler mapping, applying transabdominal and transvaginal sensors. In transabdominal examination we studied the blood flow parameters in the common uterine artery in the descending and ascending parts. In transvaginal examination we determined the blood flow parameters in the arteries of the cervical stroma and in the isthmus. We measured the resistance index (IR), systolic-diastolic ratio (SDR).

Statistical processing of the obtained results was performed using the program "STATISTICA-6". The results are presented as medians and standard deviation. The Mann–Whitney U test was used to determine the significance of the differences between the studied groups. Spearman's correlation analysis was used to assess possible correlations between cervix ripening and inflammatory cytokines IL-1β, IL-6 and TNF-α) and uterine blood flow parameters (systolic diastolic ratio SDR and resistance index RI). A P value of $\leq$0.05 was considered statistically significant.

RESULTS

The main clinical characteristics of the studied groups are presented in (Table 1). The age of the examined pregnant women ranged from 18 to 33 years and on average it was 25.7. Patients were compared with each other by age, features of sexual and menstrual function ($p \leq 0.05$). In their medical records among gynecological pathology there were inflammatory diseases of the female genital organs in 49.4% of women (group 1)

Table 1. Clinical and demographic characteristics of the participants in the studied groups

	Group 1	Group 2	Control	P
	n=29	n=31	n=15	
Age, years	25.7 (18-33)	25.7 (18-33)	25.7 (18-33)	n/a
Cervical ripening score (Bishop score)	9-13	6-8	n/a	0,02
Inflammatory disease of female genitals, n (%)	14 (48.2%)	20 (64.5%)	7 (46.5%)	0,03
Cervical ectopia, n (%)	11 (37.5%)	16 (51.6%)	6 (40%)	0,04
Childhood infections, n (%)	4 (13.7%)	15 (48.3%)	2 (13.13%)	0,02
Neurocirculatory pathology, n (%)	1 (3.4%)	3 (9.6%)	1 (6.7%)	0,03
Thyroid pathology, n (%)	2 (6.8%)	5 (16.1%)	1 (6.7%)	0,02
Miscarriage in 1st semester, n (%)	2 (6.8%)	1 (3.2%)	1 (6.7%)	0,04

Listed characteristics were compared between group 1, group 2 and the control group. Values for the age and cervical ripening score are expressed as median and ranges. n – indicates a number of patients along with percentage (%) of the total number of patients in a given group. Mann–Whitney U tests was used. A P value of ≤0.05 was considered statistically significant. n/a: non applicable.

Table 2. Comparison of cytokine levels in the blood of the control and studied groups

	Group 1	Goup 2	Control group
	n=29	n=31	n=15
IL-6 pg/ml	79.8 ± 9.6*	22.6 ± 2.7	20.5 ± 2.3
IL-1β pg/ml	197.4 ± 23.7*	64.7 ± 7.5	62.9 ± 7.2
TNF-α pg/ml	2.8 ± 0.3*	0.9 ± 0.1	0.8 ± 0.09

Concentrations of IL-6, IL-1β and TNF-α were compared between group 1 and control group and group 2 and control group. Values are expressed as mean and standard deviation. Mann–Whitney U test was used. A P value of ≤0.05 (* – p ≤0.05) was considered statistically significant.

Table 3. Characterization of the uterine and cervical blood flow in the studied groups

	Group 1	Group 2	Control group
	n=29	n=31	n=15
Common uterine artery			
SDR	1.70 ± 0.03*	1.74 ± 0.02	1.82 ± 0.03
RI	0.38 ± 0.04*	0.47 ± 0.05	0.51 ± 0.04
Ascending uterine artery			
SDR	1.71 ± 0.02*	1.85 ± 0.05	1.88 ± 0.02
RI	0.38 ± 0.04*	0.47 ± 0.05	0.49 ± 0.05
Descending uterine artery			
SDR	1.61 ± 0.17*	1.82 ± 0.25	1.86 ± 0.27
RI	0.38 ± 0.04*	0.47 ± 0.03	0.49 ± 0.05
Stromal arteries of the cervix			
SDR	2.41 ± 0.3*	2.82 ± 0.31	2.86 ± 0.4
RI	0.48 ± 0.06*	0.67 ± 0.08	0.69 ± 0.07

Systolic diastolic ratio (SDR) and resistance index (RI) were compared between group 1 and control group and group 2 and control group. Values are expressed as mean and standard deviation. Mann–Whitney U test was used. A P value of ≤0.05 (* – p ≤0.05) was considered statistically significant.

and 64.6% of patients (group 2). Cervical ectopia was present in 38.5% of group 1 representatives and 51.6% of patients in group 2 (p ≤ 0.05). Analysis of extragenital pathology showed that childhood infections and acute respiratory diseases were recorded in group 2 more often than in group 1 (48.5% in group 2 compared to 15.4% in group 1). Neurocirculatory disorders and thyroid pathology were significantly more common in group 2 (10.2%, and 16.8%) compared to group 1 (1.7%, and 3.3%) (p ≤ 0.05). Regarding the complications of the current pregnancy, significant differences were found in the frequency of miscarriage in the 1st trimester, which was 3.6% in patients of group 1 and 21% of pregnant women in group 2 (p ≤ 0.05).

Table 4. Correlation coefficient between cervical ripening score and inflammatory cytokines and uterine and cervix blood flow parameters (SDR and RI)

	Correlation coefficient	P
Cytokines		
IL-6	0,78	0,001
IL - 1β	0,7	0,001
TNF-α	0,65	0,002
SDR		
Common uterine artery	-0,478	0,012
Ascending uterine artery	-0,442	0,018
Descending uterine artery	-0,653	0,003
Stromal arteries of the cervix	-0,689	0,001
RI		
Common uterine artery RI	-0,675	0,004
Ascending uterine artery	-0,466	0,041
Descending uterine artery	-0,723	0,003
Stromal arteries of the cervix	-0,747	0,001

Spearman's correlation was used to calculate the correlation between cervical ripening and the given parameters. A P value of ≤0.05 was considered statistically significant

The analysis of the major cytokines production (IL-1β, IL-6, and TNF-α) as a possible indicator in preparing the body for labor, revealed high concentrations of studied proinflammatory cytokines (Table 2) in the serum of pregnant women of groups 1 and 2. In pregnant women of group 1, the concentration of IL-6 exceeded that in group 2 and in the control group (79.8 ± 9.6 pg / ml, 22.6 ± 2.7, and 20.5 ± 2.3 pg / ml g, respectively) ($p \leq 0.05$). The level of IL-1β in group 1 was twice as high as that in group 2, and in the control group (197.4 ± 23.7 pg / ml, 64.7±7.5, and 62.9 ± 7.2 pg / ml, respectively) ($p \leq 0.05$). The maximum concentration of TNF-α was observed during the onset of labor in pregnant women of group 1 compared to group 2 and control group (2.8 ± 0.3 pg / ml, 0.9 ± 0.01, and 0.8 ± 0.09 pg / ml, respectively) ($p \leq 0.05$) (Table 2). Patients in group 1 with high cervical ripening score had high level of major proinflammatory cytokines and displayed lack of cervix preparedness for labor. Taken together we conclude that these immune markers can serve as a prognostic factor to ensure a timely labor and to assess the effectiveness of pre-induction and induction of labor.

Over the course of the last few years, assessing the hemodynamic changes in uterine arteries using Doppler ultrasound has successfully been used to diagnose and predict pregnancy outcomes [19].

Next, we aimed to examine whether there might be a correlation between the inflammatory cytokines and the hemodynamic processes in the cervix. To address this, we measured the cervical blood flow in the studied groups. The main indicators of cervical blood flow that were taken using Doppler in the studied groups included systolic diastolic ratio (SDR) and resistance index (RI) in the vessels that feed the cervix: common uterine artery, ascending and descending parts of the uterine artery and cervical stromal arteries. We observed significantly lower rates of SDR and RI in women of group 1 compared with pregnant women of group 2 and a control group in the common uterine artery, ascending and descending parts and in the arteries of the cervical stroma (Table III). Lower SDR values were recorded in group 1 in common, ascending and descending uterine arteries as well as stromal arteries of the cervix in patients in group 1 (1.70 ± 0.03, 1.71 ± 0.02, 1.61 ± 0.17 and 2.41 ± 0.3 respectively) compared to group 2 and control groups. Similarly, resistance index in group 1 was significantly lower compared to group 2 and the control group with the values 0.38 ± 0.04 in common, ascending and descending uterine arteries and 0.48 ± 0.06 in stromal arteries of the cervix (Table 3).

Analysis of the cervix hemodynamics in the examined women showed a significant decrease in vascular resistance indices in pregnant women of group 1 in the common uterine artery, its ascending and descending parts, as well as in stromal arteries of the cervix (Table 3). This is consistent with the previous observations

that shows that during the ripening of the cervix before labor there is an increased blood supply to the cervix [20]. A significant decrease in the average blood flow in this group of pregnant women suggests that the cervix is undergoing the process of increasing the capacity of its vascular bed during blood deposition in cervical vessels, which is part of the physiological course of prenatal transformation.

Next, we investigated the correlation between the determined immunological and hemodynamic parameters. Significant correlations were found between cervix ripening and the levels of the studied pro-inflammatory cytokines IL-1β, IL-6 and TNF-α (Table 4, Spearman's r coefficient r= 0.78, 0.7, 0.65 respectively). Significant inverse correlations were observed between cervix ripening and SDR and RI parameters in the uterine arteries of the cervix and cervical stromal arteries summarized in Table 4. Statistically significant correlation indicates that there is an association between the parameters studied. The associative link between the cytokines studied, SDR and RI parameters and cervix ripening suggests that these parameters may be investigated further as predictors of women's labor.

DISCUSSION

In this study we evaluated whether cervical ripening indicators can be used in conjunction with immunological and hemodynamic paraments to accurately predict successful labor onset in female patients at 38-40 gestational weeks. Cervical ripening score (Bishop score) along with cervical length have long been used as a preferred method of defining cervical preparedness for labor. However, these methods might not be the best way to assess birth preparedness primarily due to variations in the observation along with the discomfort that these examinations bring to the pregnant women [21, 22]. In this report we aimed to expand the existent methods of assessing cervical readiness and investigate other parameters that may improve the accuracy of predication markers for labor outcomes.

Cardiovascular adaptations and immunological changes play a major role in pregnancy. The change in immunoreactivity on the eve of spontaneous labor is accompanied by a significant activation of the production of pro-inflammatory cytokines at the systemic level and local changes in cervical hemodynamics. Monitoring maternal hemodynamics has previously been explored as a tool to predict obstetric risk in early labor [23]. In line with previous studies, we used several parameters to assess maternal cardiovascular adjustments during preparedness for labor. Our results show an association between cervical ripening and hemodynamic changes implying that in early stages of labor, it is important to monitor hemodynamic indices.

Similarly, immunological adjustments are the key features of pregnancy. Systemic and local inflammatory activation is affecting preparedness for labor along with the labor and parturition. Serum cytokines and chemokines have previously been tested as reliable tools to predict a number of labor complication and pathologies such as preeclampsia and labor complications [24]. Cytokines have many different ways of regulating tissues and tissue environments. For example, IL-6 pro-inflammatory cytokine has angiogenic and mitogenic effects and plays an important role in reproductive function by regulating ovarian steroid hormone production, folliculogenesis and early implantation events. The angiogenic properties of pro-inflammatory cytokines and subsequent formation of the blood vessels can partly explain the link that we observe between the increased level of cytokines and the decrease in hemodynamic blood flow parameters that correlates with cervical ripening. This correlation may suggest an important immunoregulatory effect of cytokines during pregnancy on vascularization process and blood supply of the uterine vessels in late pregnancy. However further studies are needed to decipher the exact link between the pro-inflammatory cytokines and angiogenesis during late-stage pregnancy and labor onset.

Moving towards a better prediction of labor remains a high priority in women's health [25]. Accurate and reliable ways of monitoring late stages of labor preparedness will undoubtedly decrease labor complications and will allow for interventions to be administered timely. Our work advances our understanding of the markers that can be used as a screening tool to assess the onset of labor and paves way to discovering correlations between different parameters that can be assessed during pregnancy. Future work will involve finding additional markers that may correlate with cervical ripening and immunological and hemodynamic state of the cervix to establish an accurate template for predicting birth preparedness and labor complications.

CONCLUSIONS

The process of cervix remodeling before labor is characterized by an increase in the proinflammatory cytokines in blood serum due to increased immunological activity of peripheral neutrophils. We observe an increase in the pre-inflammatory cytokines in patients with high cervical ripening. Interestingly, high cervical ripening was associated with a decrease in the hemodynamic features of the cervix including decreased arterial blood flow in the descending uterine artery and stromal vessels. The

results presented here establish a correlation between the cervix ripening and the immunological and hemodynamic aspects of late pregnancy. Multifunctional immunoregulatory properties of proinflammatory cytokines during physiological pregnancy and labor may play an important role in ensuring hemodynamic adjustment of the cervix before labor. Thus, combining multiple parameters to identify pregnancy outcomes may help us tackle a clinical challenge posed by pregnancy risks and labor complications.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

The dynamics of recovery of external breathing function in patients after laparoscopic cholecystectomy in the acute period under the influence of the rehabilitation program

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ABSTRACT

Aim: To determine the dynamics of renewal of the function of external respiration in patients after laparoscopic cholecystectomy at the acute stage of rehabilitation under the influence of a rehabilitation program.

Materials and Methods: The study is randomized, simple with blinded assessors. The forced vital capacity (FVC, l), forced expiratory volume in the first second (FEV1, l) and peak expiratory flow rate (PEFR, l/s) were assessed. Spirometry was performed 120 patients on the first day of admission of patients to the surgical department for surgical intervention, on the second day and on the day of discharge. Methods of mathematical statistics: arithmetic mean (M) and standard error of the mean (±m), Student's t-test were calculated, differences at $p<0,05$ were considered statistically significant.

Results: It has been established that laparoscopic cholecystectomy leads to a statistically significant decrease in the parameters of respiratory function in all age categories. More pronounced positive dynamics of respiratory function in the group of respiratory therapy. It was established that without respiratory therapy on the day of discharge there was no restoration ($p<0.05$) in groups of elderly patients of group of FVC l, FEV1 l, PEFR l/s; in middle-aged patients did no restoration FEV1, l, PEFR, l/s; in younger patients there was no recovery of FEV1, l.

Conclusions: The results of the study indicate the effectiveness of the introduction of diaphragmatic breathing exercises in combination with early mobilization at the acute and subacute stages of rehabilitation in patients after laparoscopic cholecystectomy in order to restore the function of the respiratory system.

KEY WORDS: cholecystectomy, physical therapy, breathing exercises

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INTRODUCTION

Laparoscopic cholecystectomy (LCH) has long been the gold standard for the surgical treatment of calculus cholecystitis. However, it should be understood that there is an operative-anesthetic risk that increases with age and may be responsible for the high rate of postoperative complications. Thanks to the improvement of surgical tactics of treatment, a decrease in postoperative mortality in acute cholecystitis has been achieved, which currently amounts to 0,3-2,9 % [1, 2].

As is known, the acute postoperative period for patients after surgical intervention on the abdominal organs (AO) is the period when those changes in the activity of organs and systems that are a direct consequence of surgical trauma and anesthesia are most pronounced. First of all, in the immediate period after the operation, the patient feels the effects of artificial lung ventilation (ALV) during the intervention. Last but not least is the new pain in the wound. As a rule, patients instinctively avoid straining and using the muscles of the anterior abdominal wall. When breathing, patients begin to avoid the diaphragmatic type of breathing, which in turn requires additional participation in breathing of the intercostals muscles, and, as a result, the type of breathing changes from diaphragmatic to chest. A significant impact on the decrease in respiratory function has a restriction of the activity of patients, which leads to a decrease in the function of external respiration. Reducing the number of days spent in the surgical department for such patients does not eliminate the problem of incomplete recovery of patients after surgery. The patient at home continues to avoid the correct type of breathing and spares the muscles of the anterior abdominal wall due to pain, respectively,

physical performance remains at a low level. Instead of relief, patients cannot return to the activities that they had before surgery for a long time. Therefore, one of the main tasks of rehabilitation in the acute and sub-acute period should be the prevention of congestive pneumonia and the restoration of the function of external respiration with the inclusion of the muscles of the diaphragm and the anterior abdominal wall.

AIM

To determine the dynamics of renewal of the function of external respiration in patients after laparoscopic cholecystectomy at the acute stage of rehabilitation under the influence of the rehabilitation program.

MATERIALS AND METHODS

Determined the dynamics of recovery of external breathing function in patients after laparoscopic cholecystectomy at the acute stage of rehabilitation under the influence of a rehabilitation program. Research design: The study is randomized, simple with blinded assessors. The forced vital capacity (FVC, l), forced expiratory volume in the first second (FEV 1, l), in liters, and peak expiratory flow rate (PEF, l/s) were assessed. Spirometry was performed on the first day of admission of patients to the surgical department for surgical intervention, on the second day and on the day of discharge using a SPIROBANK II BASIC 7882 spirometer [3,4]. The days of discharge (M±m) in the groups were different: A1 3,75 ± 0,25; A2 3,90 ± 0,20; B1 4,65 ± 0,40; B2 4,85 ± 0,41; C1 6,20 ± 0,58; C2 6,10 ± 0,60. Patients were divided into age categories: group A – young patients aged 18 to 44 years (n=40), including men (n=7) and women (n=33); group B – patients of middle age from 45 to 59 years (n=40), including men (n=7) and women (n=33); group C – elderly patients from 60 to 74 years old (n=40), of which men (n=9) and women (n=31) Each age category of patients upon admission to the surgical department was divided by randomization by a simple random selection method with lottery in the control groups (A1, B1, C1) and groups that underwent rehabilitation intervention according to our method of the group (A2, B2, C2).

Inclusion criteria: patients with chronic calculous cholecystitis (CCC), who underwent laparoscopic cholecystectomy in the surgical department of the Ivano-Frankivsk Central City Clinical Hospital in 2019-2020. Exclusion criteria: the presence of neuropsychiatric pathology in patients; refusal of patients to participate in the study. Methods of mathematical statistics: statistical processing of research results was performed using the standard Microsoft Excel program package (Microsoft 365 for enterprises, owner nholod@ifnmu.edu.ua). The Kolmogorov-Smirnov consistency criterion was used to test the null hypothesis H0 that the studied sample obeys the normal distribution law. Arithmetic mean (M) and standard error of the mean (±m) were calculated. The probability of differences was assessed using the Student's paired t-test for dependent samples. Differences were considered statistically significant at $p<0.05$ (95% significance level). FDD was assessed in accordance with the recommendations of the European Respiratory Society/American Thoracic Society. The best value from the three tests was taken into account. There was no withdrawal from the study. The used methods of the conducted research correspond to the principles of the Declaration of Helsinki, approved by the ethics commission Ivano-Frankivsk National Medical University (IFNMU).

RESULTS

Demographic indicators of patients and the length of days spent in the department by group are presented in Table 1.

Group A1 patients aged 35,80 ± 1,41 years were in the surgical department for 3,75 ± 0,25 days; group A2 patients aged 36,30 ± 1,44 years were in the department for 3,90 ± 0,20 days. Group B1 patients aged 52,35 ± 0,99 years were in the surgical department for 4,65 ± 0,40 days; group B2 patients aged 52,15 ± 0,94 years were in the department for 4,85 ± 0,41 days. Group C1 patients aged 65,75 ± 1,00 years were in the surgical department for 6,20 ± 0,58 days; group C2 patients aged 65,60 ± 0,89 years were in the department for 6,10 ± 0,60 days. Statistical difference between age and number of days of stay between groups of each age category A1 and A2; B1 and B2; C1 and C2 were absent ($p> 0.05$).

Comparison of FVC parameters is presented in Table 2. Comparison of indicators before surgery and the first day after surgery (P0 before P1) showed a statistically significant decrease in ($p<0,05$) FVC in all groups (M±m): A1 from 2,68 ± 0,81 to 2,09 ± 0,78; A2 from 2,74 ± 0,84 to 2,04 ± 0,75; B1 from 2,49 ± 0,76 to 1,83 ± 0,69; B2 from 2,51 ± 0,67 to 1,80 ± 0,68; C1 from 2,28 ± 0,68 to 1,61 ± 0,63; C2 from 2,31 ± 0,64 to 1,57 ± 0,60. Comparing FVC indices between the first postoperative day and the day of discharge (P1 before P2), a statistically significant increase in ($p<0,05$) indices was found in groups A2 from 2,04 ± 0,75 to 2,52 ± 0,70; B2 from 1,80 ± 0,68 to 2,23 ± 0,65; C2 from 1,57 ± 0,60 to 1,97 ± 0,61, which, along with early mobilization, performed diaphragmatic exercises. Comparison

Table 1. Demographics of patients by groups

Group	Total number of persons	Including women	Including men	Age (M±m), years	Number of bed days, (M±m) days
Group A1	20	16	4	35,80 ± 1,41	3,75 ± 0,25
Group A2	20	17	3	36,30 ± 1,44	3,90 ± 0,20
Group B1	20	17	3	52,35 ± 0,99	4,65 ± 0,40
Group B2	20	16	4	52,15 ± 0,94	4,85 ± 0,41
Group C1	20	16	4	65,75 ± 1,00	6,20 ± 0,58
Group C2	20	15	5	65,60 ± 0,89	6,10 ± 0,60

Table 2. Indicators of FVC, l

Group	Indication before operative intervention, (M±m), P_0	Indicator on the first day after surgery, (M±m), P_1	Indicator on the day of discharge, (M±m), P_2	p P_1 before P_0	p P_2 before P_1	p P_2 before P_0
Group A1	2,23 ± 0,49	1,73 ± 0,43	1,88 ± 0,48	< 0,05	> 0,05	< 0,05
Group A2	2,26 ± 0,47	1,71 ± 0,42	1,99 ± 0,42	< 0,05	< 0,05	> 0,05
Group B1	2,01 ± 0,46	1,48 ± 0,38	1,63 ± 0,49	< 0,05	> 0,05	< 0,05
Group B2	1,98 ± 0,45	1,46 ± 0,38	1,71 ± 0,39	< 0,05	< 0,05	> 0,05
Group C1	1,86 ± 0,54	1,29 ± 0,53	1,51 ± 0,52	< 0,05	> 0,05	< 0,05
Group C2	1,83 ± 0,52	1,26 ± 0,51	1,60 ± 0,53	< 0,05	< 0,05	> 0,05

Table 3. Indicators of forced expiratory volume in one second of FEV 1, l

Group	Indication before operative intervention, (M±m), P_0	Indicator on the first day after surgery, (M±m), P_1	Indicator on the day of discharge, (M±m), P_2	p P_1 before P_0	p P_2 before P_1	p P_2 before P_0
Group A1	2,68 ± 0,81	2,09 ± 0,78	2,30 ± 0,85	< 0,05	> 0,05	> 0,05
Group A2	2,74 ± 0,84	2,04 ± 0,75	2,52 ± 0,70	< 0,05	< 0,05	> 0,05
Group B1	2,49 ± 0,76	1,83 ± 0,69	2,10 ± 0,73	< 0,05	> 0,05	> 0,05
Group B2	2,51 ± 0,67	1,80 ± 0,68	2,23 ± 0,65	< 0,05	< 0,05	> 0,05
Group C1	2,28 ± 0,68	1,61 ± 0,63	1,86 ± 0,62	< 0,05	> 0,05	< 0,05
Group C2	2,31 ± 0,64	1,57 ± 0,60	1,97 ± 0,61	< 0,05	< 0,05	> 0,05

Differences were considered statistically significant at $p<0.05$.

of FVC parameters on the day of discharge and before surgery (P2 before P0) found that in all patients, except for group C1 (old people), who did not engage in diaphragmatic breathing exercises, the parameters did not differ statistically.

Comparison of FEV1 parameters is presented in Table 3. Comparison of indicators before surgery and the first day after surgery (P0 before P1) also established a statistically significant decrease ($p<0,05$) in FEV1 in all groups (M±m): A1 from 2,23 ± 0,49 to 1,73 ± 0,43; A2 from 2,26 ± 0,47 to 1,71 ± 0,42; B1 from 2,01 ± 0,46 to 1,48 ± 0,38; B2 from 1,98 ± 0,45 to 1,46 ± 0,38; C1 1,86 ± 0,54 from to 1,29 ± 0,53; C2 from 1,83 ± 0,52 to 1,26 ± 0,51. Comparing the FEV1 indices between the first postoperative day and the day of discharge (P1 before P2), a statistically significant increase in indices ($p<0,05$) was found in groups A2 from 1,71 ± 0,42 to 1,99 ± 0,4; B2 from 1,46 ± 0,38 to 1,71 ± 0,39; C2 from 1,26 ± 0,51 to 1,60 ± 0,53, which performed diaphragmatic exercises with early mobilization. Comparison of FEV1 values on the day of discharge and surgery (P2 before P0) found that all patients of groups A1, B1, C1, who did not engage in diaphragmatic breathing exercises, had a statistically significant decrease ($p<0,05$) in of FEV1, there was no restoration to the preoperative level.

Comparison of PEFR parameters is presented in Table 4 Comparison of indicators before surgery and the first day after surgery (P0 before P1) showed a statistically significant decrease ($p<0,05$) in PEFR in all groups (M±m): A1 from 5,69 ± 2,04 to 3,61 ± 1,76; A2 from 5,72 ± 2,10 to 3,62 ± 1,77; B1 from 5,40 ± 1,76 to 3,46 ± 1,51; B2 from 5,42 ± 1,84

Table 4. Indicators of the peak speed of exhalation of PEFR, l/s

Group	Indication before operative intervention, (M±m), P_0	Indicator on the first day after surgery, (M±m), P_1	Indicator on the day of discharge, (M±m), P_2	p P_1 before P_0	p P_2 before P_1	p P_2 before P_0
Group A1	5,69 ± 2,04	3,61 ± 1,76	4,49 ± 1,82	< 0,05	> 0,05	> 0,05
Group A2	5,72 ± 2,10	3,62 ± 1,77	4,76 ± 1,74	< 0,05	< 0,05	> 0,05
Group B1	5,40 ± 1,76	3,46 ± 1,51	4,29 ± 1,69	< 0,05	> 0,05	< 0,05
Group B2	5,42 ± 1,84	3,40 ± 1,51	4,38 ± 1,52	< 0,05	< 0,05	> 0,05
Group C1	4,89 ± 2,09	2,73 ± 1,49	3,69 ± 1,51	< 0,05	> 0,05	< 0,05
Group C2	4,87 ± 2,09	2,69 ± 1,48	3,90 ± 1,50	< 0,05	< 0,05	> 0,05

to 3,40 ± 1,51; C1 from 4,89 ± 2,09 to 2,73 ± 1,49; C2 from 4,87 ± 2,09 to 2,69 ± 1,48. Comparing the PEFR indices between the first postoperative day and the day of discharge (P1 before P2), a statistically significant ($p<0,05$) increase in indices was found in groups A2 from 3,62 ± 1,77 to 4,76 ± 1,74; B2 from 3,40 ± 1,51 to 4,38 ± 1,52 ; C2 from 2,69 ± 1,48 to 3,90 ± 1,50, which, along with early mobilization, performed diaphragmatic exercises. Comparison of PEFR, (l/s) values on the day of discharge and before surgery (P2 before P0) revealed that in all patients of groups elderly and middle-aged C1, B1 who did not engage in diaphragmatic breathing exercises, a statistically significant decrease was observed ($p<0,05$), i.e., there was no recovery of PEFR to the preoperative level.

DISCUSSION

In developing a rehabilitation intervention, we took into account the experience of scientists [5]. Before surgery, patients of groups A2, B2, C2 underwent some training, where there was an explanation to patients about the importance of increasing physical activity and restoring respiratory function. Patients were taught proper diaphragmatic positive expiratory pressure breathing techniques and the exercises they would do after surgery for faster recovery. They taught the technique of moving from the starting position (SP) lying in the SP while sitting and standing, the technique of correct coughing.

In most cases, in all patients of groups A2, B2, C2, the goals of physical therapy were: prevention of postoperative complications, peripheral circulatory disorders, thromboembolic complications, hypostatic pneumonia, disorders of the gastrointestinal tract, complications from the postoperative wound; increased activity of the abdominal muscles, prevention of hernias, activation of intestinal motility, restoration of tolerance to physical activity, restoration of physical qualities, etc. One of the goals was to restore the function of external respiration of patients (improvement of bronchial patency and drainage function of the bronchi, restoration of lung capacity) and the correct breathing pattern. An important part of rehabilitation in groups A2, B2, C2 was the application of the principles of individualization, consciousness and activity of the patient. The next day after surgery, early mobilization of patients was performed. Performed breathing and therapeutic exercises to stretch the intercostals muscles, breathing exercises with diaphragmatic breathing, namely with positive expiratory pressure, since this technique helps to remove sputum from the main bronchi in patients with hypersecretion after upper abdominal airway surgery and improved lung function [6]. Performed therapeutic exercises in the initial positions lying, sitting, standing. Categorically avoided exercises that lead to an increase in intra-abdominal pressure. The ratio of respiratory and therapeutic exercises was 1:2. The duration of the first lesson did not exceed 10 minutes. Each patient performed the exercises 2 times a day (morning and afternoon) under the guidance of a physical therapist. A significant problem in the implementation of rehabilitation measures was that the pain in the area of the surgical wound was exacerbated by movement. As a result, patients tried to reduce the amount of physical activity as much as possible.

The presence of pain syndrome contributes to a decrease in the productivity and effectiveness of coughing, as a result, a violation of the mechanism of sputum evacuation from the tracheobronchial tree of the lungs. When developing a physical therapy program for elderly patients, we took into account the fact that physiological changes with aging

occur in all systems and organs of the body, including respiration. As a rule, elderly people experience deformity of the chest, atrophy of the intercostals muscles and diaphragm [8]. The size of the lung decreases and the structure of the alveoli changes, the elasticity of the elastic fibers' decreases, due to which the intra alveolar membranes disappear and the alveolar passages expand. There is a decrease in the gas exchange surface and a decrease in the vital capacity of the lungs, the reserve volume of inhalation and exhalation, tidal volume, and the respiratory rate increases. As a result, there is a decrease in the functional capabilities of the respiratory organs with an increase in hypoxia and hypercapnia, which is especially evident during physical activity. Elderly patients usually have bronchial obstruction with irregular lung ventilation [8-10].

When implementing a rehabilitation program for patients after LCH, special attention was paid to elderly patients, because they have a higher risk of developing congestive pneumonia. Therefore, the use of breathing exercises in elderly patients is vital [8].

Early mobilization of patients occurred in all groups, because it is important for the prevention of postoperative deep vein thrombosis and pulmonary thrombosis, the most common cause of in-hospital death. Scientists have found that pneumoperitoneum and the Trendelenburg position lead to a decrease in the volumetric blood flow velocity, prevent total femoral venous blood flow and increase venous stasis [11,12]. The control groups were trained in correct coughing and early mobilization of patients on the first day. Early mobilization in all groups included: sitting on the edge of the bed with legs down, coughing, standing, walking in place, walking in the ward, walking along the corridor and stairs. When performing early mobilization, the age, condition of the patient, etc. were taken into account.

CONCLUSIONS

1. It has been established that laparoscopic cholecystectomy leads to a statistically significant decrease in the parameters of forced vital capacity, forced expiratory volume per second and peak expiratory flow in all age categories.
2. It was established that without respiratory therapy in groups of elderly patients of group C1 there was no restoration ($p<0,05$) of FVC, l before surgery (P0) 2,28 ± 0,68, on the day of discharge (P2) 1,86 ± 0,62, FEV 1.l (P0) 1,86 ± 0,54, (P2) 1,51 ± 0,52 PEFR l/s (P0) 4,89 ± 2,09, (P2) 3,69 ± 1,51; middle-aged patients of group B2 did not recover ($p<0,05$) FEV1, l (P0) 2,01 ± 0,46, (P2) 1,63 ± 0,49, PEFR, l/s (P0) 5,40 ± 1,76, (P2) 4,29 ± 1,69; in younger patients there was no recovery ($p<0,05$) of FEV1, l (P0) 2,23 ± 0,49, (P2) 1,88 ± 0.48.
3. The use of diaphragmatic breathing exercises in combination with early mobilization leads to a statistically significant increase in the parameters of the forced vital capacity of the lungs in groups A2 from 2,04 ± 0,75 to 2,52 ± 0,70; B2 from 1,80 ± 0,68 to 2,23 ± 0,65; C2 from 1,57 ± 0,60 to 1,97 ± 0,61, the volume of forced exhalation in one second in groups A2 from 1,71 ± 0,42 to 1,99 ± 0,4; B2 from 1,46 ± 0,38 to 1,71 ± 0,39; C2 from 1,26 ± 0,51 to 1,60 ± 0,53 and the peak expiratory velocity in groups A2 from 3,62 ± 1,77 to 4,76 ± 1,74; B2 from 3,40 ± 1,51 to 4,38 ± 1,52 ; C2 from 2,69 ± 1,48 to 3,90 ± 1,50 in comparison with the indicators on the day of discharge and on the first day after surgery.
4. The results of the study indicate the effectiveness of the introduction of diaphragmatic breathing exercises in combination with early mobilization at the acute and subacute stages of rehabilitation in patients after laparoscopic cholecystectomy in order to restore the function of the respiratory system.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Analysis of cases of premature rupture of membranes and preterm births to identify effective management measures to prevent them

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ABSTRACT

Aim: Based on retrospective analysis recognize the key factors of development of premature childbirth and elaborate highly specific criteria for individual prognosis to improve perinatal outcomes.

Materials and Methods: A retrospective analysis of the birth histories of 250 women and their newborns with spontaneous preterm births at 22-36 weeks was conducted using archival data from the department for pregnant women with obstetric pathology of the State Institution "Institute of Pediatrics, Obstetrics and Gynecology named by academician OM Lukianova of the National Academy of Medical Sciences of Ukraine"

Results: Important risk factors for premature rupture of membranes (PROM) in preterm pregnancy include the presence of sexually transmitted diseases ($\chi2=31.188$, $p=0.001$), bacterial vaginosis ($\chi2=30.913$, $p=0.0001$), a history of abortion and/or preterm birth ($\chi2=16.62$, $p=0.0002$), SARS during pregnancy ($\chi2=16.444$, $p=0.0002$), chronic adnexitis in anamnesis ($\chi2=11.522$, $p=0.0031$), inflammatory cervical disease ($\chi2=11.437$, $p=0.0032$), anaemia ($\chi2=10.815$, $p=0.0044$), isthmic-cervical insufficiency (ICI) ($\chi2=10.345$, $p=0.0057$), chronic pyelonephritis with exacerbation ($\chi2=9.16$, $p=0.01$), smoking during pregnancy ($\chi2=10.815$, $p=0.0044$).

Conclusions: The results of a retrospective analysis of 250 cases of preterm birth at 22 to 36 weeks allowed us to identify ways to effectively use existing diagnostic measures to determine readiness for pregnancy and the possibility of prolonging pregnancy to the viability of the newborn. Ways to improve the prevention of preterm birth and the design of further research were identified.

KEY WORDS: pregnancy, spontaneous premature childbirth, premature rupture of membranes, vaginal microbiocenosis

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INTRODUCTION

The problem of preterm birth in modern obstetrics and perinatology remains one of the most pressing, having not only a medical but also a social aspect, due to adverse perinatal outcomes for children [1, 2]. According to the World Health Organisation (WHO), 15 million children are born prematurely every year worldwide, which is an average of 7.5 % of births (6.2 – 11.9 %). 7.5 % of preterm births account for 69 – 83 % of perinatal losses. Every year, more than 1 million premature babies die worldwide. Those children who survive are 10 times more likely to suffer from illness and disability. In 50 – 70% of cases, perinatal mortality is caused by complications resulting from premature birth. The course of pregnancy reflects the health of the mother and the environment. Disorders of the neuroendocrine systems, peculiarities of immune reactions, the nature of bacterial and viral infection can cause premature water breakage, uterine infection, preterm birth and infant mortality [3, 4].

The morbidity and mortality rate of preterm infants is 40 times higher than that of full-term infants. Perinatal morbidity and mortality in preterm births depends on the gestational age and weight of the fetus, as well as the course of pregnancy and childbirth. A special place in the structure of perinatal morbidity and mortality in preterm infants is occupied by births with premature rupture of membranes [5-7]. Rupture of the membranes between 22 and 34 weeks of gestation is a complex, not fully resolved problem for obstetric practice. When prolonging a preterm pregnancy in the case of PROM, the most dangerous complication is the possibility of uterine infection, the development of chorioamnionitis, fetal and neonatal infection. The risk of infection is higher the lower the gestational age of the fetus [1, 8, 9].

Preterm newborns are at significant risk of developing respiratory distress syndrome, hypothermia, hypoglycaemia, hyperbilirubinemia, metabolic acidosis, haemorrhagic syndrome, necrotising enterocolitis, infectious diseases, intraventricular haemorrhage (IVH)

and the risk of early neonatal mortality. The choice of rational management of preterm pregnancy in the case of PROM is a complex problem, as it is necessary to take into account the ratio of the risk of infection during pregnancy prolongation and the risk and consequences of preterm birth [10-12].

Taking into account current views on PROM in preterm pregnancy, one of the main tasks of practical obstetrics is to identify early prognostically significant markers of intrauterine infection (IUI), choose the optimal time of delivery, and justify treatment tactics to improve perinatal outcomes.

Ukrainian scientific sources do not contain data on the association of a certain infectious factor in the mother with the implementation of uterine infection of the fetus and newborn. Safe latency periods for premature rupture of membranes in preterm birth have not been determined. There are no studies of the negative impact of environmental factors on the development of preterm birth and the formation of the period of early neonatal adaptation [13, 14].

Foreign scientific publications relate to the development and implementation of optimal schemes for the prevention of intrauterine infection in preterm pregnancy complicated by PROM, and the study of the long-term effects of antibiotics during pregnancy on child development [15, 16].

In recent years, antiphospholipid syndrome has been given a leading role among the autoimmune aspects of preterm birth and miscarriage. The etiological factors of this syndrome are not fully understood [17, 18].

At the current stage, the pathogenesis of preterm labour is not fully understood; the mechanism of labour initiation is explained by various theories: a decrease in progesterone levels, oxytocin stimulation and decidual activation [19].

The risk factors for perinatal morbidity and mortality in preterm birth are gestational age and fetal weight, and the characteristics of the course of preterm birth itself [20-22]. High perinatal morbidity and mortality are associated not only with prematurity, but also with the causes of preterm birth [23].

The issue of prediction and early warning of preterm birth needs to be improved. There is no consensus in the scientific literature on the obstetric tactics for managing women with PROM and no labour in preterm pregnancy. In such cases, doctors have to choose between the risk of giving birth to a preterm immature baby with immediate induction of labour and the risk of developing infectious complications in the pregnant woman and fetus with a wait-and-see approach [24].

The likelihood of spontaneous development of labour in PROM and preterm pregnancy depends on the gestational age – the shorter it is, the longer the latency period. Thus, within 24 hours, with an expected fetal weight of 500–1000 g, spontaneous labour begins in only 25 % of women [25]. According to the literature, different methods of delivery for women with PROM and preterm pregnancy show differences in the rates of perinatal morbidity of newborns: spontaneous induction of labour increases the incidence of respiratory disorders and congenital infections, while induction of labour with oxytocin increases the incidence of children with primary asphyxia, hypoxic-ischemic central nervous system (CNS) damage, intraventricular haemorrhage and severe conjugal jaundice [26-28].

Approaches to conservation therapy in women at risk of abortion need to be reviewed and supported by evidence. The danger of prolonging pregnancy in case of premature rupture of membranes has not been proven. The association between the duration of the latent period and inflammatory diseases in preterm infants needs to be studied; technologies for preventing preterm birth need to be improved; approaches to conservation therapy and pregravid preparation in women at risk of abortion need to be reviewed.

AIM

Based on a retrospective analysis, identify the main factors in the development of preterm birth and develop highly specific criteria for individual prognosis to improve perinatal outcomes.

MATERIALS AND METHODS

An analysis of the medical records of women with preterm births that occurred in the conditions of the State Institution "Institute of Pediatrics, Obstetrics and Gynecology named by academician OM Lukianova of the National Academy of Medical Sciences of Ukraine" for the period from 2010 to 2020 was carried out. To participate in the study, 250 pregnancy and childbirth histories of women who had preterm births at 22–36 weeks of gestation were selected, and the features of the course of pregnancy, childbirth and the health status of their newborns were studied. The main group included 250 pregnant women who gave birth at 22–36 weeks, including women with premature rupture of membranes, who underwent conventional examination and treatment according to the clinical protocol approved by the Order of the Ministry of Health of Ukraine No. 782 "Preterm Birth" of 29.12.05. The results of the analysis were compared with a group of women who gave birth at full term (37–40 weeks) – the control group, which consisted of 50 women.

In pregnant women with PROM in preterm pregnancy, monitoring was carried out in accordance with Ministry of Health of Ukraine Order No. 782; in case of choice of a wait-and-see tactic, dynamic monitoring of the pregnant woman and fetus was performed in an obstetric hospital with auscultation of the fetal heartbeat twice a day and, if necessary, recording cardiotocography at least once a day from the 32-nd week of pregnancy; ultrasound examination, including Doppler blood flow measurement from the 30-th week of pregnancy. Pregnant women performed the fetal movement test on their own. Clinical and laboratory monitoring was carried out to determine the number of leukocytes in the peripheral blood, depending on the clinical course, but at least once every three days; complete blood count once every 2–3 days (with blood formula); bacterioscopic examination of vaginal discharge once every three days (with counting the number of leukocytes in the smear). From the moment amniotic fluid leakage was registered, in the absence of signs of infection in the mother, prophylactic administration of semi-synthetic penicillins or second-generation cephalosporins at medium therapeutic doses was performed. In the case of a cervical suture or an obstetric unloading pessary, they were removed with the onset of labour. In the absence of labour, preservative therapy (progesterone, tocolysis, metabolic therapy, prophylaxis of respiratory distress syndrome within the recommended timeframe according to the Order of the Ministry of Health No. 782 "Preterm delivery" from the 24-th to the 34-th week of pregnancy) was performed.

The statistical processing of the results consisted in the use of parametric and non-parametric statistics. The evaluation of the obtained quantitative and qualitative indicators was carried out on an Intel Core i3 personal computer using the STATISTICA 8.0 software package (Statistica Inc., USA).

In the case of normal distribution in a sample of the same type of traits, the student's t-criterion was used to compare them. The difference was considered significant at $p < 0.05$.

We used the logistic regression method when there are binary outcomes (presence/absence of a symptom or subject) and a number of predictors of the disease; we estimated the Odds Ratio (OR). $\chi 2$ test (null hypothesis that the logistic regression coefficient is zero and alternative hypothesis that the odds ratio of "disease" associated with this variable is one) to determine whether each variable influences the presence or absence of disease (congenital infection) and to quantify the degree of this influence.

When interpreting the results, it is taken into account that if the Confidence Interval (CI) for the OR includes one, then the difference between the groups is statistically insignificant. If all CI values are greater than one, then the chance of having the trait is statistically significantly higher in the first group than in the second. If all CI values are less than one, the chance is higher in the second group.

The operational characteristics of diagnostic tests were determined by the following formulas:

Sensitivity = a / (a + c)

Specificity = d / (d + b)

Positive predictive value (PPV) = a / (a + b)

Negative predictive value (NPV) = d / (d + c),

Where:

a – true positive results;

b – false positive results;

c – false negative results;

d – true negative results.

RESULTS

The average age of women in the study group was 31.34 ± 5.64 years and did not differ significantly from the control group, 30.54 ± 6.26 ($p > 0.05$). Among the women in the study group who gave birth prematurely, 137 (55 %) had their first birth, and 113 (45 %) had repeated births. 160 (64 %) of the women in the main group lived in urban areas, and 90 (36 %) in rural areas. Among the women in the main group, 99 (39.6 %) were single or in an unregistered marriage. Smoking during pregnancy was observed in 62 (24.8 %) pregnant women in the main group and in 4 (8.0 %) women in the control group ($p < 0.05$).

The threat of pregnancy termination, starting from the first trimester, occurred in 187 (74.8 %) women of the main group, in the second trimester – in 197 (78.8 %) patients. The anamnesis revealed that 170 (68.0 %) women in the main group had lost a pregnancy in the first trimester, including habitual miscarriage (2 to 9 abortions) in 112 (44.8 %) of the subjects. 13 (5.2 %) women had a history of ectopic pregnancy. With the help of modern assisted reproductive technologies, 26 (10.4 %) couples have repeatedly tried to get pregnant. In the past, 53 (21.2 %) women in the main group had experienced preterm births. In all cases of early preterm births, stillbirth was diagnosed; in late preterm births, babies were born alive, but with signs of prematurity, which required long-term rehabilitation. A retrospective analysis revealed that 11 (4.4 %) children with cerebral palsy grow up to be disabled from childhood.

Hormonal imbalance in the hypothalamus-pituitary-ovarian system was detected in 189 (75.6 %) of the main group: ovarian-menstrual cycle (OMC) disorders, benign tumours of the uterus and append-

Table 1. Gynecological pathology in examined women (abs. number, %)

Gynecological pathology	Main group (n = 250)	Control group (n = 50)
Inflammatory diseases of the cervix	107 (42,8)*	9 (18)
Chronic adnexitis	85 (34,0)*	6 (12)
Myoma of the uterus	15 (6,0)	2 (4)
Ovarian operations	13 (5,2)	1 (2)
Gynecological peritonitis	2(0,8)	0
Infertility I and II	15(6,0)	2 (4)
Disorders of the menstrual cycle	30 (12,0)	5 (10)
Sexually transmitted diseases	82 (32,0)*	7(14)
Vaginitis	52(20,8)	5(10)

* indicates the probability of differences compared to the control group, $p < 0,05$.

Table 2. Number of pregnant women by examination groups with extragenital pathology (abs. number, %)

Extragenital pathology	Main group (n = 250)	Control group (n = 50)
Acute or gestational pyelonephritis	25 (10,0) *	2 (4)
Chronic pyelonephritis with exacerbation	38 (15,2)*	1 (2)
Chronic sinusitis and tonsillitis with exacerbation	25 (10,0)*	0
Chronic bronchitis with exacerbation	15 (6,0) *	1 (2)
Bronchial asthma	5 (2,0)	0
Acute respiratory viral infections	22 (8,8)*	2 (4)
Diseases of the cardiovascular system	7 (2,8) *	1 (2)
Diseases of the gastrointestinal tract	8 (3,2) *	1 (2)
Cholestatic hepatosis	1 (0,4)	0
Anemia	75 (30,0)*	6 (12)
Disease of the thyroid gland	8 (3,2) *	1 (2)
Adiposity	10 (4,0)	2 (4)
Venous complications	3 (1,2)	0
Varicose veins	8 (3,2) *	1 (2)

* indicates the probability of differences compared to the control group, $p < 0,05$.

ages, endometrial pathology – 157 (62.8 %) cases, hyperandrogenism – 51 (20.4 %) observations, hyperprolactinemia – in 67 (26.8 %) women. In 108 (43.2 %) of the main group, hyperaggregation was detected, which was caused by antiphospholipid syndrome, mutation of coagulation factor V (G1691A), mutation of prothrombin (G20210A) and MTHFR (C677T), and hyperhomocysteinaemia. Hyperaggregation states (antiphospholipid syndrome, hyperfibrinogenemia, decreased Activated Partial Thromboplastin Time (APTT), increased Soluble Fibrin-monomer Complexes (SFMC), hyperhomocysteinemia) were observed in 180 (72.0 %) women. The anamnesis revealed that 101 (40.4 %) women in the main group had sexually transmitted diseases (STDs): chlamydia, ureaplasmosis, mycoplasmosis. Infection of the vagina and cervix (129 (51.6 %) cases) causes cervical dysplasia (68 (27.2 %) cases) and endometrial inflammation. Bacterial vaginosis was noted in 81 (32.4 %) women. Gynaecological pathology is presented in Table 1.

Therefore, a burdened obstetric and gynaecological history with predominantly inflammatory diseases in pregnant women in the main group makes urogenital infection a predictor of premature rupture of membranes in preterm pregnancy, along with hormonal disorders and hyperaggregation states. Concomitant extragenital pathology is important for pregnancy, the frequency of which in the study groups is shown in Table 2.

In the main group, concomitant extragenital pathology was present in 250 (100 %) cases, which is significantly more frequent compared to the control group – 18 (36.0 %), ($p < 0.05$). In women of the main group, a combination of several diseases was observed, and

Table 3. The course of pregnancy in examined women in groups (abs. number, %)

Complications of pregnancy	Main group (n = 250)	Control group (n = 50)
The threat of abortion in the I and II trimesters	105 (42,0)*	9 (18,0)
Early gestosis	33 (13,2)	5 (10,0)
Late gestosis	18 (7,2)	3 (6,0)
Polyhydramnios	20 (8,0)	4 (8,0)
low tide	45 (18,0)	5 (10,0)
Isthmic-cervical insufficiency	30 (12,0)*	0
Suture on the cervix	13 (5,2)	1 (2,0)
Fetal growth retardation I ст.	35 (14,0)	6 (12)

* indicates the probability of differences compared to the control group, $p < 0,05$.

Table 4. Distribution of women with premature birth in different periods of pregnancy according to some clinical and paraclinical indicators (abs. number, %)

Pregnancy period, weeks	The number of women with premature births (n)	The number of women with premature birth and long term PROM	Duration PROM, (год) (M±m)	Stillborn	Treat-ment in the Neonatal Intensive Care Unit	Died	Discharged home with the child
22 – 27	27	18 (66,6)	163,3 ± 58,2	25 (92,59)	2 (7,4)	1 (3,7)	1 (3,7)
28 – 31	31	26 (83,8)	92,1 ± 44,3	7 (22,5)	24 (77,4)	3 (9,7)	21 (67,7)
32 - 34	52	34 (65,4)	80,4 ± 39,9	0	52 (100)	7 (13,5)	45 (86,5)
35-36	140	111 (79,3)	30,6 ± 15,7	2 (1,4)	31 (22,1)	1 (0,7)	137 (97,9)
In total	250	189 (75,6)	91,3 ± 34,9	34 (13,6)	109 (43,6)	12 (4,8)	204 (81,6)

Table 5. Distribution of women with premature birth in different periods of pregnancy according to the presence of obstetric complications (abs. number, %)

Pregnan-cy period, weeks	Number of women from PROM more than 3 days	Premature detachment of the placenta	Prolapse of the umbilical cord	Compression of the umbilical cord
22 – 27	8 (29,6)	-	-	-
28 – 31	26 (83,8)	-	-	-
32 - 34	34 (65,4)	-	-	-
35-36	111 (79,3)	-	-	-
In total	189 (75,6)	-	-	-

Table 6. Distribution of premature newborns in different periods of pregnancy according to the presence of complications associated with prematurity and prematurity giving birth (abs. number, %)

Pregnan-cy period, weeks	The number of premature newborns in in the Neonatal Intensive Care Unit	Lung hypoplasia	Deforma-tion of the skeleton	Respira-tory distress syndrome	Internally-ventricular hemorrhage
22 – 27	2	-	-	2 (100)	1 (50)
28 – 31	24	-	-	9 (37,5) *	4 (16,6)*
32 – 34	52	-	-	1 (1,9) *	3 (5,7)*
35 – 36	31	-	-	-	-

* the probability of differences compared to the group of newborns at 22-27 weeks is marked,$p < 0,05$.

almost every second pregnant woman had a combination of extragenital pathology with the presence of an inflammatory component.

The duration of pregnancy in women in the main group with PROM had the following features: 105 (42.0 %) had a threat of miscarriage and/or preterm birth in the 1st and/or 2-nd trimester, which was significantly more frequent compared to the control group ($p < 0.05$). Early gestosis in women of the main group was observed in 33 (13.2 %) women, and late gestosis in 18 (7.2 %) pregnant women. Acute respiratory viral infection during pregnancy was experienced by 13 (13.0 %) of the study group. Preeclampsia was noted in 20 (8.0 %) pregnant women, preeclampsia in 45 (18.0 %) women, placental dysfunction and mild fetal growth retardation syndrome were observed in 35 (14.0 %). Isthmic-cervical

Table 7. The prognostic value of risk factors for predicting the realization of intrauterine infection in PROM in premature birth

Indicator (risk factor)	Calculation index
Duration of the waterless period, (min)	0,05
Bacterial vaginosis	3,05
History of pregnancy losses (from 1 to 5)	1,93
Carriers of sexually transmitted infections	1,68
Acute Respiratory Diseases during pregnancy at any time	1,07
Herpes virus infections	0,68
Threat of abortion	0,08
Hyperaggregation state	6,2

Table 8. The prognostic value of the combination of some non-parametric factors in determining the risk of premature birth at different times

Factor		Calculation index	P
Carriers of sexually transmitted infections	+ Threat of termination of pregnancy at different times	4,96	0,03
	+ Acute Respiratory Diseases during pregnancy at any time	1,79	0,04
	+ History of pregnancy losses (from 1 to 5)	2,13	0,24
	+ Lack of lactoflora	1,82	0,54
	+ Hyperaggregation state	1,98	0,99
	+ Progesterone deficiency	1,64	0,69
Herpes virus infection	+ Threat of abortion at any time	3,25	0,78
	+ Acute Respiratory Diseases during pregnancy at any time	2,01	1,00
	+ History of pregnancy losses (from 1 to 5)	207	1,00
	+ Lack of lactoflora	1,01	1,00
	+ Progesterone deficiency	2,90	1,00

Table 9. Chances and risk of intrauterine infection in pregnancy and premature pregnancy depending on the studied indicators

Indicator	Statistical indicator					
	OR	95 % CI	χ^2	p	OR	95% CI
Violation blood flow in average cerebral arteries	77,56	13,21 – 599,98	47,84	0,0006	25,50	6,77 – 153,48

Table 10. Results of the study of the influence of vaginal microflora on the risk of IUI implementation in premature newborns in premature pregnancies complicated by PROM

Microflora	OR	95% CI	χ^2	p	OR	95% CI
St. aureus	4,40	1,14 - 17,34	4,85	0,02	3,45	1,12 - 10,69
E. Coli	2,94	1,05 - 8,32	4,30	0,038	1,77	1,03 - 2,71
St. epidermidis	2,29	0,99 - 6,95	4,23	0,03	3,43	1,15 - 10,97
Enterococcus spp.	2,61	0,86 - 8,16	2,68	0,10	2,04	0,88 - 4,39
Klebsiella pneumoniae	3,45	0,76 - 15,6	2,29	0,12	2,96	0,78 - 11,06
Proteus vulgaris	3,33	0,62 - 17,79	1,57	0,20	2,96	0,64 - 13,39
Enterobacter chlochae	3,13	0,29 - 33,59	0,33	0,56	2,96	0,30 - 28,80
Proteus mirabilis	2,05	0,22 - 16,57	0,06	0,80	1,97	0,23–14,00
St. saprophiticus	1,89	0,97 - 5,55	0,19	0,65	1,42	0,89 - 4,13
St. haemoliticus	2,00	0,37 - 14,24	0,28	0,59	1,85	0,43 - 11,98
C. albicans	0,92	0,33 - 2,50	0,005	0,98	0,96	0,56 - 1,45

Table 11. Chances and risk of congenital pneumonia depending on the spectrum of the microflora of the birth canal

indicator	Statistical indicator					
	OR	95% CI	χ^2	p	OR	95% CI
Mycoplasmagenytalium	17,56	4,64 - 71,01	26,12	0,0005	8,28	3,20 - 23,72
Trichomonasvaginalis	15,77	3,39 - 83,64	18,13	0,0005	9,86	2,78 - 43,41
Chlamydiatrachomatis	8,34	2,72 - 26,29	17,27	0,0006	3,64	1,93 - 6,31
Gardnerellavaginalis	5,90	2,00 - 17,79	12,14	0,0012	2,96	1,58 - 5,07
Ureaplasmaurealyticum	2,44	0,85 - 7,03	2,60	0,10	1,80	0,89 - 3,33

insufficiency was observed in 30 (12.0 %) women, and cervical suture in 13 (5.2 %) pregnant women in the main group. Data on the course of pregnancy in the examined women in the groups are presented in Table 3.

Overall, the incidence of complicated pregnancy in women with premature rupture of membranes was observed in 119 (100 %) cases, which is an unfavourable prognostic risk factor for pregnancy and also indicates a fairly frequent combination of several complications of pregnancy in women with premature rupture of membranes in preterm pregnancy.

The microbiocenosis of the genital tract is of great prognostic importance for pregnancy. Among the isolated microflora of the vagina and cervical canal in pregnant women of the examined groups, opportunistic gram-negative microflora prevailed in 182 (72.8 %) cases in the main group and in 8 (16.0 %) cases in patients of the control group ($p < 0.05$), namely *Esch. Coli* – 70 (28 %) and 2 (4.0 %) respectively, *Enterococcus. spp*. – 62 (24.8 %) and 1 (2.0 %), *Klebsiella pneumoniae* – 12 (4.8 %) and 1 (2.0 %), *Proteus vulgaris* – 13 (5.2 %) and 1 (2.0 %), *Enterobacter chloacae* – 7 (2.8 %) and 1 (2.0 %), *Proteus mirabilis* – 5 (2 %) and 2 (4.0 %). *Providencia alcalifac* and *Enterobacter aerogenes* were found in 5 (2.0 %) and 8 (3.2 %) women of the main group and were absent in the control group.

Gram-positive flora occurred in 231 cases (92.40 %) in the main group and in 6 (12.0 %) cases in the control group ($p < 0.05$), namely: *St. epidermidis, St. saprophyticus, St. aureus* were found only in women of the main group. *Candida albicans* was found in 178 cases (71.2 %) in the main group and in 7 (14.0 %) in the control group ($p < 0.05$), *Gardnerella vaginalis* – in 82 (32.8 %) in the main group and in 2 (4.0 %) women in the control group ($p < 0.05$), which indicates the combination of several types of microorganisms in the microbiocenosis of the genital tract of pregnant women. It is known that a high concentration of microorganisms leads to upward infection of the amniotic membranes, which is the main cause of their premature rupture. Thus, in the quantitative analysis in our study, the conditionally pathogenic microflora was in a concentration of 106-7 colony-forming units per 1 ml of fluid (CFU/ml) in the main group and 103-4 CFU/ml in the control group ($p < 0.05$). Thus, a high concentration of microorganisms in the genital tract of pregnant women leads to ascending infection of the membranes, their premature rupture, infection of the fetus and newborn, and necessitates the prophylactic administration of antibiotic therapy in prolonged pregnancy complicated by PROM.

The duration of pregnancy in the main group of women had the following features: abnormalities of labour (weakness of labour, discoordinated labour) were observed in 25 women (10.0 %), incorrect fetal position, pathological presentation at the time of the onset of labour – in 47 women (18.8 %) of the main group and 4 (8.0 %) of the control group ($p < 0.05$). Fetal distress was diagnosed in 30 women of the main group (12.0 %) and 2 (4.0 %) women of the control group ($p < 0.05$), chorionamnionitis clinic was not noted in any of the subjects of the main and control groups ($p < 0.05$).

According to the analysis of the course of labour in the study groups, the third period was complicated by a defect in the placenta, partial tight attachment of the placenta with manual separation and discharge of the placenta in 27 women (10.8 %) of the main group and was not observed in women of the control group ($p < 0.05$). Premature placental abruption was observed in 5 women (2.0 %) in the intervention group and 1 woman in the control group (2.0 %) ($p > 0.05$). Surgical delivery was performed in 47 women in the intervention group (18.8 %). In the control group, 5 women underwent caesarean section (10.0 %). Indications for surgical delivery were premature placental abruption, fetal malposition, uterine scarring, and fetal distress.

In a retrospective analysis of uteroplacental and fetal-placental blood flow disorders (assessment of

blood flow velocity curves in the uterine arteries and umbilical cord arteries), Doppler (comparison of vascular resistance indices, diastolic component of blood flow) made it possible to establish parameters in which it was inappropriate to prolong pregnancy, which led to an urgent delivery regardless of gestational age in 98 (39.2 %). The distribution of women with preterm births at different gestational ages is shown in Table 4.

From the data presented, it can be argued that the greatest obstetric losses are associated with the gestational age of the newborn. That is, the very fact of preterm birth, rather than the duration of the latent period, is a factor in the development of postnatal complications. Therefore, the main task of obstetricians and gynaecologists is to effectively prevent early preterm birth or to delay delivery as much as possible. The distribution of women with preterm births at different gestational ages according to the presence of certain obstetric complications is shown in Table 5.

The analysis of the postpartum period showed that there were no cases of postpartum endometritis in both the main and control groups, and uterine subinvolution occurred in 30 women (12.0 %) in the main group and 3 (6.0 %) in the control group.

The clinical parameters of 109 newborns born prematurely and treated in the neonatal intensive care unit (NICU) were analysed. The gestational age of children treated in the NICU was as follows: 22–27 weeks – 2 (10.5 %) children, 28–31 weeks – 24 (22.01 %), 32–34 weeks – 52 (47.7 %), 35–36 weeks – 31 (28.5 %) children.

There were 42 (38.53 %) children on artificial lung ventilation (ALV). The average length of stay for a newborn on mechanical ventilation was 7–10 days. There were 21 (19.3 %) children on SiPAP. Kurasuf was administered to 46 (42.2 %) newborns. After birth, 12 preterm infants died on days 3–12: 3 (25 %) due to congenital pneumonia, 8 (66.7 %) from hypoxic-ischemic CNS damage.

The distribution of preterm infants by weight is as follows: from 500 g to 999 g – 2 (1.83 %) infants, from 1000 g to 1499 g – 24 (22.01 %), from 500 g to 1999 g – 52 (47.7 %), from 2000 g to 2499 g – 31 (28.4 %) infants.

The distribution of women with preterm births at different stages of pregnancy by the presence of complications in the newborn is shown in Table 6

Hypoxic-ischemic damage to the central nervous system (in the form of depression syndrome) and respiratory distress syndrome were present in 100 % of infants born prematurely before 29–30 weeks of gestation; intrauterine infection in the form of congenital bilateral pneumonia, rhinitis, conjunctivitis, omphalitis – 87 (79.81 %) of newborns; intraventricular hemorrhage of the P-S degree – 45 (41.3 %) of babies in the main group.

We conducted a regression analysis to determine the role of some factors in the development of preterm birth. Thus, smoking can be considered a risk factor for PROM in preterm pregnancy ($\chi 2=10.815$, $p=0.0044$). Factors were selected to predict the occurrence of uterine infection in preterm birth using statistically significant predictors (Table 7).

As the data show, the duration of the waterless period has the least impact on the development of uterine infection in preterm birth. Thus, the calculated index of the impact of a history of pregnancy loss increases the likelihood of this event by 39 times compared to a long latency period under conditions of waiting tactics.

We also determined the prognostic value of the combination of some non-parametric factors in determining the risk of preterm birth at different times (Table 8).

No significant difference was found between the weights of the born and deceased children in the respective age categories ($p > 0.05$).

The influence (increased chances of developing an event) of some laboratory and clinical parameters on the risk of developing PROM in preterm pregnancy was analysed. For C-reactive protein in pregnant women's serum +++ (OR 110.07, 95 % CI 18.63 – 865.36), amniotic fluid index < 3 cm according to ultrasound (OR 55.20, 95 % CI 12.50 – 276.57), placental hypoplasia (corresponding to gestational age 5 mm) (OR 7.07, 95 % CI 3.68 – 18, 36) can be considered reliable prognostic criteria for the occurrence of intrauterine infection in a preterm newborn in preterm pregnancy with PROM and recommend determining the prognosis of the risks of delivery or prolongation of the latent period.

We also analysed the prognostic significance of Doppler in the middle cerebral artery for the risk of antenatal infection. The results of the distribution of prognostic indicators are presented in Table 9.

At the antenatal phase, Doppler ultrasound in the fetal middle cerebral artery (OR 77.56, 95 % CI 13.21 – 599.98) can be used to predict the realisation of IUI in a preterm infant and timely delivery in combination with the above methods based on the determination of C-reactive protein in pregnant women's serum and amniotic fluid index. An early sign of fetal distress should be considered a decrease in the S/D ratio.

The prognostic significance of the data of bacteriological examination of vaginal contents was studied. The role of certain pathogens of urogenital infections in the development of intrauterine infection in preterm birth and PROM was investigated using polymerase chain reaction (PCR). An analysis of the results of the study of the impact of vaginal microflora on the risk of VUI in preterm infants with preterm pregnancy complicated by PROM is presented in Table 10.

The presence of *St. aureus* (OR 4.40, 95 % CI 1.14 – 17.34) and *E. Coli* (OR 2.94, 95 % CI 1.05 – 8.23) in high concentrations in the birth canal of a pregnant woman at the time of PROM significantly increases the risk of congenital infection in a preterm infant and justifies the prophylactic use of antibiotics. At the same time, *St. epidermidis*, according to our study, reduces the risk of congenital infection in preterm pregnancy (OR 0.29, 95 % CI 0.08 – 0.95).

We investigated the impact of certain pathogens of urogenital infections and TORCH infections on the risk of congenital infection in preterm pregnancy against the background of PROM. The results are shown in Table 11. In the examination for TORCH infections, according to the retrospective analysis, it was found that 41 (20.7 %) had Ig M, and exacerbation of herpes virus infection (high Ig G titres) was detected in 138 (69.7 %) pregnant women.

Thus, the presence of markers of urogenital infection in the labour tract of pregnant women, namely *Mycoplasma genytalium* (OR 17.56, 95 % CI 4.64 – 71.01), *Trichomonas vaginalis* (OR 15.77, 95% CI 3.39 – 83.64), *Chlamydia trachomatis* (OR 8.34, 95 % CI 2.72 – 26.29), *Gardnerella vaginalis* (OR 5.90, 95 % CI 2.00 – 17.79), significantly increases the risk of having a child with congenital infection in PROM and preterm pregnancy.

DISCUSSION

The risk factors for perinatal morbidity and mortality in preterm birth are gestational age and fetal weight, and the characteristics of the course of preterm birth itself [20, 21]. High perinatal morbidity and mortality are associated not only with prematurity, but also with the causes of preterm birth [22].

The issue of prediction and early warning of preterm birth needs to be improved. There is no consensus in the scientific literature on the obstetric tactics for managing women with PROM and no labour in preterm pregnancy. In such cases, doctors have to choose between the risk of giving birth to a preterm immature baby with immediate induction of labour and the risk of developing infectious complications in the pregnant woman and fetus with a wait-and-see approach [23].

The likelihood of spontaneous development of labour in PROM and preterm pregnancy depends on the gestational age – the shorter it is, the longer the latency period. Thus, within 24 hours, with an expected fetal weight of 500–1000 g, spontaneous labour begins in only 25 % of women [5, 7, 24]. According to the literature, different methods of delivery for women with PROM and preterm pregnancy show differences in the rates of perinatal morbidity of newborns: spontaneous induction of labour increases the incidence of respiratory disorders and congenital infections, while induction of labour with oxytocin increases the incidence of children with primary asphyxia, hypoxic-ischemic central nervous system (CNS) damage, intraventricular haemorrhage and severe conjugal jaundice [13, 18, 24].

A detailed analysis of the effect of the duration of the water-free interval on the incidence of clinical symptoms of chorionamnionitis depending on the gestational age suggests the need to find more sensitive and early markers of intrauterine infection than clinical signs of chorionamnionitis in order to prevent severe forms of congenital infection and improve perinatal outcomes [8, 16, 25].

Thus, in the case of PROM, the timing of pregnancy prolongation should depend on the gestational age, expected weight of the newborn, clinical condition of the mother and fetus, and the onset of infection symptoms. Thus, a complicated obstetric and gynaecological history (even with one fetal loss in the history) with the presence of predominantly inflammatory diseases in pregnant women of the main group, the presence of acute respiratory disease in the 1-st and 2-nd trimester, hyperaggregation and hormonal dysfunction are key risk factors for premature rupture of membranes in preterm pregnancy [11, 12, 26].

Prolongation of pregnancy with PROM from the 28-th week of pregnancy significantly reduces the incidence of type I respiratory distress syndrome in preterm infants, thus reducing the need for mechanical ventilation and exogenous surfactant, the average duration of mechanical ventilation and the length of stay in the intensive care unit [26,27].

Approaches to conservation therapy in women at risk of abortion need to be reviewed and supported by evidence. The danger of prolonging pregnancy in case of premature rupture of membranes has not been proven. The association between the duration of the latent period and inflammatory diseases in preterm infants needs to be studied; technologies for preventing preterm birth need to be improved; approaches to conservation therapy and pregravid preparation in women at risk of abortion need to be reviewed.

CONCLUSIONS

1. Important risk factors for premature rupture of membranes in preterm pregnancy include the presence of sexually transmitted diseases ($\chi2=31.188$, $p=0.001$), bacterial vaginosis ($\chi2=30.913$, $p=0.0001$), a history of abortion and/or preterm birth ($\chi2=16.62$, $p=0.0002$), SARS during pregnancy ($\chi2=16.444$, $p=0.0002$), chronic adnexitis in anamnesis ($\chi2=11.522$, $p=0.0031$), inflammatory cervical disease ($\chi2=11.437$, $p=0.0032$), anaemia

($\chi2=10.815$, p=0.0044), isthmic-cervical insufficiency ($\chi2=10.345$, p=0.0057), chronic pyelonephritis with exacerbation ($\chi2=9.16$, p=0.01), smoking during pregnancy ($\chi2=10.815$, p=0.0044).

2. The highest infant mortality and stillbirth rates are associated with gestational age of less than 34 weeks, which requires an effective system of prevention of very early preterm birth and methods of its prediction.
3. In the case of premature rupture of membranes up to 32–33 weeks of gestation, prolongation of pregnancy should be ensured to the maximum extent possible to increase the viability of the newborn. Prolongation of pregnancy in this period should be confirmed by the absence of threatening signs of septic complications in the mother and fetus.
4. Depending on the gestational age, concomitant pathology, obstetric situation, obstetric and gynaecological history, an individual tactic for the management of preterm pregnancy against the background of premature rupture of membranes is chosen.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Structure and features of psychopathological symptoms in forced migrants and internally displaced persons

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ABSTRACT

Aim: To study the structure and characteristics of psychopathological symptoms in FM who left Ukraine as a result of the full-scale armed aggression of the Russian Federation against Ukraine, and internally displaced persons, in a comparative aspect.

Materials and Methods: Examination was performed in compliance with the principles of biomedical ethics, based on informed consent. Research was provided on the basis of the Ternopil Regional Clinical Psychoneurological Hospital. Inclusion criteria were women who were forced to leave the territory of Ukraine as a result of hostilities after February 24, 2022, and who left for temporary residence in the territory of the Republic of Poland (Poland) (FM), and women who were temporarily relocated within Ukraine in connection with connection with hostilities (IDP). Exclusion criteria from the study were presence of language disorders, pronounced cognitive disorders, severe somatic condition. The examination was organized by the method of a semi-structured clinical interview according to the developed by us protocol and was conducted remotely. During the examination, depressive, anxiety-phobic, asthenic and dyssomnic disorders, addictive behavior and symptoms of PTSDwere identified and verified. Statistical and mathematical processing a was carried out using Fisher's exact test.

Results: The data we obtained indicate a significant spread of psychopathological symptoms in FM and IDP.

Conclusions: FM and IDP are characterized by a high incidence of psychopathological symptoms. The most frequent were: depressed mood (FM – 67.2%, IDP – 58.5%), feelings of anxiety and fear (FM –52.5%, IDP – 43.6%), obsessive thoughts (FM – 58.9 %, IDP – 49.5%).

KEY WORDS: treatment, psychopathological symptoms, internally displaced persons, forced migrants

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INTRODUCTION

The full-scale invasion of the Russian Federation into Ukraine led to radical societal, social and psychological transformations in Ukrainian society. One of the most important public, social and psychological phenomena associated with war is forced migration. According to UN data in the end of May 2022, more than 6.5 million Ukrainians temporarily emigrated to neighboring countries, and more than 8 million people became internally displaced persons (IDP) [1].

Emigration is a serious psychological stress that carries risks for a person's mental health. In previous studies, we established the presence of pronounced psychopathological changes in emigrants, which primarily related to the affective sphere, in particular, depressive and anxiety disorders [2-6].

At the same time, the socio-psychological situation of emigration before and after the start of the full-scale invasion of the Russian Federation into Ukraine differs significantly. Pre-war migration was planned: the recipient country was carefully chosen by the potential migrant, the possibilities and prospects of migration, the situation on the labor market were analyzed, employment, provision of housing, food, medical, legal assistance, etc. was planned, certain preparatory actions were carried out; quite often, such migration had a group character (family or as a part of professional groups), which significantly reduced the stress of adaptation, provided the migrant with the necessary level of psychological and social support and contributed to better integration into the social environment of the recipient country. The main motive for pre-war migration was economic – the desire to improve one's financial situation or move to a country with a higher standard of living. Migration caused by hostilities is forced, usually spontaneous, is carried out under the influence of an immediate threat to life and health, is not planned in advance, the choice of the recipient country is often random, and the place of stay and the conditions of stay are determined not by the migrant, but by the side that accepts. The stress of adaptation in such migrants is exacerbated

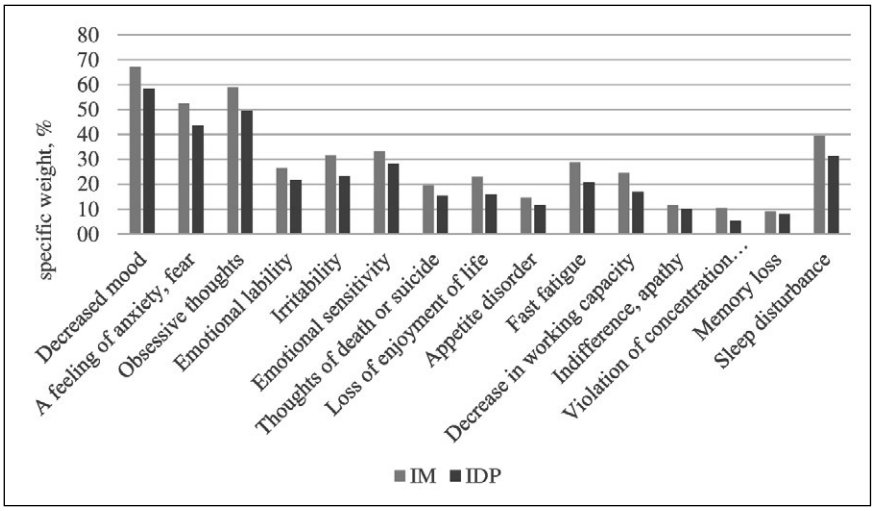

Fig. 1. The structure and prevalence of complaints from the psycho-emotional sphere among forced migrants and internally displaced persons.

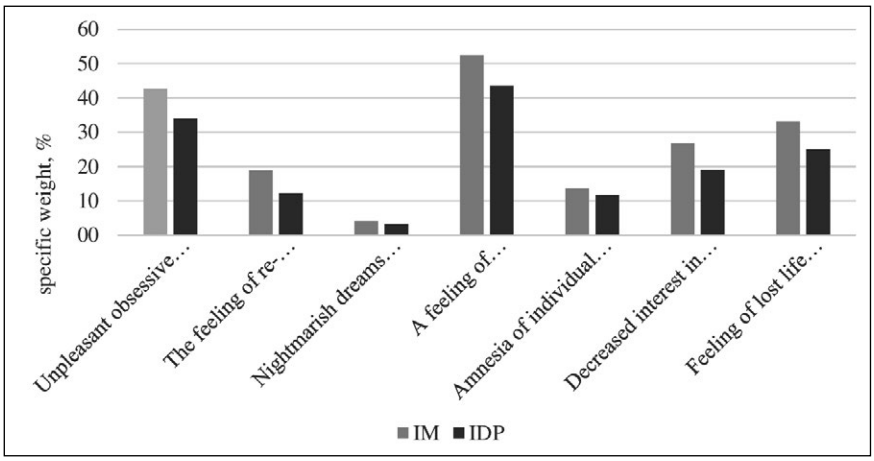

Fig. 2. Structure and prevalence of symptoms of post-traumatic stress disorder in forced migrants and internally displaced persons.

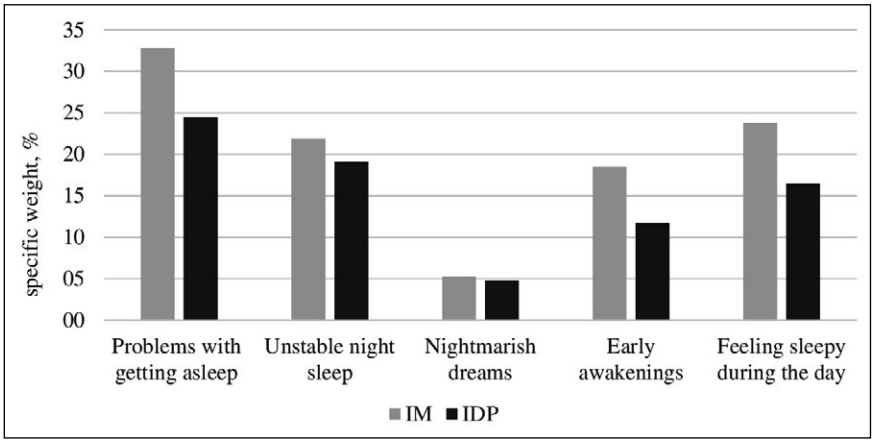

Fig. 3. The structure and prevalence of sleep disorders in forced migrants and internally displaced persons.

by unpreparedness for a new linguistic and social environment, financial problems, difficulties in employment and housing, ignorance of local legislation and related legal insecurity, insufficient medical and psychological support, uncertainty about the future, worries about the fate of relatives and ones who left in the war zone, etc.

In this regard, the study of the peculiarities of the structure and nature of psychopathological symptoms in forced migrants (FM) becomes especially relevant. The data of such a study can form the basis for the development of targeted treatment and rehabilitation and psychocorrective measures for this category of persons.

AIM

The aim of this study was to study the structure and characteristics of psychopathological symptoms in FM who left Ukraine as a result of the full-scale armed aggression of the Russian Federation against Ukraine, and internally displaced persons, in a comparative aspect.

Table 1. The subjective structure of complaints from the psycho-emotional sphere in FM and IDP

Complaint	FM		IDP		p
	abs.	%	abs.	%	
Low mood	178	67.2	110	58.5	< 0.05
A feeling of anxiety, fear	139	52.5	82	43.6	< 0.05
Obsessive thoughts	156	58.9	93	49.5	< 0.05
Emotional lability	70	26.4	41	21.8	> 0.05
Irritability	84	31.7	44	23.4	< 0.05
Emotional sensitivity	88	33.2	53	28.2	> 0.05
Thoughts of death or suicide	52	19.6	29	15.4	> 0.05
Loss of enjoyment of life	61	23.0	30	16.0	< 0.05
Appetite disorder	39	14.7	22	11.7	> 0.05
Fast fatigue	76	28.7	39	20.7	< 0.05
Decrease in working capacity	65	24.5	32	17.0	< 0.05
Indifference, apathy	31	11.7	19	10.1	> 0.05
Violation of concentration of attention	28	10.6	10	5.3	< 0.05
Memory loss	24	9.1	15	8.0	> 0.05
Sleep disturbance	105	39.6	59	31.4	< 0.05

Table 2. The structure of symptoms of post-traumatic stress disorder in FM and IDP

Symptom	FM		IDP		p
	abs.	%	abs	%	
Unpleasant obsessive memories of a traumatic event	113	42.6	64	34.0	< 0.05
The feeling of re-experiencing the traumatic event	50	18.9	23	12.2	< 0.05
Nightmarish dreams with the content of a psychotraumatic event	11	4.2	6	3.2	>0.05
A feeling of psychological distress	139	52.5	82	43.6	< 0.05
Amnesia of individual elements of the experienced event	36	13.6	22	11.7	>0.05
Decreased interest in everyday life	71	26.8	36	19.1	< 0.05
Feeling of lost life (pessimistic assessment of perspectives)	88	33.2	47	25.0	< 0.05

Table 3. The structure of sleep disorders in FM and IDP

Symptom	FM		IDP		p
	abs.	%	abs.	%	
Problems with getting asleep	87	32.8	46	24.5	< 0.05
Unstable night sleep	58	21.9	36	19.1	>0.05
Nightmarish dreams	14	5.3	9	4.8	>0.05
Early awakenings	49	18.5	22	11.7	< 0.05
Feeling sleepy during the day	63	23.8	31	16.5	< 0.05

MATERIALS AND METHODS

We clinically examined 265 women who were forced to leave the territory of Ukraine as a result of hostilities after February 24, 2022, and who left for temporary residence in the territory of the Republic of Poland (Poland) (FM), and 188 women who were temporarily relocated within Ukraine in connection with connection with hostilities (IDP). The average age of the examined FM was 31.8 ± 9.4 years, IDP – 33.1 ± 8.7 years (p>0.05). The examination was organized by the method of a semi-structured clinical interview and was conducted remotely in the mode of an online video conference using technical tools and computer platforms that provided constant two-way video and audio communication. During the examination, elucidation and detailing of complaints from the psycho-emotional sphere was carried out, the psychopathological manifestations present in the examinees, the peculiarities of their occurrence and

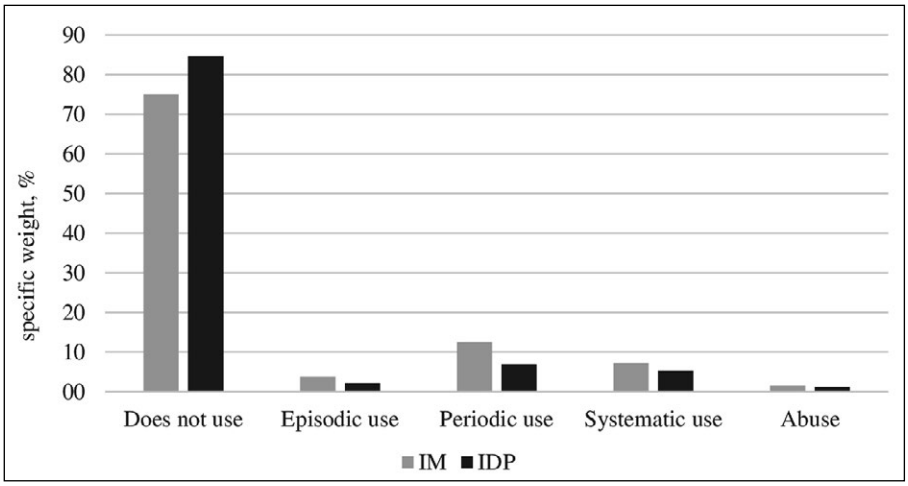

Fig. 4. Prevalence of various forms of smoking among forced migrants and internally displaced persons.

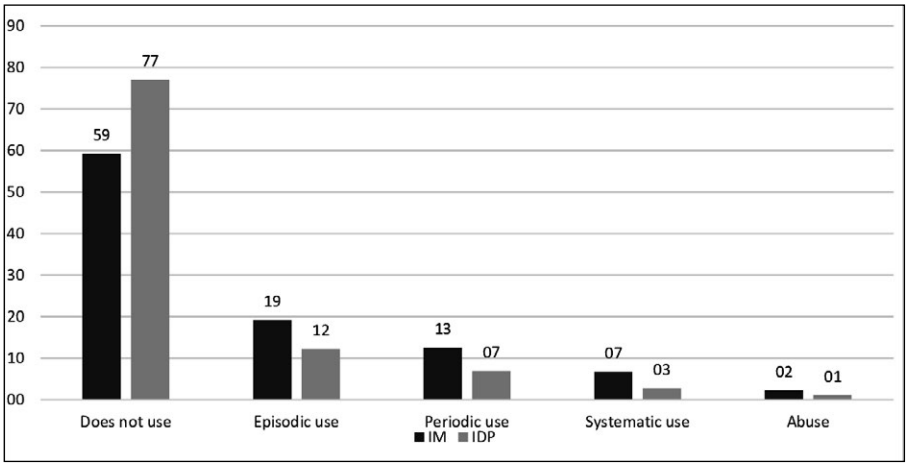

Fig. 5. Prevalence of various forms of alcohol consumption among forced migrants and internally displaced persons.

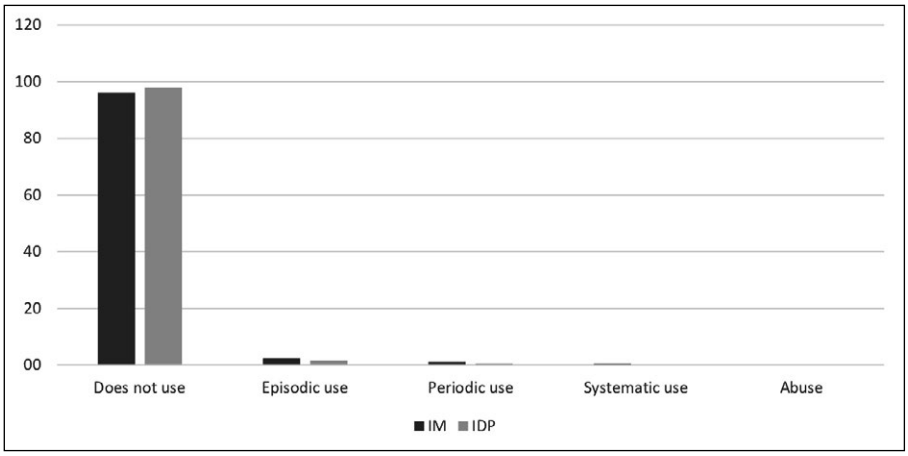

Fig. 6. Prevalence of various forms of drug use among forced migrants and internally displaced persons.

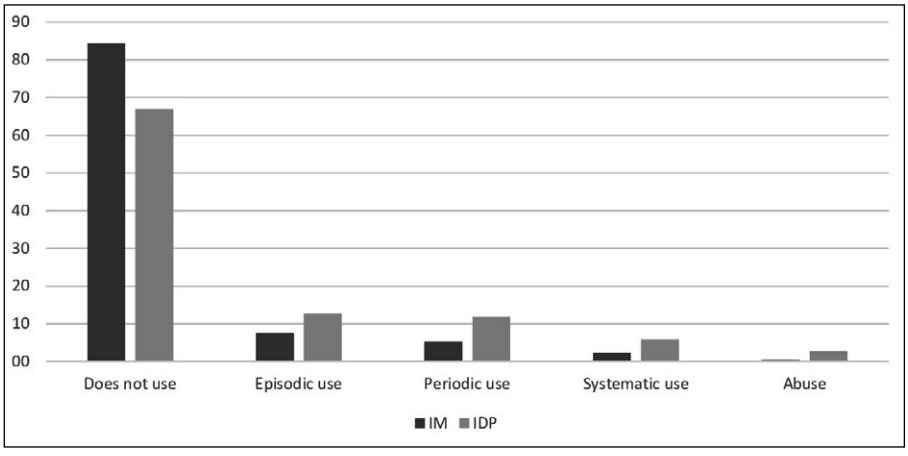

Fig. 7. Prevalence of various forms of drug addiction among forced migrants and internally displaced persons.

Table 4. The structure of addictive disorders in FM and IDP

Types of dependencies	FM		IDP		p
	abs.	%	abs.	%	
Smoking and tobacco substitutes (vapes)					
Does not use	199	75.0	159	84.6	< 0.01
Episodic use	10	3.8	4	2.1	> 0.05
Periodic use	33	12.5	13	6.9	< 0.05
Systematic use	19	7.2	10	5.3	> 0.05
Abuse	4	1.5	2	1.1	> 0.05
Alcohol					
Does not use	157	59.2	145	77.1	< 0.01
Episodic use	51	19.2	23	12.2	< 0.05
Periodic use	33	12.5	13	6.9	< 0.05
Systematic use	18	6.8	5	2.7	< 0.05
Abuse	6	2,3	2	1.1	> 0.05
Narcotics (cannabis, psychostimulants)					
Does not use	255	96.2	184	97.9	> 0.05
Episodic use	6	2,3	3	1.6	> 0.05
Periodic use	3	1.1	1	0.5	> 0.05
Systematic use	1	0.4	0	0.0	> 0.05
Abuse	0	0.0	0	0.0	> 0.05
Medicines and medicinal products					
Does not use	224	84.5	126	66.9	< 0.01
Episodic use	20	7.5	24	12.8	< 0.05
Periodic use	14	5.3	22	11.7	< 0.01
Systematic use	6	2,3	11	5.9	< 0.05
Abuse	1	0.4	5	2.7	< 0.05

pathodynamics were identified and verified. Statistical and mathematical processing of the obtained data was carried out using Fisher's exact test.

RESULTS

A wide range of complaints from the psycho-emotional sphere was found in the FM and IDP (Table 1, Fig. 1).

The most common complaints in FM and IDP were complaints of low mood, obsessive thoughts and feelings of anxiety or fear, somewhat less common – various forms of dyssomnia, irritability, anhedonia (loss of pleasure from life and activities that were previously interesting and enjoyable), rapid fatigue and reduced work capacity; these symptoms were significantly more common in FM. An important place in the structure of complaints was also belongs to emotional lability and sensitivity; these complaints were also found more often in FM, however, the differences compared to IDP are not statistically significant. Complaints about suicidal thoughts, loss of appetite, apathy, memory loss and impaired concentration turned out to be less frequent; the last complaint was significantly more frequent in the FM, for the rest of the complaints, the differences are not statistically significant with a higher specific weight of complaints in the FM compared to the IDP.

The most common post-traumatic symptoms of post-traumatic stress disorder in FM and IDP were the feeling of psychological distress , unpleasant memories of the experienced stress that had an obsessive nature, a pessimistic assessment of perspectives, a decrease in interest in everyday life, as well as a feeling of re-experiencing a traumatic event (flashbacks); all these symptoms were significantly more common in FM. Amnesia of certain elements of the experienced event and nightmare dreams with the content of psychotrauma were less common, which were more often found in FM, however, the differences with IDP were not statistically significant (Table 2, Fig. 2).

The structure of dyssomnic symptoms in FM and IDP was dominated by disturbances in falling asleep and unstable night sleep, as well as a feeling of sleepiness during the day and early awakenings; these symptoms were more often found in FM, and the differences with

IDP were statistically significant (with the exception of unstable night sleep) (Table 3, Fig. 3).

Nightmares were the rarest dyssomnic symptom in FM and IDP; they were found insignificantly more often in FM.

Forced migration and internal displacement are associated with an increased risk of addictive behavior (Table 4).

The prevalence of tobacco smoking (including the use of tobacco substitutes) was higher in FM, and the most significant differences were regarding the periodic use of tobacco and its substitutes (Fig. 4).

Differences in alcohol consumption turned out to be more significant (Fig. 5). FM significantly more often used alcohol episodically, periodically and systematically compared to IDP.

The prevalence of narcotization (cannabis derivatives and psychostimulants) among the studied persons was insignificant, and did not differ significantly in FM and IDP (Fig. 6, Fig. 7).

The only exception was the use of medications and drugs (mainly anxiolytic, antidepressant, sedative, as well as sleeping pills), which was significantly more common among IDP. To our opinion, the explanation of this phenomenon lies in the much greater availability of psychotropic drugs for the population in Ukraine compared to the countries of the European Union, the need to comply with complex and lengthy procedures for obtaining prescriptions for psychotropic drugs in EU countries, which make it impossible for migrants to freely purchase such drugs. On the other hand, in Ukraine, it is easier to buy a wide range of psychotropic drugs in pharmacies, as well as to order them via the Internet, bypassing formal procedures, which leads to a much greater prevalence of this type of addiction among IDP.

The data we obtained indicate a significant spread of psychopathological symptoms in FM and IDP. At the same time, a clear tendency was revealed to be more affected by psychopathological manifestations of FM compared to IDP. To our opinion, this may be due to the influence of the language barrier, the difficulties of acculturation in a new social, cultural and religious environment, the absence or insufficiency of social support groups, separation from family members and loved ones, and significantly fewer opportunities for direct communication with them. In addition, FM face significantly greater difficulties in finding employment, housing, medical care, legal support, etc. Also important is the psychologically difficult feeling of being a foreigner in another country, awareness of one's own vulnerability and dependence on the actions of the authorities and the local population. All these factors have a complex synergistic negative impact on the psyche of forced migrants, leading to a higher prevalence of various forms of psychopathological symptoms.

DISCUSSION

In the literature there are results that are similar to ours:

- Prevalence of depression and anxiety may be higher among forced migrants and internal migrants at different stages of displacement and migration experience.
- Forced migrants and internal migrants affected by conflict and war show higher rates of PTSD and other mental health problems, especially among younger migrants and adolescents.
- The incidence of psychosis has been shown to be higher among migrants in a number of countries, which is related to the cumulative effect of social disadvantage before, during and after migration.
- Forced migrants and internal migrants, asylum seekers and irregular migrants, in particular, show a higher prevalence of mental health problems compared to the population of receiving countries [7-11].

When a person becomes a forced migrants and internal migrants, it can be associated with a number of stressors that affect their mental health. Migrants and refugees may be exposed to a variety of stressors that affect their mental health and psychosocial well-being before and during the migration journey, as well as during the settlement and integration process. This can lead to a wide range of mental illnesses, including depression, anxiety, PTSD, psychotic disorders, and more. Forced migrants and internal migrants may experience a variety of mental disorders, which vary depending on social and environmental factors such as lack of family or social support, discrimination, age, ethnicity, and length of time spent in the host country. The results indicate that the prevalence of mental health problems may be quite high. Many internal migrants and forced migrants do not have access to, or face barriers to, mental health services. There may also be a disruption in the continuity of medical care [7, 10].

Recent prevalence have shown that the burden of mental disorders in conflict-affected populations is as high as 22.1% [12]. Certain populations exposed to conflict and war, such as young migrants and adolescents, are more likely to be characterized by poor mental health. Groups such as forced migrants and internal migrants tend to have a higher prevalence of depression; however, this largely depends on their living conditions and the presence of injuries received during the relocation. It is necessary to approach the mental health of forced migrants and internal migrants comprehensively, providing them with treatment while considering the determinants of health, including migration status.

Some studies in groups of forced migrants resettled in high-income countries have shown an increased risk of suicidal behavior, likely resulting from a combination of adverse socioeconomic conditions, exposure to potentially traumatic events, the burden of mental disorders, and the lack of adequate and accessible health care.

The high prevalence of depression among forced migrants and internally displaced persons in WHO regions is widely documented. It can develop at different points along the path of movement and migration. For example, depression may begin in the home country as a result of traumatic events, after experiencing violence during displacement and migration, or while living in host countries due to discrimination, marginalization, and loss of resources. A global meta-analysis found that forced migrants, internal migrants and asylum seekers were characterized by high and persistent rates of PTSD and depression [8]. However, the prevalence of depression and anxiety among forced migrants and internal migrants varies considerably across different regions, due to a number of regional and contextual factors. In the European region, it is noted a similar prevalence of anxiety both among forced migrants (13%) and among the general population (9%), but a significantly higher frequency of depressive disorders in the first category (32% vs. 4%). It should be noted that regarding the influence of length of stay in the destination country on the prevalence of depression and anxiety, the data differ [13]. The results of a study among young forced migrants (aged 19–25) in Canada showed that the prevalence of mental disorders decreased with increasing educational attainment, and PTSD rates decreased with increasing length of stay in the country. Isolation has been shown to be significantly associated with depression and anxiety among migrants [10]. Therefore, the formation of deep social ties with the host country community, as well as the provision of social integration services, are considered valuable in promoting the mental well-being of migrants [13].

Events involving interpersonal violence are associated with the highest risk of developing PTSD. Long-term effects of violence or other traumatic events can include severe anxiety, stress, or fear; alcohol or drug use; depression; eating disorders; self-harm or suicide. Studies have shown relatively high rates of PTSD among forced migrants and internal migrants: a prevalence of 24.3% was found among forced migrants in Berlin and 35.7% among asylum seekers living in three collective accommodation centers in Erlangen, Nimes [7].

CONCLUSIONS

1. FM and IDP are characterized by a high incidence of psychopathological symptoms.
2. The leading place in the structure of psychopathological symptoms in FM and IPD belongs to depressive symptoms, post-traumatic symptoms and anxiety symptoms, as well as various forms of dyssomnias.
3. The prevalence of the majority of psychopathological symptoms in FM is higher compared to IDP, which can be explained by the difficulties of social and psychological adaptation and acculturation in a cultural, social, foreign language and religious environment.
4. Forced migration and internal displacement is a factor that contributes to the activation of addictive behavior; at the same time, the prevalence of smoking and alcoholism is higher among forced migrants, and the use of psychotropic medications and medicinal products is higher among internally displaced persons.
5. The revealed regularities should be taken into account when developing treatment and rehabilitation and preventive measures for forced migrants and internally displaced persons.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

The results of the corrective rehabilitation program on the gait of amateur athletes with long-term consequences of brain injury

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ABSTRACT

Aim: To study the results of the quality of life, the state of vestibular disorders and the nature of walking of amateur athletes with the consequences of a combat craniocerebral injury after rehabilitation treatment according to a correctional program.

Materials and Methods: The study was conducted on the basis of the Ukrainian Scientific Research Institute of Prosthetics in Kharkov. Under observation were 38 men aged 25-42 years with long-term consequences of a closed craniocerebral injury in the late long-term period. In all patients, complications after TBI were persistent headache, decreased muscle strength in the lower extremities, impaired coordination and balance, and walking patterns. All patients were involved in amateur sports before injury. The following research methods were used during the examination: visual analogue pain scale (VAS), Lovett manual muscle test, Bohannon test, «Timed Up and Go test».

Results: All patients were randomly divided into two groups. Patients Gr.1 (n=20) were trained according to the developed program, which included training according to the PNF method, kinesiotherapy, classes on the C-mill sensory treadmill and the Hunova computer device, segmental reflex massage. Patients Gr. 2 (n=18) underwent a course of physical rehabilitation according to the generally accepted methodology of the Ministry of Health of Ukraine. After working with patients according to the developed correction and rehabilitation program, the following dynamics were observed: the quality of life on the VAS scale in Gr.1 patients had a statistically significant difference ($p<0.05$) compared to the primary indicator. The dynamics of the Lovett manual muscle test indicated an increase in the muscle strength of the extensor and flexor muscle groups of the lower extremities, the dynamics of the balance indicator in the standing position behind Bohann in all Gr.1 patients and acquired statistical significance ($p<0,05$). According to the test "Timed Up and Go" patients Gr.1 approached the standard value ($p<0,05$). In all patients of Gr. 2, the studied characteristics had a positive trend ($p>0,05$).

Conclusions: Individual selection of physical exercises, development of correctional and rehabilitation programs, multidisciplinary approach has a positive impact on changes in the functional state of amateur athletes, quality of life and contributes to the return to an active social life.

KEY WORDS: amateur athletes, traumatic brain injury, correctional rehabilitation program

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INTRODUCTION

Today, a full-scale invasion of the aggressor country continues on the territory of our state, which has changed the lives of many Ukrainians. Many athletes defend their hometowns in the ranks of the territorial defense and the Armed Forces of Ukraine. Everyone has faith in victory and dreams of returning to normal life. Unfortunately, not everyone returns without being wounded in the war. However, everything will end and amateur athletes will return to their real lives.

Among the combatants in the East of Ukraine since 2014, the second place among all the injuries received was occupied by damage to the central nervous system, which were caused by the blast wave [1, 2]. An integral part of all barotraumas is a true concussion due to the action of an air wave, resembling a short massive impact with a wide dense surface [3-5]. It is known that 73% of cases of combat injuries are accompanied by brain contusion, which occurs three times more often than other injuries. However, most often the military do not recognize this injury as severe and do not seek medical help [1]. The main problem of closed craniocerebral injury (CTBI) is that complications appear after some time. However, the consequences of CTBI are very significant and can cover disorders not only from the side of the physical state, but also from the side of the psychosomatic sphere. This problem is also gaining urgency from an economic point of view, because in most cases, CTBI during the hostilities will be received by people of working age, who eventually receive the status of disabled people. CTBI, obtained during the period of combat operations, is a complex of structural and functional changes in the

Table 1. The interpretation of the assessment of muscle strength according to the Lovett test

Score	Description of the value
0	This is the absence of pain, a person does not feel it at all
1	Discomfort is extremely mild
2	Unpleasant sensations are mild
3	The pain disturbs regularly, the patient is constantly distracted by it.
4	Moderate pain
5	Pain is moderately intense
6	Pain is still moderate
7	Pain is heavy. She literally subjugates all other sensations
8	Feelings are intense. Physical activity is extremely limited
9	Pain is very severe
10	Pain is unbearable. The patient is bedridden, he often dreams

Table 2. The interpretation of the evaluation of muscle strength according to the Lovett test, ball

Score, ball	Description of the value
0	complete absence of muscle tension
1	weak muscle contraction
2	expressive muscle tension and the ability to perform movements in an incomplete volume
3	full range of motion without additional resistance
4	full range of motion with medium resistance over the entire range
5	full amplitude with maximum resistance

nervous system of an adaptive plan, which is a dynamic, multi-level process. The degree of expression and dynamics of clinical manifestations of structural and functional disorders of the main pathogenetic processes directly depends on the severity of the injury [3-8]. Local disorders are detected only after a few days through disorders of the functions of the cranial nerves; paralysis and paresis of the limbs; disorders of coordination and balance; convulsions, etc. [9, 10].

The question of the renewal of amateur athletes with the help of individual selection of correctional and rehabilitation programs remains open. Indeed, in the scientific literature almost no attention is paid to the problem of the physical rehabilitation of such patients, as well as the restoration of amateur athletes who participated in hostilities. Movement disorders after blast injury are the most common complication. The recovery of such patients is possible only with a timely and comprehensive approach using the selection of methods and means of physical rehabilitation. The selection of correctional and rehabilitation programs aimed at restoring the balance and walking pattern will improve the quality of life and the ability to return to amateur sports.

AIM

To study the results of the quality of life, the state of vestibular disorders and the nature of walking of amateur athletes with the consequences of a combat craniocerebral injury after rehabilitation treatment according to a correctional program.

MATERIALS AND METHODS

The study was conducted on the basis of the Ukrainian Scientific Research Institute of Prosthetics in Kharkov. The organization of the study was based on the provisions of the Helsinki Declaration of the World Medical Association. All patients provided written informed consent to participate in the study. Under observation were 38 men aged 25-42 years with long-term consequences of a closed craniocerebral injury in the late long-term period.

The duration of the post-traumatic period is from six months. The cause of disability was wounds and contusions associated with military operations. In all patients, complications after TBI were persistent headache, decreased muscle strength in the lower extremities, impaired coordination and balance, and walking pattern. All patients were involved in amateur sports before the injury.

During the examination, the following research methods were used:

1. Visual analogue pain scale (VAS). VAS is a horizontal 10 cm line with "no pain" written on one end and "worst pain imaginable" on the other end, from 0 to 10. The analysis of the results is given in Table 1 [11]:

Table 3. The interpretation of the balance assessment in a standing position according to the Bohannon test, ball

Score, ball	Description of the value
0	Can't stand
1	Can balance for less than 30 seconds with feet shoulder-width apart
2	Can balance for more than 30 seconds with feet shoulder-width apart
3	In S.P. feet together, stand for less than 30 seconds
4	In S.P. standing, feet together, stand for 30 seconds or more

Table 4. The indicator of quality of life index of patients in Group 1 (n=20) and Group 2 (n=18), cm

Group	Before the program, cm	After the program, cm	Difference, cm	p
Gr. 1 (n=20)	8,37±2,4	5,24±1,6	3,16±0,8	<0,05
Gr. 2 (n=18)	8,37±2,4	7,10±0,8	1,27±1,6	>0,05

Table 5. The indicator of muscle strength of patients in Group 1 (n=20) and Group 2 (n=18), ball

Lovett's muscle strength rating scale	Gr. 1 (n=20), ball		Gr. 2 (n=18), ball	
	Before rehabilitation M±m	After rehabilitation M±m	Before rehabilitation M±m	After rehabilitation M±m
Abdominal muscles	3,2±0,24	4,1±0,28*	3,2±0,24	3,6±0,7
Spinal extensor muscles	3,1±0,17	4,2±0,12*	3,1±0,17	3,3±0,4
Square muscle of the lower back	3,4±0,14	4,2±0,18*	3,4±0,14	3,7±0,12
Iliopsoas muscle	2,4±0,25	3,8±0,34*	2,4±0,25	2,9±0,12
Adductor thigh muscles	3,2±0,12	4,3±0,15*	3,2±0,12	3,6±0,11
Quadriceps femoris	2,2±0,16	3,5±0,18*	2,2±0,16	2,7±0,13
Tibialis anterior	2,5±0,14	3,6±0,12*	2,5±0,14	3,1±0,11
Triceps muscle of the leg	2,1±0,17	3,5±0,14*	2,1±0,17	2,6±0,12
Biceps femoris	2,3±0,15	3,4±0,17*	2,3±0,15	2,8±0,14
Gluteus medius thigh	2,2±0,13	4,2±0,12*	2,2±0,13	2,6±0,15
Gluteus maximus muscle	2,3±0,17	3,6±0,14*	2,3±0,17	2,9±0,12

* $p<0.05$ (statistically significant difference)

1. *Lovett test* – a special test for manual determination of the strength of the patient's muscles. The abdominal muscles, spinal extensors, quadratus lumborum, iliopsoas, and hip adductors were assessed; quadriceps femoris; anterior tibial (when the foot is extended at the ankle joint); three-headed shins (when the foot is bent at the ankle joint); biceps femoris; middle sciatic muscle of the thigh; large ischial. The assessment of muscle strength according to the Lovett test is presented in Table 2 [10, 11]:
2. The assessment of balance in the standing position was performed using the *Bohannon test* [10, 1] (Table 3).
3. *Test "Timed Up and Go" (TUG).* Assesses functional mobility, balance, walking ability and determines the risk of falling. It is an easy-to-survey test that is both sensitive and specific about the likelihood of a fall. To conduct the test, you must prepare a chair with an armrest, a stopwatch and mark the distance of 3 meters. The patient sits on a chair, follows the command, gets up, reaches the 3-meter mark, comes back and sits down. Fall risk score for vestibular disorders – >11 seconds.
4. *Pedagogical experiment.* In order to test the effectiveness of the developed correctional and rehabilitation program, a pedagogical experiment was conducted, which included ascertaining and forming stages. The ascertaining stage of the pedagogical experiment made it possible to find out the current state of the study of the problem of physical rehabilitation of patients and, on the basis of the primary examination (conversations, observations, functional testing), to determine the problems of patients with the consequences of post-traumatic brain injury and form homogeneous groups. The formative stage of the pedagogical experiment involved the implementation of the developed program and verification of its effectiveness by comparing the studied indicators in patients of both groups.

Table 6. The indicator of balance in the standing position behind in patients Gr. 1 (n=20) and Gr.2 (n=18), in points

Group	Before the program	After the program	difference	p
Gr. 1 (n=20)	1,8±0,9	3,1±0,7	1,9±0,2	<0,05
Gr. 2 (n=18)	1,8±0,9	2,1±0,8	0,2±0,9	>0,05

METHODS OF MATHEMATICAL STATISTICS

Statistical data processing was carried out using the statistical package STATISTICA 13.0 (StatSoft). The arithmetic mean value was calculated – M; standard deviation – δ; dispersion – D; the error of the arithmetic mean is ±m. Verification of the conformity of the distribution of the sample population to the normal law was carried out using the Shapiro-Wilk test. To determine significant differences, Student's parametric test (t) was used; differences were considered statistically significant at $p<0,05$.

When building a correctional rehabilitation program, the principles of physical rehabilitation and pedagogical interaction were followed, namely, accessibility, complexity and multidisciplinarity [3, 12-23]. All patients were randomly divided into two groups.

Patients Gr.1 (n=20) were trained according to the developed correctional rehabilitation program. The developed correction and rehabilitation program included training according to the PNF method, kinesiotherapy, classes on the C-mill sensory treadmill and the Hunova computer device, and segmental reflex massage. The course of physical therapy lasted 24 days. Classes were held 6 times a week, in the morning with a physical therapist, every day except Sunday. Group 2 patients (n=18) underwent a course of physical rehabilitation according to the generally accepted methodology of the Ministry of Health of Ukraine.

A PNF training method based on neurophysiological mechanisms that improve muscle responses to their active contraction through stimulation of spinal motoneurons with impulses in response to proprioceptive stimulation from the periphery. This is achieved through special models of spiral-diagonal movements, actively performed by the patient with the help of the hands of a specialist in physical rehabilitation with a dosed counter resistance. [2].

Kinesiotherapy. Active movements in the joints of the extremities were prescribed with full amplitude and multiple repetitions with and without additional weights. The exercises included coordination exercises (a combination of simple and then more complex movements in all joints of the limbs), development of the amplitude and accuracy of active movements. Exercises were used in the starting position standing, sitting and lying down. Patients necessarily performed relaxation exercises in combination with breathing exercises. With the help of special exercises, the sensory support of motor acts was improved (proprioceptive, visual, verbal, tactile control) [15, 22-25].

Classes on the C-mill sensory treadmill with built-in power platforms and biofeedback. The technique is used for diagnosing and training walking, provides gradual progress and a high level of patient motivation throughout the rehabilitation process, gradually returning the patient to a natural walking style.

The HUNOVA device is an automated rehabilitation process that improves the sense of balance and balance while walking. It also allows, thanks to the automation of the rehabilitation process, to increase the intensity of rehabilitation programs and evaluate the patient's capabilities in terms of movement, speed, strength and other derived parameters.

To activate physiological and trophic processes in the tissues of the lower extremities, *segmental-reflex massage* was performed, namely, massage of the paravertebral zones of the spinal segments of the lumbosacral spine, from which the innervation of the lower extremities is carried out. The purpose of the massage was to apply mechanical stimulation to the root of the spinal nerves at the points of their exit from the spinal column. This contributed to the provision of a stimulating effect on tissue and physiological processes in the reflex-related tissues of the lower extremities. This procedure was carried out in the initial position of the massaged person lying on his stomach, under which a small massage roller was placed. After stroking the massaged area, connective tissue massage was performed sequentially. The exit points of the spinal nerve roots were studied. Then the "Rhombus of Michaelis" zone was rubbed in different directions, paying special attention to the lower borders of the sacrum [4, 5]. In conclusion, continuous vibration of the paravertebral zones of the massaged area was carried out. The duration of the procedure is 10-12 minutes.

ETHICAL APPROVAL

The research related to human use has been complied with all the relevant national regulations and institutional policies, principles of the Helsinki Declaration, adopted by the General Assembly of the World Medical Association (1964-2000), the Council of Europe Convention on Human Rights and Biomedicine (1997).

INFORMED CONSENT

Informed consent has been obtained from all individuals included in this study.

RESULTS

The clinical picture of all patients was almost the same. All the subjects had the main neurological syndromes that limited their vital activity: vegetative disorders and discoordination of the vestibular genesis.

At the level of the structure and function of the ICF, mono- or hemiparesis of the lower extremities was observed in all patients. Loss of sensation below the neurological level. Violation of proprioceptive sensitivity in the feet and toes. Limitation of the range of motion in the joints of the lower extremities.

At the ICF activity level, all self-care patients were independent of outside help.

At the ICF participation level: all patients complained of being able to walk non-stop only for a distance of less than a kilometer. Not an opportunity to return to amateur sports.

Personal factors: purposeful and motivated return to amateur sports.

After working with patients, the following dynamics was observed behind the developed correctional and rehabilitation program. Thus, when assessing the quality of life according to the VAS scale, the dynamics of pain syndrome parameters in Gr. 1 patients had a statistically significant difference ($p<0,05$) compared with the primary indicator. However, in patients Gr. 2 showed positive dynamics, but it did not acquire statistical significance ($p>0,05$) (Table 4).

When testing on the Lovett scale, the study of simple movements performed in one plane was carried out. According to the Lovett Manual Muscle Test (MMT), during the initial examination, signs of loss of muscle strength of the extensor and flexor muscle groups of the lower extremities were observed in all patients. It was found that the MMT indices of both the anterior and posterior thigh muscle groups tended to a statistically significant decrease, i.e., lower back. The assessment of muscle strength according to the Lovett test in patients indicated a decrease in the strength of all studied muscle groups (Table 5).

After a course of rehabilitation in patients Gr. 2 observed a trend towards improvement in all indicators according to the Lovett test ($p>0,05$). Patients Gr.1 showed statistically significant dynamics of all studied parameters ($p<0,05$). Thus, the indicators of the abdominal muscles increased by 0,9 points, the extensor muscles of the spine by 1,1 points, the square muscle of the lower back by 0,8 points, the iliopsoas muscle by 1,4 points, adductor muscles of the thigh by 1,1 points, quadriceps femoris by 1,3 points, anterior tibial muscle by 1,2 points, triceps muscle of the lower leg by 1,4 points, biceps femoris by 1,1 points, gluteus medius femoris by 2 points and the gluteus maximus muscle by 1,3 points, which was statistically confirmed ($p<0,05$).

The average balance in the standing position according to Bohann was 1,8±0,9 points in the initial study, which indicated instability to more maintain one's standing position, independently on both legs. After working on the program in patients Gr. 1 determined a statistically significant positive trend ($p<0.05$) in patients Gr. 2 positive changes were observed but did not acquire statistical significance ($p>0.05$). The dynamics of balance indicators is presented in Table 6.

In the primary study of testing vestibular coordination and pattern walking, the indicator in all patients indicated a statistically significant decrease in the obtained data compared to the standard indicator ($p<0,05$). The average execution time was 20 seconds or more. When observing patients during the test, attention was paid to walking, during which 13 patients lost their balance; 14 had short steps; in 12 people, a small arm swing was observed. After rehabilitation according to the developed program, patients Gr. 1 on average passed the test in 12-14 seconds and almost approached the standard value (11 seconds).

DISCUSSION

Thus, the results of the study indicated that in amateur athletes in the late long-term period, the complications of TBI were a decrease in muscle strength in the lower extremities, impaired coordination and balance, a walking pattern, and a decrease in the quality of life. All of the above confirmed the opinions of some scientists that after TBI of an explosive genesis, local disturbances are detected only after a few days in the form of disorders of the functions of the cranial nerves; paralysis and paresis of the limbs; disorders of coordination and balance; convulsions, etc. [5, 9, 25-27].

We agree with the opinion of A. Matveiko et al. (2019) that in order to stimulate new neural pathways after brain contusion, it is necessary to develop correctional and rehabilitation programs, the main tool of which is kinesiotherapy [1].

The conclusions of Voronova V. Ya., Lazareva O. B., Kovelskaya A. V. and Kobinsky O.V. (2021) were confirmed, indicating that in order to restore walking in patients with TBI, it is necessary to form an examination and intervention plan based on SMART -objectives, which are to get an idea of the needs and potential of the patient, allow you to choose the intervention that best meets the patient's main problem [13, 18, 20, 21].

Based on the findings of many scientists, we have determined that it is the individual selection of physical exercises, the development of correctional and rehabilitation programs, the multidisciplinary approach that positively affects the changes in the functional state of amateur athletes, the quality of life and contributes to the return to an active social life. [10, 21-24].

LIMITATIONS

The study presented has some limitations. Firstly, the small number of patients who were involved in the study, limiting the ability to generalize to other populations. Secondly, the study was conducted only within the framework of one social sphere; it may be a limitation for summarizing the results.

CONCLUSIONS

In amateur athletes with TBI in the late recovery period, at the level of structure and function according to the ICF, there is a violation of proprioceptive sensitivity in the feet and toes. At the level of participation, according to the ICF, there are complaints about not being able to return to amateur sports. After the course of rehabilitation according to the author's program, patients of Group 1 observed a statistically significant improvement of all studied indicators, namely, the quality-of-life indicator according to the VASH improved by 3.16 points; according to the scale of the Lovett test, an increase in muscle strength of both the front ($p<0.05$) and the back group of the thigh and lower back muscles ($p<0.05$). The balance score according to the Bohannon test in Gr.1 patients increased by 1.9±0.2 points ($p<0.05$). Test for "Timed Up and Go" patients Gr. 1 on average passed the test in 12-14 seconds ($p<0.05$). In Gr.2 patients, a tendency to improvement was observed for all the above-mentioned indicators, but they did not reach statistical significance ($p>0.05$).

Prospects for further research involve the development of a correctional rehabilitation program for amateur athletes with the consequences of brain contusion and a violation of the walking pattern for a complete recovery of physical condition and return to sports activities.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Clinical anatomy of pulmonary connections in young people

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ABSTRACT

Aim: To study the clinical anatomy of the pulmonary ligaments of young people.

Materials and Methods: The study was carried out when performing 28 autopsies of young people aged 25 to 44 years. Methods of dissection of chest organocomplexes, macro-microscopy, morphometry and planimetry, and statistical processing were used. The shape and topography of the pulmonary ligaments was assessed, their area, the localization of lymph nodes was examined.

Results: The pulmonary ligament is an anatomical formation, which is formed as a result of a combination of leaves of the mediastinal pleura, which, covering the surfaces of the roots of the lungs, descend towards the diaphragm and are located between the mediastinal organs and the lungs. Pulmonary connections on both sides have a few edges: the inner, outer and lower free. The pulmonary ligaments with lower free edges do not pass to the diaphragmatic surface of the pleura, but only with inner ones, which are located on the right along the esophagus, and on the left along the aorta. Pulmonary ligaments on both sides pass into the mediastinal part of the pleura, covering the pericardium.

Conclusions: There are individual differences between the shape and size of the right and left pulmonary ligaments in males and females. There is no significant difference between the sizes of the right and left pulmonary ligaments, but such dimensions as: the width, the angle of inclination and the ratio of their lower free edge to the lower edge of the lungs are not found in all cases.

KEY WORDS: young age, people, clinical anatomy, pulmonary ligaments

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INTRODUCTION

Respiratory diseases remain a very common pathology in the morbidity structure of the population of Ukraine and an important health problem due to their frequency among the working population and children, a combination of various lung pathologies and a negative impact on concomitant diseases, and the development of disability [1-3]. Thus, the average duration of treatment of a patient in the thoracic department is 15.2 days, and the mortality rate from chronic diseases of the lower respiratory tract reaches 12.6 (per 100,000 populations).

In recent years, more and more attention has been paid to improving the methods of surgical treatment of pathology of the lungs and mediastinal organs. At the same time, they also mention the pulmonary ligament, the expediency of its intersection and ligation during both open and video-assisted thoracoscopic surgical interventions [4]. However, in modern scientific literature there is practically no data on the size, shape, structure and anatomy of the pulmonary ligaments in people, the differences between them on the left and right, their age and gender characteristics. Definitions, which are mainly found in scientific works devoted to surgical interventions on the lungs, indicate that the pulmonary ligament is a two-layer pleural structure connecting the visceral pleura in the lower medial part of the lung with the parietal pleura, which extends sheet-like down from the level of the inferior pulmonary vein to the diaphragmatic pleura, where it is either fixed or ends with a free crescent-shaped edge [5]. Some authors call it the inferior pulmonary ligament [6, 7]. However, its size, content and features of placement both on the left and on the right in people of all ages are not discussed in scientific works of anatomical or surgical directions.

In the literature, much more attention is paid to studying its role during surgical interventions, especially when performing upper lobectomy using video-assisted thoracoscopic surgery in the early stage of lung cancer [6]. Some thoracic surgeons believe that incision of the inferior pulmonary ligament during an upper lobectomy leads to positive postoperative

results of lung expansion, reduction of pleural effusion, and prevention of atelectasis [7]. However, there are reports that excessive lung expansion can lead to serious changes in the angle of the bronchi, which ultimately causes their deformation [8]. Other surgeons believe that the preservation of the lower pulmonary ligaments during surgery may be beneficial in terms of postoperative pleural fluid drainage by ensuring normal lymphatic drainage [5] and to expand the left lower lobe and reduce movement and repositioning of the left main bronchus [6].

With the development of lung cancer and the occurrence of metastases, it is proposed to perform an approach through the inferior pulmonary ligament to perform resection of the posterior or lateral basal segments. With such approaches, surgical trauma and postoperative complications are reduced [2]. However, it requires surgeons to know a clear definition of anatomical structures and the best surgical skills [9, 10].

So, given that in the available modern scientific literature there is no data on the size and clinical anatomy of the pulmonary ligaments in people, we set out to conduct a study aimed at determining the size, shape, area, content and syntopy of the left and right pulmonary ligaments in people. young age is normal, contributing to the improvement of surgical interventions on the lungs and mediastinal organs. Their study began with people aged 25 to 44 years, which, according to the latest WHO classification, is considered young. We also hope that these studies will to some extent fill the gap in the clinical anatomy of the pulmonary ligaments of young people.

AIM

The aim of this research was to study the size, shape, area, content and clinical anatomy of the left and right pulmonary ligaments in young people.

MATERIALS AND METHODS

When writing the article, the following methods were used: bibliosemantic, content analysis, statistical, macroscopic analysis. Macroscopic studies were carried out on preparations of the chest organs during 28 autopsies of young people aged 25 to 44 years who died from various causes at the Poltava Regional Pathological Anatomical Bureau (inclusion criterion – young age of the person (25-44 years according to the WHO classification) Among persons of this age period, there were 15 male and 13 female specimens, their average age was 39.3±2.4 years.In this study, methods were used for dissecting organ complexes of the breast in order to access macroscopic preparations of the pulmonary ligaments, macroscopy, and macro-microscopy according to V.P. Vorobyov, syntopy of pulmonary ligaments, morphometry and planimetry of pulmonary ligaments, statistical processing of quantitative data.

Before opening the chest, the trachea was clamped with a clamp to prevent the decrease of the lungs. For a better study, the preparation of organocomplexes on both sides was performed, followed by the study of the right and left pulmonary ligaments. When conducting a study using a caliper, the height was measured from the apex at the lower semicircle of the inferior pulmonary vein to the middle of its base, the width at the upper edge, in the middle and along the lower edge. An anthropometric conveyor was used to determine the angles of deviation of the pulmonary ligaments from the frontal plane. The distance from the lower edge of the pulmonary ligaments in the lung to the lower edge of the lower particles was also measured, and when they passed to the diaphragmatic surface, this distance was determined. The distance from the lower edge of the pulmonary ligaments in the lung to the lower edge of the lower particles was measured. Attention was paid to in which cases the pulmonary ligaments with their pulmonary edge reached the lower edge of the lower part of the lungs, and in which cases they did not reach or passed to their diaphragmatic surface and measured this distance. The shape of the pulmonary ligaments was assessed, after their excision they were stretched on millimeter paper, outlined and the area was determined, after which their content was examined. The number and location of lymph nodes in them were determined.

We studied the topography of the left and right pulmonary ligaments in relation to the inferior pulmonary veins, the lower edge and diaphragmatic surface of the lower lobes of the lungs, the esophagus with the vagus nerves, the descending part of the thoracic aorta, the pericardium, and the diaphragm.

The obtained digital material of the research results was subjected to statistical processing using the Statistica 9.0 program and a comparison of average indicators between the right and left pulmonary ligaments of men and women was carried out. The results were considered statistically significant at $p<0.05$.

RESULTS

Upon receipt of the results of the study, it was established that in young people, pulmonary ligaments are a doubling of the mediastinal part of the parietal pleura, which passes into the pulmonary pleura and covers the roots of the left and right lungs along the anterior and

posterior surfaces. Below the roots of the lungs, these two sheets do not immediately converge and are placed between the organs of the mediastinum and the lower lobe of the lungs, forming the pulmonary ligament. The tops of these ligaments are below the inferior pulmonary vein, although the latter is sometimes placed between its leaves. This must be taken into account by surgeons when accessing the root of the lungs, when performing surgical interventions on the lungs, such as lower lobe lobectomy or pulmonectomy, and mediastinal organs.

When studying topographic anatomy, it was found that the inner edges of the pulmonary ligaments, both on the right and on the left, are located at the nearby sections of the esophagus and aorta, and then they go to the mediastinal surface of the lower particles, where they pass into its pulmonary pleura. Pulmonary ligaments on both sides, except for the apex, have two edges: the inner or mediastinal and outer, or pulmonary and lower free edge, hanging over the diaphragm. Between the lower edge of the pulmonary ligaments and the diaphragm there is a certain gap, the height of which depends on the distance at which the ligaments with their outer edge pass into the pulmonary pleura of the lower lobe of the lungs. So, the higher the diaphragmatic surface of the lung, the lower edge of the ligaments passes into the pulmonary pleura, the greater the height of this gap, and the lower, the smaller its height. Pulmonary ligaments with their lower free edges from the outside do not pass to the diaphragmatic surface of the pleura, but only with their inner edge, located on the right along the esophagus, and on the left – along the aorta, can continue into the diaphragmatic part of the pleura. Pulmonary ligaments with the inner edge of the anterior leaf on both sides pass into the mediastinal part of the pleura, covering the pericardium. However, in one (3.6%) female person, the anterior and posterior sheets of the pulmonary ligament passed into the mediastinal part of the parietal pleura that covered the pericardium. The right pulmonary ligaments in people from the inner edge also passed into the mediastinal part of the parietal pleura, which covered the pericardium, and the back leaf – in the mediastinal part of the parietal pleura that covered the esophagus. In two (7.1%) preparations (male and female), both sheets from the inner edge passed into the mediastinal part of the parietal pleura, which covered the thoracic part of the esophagus. In 11 (73.3%) men, the left and in 8 (53.3%) men, the right pulmonary ligaments from the side of the mediastinum with their lower edge passed into the pleura, which covered the diaphragm. Such a transition of the pulmonary ligaments into the diaphragmatic part of the parietal pleura in females was observed in 7 (53.8%) cases on the left and in 9 (69.2%) cases on the right. In one (7.7%) female preparation, a transition of the posterior leaf of the pulmonary ligament on one side to the posterior leaf of the pulmonary ligament of the opposite side was detected.

When studying the question of what shape of the pulmonary ligaments young people have, it was found that 10 (66.7%) of the left pulmonary ligaments of the male subjects had a triangular, 4 (26.7%) – trapezoid and 1 (6.7%) – quadrangular forms. On the right side, 8 (53.4%) pulmonary ligaments were triangular, 5 (33.3%) were quadrangular, and 2 (13.3%) were trapezoidal. Among women, 9 (69.2%) had a triangular shape, 3 (23.1%) trapezoidal, and 1 (7.7%) quadrangular left pulmonary ligaments.

The right pulmonary ligaments were distributed in shape as follows: 6 (46.1%) were triangular, 4 (30.8%) were quadrangular and 3 (23.1%) were trapezoidal. That is, 19 (67.9%) left and 14 (50.0%) right ones had a triangular shape, 7 (25.0%) left and 5 (17.9%) right ones had a trapezoidal shape, and 2 (7. 1%) left and 9 (32.1%) right pulmonary ligaments.

Research continued by measuring the height of the pulmonary ligaments. Thus, the average height of the left pulmonary ligaments in young people was 58.4 ± 3.2 mm, and the right ones – 54.5 ± 2.8 mm ($p > 0.05$).

The width of the pulmonary ligaments was also measured at three levels: along the upper and lower edges and in the middle of the height. Only trapezoidal and quadrangular pulmonary ligaments had width at the upper edge. The average width at the center of the height of the left pulmonary ligaments was 27.7±3.4 mm, and that of the right ones – 30.9±3.2 mm ($p > 0.05$). The width at the lower edge of the left pulmonary ligaments in young people averaged 48.9±3.7 mm, and the average value of the same indicator for the right pulmonary ligaments was 51.3±3.2 mm ($p > 0.05$).

The areas of the pulmonary ligaments were determined using the planimetric method. Thus, the average area of the left pulmonary ligaments was 1008.9±110.5 mm2, and that of the right ones was 1138.6±115.3 mm2 ($p>0.05$).

Data on the average height, width of the left and right pulmonary ligaments at different levels and their areas in young men and women are shown in Table 1.

In young males, 4 (14.3%) left and 6 (21.4%) right pulmonary ligaments did not reach the lower edge of the lower lobe of the lungs, and 2 (7.1%) left and 3 (10.7%) of the right pulmonary ligaments passed to the diaphragmatic surface of the lower particles of the lungs. In women, on the left, 5 (17.9%) pulmonary ligaments did not reach and 7 (25.0%) – passed to the diaphragmatic surface of the lower lobes, and on the right, 5 (17.9%) pulmonary ligaments passed and 8 (28.6%) did not reach the diaphragmatic surface of

Table 1. Average sizes of pulmonary ligaments in young male and female people

No.	Average indicator sizes	Pulmonary ligaments in young people				Confidence level (p)
		men		women		
		left	right	left	right	
1.	height of pulmonary ligaments (mm)	60,7±3,4	57,6±3,3	56,2±2,9	51,8±3,1	$p_1 > 0,05$ $p_2 > 0,05$
2.	width of pulmonary ligaments at the upper edge (mm)	12,1±3,2	15,5±3,2	11,3±2,7	13,7±2,6	$p_1 < 0,05$ $p_2 < 0,05$
3.	width of pulmonary ligaments at mid-height (mm)	28,6±2,9	30,1±2,8	26,7±3,1	29,2±2,7	$p_1 > 0,05$ $p_2 > 0,05$
4.	width of pulmonary ligaments at the lower edge (mm)	49,6±3,2	52,1±3,3	47,4±2,9	48,3±2,8	$p_1 > 0,05$ $p_2 > 0,05$
5.	area of pulmonary ligaments (mm2)	1124,6 ± 109,8	1184,3± 116,4	887,5± 103,6	975,4± 99,8	$p_1 < 0,05$ $p_2 > 0,05$

Note: p_1 – level of reliability of average indicators of the sizes of the left pulmonary ligaments between men and women; p_2 – level of reliability of average indicators of the sizes of the right pulmonary ligaments between men and women.

the lower particles of the lungs. The average distance from the lower edge of the left pulmonary ligaments to the lower edge of the lower particles of the lungs in males was 4.7±1.8 mm, and in females – 8.9±2.8 mm ($p<0.05$), which among all left ligaments, the average was 6.8±2.5 mm. The average distance from the lower edge of the right pulmonary ligaments to the lower edge of the lower particles of the lungs was 4.4±1.3 mm, in men it averaged 2.8±1.1 mm, and in women it was 5.7±1.9 mm ($p<0.05$).

Upon further study, it was revealed that some pulmonary ligaments passed from top to bottom with a backward deviation from the frontal plane. This feature of the passage of the left pulmonary ligaments was observed in 11 (39.3%) cases, of which 5 (33.3%) men and 6 (46.2%) women. The angle of deviation of the ligaments from the frontal plane was also measured. It averaged 20.3±4.5 in males and 29.8±3.9 in females ($p<0.05$). In 6 (21.4%) men and 8 (28.6%) women, the pulmonary ligaments deviated backward from the frontal plane, while the average angles of deviation were 18.9±3.6 in men and 27.7±4.1 – in women ($p<0.05$).

However, such dimensions as: width at the upper edge, the angle of inclination of the pulmonary ligaments back from the frontal plane and the ratio of their lower free edge to the lower edge of the lower particles of the lungs are not found in all pulmonary ligaments of young people.

According to the data obtained in men, the inferior pulmonary vein was located in the thickness of 4 (14.3%) of the left and 2 (7.1%) of the right pulmonary ligaments. In females, such placement of the inferior pulmonary vein was observed in 2 (7.1%) cases on the left and in one (3.6%) on the right. In such preparations, the distance from the upper edge of the pulmonary ligaments to the upper semicircle of the inferior pulmonary veins was measured. The average value of this distance in men is 2.1 ± 0.5 mm on the left and 1.8 ± 0.7 mm on the right ($p> 0.05$). And the average distance between the top of the pulmonary ligaments and the upper semicircle of the lower pulmonary veins in young women is 2.0 ± 0.2 mm on the left and 1.5 ± 0.4 mm on the right.

During dissection, lymph nodes of various sizes were found in the thickness of the pulmonary ligaments. So, in the thickness of 12 (42.9%) of the left pulmonary ligaments, 23 lymph nodes were found, of which 11 lymph nodes were found in men on the left in the thickness of 5 (33.3%) ligaments: 4 at the apex, 3 in the middle of the height and 5 at the lower edge pulmonary ligaments. In females, in the thickness of 7 (53.8%) of the left pulmonary ligaments, 5 lymph nodes were located at the upper and lower edges and 2 in the middle of the height. Examination of 13 (46.4%) right pulmonary ligaments revealed 22 lymph nodes between their sheets. In 8 (53.3%) males, in the thickness of the right pulmonary ligaments at the upper edge and in the middle of the height there were 3 lymph nodes and at the lower edge – 6 lymph nodes. And in women, 5 (38.5%) of the right pulmonary ligaments in their thickness had 10 lymph nodes, which were located: at the upper edge – 2 and in the middle of the height and at the lower edge – 4 each. When conducting a macro-microscopic study, it was found that between the leaves of the pulmonary ligaments in the loose connective tissue, in addition to the lymph nodes, are blood vessels and bundles of nerve fibers, limited by the perineurium.

DISCUSSION

According to the data obtained, the pulmonary ligament of young people is a doubling of the pleura,

which forms below the root of the lungs and stretches to the diaphragmatic pleura and connects the visceral pleura to the mediastinal pleura in the lower part of the lung. These results of the study coincide with the data of other authors [12]. However, we do not agree with the data of scientists who call the pulmonary ligament inferior [6, 7], since a person does not have other pulmonary ligaments, including the upper ones, and they exist only on the right and left.

The pulmonary ligaments with their lower free edges from the outside do not pass to the diaphragmatic surface of the pleura, but with their inner edges, which are located on the right along the esophagus, and on the left along the aorta, they can continue into the diaphragmatic part of the pleura. The pulmonary ligaments, with the inner edge of the anterior leaf on both sides, pass into the mediastinal part of the pleura, covering the pericardium.

Lymph nodes of different sizes were found in the thickness of the pulmonary ligaments at different levels, which indicates the existence of sufficient lymphatic drainage, which plays a significant role in the outflow of pleural fluid after surgical interventions on the lungs and mediastinal organs. This confirms the opinion of other scientists about the advisability of preserving the lower pulmonary ligaments when performing surgical interventions for postoperative outflow of pleural fluid [5].

In this scientific study, the forms and average sizes of the pulmonary ligaments in young males and females were established. The features of the transition of the inner, outer and lower edges of these ligaments to the mediastinal, visceral and diaphragmatic parts of the pleura are indicated. So, the pulmonary ligaments, with their inner edges of the back sheet, pass into the mediastinal pleura, covering the esophagus on the right, and the thoracic aorta on the left.With the inner edge of the anterior sheet, the pulmonary ligaments on both sides pass into the mediastinal part of the pleura covering the pericardium, and the lower edge can continue into the diaphragmatic part of the pleura. Also, during the study, an interesting feature of the placement in the thickness of the left and right pulmonary ligaments of the lower pulmonary vein in some young males and females was revealed. All these data must be taken into account when performing accesses through the pulmonary ligaments to the root of the lungs, when performing open and video-assisted thoracoscopic operations, as some authors point out in their scientific articles [4, 7, 8], as well as when performing upper lobectomy at an early stage of lung cancer [6] and resection of the posterior or lateral basal segments [11].

Thus, to improve the results of performing surgical interventions on the lung root, lower lobe, lungs and mediastinal organs, it is necessary to have a clear knowledge of the clinical anatomy of the chest organs and pulmonary ligaments.

CONCLUSIONS

Thus, the size, shape, area, content and clinical anatomy of the left and right pulmonary ligaments in young people were studied. It has been established that in young people there are individual differences between the shape and size of the right and left pulmonary ligaments in males and females. In most cases, there was no significant difference ($p > 0.05$) between the values of different sizes of the right and left pulmonary ligaments. It was revealed that the upper edge of these ligaments is located below the inferior pulmonary vein, although the latter one in 4 (14.3%) cases on the left and in 2 (7.1%) on the right is located between its leaves. In the thickness of 12 (42.9%) left pulmonary ligaments there were 23 lymph nodes at different levels, and between the layers of 13 (46.4%) right pulmonary ligaments there were 22 lymph nodes. In addition to the lymph nodes, between the leaves of the pulmonary ligaments in the loose connective tissue there are blood vessels and bundles of nerve fibers.

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ORIGINAL ARTICLE

CONTENTS

Comorbid pathology of the mammary glands and endometriosis: risk factors and prognosis

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ABSTRACT

Aim: based on a retrospective analysis, the relationship between external genital endometriosis and comorbid breast pathology was established and risk factors were identified, their comparison and the formation of a prognostic risk criterion were determined.

Materials and Methods: to address the objectives of the study, a retrospective analysis of 470 cases of patients treated for external genital endometriosis after surgical treatment and comorbid breast pathology was conducted. The control group included 30 healthy non-pregnant women. Statistical processing was performed on a personal computer using the statistical software package Statistica 10.

Results: As a result of the analysis, the age of the patients ranged from 23 to 40 years. The average age of patients in the study group was (32.2±1.18) years, and in the control group (31.1±1.35) ($p>0.05$). The groups were homogeneous in terms of age ($p>0.05$), marital status ($p>0.05$) and level of education ($p>0.05$). Close relatives in 208 (44.25±2.18) % (OR=8.86; 95 % CI: (0.68-10.53); $p<0.002$) cases suffered from benign (hormone-dependent) tumours and tumour-like diseases of the uterus and appendages in isolation or in various combinations (fibroids, adenomyosis, endometrial hyperplasia). It was also found that 102 (21.70±1.67) % of patients had endometriosis, which may indicate a genetic predisposition to this disease. In the closest relatives of EM patients: in 118 (25.10±2.01) % of the examined parents, breast problems were noted, in 66 (14.04±1.12) % – diabetes mellitus, and in 98 (20.85±1.22) % thyroid diseases were detected, which in total amounted to (60.00±2.23) % (OR=9.12; 95 % CI: (0.58-11.54); $p<0.002$). Early menarche almost tripled the risk of EM (OR=2.72; 95% CI: (1.02-5.11); $p<0.002$), and menstrual irregularities doubled it (OR=2.04; 95% CI: (1.09-3.14); $p<0.05$), higher education, urban residents – 2.2 times higher (OR= 2.27; 95 % CI: (1.11-3.63); $p<0.05$), diseases of the gastrointestinal tract and hepatobiliary complex – 5.2 times higher (OR=5.27; 95 % CI: (1.89-12.03); $p<0.05$), frequently recurrent inflammatory diseases of the appendages – 3 times higher (OR=3.14; 95 % CI: (0.91-5.14); $p<0.05$), dysmetabolic manifestations (thyroid dysfunction) – 5 times higher (OR=5.11; 95 % CI: (1.61-9.503); $p<0.002$).

Conclusions: Thus, in endometriosis and dyshormonal diseases of the mammary glands, menstrual and generative function disorders, along with clinical symptoms of pelvic pain, dysmenorrhoea, autonomic nervous system disorders and sexual dysfunction, are significant components of this problem, initiating comorbidity processes in target organs in the setting of hormonal maladaptation. Therefore, these comorbidities become a trigger for the activation of systemic hormonal imbalance and become an urgent interdisciplinary problem that requires further study.

KEY WORDS: endometriosis, mammary glands, risk factors, hormonal imbalance, inflammation

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INTRODUCTION

The problem of combined damage to hormone-dependent target organs in the structure of gynaecological pathology is a leading one [1, 2]. The peculiarities are changes in their condition in accordance with the hormonal background of a woman as a result of physiological processes (menstrual cycle dynamics, different age periods of a woman) and in pathology of the reproductive system [3, 4]. According to scientific publications, the frequency of dyshormonal diseases of the reproductive system has been increasing in recent years [5]. A patient with dyshormonal disorders is examined by various narrow-profile specialists, such as obstetrician-gynaecologist, mammologist, endocrinologist. However, there is a lack of a holistic view of the patient, prescription of complex medications, when one pathology is defined as the main one and the other as concomitant, although the cause and effect relationship is not always clearly traced. According to recent scientific studies, in this cohort of patients, endometriosis is diagnosed in 10–15 % of women of reproductive age, 70 % of women with chronic pelvic pain, and 40–60 % of women with algodysmenorrhoea [6, 7].

To date, the causes and triggering mechanisms for the development of benign and malignant breast tumours have not been fully elucidated. However, the results

of multi-purpose epidemiological and experimental studies have identified a number of factors that increase the risk of breast tumours [6].

Modern types of surgical and medical treatment of this disease are not effective in all cases and are accompanied by a high frequency of relapses. Recent scientific developments indicate that women with endometriosis have a significantly lower pregnancy rate than healthy women [8, 9]. It has been established that in the population, 10–15 % of fertile women are diagnosed with endometriosis during laparoscopy, while in patients with infertility, 15–80 % are diagnosed with endometriosis [10]. According to WHO statistics, more than a million new cases of breast cancer are diagnosed worldwide every year.

Mortality from this pathology exceeds 50 % of all patients. The reduction of this figure is hampered by the lack of organised, high-quality preventive screening of the population for the early detection of malignant breast tumours. An analysis of breast cancer screening methods shows that mortality among high-risk women who participated in a preventive treatment programme for diffuse breast disease is 30-50% lower than in groups where breast cancer prevention was not carried out. The search for the causes and ways of developing this disease is ongoing to develop optimal treatment methods. The issues of early diagnosis, search for new methods of treating dyshormonal breast diseases and improving the effectiveness of therapy, especially in combination with infertility, require further study [11, 12]. The relationship between benign breast pathology and endometriosis and infertility is well known, but the mechanisms of fertility disorders in this pathology have not been fully studied [13].

That is, the condition of the mammary glands depends on the function of the hypothalamic-pituitary-ovarian system both in different periods of a woman's life and in various pathological conditions [14]. It should be noted that much attention is paid in the literature to the interaction of the target organs of the reproductive system, but there is virtually no data on the possibility of development and the relationship between endometriosis and benign breast dysplasia in women with various types of infertility [15, 16].

Recently, scientists and doctors have been paying attention to the potential of mesenchymal stem cells as a new approach to treating endometriosis. Mesenchymal stem cells are a special type of cell that have the ability to self-renew and differentiate into different types of tissues in the body [17, 18].

AIM

To conduct a retrospective analysis of the relationship between comorbid breast pathology and external genital endometriosis in order to identify risk factors and form a prognostic risk criterion.

MATERIALS AND METHODS

At the first stage, we studied the correlation between benign diseases and breast cancer over 5 years in the Ternopil region.

To address the study objectives, a retrospective analysis of 470 medical records of patients treated for comorbid breast disease and external genital endometriosis after surgical treatment and in the gynaecological department of 'Municipal non-commercial enterprise ternopil municipal city hospital №2', Ternopil, Ukraine was conducted. The main source of information for the clinical and anamnestic analysis was the «patient's medical record» (f. 003/o). A questionnaire was developed for the patients included in the study, which included (age of menarche, characteristics of the menstrual cycle, previous pregnancies and their outcomes, use of hormonal therapy, surgical history, family history, family history regarding endometriosis and dyshormonal breast and thyroid diseases), gynaecological examination (bimanual or rectovaginal) and imaging studies such as transvaginal ultrasound, MRI or cystoscopy if necessary.

Statistical processing was carried out on a personal computer using the Statistica 10 statistical software package, namely, using the Student's t test. The difference between comparative means was considered significant at $t > 3.85$ and $p < 0.001$.

Prior to the study, ethical approval was obtained from the Clinical Trials Ethics Committee of the I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine (Protocol No. 72 of 6 January 2023) in accordance with the Declaration of Helsinki. The study was conducted retrospectively, and signed informed consent was obtained from all subjects.

RESULTS

At the first stage of the study, a comparative assessment of the ratio of breast surgery for benign breast disease and cancer was carried out. The analysis revealed that since 2016, there has been a stable ratio between surgical interventions for benign breast disease and cancer (Fig. 1). Our results indicate that breast cancer accounted for (23.2) % in 2016, (24.2) % in 2017, (24.6) % in 2019, and (25.5) % in 2021. Thus, the ratio of surgical interventions for benign and malignant tumours remained stable.

As a result of the retrospective analysis at the second stage, the patients' ages ranged from 23 to 40 years. The control group included 30 healthy non-pregnant women.

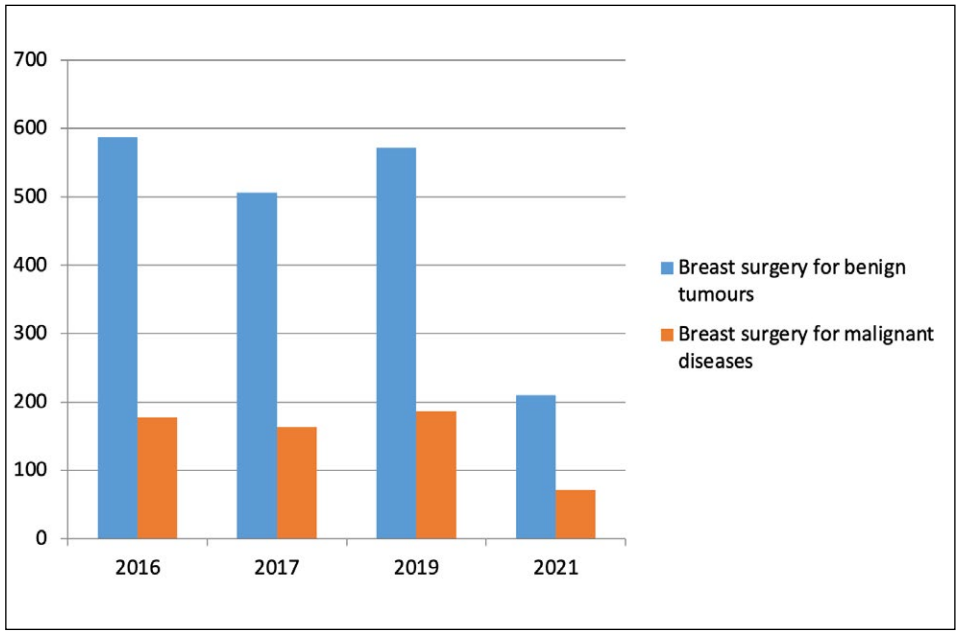

Fig. 1. Comparative data of breast surgery.

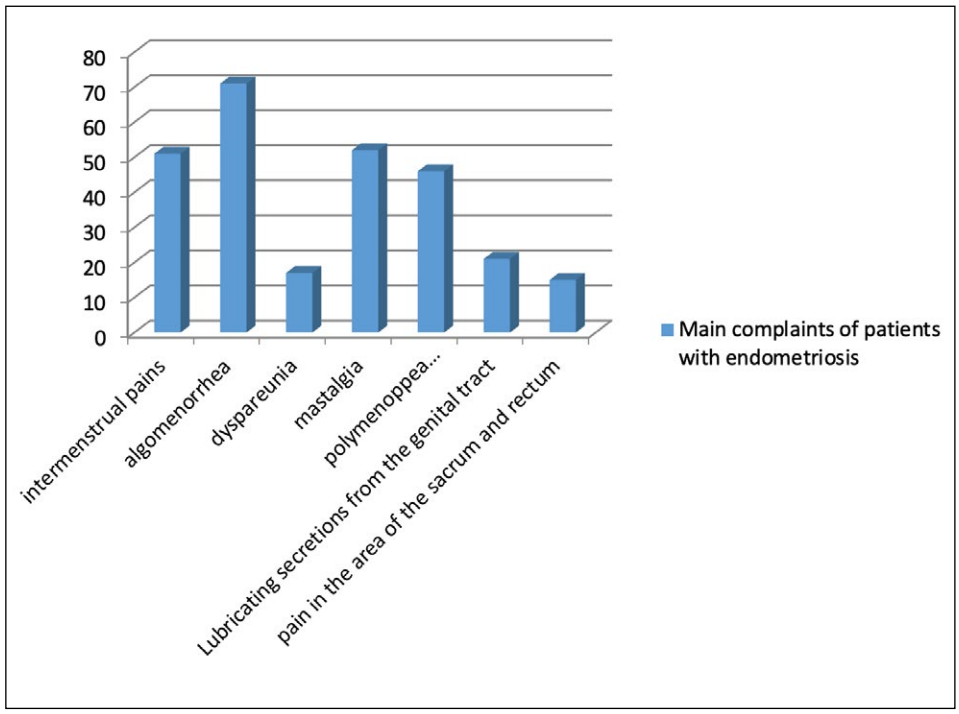

Fig. 2. Main complaints of patients with endometriosis.

The average age of patients in the study group was (32.2 ± 1.18) years, and in the control group (31.1 ± 1.35) ($p > 0.05$). The groups were homogeneous in terms of age ($p > 0.05$), marital status ($p > 0.05$) and level of education ($p > 0.05$). When studying the family history of the examined patients, it was found that close relatives in 208 (44.25 ± 2.18) % (OR=8.86; 95 % CI: (0.68-10.53); $p < 0.002$) cases suffered from benign (hormone-dependent) tumours and tumour-like diseases of the uterus and appendages in isolation or in various combinations (fibroids, adenomyosis, endometrial hyperplasia). It was also found that 102 patients (21.70 ± 1.67) % had endometriosis, which may indicate a genetic predisposition to this disease. Gynaecological surgeries in relatives.

The high frequency of endocrine disorders in the closest relatives of patients with endometriosis is noteworthy: 118 (25.10 ± 2.01) % of the examined parents had breast problems, 66 (14.04 ± 1.12) % had diabetes mellitus, and 98 (20.85 ± 1.22) % had thyroid diseases, which totalled (60.00 ± 2.23) % (OR=9.12; 95 % CI: (0.58-11.54); $p < 0.002$).

Thus, among the factors that have prognostic significance in the development of endometriosis, we can name the factor of burdened heredity, more often on the maternal side (first-degree relatives), mainly benign and malignant tumours of the genital organs and tumours of extragenital localisation of various etiologies.

Table 1. Structure of breast pathology in the examined patients

Group	Distribution of patients by type of mastopathy							
	Diffuse pathology						Nodal pathology	
	fibrous		adenosis		cystic			
	n	%	n	%	n	%	n	%
418	234	6	9	4,6	19	4,5	104	4,9

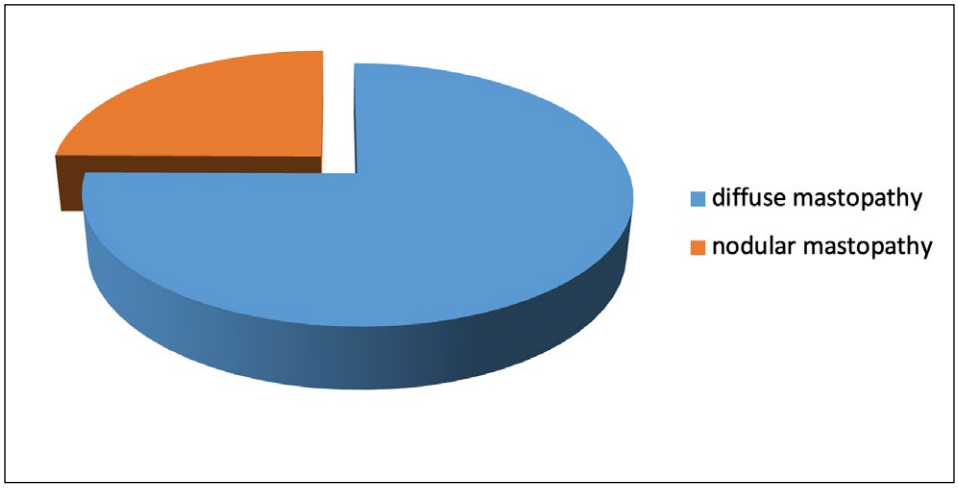

Fig. 3. Distribution of patients by type of mastopathy.

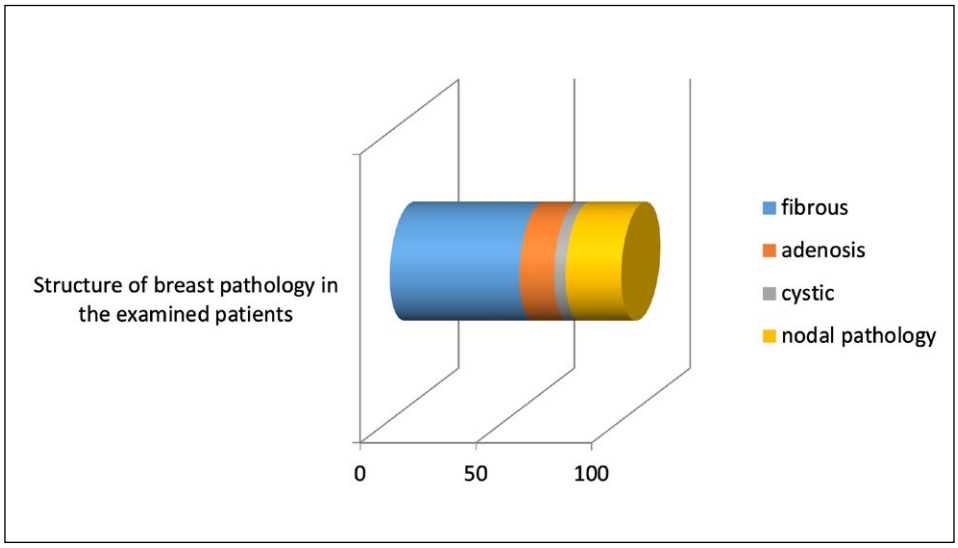

Fig. 4. Structure of breast pathology.

In addition, a high percentage of endocrine tumours was found – (60.00 ± 2.23) %.

An analytical assessment of the significance of risk factors for endometriosis suggested that early menarche almost tripled the chances of developing endometriosis (OR=2.72; 95 % CI: (1.02-5.11); $p < 0.002$), menstrual irregularities – twice (OR=2.04; 95% CI: (1.09-3.14); $p < 0.05$), chronic inflammatory diseases of the appendages (OR=3.14; 95% CI: (0.91-5.14); $p < 0.05$).

The analysis of childhood infections (measles, rubella, chickenpox, scarlet fever, mumps in various combinations), diseases of the ENT organs (chronic tonsillitis, deviated nasal septum, sinusitis, etc.), as well as influenza and acute respiratory virus infections in patients, revealed a high proportion (90.11 ± 1.48) % of infectious diseases in childhood and adolescence.

When analysing the history of chronic extragenital diseases in the study group, it was found that more than half of the patients had a combination of two or more extragenital diseases.

Diseases of the gastrointestinal tract and organs of the hepatobiliary complex (chronic gastritis, enterocolitis, cholecystitis, hepatitis) were detected in (OR=5.27; 95 % CI: (1.89-12.03); $p < 0.05$), cardiovascular diseases (hypertension, hypotension) – in 66 (14.0 %), mastalgia – in 400 (85.1 %), chronic inflammatory diseases of the upper respiratory tract – in (30.1 %), chronic pyelonephritis – in 16.0 %.

The main symptoms of endometriosis were pain, dyspareunia, dysfunction of adjacent organs (dysuria), psychoneurological disorders, reproductive disorders (infertility and miscarriage), accompanied by mastalgia of varying severity (Fig. 2).

All the examined women complained of meno- and metrorrhagia. The occurrence of cyclic pain syndrome, which increased from the moment of menarche, was detected in 405 (86.17 ± 1.23) % of patients. The duration of menstruation ranged from 7 to 10–12 days, with the duration of the menstrual cycle ranging from 21 to 26 days (Fig. 3).

In 78 (16.59 ± 1.98) % of EM patients, there was a history of 1 delivery, in 36 (7.65 ± 1.21) % – 1–2 spontaneous miscarriages and frozen pregnancies of different gestational ages, in 8 (3.82 ± 0.62) % – postpartum complications (lochiometra, uterine subinvolution, metoendometritis).

Infertility was detected in 236 (50.20 ± 2.51) % of women, of which 191 (80.93 ± 1.27) % were primary and 45 (19.07 ± 0.46) % were secondary. The duration of infertility was (5.7 ± 2.2) years.

The structure of breast pathology revealed during mammological ultrasound screening revealed mastopathy in 418 (88.93 ± 1.98) %, of which: in 314 (75.1 %) women diffuse forms of breast mastopathy were detected during the examination and in 104 (24.5 %) % nodular forms.

Benign breast changes are more common in women of childbearing age. Of the diffuse forms of mastopathy in patients with endometriosis, fibrous 234 (55.9 %) prevailed, which is associated with the unity of pathogenetic proliferative processes in the target organs (endometrium, mammary gland) of the reproductive system (Table 1, Fig. 4).

Therefore, women with these factors should be considered to be at high risk of developing complicated endometriosis. Early menarche almost tripled the odds of developing endometriosis (OR=2.72; 95 % CI: (1.02–5.11); $p < 0.002$), menstrual irregularities doubled the odds (OR=2.04; 95 % CI: (1.09-3.14); $p < 0.05$), higher education and urban residence increased the odds 2.2 times (OR=2.27; 95% CI: (1.11–3.63); $p < 0.05$), diseases of the gastrointestinal tract and organs of the hepatobiliary complex – 5.2 times higher (OR=5.27; 95 % CI: (1.89–12.03); $p < 0.05$), frequently recurrent inflammatory diseases of the appendages – 3 times higher (OR=3.14; 95 % CI: (0.91–5.14); $p < 0.05$), dysmetabolic manifestations (thyroid dysfunction) – 5 times higher (OR=5.11; 95 % CI: (1.61–9.503); $p < 0.002$).

DISCUSSION

Adenous mastopathy and cystic mastopathy were detected less frequently. Adenous mastopathy was more commonly detected in women who were pregnant but did not give birth (history of pregnancies that did not develop or ended in early termination).

In cystic mastopathy, depending on the size of the cyst, a puncture biopsy was additionally performed under ultrasound guidance.

Mortality from this pathology exceeds 50 % of all patients. The reduction of this figure is hampered by the lack of organised, high-quality preventive screening of the population for the early detection of malignant breast tumours. An analysis of breast cancer screening methods shows that mortality among high-risk women who participated in a preventive treatment programme for diffuse breast disease is 30-50% lower than in groups where breast cancer prevention was not carried out. The search for the causes and ways of developing this disease is ongoing to develop optimal treatment methods. The issues of early diagnosis, search for new methods of treating dyshormonal breast diseases and improving the effectiveness of therapy, especially in combination with infertility, require further study [11, 12]. The relationship between benign breast pathology and endometriosis and infertility is well known, but the mechanisms of fertility disorders in this pathology have not been fully studied [13].

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Recently, scientists and doctors have been paying attention to the potential of mesenchymal stem cells as a new approach to treating endometriosis. Mesenchymal stem cells are a special type of cell that have the ability to self-renew and differentiate into different types of tissues in the body [17, 18].

CONCLUSIONS

Thus, given the significant percentage of surgical treatment of breast pathology, it is advisable to expand the search for predictors of dyshormonal breast diseases.

Dyshormonal diseases of the mammary glands and endometriosis accompanied by menstrual and generative function disorders, pelvic pain clinic, dysmenorrhoea, autonomic nervous system disorders and sexual dysfunction are significant components of this problem, initiating comorbidity processes in target organs in case of hormonal maladaptation. Therefore, these comorbidities become a trigger for the activation of systemic hormonal imbalance and become an urgent interdisciplinary problem that requires further study.

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CONFLICT OF INTEREST

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ORIGINAL ARTICLE

CONTENTS

Application of roc-analysis to assess the quality of predicting the risk of chronic rhinosinusitis recurrence

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ABSTRACT

Aim: To propose a new, original approach to assessing the quality of a multivariate regression model for predicting the risk of recurrence in patients with chronic rhinosinusitis based on ROC analysis with the construction of appropriate curves, estimating the area under them, as well as calculating the sensitivity, accuracy, specificity, and predictive value of a positive and negative classification results, the likelihood ratio of positive and negative patient detection results.

Materials and Methods: 204 patients aged with a diagnosis of chronic rhinosinusitis were examined.

Results: To build a multivariate regression model 14 probable factors of chronic rhinosinusitis occurrence were selected to determine the diagnostic value of the proposed model we calculate the sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), the likelihood ratio of a positive test (LR+), the likelihood ratio of a negative test (LR-) and prediction accuracy % of the proposed mathematical model. In order to determine the prognostic value of the risk ratio of CRS recurrence model, ROC- analysis was performed, ROC curves were obtained

Conclusions: The multivariate regression model makes it possible to predict potential complications and the possibility of disease recurrence. The construction of ROC-curves allows us to assert the excellent classification quality of chronic rhinosinusitis recurrence.

KEY WORDS: recurrence, multivariate regression analysis, chronic rhinosinusitis, ROC analysis

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INTRODUCTION

Chronic rhinosinusitis (CRS) is a rather broad concept that includes several nosological forms. It is defined as "infection of the sinuses and Schneiderian membrane lasting more than 3 months (or 12 weeks) per year". In the structure of sinusitis, 56-73% are lesions of the maxillary sinus due to its large volume, high natural conjunctiva, and close contact with the roots of the teeth (premolars of the upper jaw).

According to the EPOS 2020 classification, CRS is divided into primary and secondary. The primary includes localized forms (allergic fungal rhinosinusitis, isolated sinusitis) and diffuse – chronic rhinosinusitis with polyps (polyps visualized endoscopically in the nasal passage), as well as chronic rhinosinusitis without nasal polyps. A separate distinction is made between chronic rhinosinusitis with an altered mucous membrane of the sinuses or nasal cavity as at polyposis, but there are no polyps of the nasal passage that cover the nasal passage [1, 2].

Secondary CRS is also divided into localized processes (odontogenic sinusitis, maxillary sinus cyst, mycetoma) and bilateral or widespread (primary miliary dyskinesia, Wegener's disease, chronic rhinosinusitis against the background of selective immunodeficiency) [3-5]. However, this classification by phenotypes does not consider all the pathogenetic mechanisms of the development of the disease, which in turn complicates the choice of the correct treatment tactics and makes it impossible to predict the potential recurrence of the disease. Despite numerous studies, in approximately 30% of CRS cases, the etiology and pathogenesis remain unclear, and the question of predicting potential relapses of chronic rhinosinusitis depending on its form of manifestations remains open and relevant.

Today, one of the popular and fairly accurate methods of predicting the recurrence of various diseases, including CRS, is the construction of a multivariate regression model, which includes a number of predictors that may be the cause of a repeated inflammatory process, which was described by us in a previous publication [6]. However, determining the sensitivity, accuracy and specificity of the proposed model requires an additional ROC analysis with the construction of an ROC curve.

The ROC curve is a characteristic curve that shows the dependence of the number of correctly diagnosed positive cases on the number of incorrectly diagnosed negative cases when varying the threshold of the decisive rule [7].

Approaches to building multivariate regression forecasting models in medicine are considered in the works of Musiienko V. et all. (2021); Musiienko V. et all. (2022) [8, 9].

The results of ROC-analysis for 3 degrees of climacteric syndrome are considered in the work of Chukur O. et all. (2022) [10]. This is the approach used in this work to evaluate the quality of the proposed CRS model.

In recent years, there has been an increased interest in modern methods of predicting CRS using machine learning methods in the form of recurrent neural networks [11-13]

AIM

The aim of the work is to propose a new, original approach to assessing the quality of a multivariate regression model for predicting the risk of recurrence in patients with three degrees of chronic rhinosinusitis based on ROC analysis with the construction of appropriate curves, estimating the area under them, as well as calculating the sensitivity, accuracy, specificity, and predictive value of a positive and negative classification results, the likelihood ratio of positive and negative patient detection results.

MATERIALS AND METHODS

We examined 204 patients aged 18 to 80, including 107 women and 97 men, with a diagnosis of chronic rhinosinusitis, who were undergoing inpatient treatment in the otolaryngology department of the communal noncommercial enterprise "Ternopil Regional Hospital" under Ternopil Regional Council. The average age of the patients was 45 years, and the duration of the disease varied within 5-8 years.

All patients signed an informed consent to participate in the study. After receiving the opinion of the bioethics commission at Ivan Horbachevsky Ternopil National Medical University (minutes No. 63 dated 16/03/2020) the study was conducted in compliance with all moral and ethical principles, considering World Medical Association Declaration of Helsinki on Biomedical Research.

All patients underwent a comprehensive clinical and laboratory examination, which included an examination, anamnesis collection, complete blood count with formula, biochemical blood analysis, and radiological examination (radiography of the paranasal sinuses, computer tomography or MRI of the head).

According to a specially developed questionnaire for predicting the level of recurrence of CRS, all patients were surveyed, which included 15 risk factors for the development of CRS: age, gender, environmental living conditions, nasal septum deviation, presence of an allergic component, carious or damaged teeth (upper premolars), nasal or facial skeleton injuries, the presence of leukocytosis (according to the leukocyte formula), the ESR level, the presence of diagnosed diabetes, the level of glycemia, the degree of bronchial asthma, radiological signs, smoking, and the incidence of SARS during the last 12 months, and their gradation was established from numerical values.

Construction of a prognostic model of the risk of CRS recurrence was carried out using multivariate regression analysis. The statistical processing of the obtained research results was carried out using the statistical package Statistica 10.0 and the table editor Microsoft Excel 2019.

To obtain a numerical value of the clinical significance of the test, as well as to compare several tests, calculations of ROC analysis were carried out in the Matlab program using the integral indicator of the area under the ROC curve – AUC (Area Under Curve).

RESULTS

The method of multivariate regression analysis for predicting CRS recurrence, taking into account the most informative factors and variants of their severity, makes it possible to create a mathematical model for predicting this disease and predict the probability of recurrence, which helps in the development of effective methods of treatment, prevention, development and progression of the pathology.

To build a multivariate regression model for predicting CRS recurrence, 14 probable factors of CRS occurrence were selected with the calculation of the regression coefficient "b" (Beta), which reflects for each selected factor the relationship regarding the influence on the development of CRS relapse in the examined patients. A risk factor with a significance level of $p>0.05$ was excluded from further analysis (Table 1). Since the significance levels of thirteen risk factors were less than 0.05, they were included in the mathematical model for predicting CRS recurrence (Fig. 1).

Based on the results of the multivariate regression analysis of predicting the level of CRS recurrence, a mathematical model was built to determine the risk ratio of CRS recurrence (RRCRSR).

RRCRSR=X1*0.059+X2*1.112+X3*0.968+X4*1.029+X5*1.114+X6*1.049+X7*1.031+X8*0.039+X9*1.075+X10*0.362+X11*1.012+X12*1.161+X13*0.92

-3.022,

where RRCRSR is the risk ratio for CRS recurrence;

X1 – X13 – selected risk factors for CRS recurrence (Table I) with regression coefficients; -3.022 is a constant.

N=104	Regression Summary for Dependent Variable: ChRS Relapse (1 R= ,99386421 R?= ,98776607 Adjusted R?= ,98599894 F(13,90)=558,97 p<0,0000 Std.Error of estimate: ,40287 b*	Std.Err. of b*	b	Std.Err. of b	t(90)	p-value
Intercept			-3,02163	0,349667	-8,64147	0,000000
Age	0,285824	0,013378	0,05927	0,002774	21,36604	0,000000
Sex	0,162198	0,016548	1,11240	0,113489	9,80177	0,000000
Working conditions	0,345134	0,012476	0,96780	0,034983	27,66464	0,000000
NSD (Nasal Septum Deviation)	0,277670	0,012822	1,02917	0,047525	21,65524	0,000000
Allergy comp	0,055010	0,012700	1,11361	0,257092	4,33158	0,000038
Dental caries	0,200789	0,012404	1,04883	0,064791	16,18783	0,000000
White blood comp	0,617377	0,012907	1,03118	0,021558	47,83240	0,000000
ESR	0,112440	0,012527	0,03885	0,004328	8,97582	0,000000
Diabetes	0,068969	0,013153	1,07513	0,205044	5,24341	0,000001
Glucose	0,097594	0,013685	0,36158	0,050704	7,13131	0,000000
X-ray, CT, MRI	0,362671	0,013325	1,01199	0,037182	27,21704	0,000000
Smoking	0,146406	0,015757	1,16090	0,124939	9,29170	0,000000
Flu infection	0,148273	0,012260	0,92034	0,076099	12,09392	0,000000

Fig. 1. The result of obtaining significant factors for predicting CRS recurrence when conducting a multivariate regression analysis in the Statistica 10.0 program with a significance level of $p<0.05$.

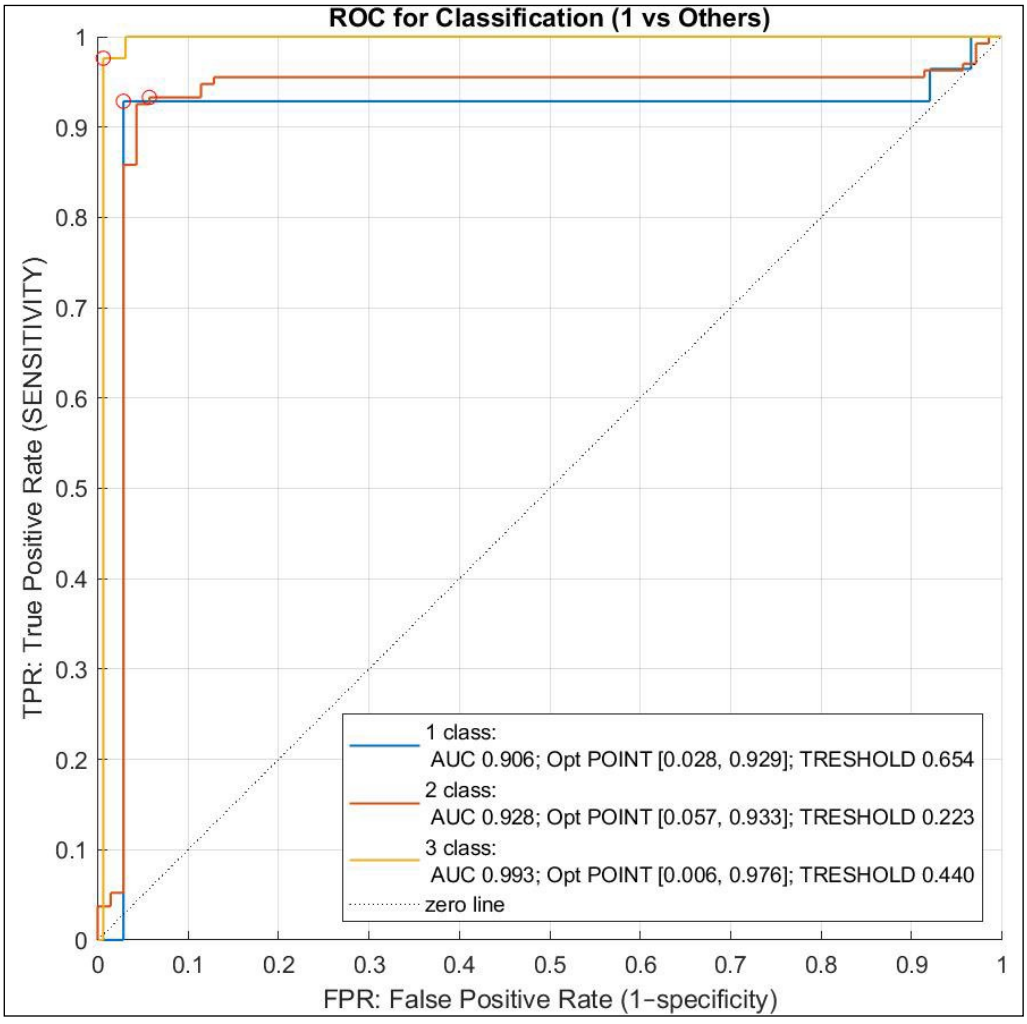

Fig. 2. ROC-curves for predicting the risk factor of chronic rhinosinusitis recurrence of R-1, R-2 and R-3 degrees.

To additionally assess the quality of the mathematical model of the RRCRSR, the coefficient of determination (R^2) was analyzed, which shows what part of the factors is considered during forecasting. The coefficient of determination in the proposed mathematical model of RRCRSR is R^2=0.987 (in the Statistica 10.0 program R^2= .98776607). So, in our case, 98.7% of factors are considered in the model for predicting the risk of CRS recurrence (RCRS), which indicates how well the obtained observations confirm the mathematical model [6].

Table 1. Significant risk factors for CRS recurrence

Name of factors	Conventional designations of factors in the mathematical forecasting model	Factor ranges and names of their possible variants	Numerical values of factor ranges
Age	**X1**	18-25	0
		25-44	1
		44-60	2
		60-75	3
		75-90	4
Gender	**X2**	M	1
		F	2
Working conditions	**X3**	Maternity leave/ Does not work/ Pensioner/ Disabled of II-III grade	1
		Nurse/ Doctor	2
		Student/ Educator/ Junior researcher/ Teacher/ Lecturer/ Librarian/ Accountant/ Leading specialist/ Manager/ Engineer/ Private entrepreneur/Operator	3
		Barista/ Waiter/ Make-up artist/ Salesman/ Cook/ Cleaner/ Watchman/ Driver/ Plant worker/ Warehouse administrator/ Foreman/ Tractor driver/ Police inspector/ Storekeeper/ Carpenter/ Crane operator	4
Nasal Septum Deviation	**X4**	1/3 of nasal meatus	1
		2/3 of nasal meatus	2
		Completely	3
		S-shaped	4
Allergic component	**X5**	No	0
		Yes	1
Carious (damaged) teeth (premolars)	**X6**	1 tooth	1
		2 teeth	2
		3 teeth	3
Level of WBC	**X7**	Normocytosis	0
		Eosinophilic leukocytosis	1
		Basophilic	2
		Monocytic	3
		Neutrophil leukocytosis	4
		Lymphocytic	5
ESR level	**X8**	Norm	0
		Increased	1
Presence of diabetes	**X9**	Absent	0
		Diabetes of I type	1
		Diabetes of II type	2
Glycemic level	**X10**	Nrml 3.3-5.5 mMol/L	0
		Light 6.7-8.2 mMol/L	1
		Medium 8.3-11.0 mMol/L	2
		Severe more than 11.0 mMol/L	3
X-ray signs (CT, MRI)	**X11**	Swelling of the mucous membrane	1
		Fluid level	2
		Cyst	3
		Alien body/ Mycetoma	4
		Tumor process/ Osteoma/ Polyps	5
Smoking	**X12**	No	0
		Yes	1
Flu infection	**X13**	Wasn't sick	0
		1-2 times a year	1
		3-4 times a year or more	2

Table 2. Initial data for the calculation of operational characteristics in the classification of the average (R-2) degree of risk of chronic rhinosinusitis recurrence, relatively mild (R-1) and severe (R-3) degrees

Degree of risk of CRS recurrence	The number of patients for the verification of the RCRS model with classification R-2, relative to R-1, R-3 among patients with chronic rhinosinusitis				
	True positive R 1, R 3 (a_{213})	Sum R 1, R 3	False positive R 2 (b_{213})	Sum R 2	Total ($a_{213}+b_{213}$)
R 1	28	66	-	4	70
R 3	38		4		
R 2	False negative (c_{213})	6	True negative (d_{213})	128	Total ($c_{213}+d_{213}$) 134
Total	$a_{213}+c_{213}$ 72		$b_{213}+d_{213}$ 132		$a_{213}+b_{213}+c_{213}+d_{213}$ 204

Table 3. Generalized operational characteristics of the mathematical model for predicting the risk of chronic rhinosinusitis recurrence

Designation of operational characteristics	Levels of risk of chronic rhinosinusitis recurrence			Average values of operational characteristics
	R-1	R-2	R-3	
Se, %	98,8	91,6	97,5	95,9
Sp, %	83,8	96,9	97,4	92,7
PPR, %	97,1	94,2	99,3	96,8
NPR, %	92,8	95,5	90,4	92,9
LR+	6,09	29,5	37,5	24,3
LR-	0,014	0,08	0,025	0,039
Prediction accuracy, %	96,5	95,09	97,5	96,3

Se - sensitivity, Sp - specificity, PPV - positive predictive value, NPV - negative predictive value, LR+ - likelihood ratio of a positive test, LR- - likelihood ratio of a negative test.

To determine the diagnostic value of the proposed model, based on the obtained results, we calculate the sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), the likelihood ratio of a positive test (LR+), the likelihood ratio of a negative test (LR-) and prediction accuracy % of the proposed mathematical model.

Let's consider an example of calculating operational characteristics (Se, Sp, PPV, NPV, LR+, LR- and prediction accuracy) of the proposed mathematical model on the example of an average (R-2) degree of risk of developing of chronic rhinosinusitis recurrence (table 2).

The sensitivity of detection of RCRS R-2 relative to R-1, R-3 was calculated according to the formula

$$Se_{213}= (a_{213}/(a_{213}+c_{213}))*100\%;$$

Considering the numerical values (Table II), we get

$$Se_{213}= (66 / (66+6))*100\%=(66/72)*100\%=91,6\%.$$

The determination of the specificity of the detection of RCRS R-2 in relation to R-1, R-3 was carried out according to the following formula:

$$Sp_{213}=(d_{213}/ (b_{213}+d_{213}))*100\%$$

$$Sp_{213}=(128 / (4+128))*100\%=(128/132)*100\%=96,9\%.$$

The Positive Predictive Value (PPV) in the classification of patients with RCRS R-2 relative to R-1, R-3:

$$PPV_{213} =(a_{213} / (a_{213}+ b_{213}))*100\%$$

$$PPV_{213}=(66 / (66+ 4))*100\%=(66/70)*100\%=94,2\%.$$

The probability of identifying patients with RCRS R-2 with a positive classification result, relative to R-1, R-3, is 94.2%.

The Negative Predictive Value (NPV) of the classification of patients with R-2 relative to R-1, R-3:

$$NPV_{213} =(d_{213}/ (c_{213}+ d_{213}))*100\%$$

$$NPV_{213}=(128 / (6+128))*100\%=(128/134)*100\%=95,5\%.$$

Therefore, the probability of identifying patients with RCRS R-2 with a negative classification result, relative to R-1, R-3, is 95.5%.

The likelihood ratio of a positive test of detecting patients with RCRS R-2 relative to R-1, R-3 is calculated as follows:

$LR+_{213}=(Se_{213}/ (100-Sp_{213}))$

$LR+_{213}=(91,6 / (100-96,9))= 91,6/3,1=29,5$

Based on this, the probability of receiving a positive result of RCRS in patients with R-1, R-3 is 29.5 times greater, compared to the probability of a positive result in patients with R-2.

The likelihood ratio of a negative test of detecting patients with R-2 relative to R-1, R-3 will be:

$LR-_{213}=((100-Se_{213})/ Sp_{213})$

$LR-_{213}=((100-91,6)/ 96,9)=0,08$

which means the possibility of obtaining a negative result of RCRS in patients with R-2 is 12.5 times greater (1/0.08), compared to the probability of a positive result in patients with R-1, R-3.

The accuracy of RCRS R-2 of the proposed mathematical model was calculated according to the formula:

Accuracy of $RCRS_{213}=((a_{213}+ d_{213})/(a_{213}+ b_{213}+c_{213}+ d_{213}))*100\%$

Accuracy of $RCRS_{1234}=((66+128)/(66+4+6+128))*100\%=(194/204)*100\%=95,09\%$

and accordingly, the share of the correct prediction results of CRS R-2 is 95.09%.

Similarly, the calculation of operational characteristics was carried out for the second and third degrees of risk of chronic rhinosinusitis recurrence (R-2 and R-3). The obtained operational characteristics of the mathematical model for predicting the risk of recurrence of chronic rhinosinusitis (R-1, R-2, R-3) and their average values are shown in Table 3.

In order to determine the prognostic value of the RRCRSR model, ROC- analysis was performed, ROC curves were obtained for mild (R-1), medium (R-2), and high (R-3) degrees of risk of CRS recurrence, and the corresponding areas under the curves (AUC) were determined for assessment of the quality of the proposed mathematical model.

Previously, we examined 204 patients aged 18 to 80, including 107 women and 97 men, with a diagnosis of chronic rhinosinusitis, who were undergoing inpatient treatment in the otolaryngology department of the communal noncommercial enterprise "Ternopil Regional Hospital" under Ternopil Regional Council.

It is recommended that the diagnostic test be both highly sensitive and highly specific. However, this rarely happens in practice. To achieve a compromise between sensitivity and specificity, to adequately choose a diagnostic criterion and distinguish patients (sick) from healthy, it is recommended to build a ROC curve.

After constructing the ROC curve, the corresponding data of the integral indicator of the area were obtained.

As can be seen from fig. 2, the area under the curve AUC1 =0.906 (classification quality of R-1 RRCRSR); AUC2 =0.928 (classification quality of R-2 RRCRSR); AUC3 =0.993 (classification quality of R-3 RRCRSR). Therefore, according to the ROC analysis, the prediction of R-1, R-2 and R-3 degrees of risk of developing of CRS recurrence is excellent.

DISCUSSION

The use of the mathematical model proposed by us, which considers possible risk factors for the development of CRS recurrence, provides the possibility of early prediction of potential complications and the probability of disease recurrence. This, in turn, contributes to early diagnosis and the choice of more effective and less harmful methods of CRS treatment.

The concept of reliability in medicine is multifaceted and includes a set of criteria for evaluating the results of diagnostic studies [7]. The main components of this complex include the following operational characteristics: sensitivity, specificity, prediction value of positive and negative results. Less relevant indicators of accuracy and the ratio of the likelihood of a positive and negative test. Each of these criteria is a specific statistical indicator.

Sensitivity indicator (Se) – shows the proportion of persons with a positive test result among persons with the disease under investigation; or the proportion of really sick people in the examined population who, according to the results of a diagnostic test, are found to be sick.

Specificity (Sp) indicates the proportion of individuals with a negative test result among individuals without examined disease or the proportion of those with a negative diagnostic test among all individuals without the disease.

In our case, the mathematical model shows a sensitivity and specificity of more than 90% (Se – 95.9%, Sp – 92.7%), which indicates that more than 90% of cases were diagnosed correctly.

The positive predictive value (PPV) indicates the probability of a disease with a positive (pathological) test result. The negative predictive value (NPV) indicates the probability of the absence of the disease with a negative (normal) test result.

The higher the indicators of specificity and sensitivity, the greater the value of PPV and NPV. In our case, Se is 95.9%, Sp is 92.7%, respectively, PPV is 96.8%, and NPV is 92.9%.

Based on the obtained results, we believe that the accuracy of predicting the risk of chronic rhinosinusitis recurrence is 96.3%, and the constructed ROC curves approach the upper left corner (AUC1 = 0.906 (classification quality of R-1 RRCRSR); AUC2 = 0.928 (classification quality of R -2 RRCRSR); AUC3 =0.993 (classification quality of R-3 RRCRSR)). All this indicates the strong diagnostic validity of this model and suggests that the model can be a useful application for doctors in identifying patients with different degrees of risk of developing chronic rhinosinusitis recurrence and making decisions about its treatment.

CONCLUSIONS

1. The multivariate regression model, which takes into account a number of predictors of the risk of CRS recurrence, makes it possible to predict potential complications and the possibility of disease recurrence with high values of sensitivity (95.9%), specificity (92.7%) and accuracy (96.3%) .
2. The construction of ROC-curves with the evaluation of the corresponding areas allows us to assert the excellent classification quality of mild (R-1; AUC1 =0.906), medium (R-2; AUC2=0.928) and severe (R-3; AUC2=0.993) degrees the risk of chronic rhinosinusitis recurrence, which allows timely and correct diagnosis of the severity of the inflammatory process, which makes it possible to choose the optimal method of treatment.
3. The application of this technique can be used for the development of medical calculators for assessing the severity of the risk of chronic rhinosinusitis recurrence, as well as for the design of relevant information and diagnostic systems in otolaryngology.

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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

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ORIGINAL ARTICLE

CONTENTS

Adenosine triphosphate binding cassette transporters G5 and G8 early diagnostic tools for cardiovascular disease in human

Amina A. B. Al-Dejeli, Murtadha A. AL-Mudhafar, Imad K. A. AL-Sabri
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ABSTRACT

Aim: The current study was designed to investigate the role of ABCG5 and ABCG5 in serum with normal and expected cardiac complaints with CVDs as individual early diagnostic tools.

Materials and Methods: Data was collected in paper form and recorded from 100 healthy personals and 100 personals suspected with CVS after take the case history and clinical signs in private clinical hospital and the serum was collected for measurements the activity of ABCG5 and ABCG5 by used ELISA reader and the results illustrated that activity of ABCG5 and ABCG5 in all aged groups.

Results: Activity of ABCG5 and ABCG5 in all aged groups periods in patient person male and female significant decrease as compared with same age in same period of live, so that the researched depicted that can used the serum activity of ABCG5 and ABCG5 as a diagnostics tools for atherosclerotic cardiovascular disease.

Conclusions: We identified areas of further exploration on cholesterol transport related with CVD risk and concluded that changes in the Adenosine Triphosphate Binding Cassette transporters mainly G5 and G8 early diagnostic tools for cardiovascular disease in Human. We correlated areas of farther disquisition on nutrient cholesterol and CVD threat, in the included trials, healthy grown-ups consumed high doses of dietary cholesterol.

KEY WORDS: Cardiovascular diseases, ABCG5, ABCG8

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INTRODUCTION

Cardiovascular disease (CVD) is the most important prevalent disease in character in determining the general factors of movement in nature, disability and profitable loss, especially in advanced industrial countries. It has been proven that dyslipidemia, such as high serum total cholesterol and triglyceride level [1], is one of the most important risk factors for cardiovascular disease. Serum dyslipidemia is thought to result from the relationship and overlap between environmental and genetic factors [2]. There are many research evidence in clinical trials and molecular biology in selective susceptibility to cardiovascular diseases consistent with life-scales, such as excessive smoking [3], health and age status [4], exercise [5], obesity [6] and psychological effects [7]. Groups of transport proteins such as adenosine triphosphate (ATP) – binding cassette (ABC) have been investigated and found to have a critical role in cardiovascular diseases such as high blood pressure caused by atherosclerosis and heart attacks as a result of excessive smoking. These proteins play a role in regulating cholesterol level, blood pressure regulation, physiological activity of endothelial cells, inflammatory reaction of blood vessels, and platelet production, it also has the effect of ABC cassette carrier having similar effects to transporter groups. Of the most famous types are ABCA1, ABCG5 and ABCG8, those were originally responsible for genetic disorders e.g. Tangiers conditions and sitosterolemia [8]. These disorders have helped to understand the role of these transporters in regulating cholesterol flow and its relationship to heart disease including atherosclerosis and cardiovascular disorders [9]. Lots of data have shown that the family of ABC transporters including ABCG5 and ABCG8 has a close relationship with thermodynamic processes in living bodies by altering the metabolic activity of sterols in the blood. Genetically, ABCG5 and ABCG8 are found on chromosome 2p21, each encoding a 'semi-carrier' protein with nonfunctional activity in the monomeric state [10]. Both genes interfere with adipocytes by regulating the activity of Leptin leading to the complete downregulation of the ABCG5/G8 transporter as a positive feedback mechanism, and historically the first study on cytosterolemia showed that mutation in both ABCG5 and ABCG8 interfered with this disorder in vivo. A rare mutation in these genes results in a loss of function resulting in increased production of sitosterol from dietary intestinal absorption. Clinically it has been investigated that the ABCG5 and ABCG8 transporters are closely related to the incidence of atherosclerotic cardiovascular disease,

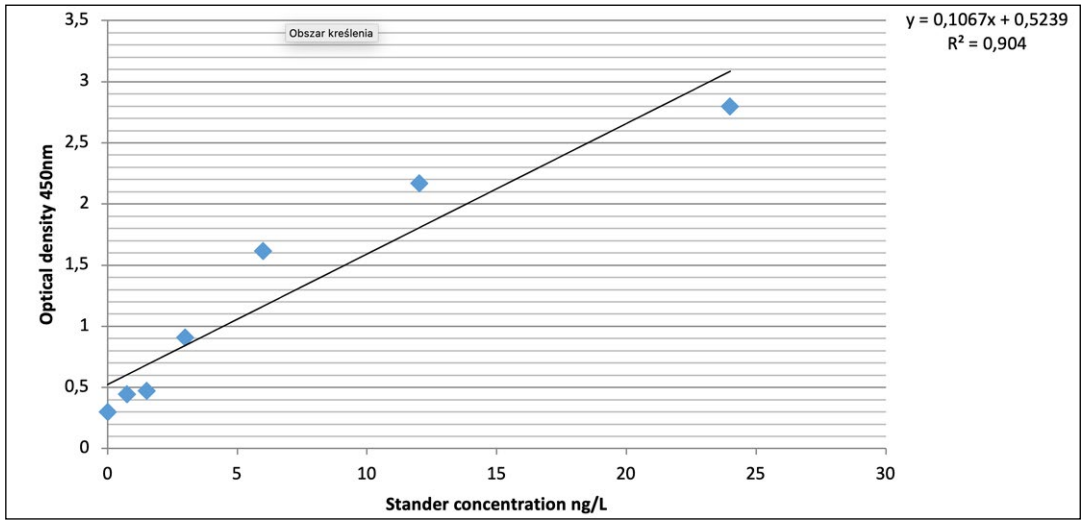

Fig. 1. Standard curve: Human ATP-binding cassette, Sub-family G, Member 5.

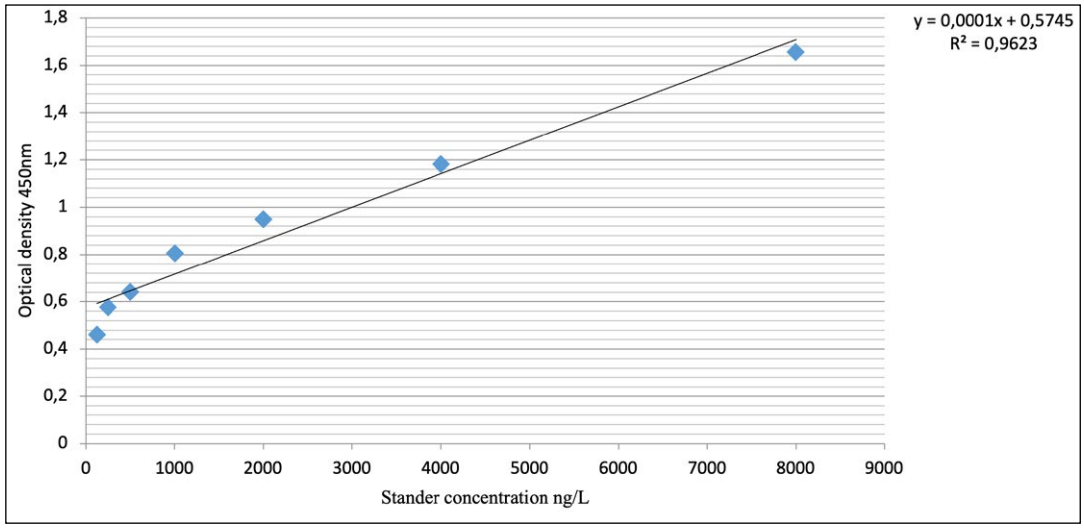

Fig. 2. Standard curve: Human ATP-binding cassette Sub-family G Member 8.

angina pectoris and myocardial infarction. ABCG5/G8 protein physiologically as expressed in enterocytes especially enterocytes and hepatocytes [11]. These transport processes are responsible for the synthesis of cholesterol sterols that flow into living cells and then are excreted with the disposable faces. Experimentally, the ABCG5/G8 transporter knockout model showed an increase in plasma cholesterol concentration within 2-3 above the normal range. However, the gene overexpression of these transporters takes on potentially lethal roles in lowering the cholesterol level and then lowering the lesion of aortic atherosclerosis [12]. Therefore, the current study was designed to investigate the role of ABCG5 and ABCG5 in serum with normal and expected cardiac complaints with CVDs as individual early diagnostic tools.

AIM

The current study was designed to investigate the role of ABCG5 and ABCG5 in serum with normal and expected cardiac complaints with CVDs as individual early diagnostic tools.

MATERIALS AND METHODS

The research was conducted with case-control study design. At the appointment of patients, written informed consent was obtained, a standardized medical history was taken, and clinical examinations were performed. Data was collected in paper form and recorded from 100 healthy personals regarded as control groups and 100 personals suspected with CVS after take the case history and clinical signs in private clinical hospital regarded as a patient group and the serum was collected for measurements the activity of ABCG5 and ABCG5 by used enzyme-linked immunosorbent assay, technique used Human research kit from Bioassay technology laboratory (Korain Biotech Co., Ltd, Shanghai), and later the concentration was calculated using the standard curve for ABCG5 and ABCG5 respectively (Fig.1., Fig.2.).

STATISTICAL ANALYSIS

Statistical analysis of the experimental results was conducted using SPSS version 13.00. The data were expressed as mean ± standard errors (SE) and P value<0.01 was considered statistically among means of group.

Table 1. The mean±SEM values of level of Human ATP-binding Cassette Sub-family G Member 5

Parameters (Gender) Groups (Years)	Human ATP-Binding cassette sub-family G member 5	
	Female (ng/l)	Male (ng/l)
15-30 patient	11.99±0.23 ^{c}	15.58±0.31 ^{c}
31-45 patient	11.78±0.34 ^{c}	14.86±0.34 ^{c}
46-60 patient	9.71±0.60 ^{bc}	11.21±0.24 ^{b}
61-75 patient	8.68±0.57 ^{ab}	9.96±0.41 ^{b}
75- above patient	6.60±0.36 ^{a}	7.51±0.83 ^{a}
15-30 control	15.10±1.06 ^{d}	19.04±0.91 ^{d}
31-45 control	17.22±0.91 ^{d}	19.17±0.45 ^{d}
46-60 control	15.53±2.49 ^{d}	20.33±0.86 ^{d}
61-75 control	15.70±0.77 ^{d}	15.81±1.53 ^{c}
75- above control	16.94±0.68 ^{d}	10.90±0.89 ^{b}

$^{a, ab, b, bc, c, d}$ - significance ($p \geq 0.01$) within same gender.

Table 2. The mean±SEM values of level of Human ATP-binding Cassette Sub-family G Member 8

Parameters (Gender) Groups (Years)	Human ATP-Binding cassette sub-family G member 8	
	Female (ng/l)	Male (ng/l)
15-30 patient	1096.80±45.13 ^{cd}	1390.00±64.59 ^{c}
31-45 patient	1011.62±13.30 ^{c}	1207.57±59.48 ^{bc}
46-60 patient	956.22±18.86 ^{bc}	1250.00±77.74 ^{bc}
61-75 patient	780.60±22.89 ^{b}	989.40±20.96 ^{b}
75- above patient	558.80±34.89 ^{a}	646.80±91.82 ^{a}
15-30 control	4213.40±21.94 ^{h}	7866.25±94.10 ^{h}
31-45 control	3155.60±57.72 ^{g}	7247.40±216.76 ^{g}
46-60 control	2385.00±37.85 ^{f}	4068.33±277.77 ^{f}
61-75 control	1645.00±104.08 ^{e}	3376.50±106.54 ^{e}
75- above control	1290.00±41.88 ^{d}	2197.75±95.93 ^{d}

$^{a, b, bc, c, cd, d, e, f, g, h}$ - significance ($p \geq 0.01$) within same gender.

RESULTS

The results in tables 1 and 2 and in figures 3 (A-B) and 4 (A-B) show the concentration of human ABCG5 and ABCG8 activity in serum, respectively. The results illustrated that the activity of ABCG5 and ABCG8 in all age groups showed a significant decrease in all female and male patient groups as compared with all ages of control groups, additionally, the results showed a significant graded decrease in female and male patient groups within increase the older ages when compared with same gender.

DISCUSSION

Cholesterol is one of the main chemical compounds involved in the normal physiological function in living bodies, and also plays a major role in the development of vascular and vascular problems such as high blood pressure and atherosclerosis. Chylomicron is the main carrier of cholesterol lipoprotein in the bloodstream because of its lipid solubility and cannot be carried by the blood. It is also an important component of the cell membrane and is a precursor to most steroid hormones in living organisms [13]. Cholesterol cannot be metabolized to carbon dioxide and water in humans. Instead, the entire cycle of sterols is eliminated from the body [14] by converting to corrosive acids, which are excreted in the stool or erode cholesterol, which transports it to the intestines for disposal. Bile salts are mainly used to emulsify fatty acids and monoacylglycerols and package them into micelles [15], along with fat-soluble vitamins, phospholipids and cholesteryl esters, to reabsorb the villi in the small intestine. The end products of cholesterol utilization are bile acids [16], ABCG5/8 ATP and Mg2 were used as cofactors in the active transport of sterol-carrying across cell membranes [17]. However, it plays an important role in the tissue transport of phytosterols and cholesterol between the extracellular and intracellular fluid in the intestinal and hepatic cells and the secretion of sterols with bile [18]. Later any disturbance in the mechanism of cholesterol metabolism leads to a disturbance in the transport of cholesterol and phytosterols in the intestinal cells [19], and this causes an imbalance in the process of secretion of dietary

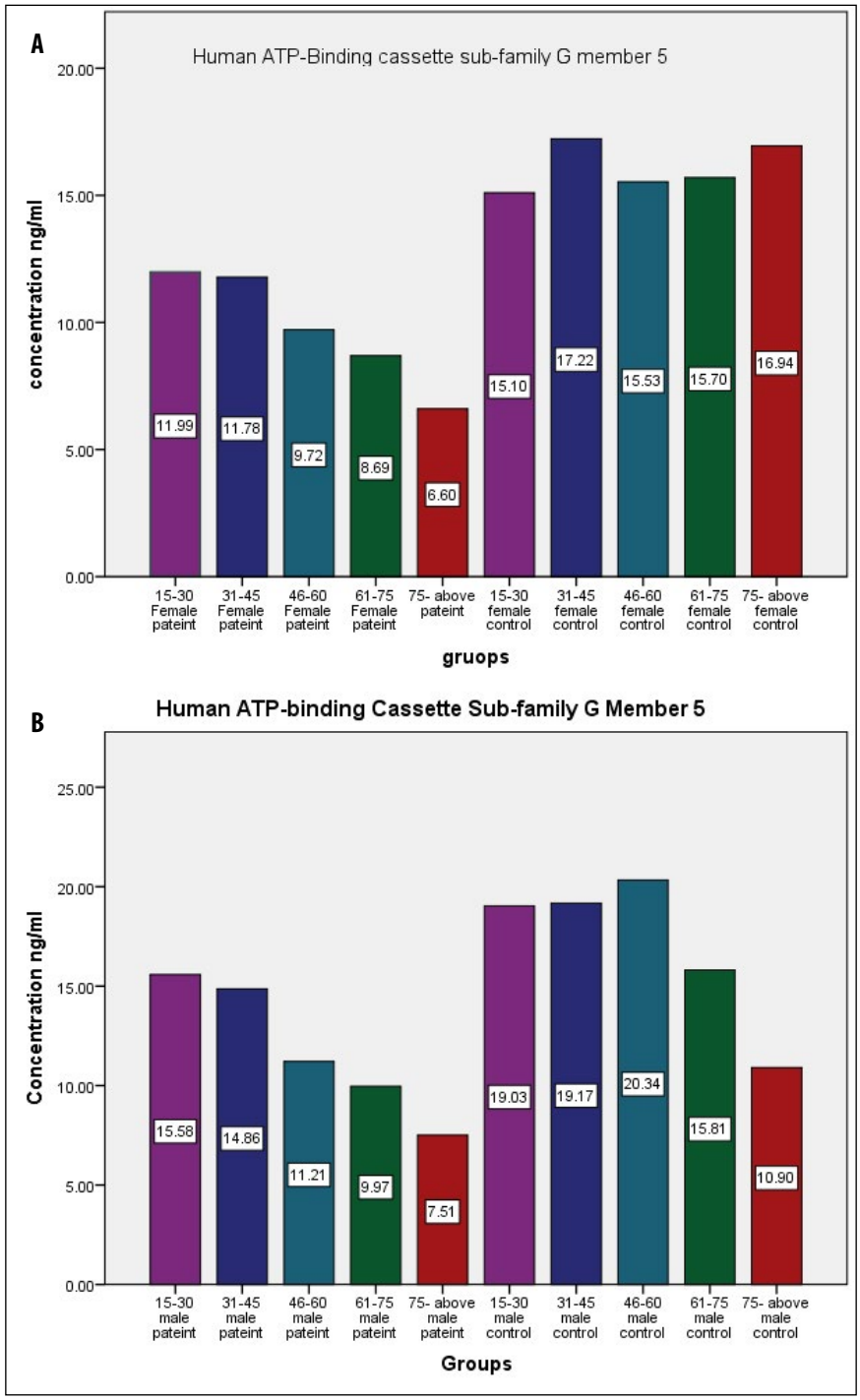

Fig. 3. Human ATP-binding Cassette Sub-family G Member 5 (A: in Female; B: in Male).

sterols leading to the development of hypercholesterolemia, a significant increase in phytosterols in the blood stream and acceleration of the development of cardiovascular diseases blood vessels such as atherosclerosis and coronary artery disease. Various studies have shown that any disturbances in ABCG5/8 gene expression in BCG5/8 mice in the cell membrane of enterocytes and hepatocytes will reverse the synthesis of the ABCG5/8 transporter and the development of cytosterols, a condition in which cholesterol and sterols are increased. Which leads to a problem with the heart and blood vessels [20].

CONCLUSIONS

In this review, we identified areas of further exploration on cholesterol transport related with CVD risk and concluded that changes in the Adenosine Triphosphate Binding Cassette transporters mainly G5 and G8 early diagnostic tools for cardiovascular disease in Human. In this review, we correlated areas of farther disquisition on nutrient cholesterol and CVD threat, in the included trials, healthy grown-ups consumed high doses of dietary cholesterol.

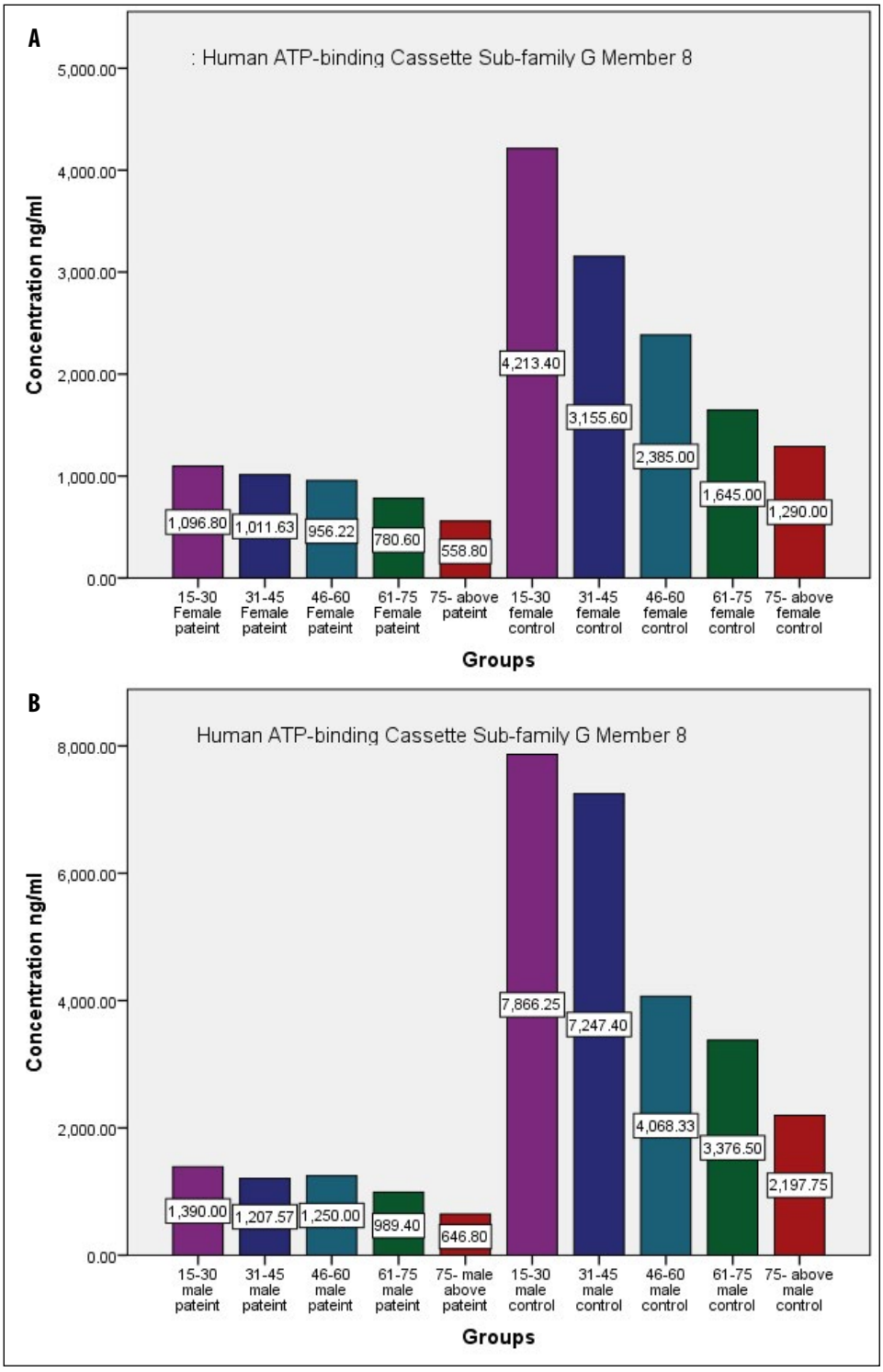

Fig. 4. Human ATP-binding Cassette Sub-family G Member 8 (A: in Female; B: in Male).

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Quantitative morphological analysis of age structural changes in prostate of experimental animals with ethanol poisoning

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ABSTRACT

Aim: To find out the age remodeling of the structural components of the prostate gland at alcohol poisoning using quantitative morphological analysis.

Materials and Methods: The structure of the prostate gland of 4 white male rats groups were morphologically investigated. The 1 group included 30 control intact animals aged 8 months, the 2-nd group – 30 rats aged 24 months, the 3-rd group – 30 8-month-old animals with ethanol intoxication, and the 4-th group included 30 24-month-old rats with the specified simulated pathology. Ethanol intoxication was modeled by intragastric administration of 30% ethyl alcohol solution at a dose of 20 ml/kg once daily for 28 days. Rats were euthanized by bloodletting under general thiopental anesthesia 28 days after the beginning of the experiment. The area of glands, the height of glandular epithelial cells, the area of their nuclei and cytoplasm, the nuclear-cytoplasmic ratio in these cells and the stromal-parenchymal ratio in the organ were studied using light microscopy and were determined morphometrically. Morphometric parameters were processed statistically.

Results: It was established that with age in the intact prostate of laboratory sexually mature white male rats, the area of glands, the height of glandular epitheliocytes, the area of their nuclei and cytoplasm, with the stability of nuclear-cytoplasmic ratios in the epithelial cells of the glands, significantly decreases, and the stromal-parenchymal ratio in the organ under study increases. Long-term ethanol poisoning leads to pronounced structural changes in the prostate, which is characterized by pronounced atrophy of the glandular epithelium, a decrease in the area of the glands, a decrease in the height of epithelial cells, a violation of nuclear-cytoplasmic relations in them, an increase in stromal-parenchymal ratio, and a prominent growth of the muscle-elastic stroma. The revealed structural changes of the studied components of the prostate dominated in 24-month-old experimental animals.

Conclusions: Morphological analysis of the prostate gland established that morphometric and morphological changed significantly according to the age and were depend on the ethanol poisoning.

KEY WORDS: prostate gland, ethanol poisinisng, age, morphology, morphometry

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INTRODUCTION

Alcoholism is a widespread pathology that hs possibility to spread among people in the worlds, it often leads to disability and mortality of the population and is an important medical and social problem. Prolonged ethanol intoxication damages almost all organs and systems, the degree of functional and structural disorders of which is different and depends on the duration and severity of intoxication [1-4].

Ethanol and its metabolites have a powerful membranotropic effect, are complicated by increased lipoperoxidation, decreased antioxidant protection, deterioration of microcirculatory bed circulation, disruption of metabolic processes in the body, structural and functional changes in all organs and systems [5, 6].

It should be noted that until today, researchers are interested in the structural components of the prostate gland, its changes in pathological conditions [7-10]. In modern medical and biological scientific literature, there is not enough data on age-related changes in the structures of the prostate gland in conditions of long-term ethanol poisoning [11-13]. The study of the above will help to expand modern ideas about the structural and functional phenomena that occur in the prostate gland under the conditions of long-term alcohol consumption.

Because the prostate gland is an accessory gland of the male reproductive system that is found only in mammals [12, 14], it seems logical to use experimental animal model to investigate the mechanisms of ethanol poisonign.

Morphometry is widely used method to study the architectonics of the blood vessels and intraorgan vascular microcirculatory bed and the structure of intact organs and in various pathological conditions [14]. At the same time, it is known that the age-related

features of remodeling of the structural components of the prostate gland during long-term ethanol poisoning have not been studied in detail. When the structures of the prostate gland are damaged, male fertility, urination, hormonal homeostasis, and immune protection of the urinary system is deteriorate and decrease [15].

AIM

To find out the age remodeling of the structural components of the prostate gland at alcohol poisoning using quantitative morphological analysis.

MATERIALS AND METHODS

The work was performed on 120 laboratory sexually mature male rats, which were divided into 4 groups: 1 group included 30 control intact animals aged 8 months, the 2-nd group – 30 rats aged 24 months, the 3-rd group – 30 8-month-old animals with ethanol intoxication, and the 4-th group included 30 24-month-old rats with the specified simulated pathology. Experimental animals were the same in weight: 8-month-old rats (166-170 g), 24-month-old rats (295-300 g).

Ethanol intoxication was modeled by intragastric administration of 30% ethyl alcohol solution at a dose of 20 ml/kg once daily for 28 days. According to laboratory practice, intragastric administration of medicinal agents to experimental animals does not require anesthesia.

Rats were euthanized by bloodletting under general thiopental anesthesia 28 days after the beginning of the experiment using institution-approved methods. The dose of ethanol was calculated for each animal separately according to its weight.

Cut pieces were fixed in Bouin's solution, passed through ethyl alcohols of increasing concentration and placed in paraffin blocks. After deparaffinization, microtome sections with a thickness of 5-6 μm were stained with hematoxylin and eosin according to Van Gieson, Mallory, Masson, and toluidine blue [16] and were studied using light microscopy and morphometrical method.

Quantitative morphological analysis of prostatic gland was used to determine the area of glands, the height of glandular epithelial cells, the area of their nuclei and cytoplasm, the nuclear-cytoplasmic ratio in these cells, and the stromal-parenchymal ratio in the organ. Morphometric parameters were processed statistically.

50 measurements were performed on each histological specimen. Morphometry was performed with the help of a light microscope «Olimpus BX-2» with a digital video camera and a package of application programs «Video Test 5.0» and «Video size 5.0».

Statistical processing of digital data was carried out using Excel (Microsoft, USA) and STATISTICA 6.0 (Statsoft, USA) software. The analysis of the research results was carried out using parametric statistical methods, the choice of which was based on the correctness of the distribution of values. The processing of the results was carried out in the systematic statistical research Department of I. Horbachevsky Ternopil National Medical University, Ministry of Health of Ukraine. For all indices, the average arithmetic mean of the sample (M) and the error of the average arithmetic mean (m) were calculated. The reliability of the difference in values between independent quantitative values was determined in the case of a normal distribution according to the Student's t-test, and it was considered statistical at a value of $p < 0.05$ [17, 18].

Laboratory animals were kept on the standard ration of the vivarium of I. Horbachevsky Ternopil National Medical University, all manipulations were carried out in compliance with the rules of the «European Convention on the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes» (Strasbourg, 2005), according to the Law of Ukraine No. 3447-IV «On the Protection of Animals from Cruelty» dated February 21, 2006, and due to the requirements of the Commission on Bioethics of I. Horbachevsky Ternopil National Medical University.

RESULTS

The rats' prostate gand has a distinct morphological structure in spite of similar embryological origin, tissue and cellular composition, and molecular characteristics to human prostate gland [19-21].

As a result of morphological investigations, it was found that in group of the control animals the prostate gland was represented as lobulated organ and consisted of an acini and ducts with three types of epithelial cells: basal cells, columnar luminal secretory cells, and neuroendocrine cells [19]. The last had neural and epithelial characteristics, and were found in very small number between basal cells, were present in ducts and acini [20, 21]. The stromal component was not very well developed, it contains few smooth muscle cells [22].

Lobes of the prostate gland were surrounded by a thin connective tissue capsule, which was lined by simple squamous epithelium (mesothelium); capsule separated lobes from each other by fibrous connective tissue. The acini, which are the components of the prostatic lobes, were surrounded by a delicate and thin fibromuscular tunica, and were embedded in a loose connective tissue with large number of collagen fibers and few stromal cells [22, 23].

Table 1. Morphometric parameters of the structural components of the prostate gland (M±m)

Indicators	groups			
	1 (control)	2 experimental	3 experimental	4 experimental
Glands area, μm²	137452,3±724,2	115349,6±975,2***	33574,9±204,3***	22242,7±183,6***
Height of glandular epithelial cells,	16,9±0,3	14,8±0,3**	9,43±0,09***	6,51±0,05***
Nuclei area of epithelial cells, μm²	36,7±0,4	28,1±0,3**	23,8±0,3***	14,9±0,2***
Cytoplasm area of epithelial cells, μm²	262,4±2,1	220,3±1,8***	82,1±0,5***	45,2±0,4***
Nuclear-cytoplasmic ratio	0,14±0,01	0,13±0,01	0,29±0,02***	0,33±0,02***
Stromal-parenchymal ratio	0,14±0,01	0,17±0,01*	0,22±0,02**	0,28±0,02***

*-p<0,05; **-p<0,01; ***-p<0,001 comparatively to the 1-st group.

The morphometric parameters of the studied structures of the prostate gland are presented in Table 1.

A comprehensive analysis of the obtained quantitative morphological indicators established that they changed significantly according to the age and were depend on the ethanol poisoning. It was found that age led to remodeling of the studied structures of the prostate gland, which was confirmed by their morphometric indicators. Thus, the glands area of the organ in 24-month-old male laboratory white rats (the second experimental group) with a pronounced statistically significant difference (p<0.001) decreased by 16.1%, the height of glandular epithelial cells – by 10.1%, the area of nuclei and the area of the cytoplasm of the studied cells – by 23.4% and 16.0%, respectively. Established changes in the morphometric parameters of glandular epithelial cells indicated their age-related atrophy.

At the same time, the nuclear-cytoplasmic ratio in glandular epithelial cells did not change significantly, which indicated the stability of cellular structural homeostasis. With age, the stromal-parenchymal ratio in the prostate gland increased by 21.4% (p<0.05), which indicated an increase in the number of stromal structures in the examined organ.

With long-term ethanol poisoning, pronounced remodeling of the studied structures of the prostate gland was observed, which was confirmed by a change in their quantitative morphological indicators. Thus, the area of prostate glands in 8-month-old animals under the influence of ethanol decreased statistically significantly (p<0.001) by 4.1 times, in 24-month-old animals – by 5.2 times (p<0.001). The height of glandular epithelial cells changed almost similarly. Thus, in 8-month-old laboratory white male rats of the control group, the specified morphometric parameter was equal to (16.9±0.3) μm, and in ethanol poisoning – (9.43±0.09) μm. A statistically significant difference (p<0.001) was found between the given quantitative morphological indicators.

At the same time, the last morphometric parameter was smaller than the previous one by 44.2%, in 24-month-old experimental animals this decrease was 56.0% (p<0.001). The area of the nuclei of epithelial cells and the area of their cytoplasm changed almost similarly. Thus, the area of the nuclei of glandular epithelial cells in 8-month-old experimental animals with ethanol poisoning was statistically significantly (p<0.001) reduced by 35.1%, in 24-month-old animals by 46.9% (p<0.001), the area of cytoplasm of the studied cells was changed by 68.7% and 79.5% (p<0.001), respectively.

Uneven changes in the morphometric parameters of the nuclei and cytoplasm of glandular epithelial cells led to violations of the ratios between the indicated components of the nucleus and cytoplasm in the studied cells. Thus, in 8-month-old white rats, this morphometric parameter under the influence of ethanol increased with a high degree of statistically significant difference (p<0.001) from (0.14±0.01) to (o.29±0.02), i.e. in 2.07 times, in 24-month-old animals – 2.5 times (p<0.001). The established changes in the given morphometric parameters indicated a violation of structural cellular homeostasis.

It was also established that the stromal-parenchymal relations in the prostate gland were also changed in the simulated conditions of the experiment. Thus, in the 3rd experimental group (8-month-old animals with long-term ethanol consumption), the indicated morphometric parameter increased by 57.1% with a pronounced statistically significant difference (p<0.001), in 24-month-old animals – by 64.7% (p<0.001).

DISCUSSION

Light microscopy of the prostate gland during long-term ethanol poisoning showed an expansion, pronounced fullness of mainly venous vessels, and pronounced perivascular and stromal edema. In the venous vessels of the microcirculatory bed, the expansion of intraendothelial gaps, desquamation of the endothelium, swelling and fragmentation of the basement membrane of hemocapillaries, plasmarrhagia of the walls and paravasal tissues were observed. In the lumens of the glands there was a different unequal amount of

secretion, which was characterized by various tinctorial properties. Coagulation of contents was noted in some glands. Growth of the muscle-elastic stroma, reduction of folds and atrophic changes of the glandular epithelium, pronounced reduction of the glandular component of the prostate gland, dystrophic, necrobiotic changes of endothelial cells, epithelial cells, stromal structures, and the appearance of foci of cellular infiltration were noted. The revealed morphological changes prevailed in the prostate gland of 24-month-old laboratory sexually mature white male rats [10].

The conducted research and obtained results showed that with age in the intact prostate gland there is atrophy of glandular structures and a decrease in their number, the number of stromal structures also increases, which was objectively confirmed by an increase in the stromal-parenchymal ratio. Long-term ethanol poisoning leads to more pronounced atrophic processes, a decrease in the area of glands, the height of glandular epithelial cells, the area of their nuclei and cytoplasm, and disruption of cellular structural homeostasis in them. At the same time, the nuclear-cytoplasmic ratio increased markedly. The identified structural changes in the components of the prostate dominated in 24-month-old rats [15].

CONCLUSIONS

The conducted studies and obtained results show that with age in the intact prostate gland of laboratory sexually mature white male rats, the area of the glands, the height of the glandular epitheliocytes, the area of their nuclei and cytoplasm significantly decreases with the stability of the nuclear-cytoplasmic ratio in the epithelial cells of the glands, and the stromal-parenchymal ratio increases in the studied body.

Long-term ethanol poisoning leads to pronounced structural changes in the prostate gland, which is characterized by pronounced atrophy of the glandular epithelium, a decrease in the glands area, a decrease in the height of epithelial cells, a violation of their nuclear-cytoplasmic ratio, an increase in stromal-parenchymal ratio, and a prominent growth of the muscle-elastic stroma. The revealed structural changes of the studied components of the prostate dominated in 24-month-old experimental animals.

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ORIGINAL ARTICLE

CONTENTS

Hand telerehabilitation for polytrauma patients following road traffic accidents

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ABSTRACT

Aim: This study aimed to examine the characteristics of upper limb and shoulder injuries combined with chest trauma in road accident victims and evaluate the effectiveness of telemedical monitoring and a newly developed telerehabilitation model in patient recovery.

Materials and Methods: Our study incorporated 136 medical records of inpatients who had sustained upper extremity and chest injuries, constituting a retrospective group. Additionally, in the main group, we included 73 patients with similar injuries of the upper extremity and chest.

Results: We analyze the functional results between the retrospective group and the main group, providing valuable insights into the effectiveness of traditional rehabilitation versus telerehabilitation. Focusing first on the average time spent on rehabilitation exercises per day, we observe a noticeable difference: while the retrospective group dedicated an average of 29±8 minutes daily, the main group invested more time, averaging 42±4 minutes. The retrospective group reported an average of 12±2 visits, in stark contrast to the main group, which averaged only 4±2 visits. The rehabilitators spent considerably less time with each patient in the main group (92±14 minutes) compared to the retrospective group (263±15 minutes), with a significant difference ($p<0.005$). The discovery in our study that there was no notable statistical difference in the functional outcomes, as evaluated by QuickDASH scores, between patients undergoing telerehabilitation and those receiving traditional rehabilitation is of significant importance.

Conclusions: The findings reveal that telerehabilitation can significantly increase patient engagement in rehabilitation exercises, primarily due to its convenience and accessibility.

KEY WORDS: telerehabilitation, polytrauma, upper limb, chest, road trauma

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INTRODUCTION

Injury remains a significant global health issue as it is associated with high morbidity and mortality in both developed and developing countries, causing approximately 5.8 million deaths worldwide [1]. Research indicates that injury is the leading cause of death, hospitalization, and disability in the first four decades of life [2, 3].

Moreover, research by Briese T. et al. delved into the trends of orthopedic injuries in traffic accident victims, underscoring the profound effect these events have on the victims' health and life quality [4]. Paryavi's studies offer a perspective on the intricacies of injuries to the shoulder area, including the upper limb and shoulder girdle, along with their management [5].

The research authored by Moulaei K. et al., provides an in-depth analysis of telerehabilitation technologies for upper limb disabilities [6]. The study conducted a scoping review by searching databases like Web of Science, PubMed, and Scopus until July 2021. The most widely used services were the evaluation of exercises and musculoskeletal function of patients by therapists, recording of patients' rehabilitation exercises, and prescribing new rehabilitation exercises. The study found that virtual reality technologies, smart wearables, and robots were commonly used in telerehabilitation services. The most important outcomes identified were improvement in musculoskeletal functions, increased patient interest and motivation, and greater adherence to rehabilitation exercises. This comprehensive review underscores the potential of telerehabilitation in providing equitable access to rehabilitation services, improving musculoskeletal function, and empowering individuals with a variety of rehabilitation capabilities.

The study led by Samantha G. Rozevink et al. explores the long-term effects of using an unactuated training device combined with a telerehabilitation platform for upper limb rehabilitation in stroke patients [7]. The study concludes that training effects were still present at six months follow-up, but due to the small sample

size and study design, the results should be interpreted with caution. This research contributes to understanding the potential and limitations of telerehabilitation for long-term recovery in stroke patients.

Chingyi Nam et al. presents a study on the feasibility and effectiveness of a home-based telerehabilitation program for upper limb rehabilitation in stroke patients [8]. This program utilizes an electromyography (EMG)-driven wrist/hand exoneuromusculoskeleton (WH-ENMS) to assist patients in their rehabilitation exercises. The study involved 11 chronic stroke patients who participated in a single-group trial, where their training progress, including frequency and duration, was telemonitored. The study concluded that the home-based self-help telerehabilitation program is feasible and effective for improving the motor function of the upper limb.

While existing scientific research has largely focused on telerehabilitation for stroke patients, the potential benefits of this technology for those recovering from road accidents remain underexplored [9, 10].

AIM

This study aimed to examine the characteristics of upper limb and shoulder injuries combined with chest trauma in road accident victims and evaluate the effectiveness of telemedical monitoring and a newly developed telerehabilitation model in patient recovery. Such insights are crucial for aiding clinical decision-making, formulating treatment strategies and preventive measures, and potentially reducing the incidence of complications and mortality rates.

MATERIALS AND METHODS

Our study incorporated 136 medical records of inpatients who had sustained upper extremity and chest injuries, constituting a retrospective group. Additionally, in the main group, we included 73 patients with similar injuries of the upper extremity and chest. These patients were consecutively enrolled in the study over a 5-year period at the same hospital, from September 2019 to November 2023.

Our analysis focused on patient demographics such as age, gender, specific diagnoses, and the nature of the injuries sustained. We categorized the results based on gender, age groups, and types of road users, and conducted comparative analyses across these groups.

To ensure the confidentiality and protection of the patients' personal data, any identifying information was omitted from the analysis. This data was securely stored in an electronic format, with restricted access to uphold privacy standards.

In our study, the control group, consisting of 136 patients, underwent traditional rehabilitation procedures for a period of three weeks following their injury. This group received the usual care, which encompassed generally accepted methods of rehabilitation therapy. These methods included treatments like massage, myostimulation, and exercises conducted in a pool.

On the other hand, a total of 73 subjects were enrolled in the telerehabilitation group. This group also participated in the study for a three-week period post-injury. However, instead of the conventional rehabilitation methods, they were trained with a specially designed set of exercises using a prototype device intended for home use. This approach aimed to assess the efficacy and practicality of telerehabilitation in comparison to traditional rehabilitation methods.

To evaluate the effectiveness of rehabilitation in both groups, we utilized the QuickDASH (Disabilities of the Arm, Shoulder, and Hand) questionnaire [12], a universally recognized tool for assessing functional limitations of the arm, shoulder, and hand. This method encompasses 11 criteria designed to evaluate physical capabilities and symptoms in patients with either single or combined injuries of the upper limb and shoulder girdle.

Each question in the QuickDASH offers five response options, reflecting the varying degrees of difficulty patients experience while performing specific tasks. These responses range from 1, indicating the ability to perform the task freely, to 5, denoting that the task is impossible to perform. The intermediate options include 2 for minor difficulties, 3 for moderate difficulty, and 4 for tasks that are very difficult to perform. This graded approach allows for a nuanced assessment of the rehabilitation process's effectiveness.

For home remote monitoring, 73 subjects in the test group used a portable device equipped with an Axis-sensor, temperature, volume, and pulse sensors, which were attached to the injured limb (Fig 1.). The device's software enabled the monitoring of several key parameters: biomechanical movement, local temperature, the frequency of active movements, and the volume of the injured limb.

During the execution of prescribed home exercises, data from the subjects' portable devices were continuously recorded. This data was then transmitted to a server via a cellular Internet connection. Additionally, the information was sent to the personal smartphones of the rehabilitation doctors. The data was presented both in digital form and graphically, allowing for real-time monitoring and assessment of the rehabilitation progress. This advanced monitoring method aimed to enhance the effectiveness and customization of the rehabilitation process.

Fig. 1. Portable device equipped with sensors.

The tele-rehabilitation protocol in our study included several key components:

1. Fixation of the Portable Device: Patients were instructed to attach the portable device to their injured limb. This device was integrated with customized software specifically designed for monitoring various health parameters.
2. Home Exercises for Rehabilitation:
- Passive Flexion-Extension in the Elbow Joint: This exercise involved gentle bending and straightening of the elbow, done passively without the patient's muscular effort.
- Active Flexion-Extension in the Elbow Joint: Unlike the passive exercise, this involved the patient actively bending and straightening their elbow, using their own muscle strength.
3. Pain Assessment Training: All patients were trained to assess and report their pain levels using a 10-point scale. This subjective assessment was crucial for monitoring their progress and adjusting rehabilitation exercises accordingly.
4. Software Utilization: The software used in this model served as a personal rehabilitation record. It facilitated the storage of health information and communication between the patient and health professionals.
5. Basic Measures Recorded: For each patient, the software recorded essential health metrics, including blood pressure, limb volume, waist and chest measurements, pulse, weight, height, sex, blood oxygen saturation, local temperature, movement activity, and the condition of connective tissue.

It's important to note that the initial implementation of this telerehabilitation model did not involve the prescription of medications or joint injections. This approach was focused on the use of telemedicine and physical rehabilitation exercises to aid recovery.

In our study, each patient's rehabilitation process was highly personalized. Based on the individual condition of each patient, the rehabilitation doctor crafted a tailored rehabilitation plan for every subject. This plan included a detailed activity schedule, ensuring that the rehabilitation exercises were aligned with the patient's specific needs and capabilities.

Key to this approach were personal goals set for daily movement activity and various steps in the rehabilitation program. These goals were designed to be both achievable and progressive, helping patients to gradually regain their physical capabilities.

The distinction between the telerehabilitation group and the control group in our study was a pivotal factor in assessing the effectiveness and benefits of these two approaches to rehabilitation.

In the telerehabilitation group, each patient was paired with a rehabilitation doctor who offered guidance and support from a distance. This arrangement facilitated continuous monitoring, enabling the rehabilitation plan to be dynamically adjusted according to the patient's individual progress and feedback. The essence of this approach was its personalized nature; the rehabilitation was not a one-size-fits-all regimen but rather a tailored program that evolved in response to the specific needs and conditions of each patient.

Table 1. Functional results comparing the retrospective and main groups

	Retrospective group	Main group	p-value
The average time spent by patients on rehabilitation exercises per day.	29±8 min	42±4 min	p<0,005
The number of patient visits to the medical facility over a period of 3 weeks.	12±2	4±2	p<0,005
The total time dedicated by the rehabilitator to each patient during the 3-week period.	263±15 min	92±14 min	p<0,005
qDISH last day of rehabilitation			
Excellent (0-25 points)	9 (6.62 %)	11 (15.07 %)	
Good (26-50 points)	97 (71.32 %)	52 (71.23 %)	p=0,152
Satisfactory (51-84 points)	24 (17.65 %)	8 (10.96 %)	
Unsatisfactory (85-100 points)	6 (4,41 %)	2 (2,74 %)	

p-values were obtained using the chi-square test for categorical variables and analysis of variance (ANOVA test) for continuous variables.

On the other hand, the control group received traditional rehabilitation at home, but this did not include the dedicated oversight of a personal doctor. They adhered to standard rehabilitation protocols that were not customized to the individual patient's evolving requirements. This meant that while they received the necessary exercises and treatments, these were not modified in real-time based on their specific recovery trajectories or feedback.

This fundamental difference in approach was key to our study. It allowed us to explore the impact of personalized, remote rehabilitation support, particularly in terms of patient outcomes, engagement, and satisfaction, compared to the more generalized approach of traditional home-based rehabilitation. By contrasting these two groups, we aimed to glean insights into the potential advantages of a more personalized and adaptive rehabilitation model, as provided by telerehabilitation, over the conventional methods.

RESULTS

In the study groups, the percentage distribution of men and women was as follows: Comprising 136 patients in retrospective group, there were 98 men (72.1%) and 38 women (27.9%). Among the 73 patients in main group, there were 52 men (71.2%) and 21 women (28.8%). These percentages indicate a higher incidence of injuries among men compared to women in both groups. However, the proportion of men to women was fairly consistent between the retrospective and main groups. In terms of injury patterns, a significant portion of patients, regardless of their gender, were injured while cycling or walking as pedestrians. This observation underscores the need for focused safety measures and awareness campaigns for these particular groups to potentially reduce the risk of road accidents.

Regarding the age distribution of the patients in our study, the most common age group was those of working age, specifically between 25 to 44 years old. This age group constituted more than forty percent of patients in both the retrospective and main groups, indicating a high incidence of injuries among individuals in their prime working years.

Conversely, the smallest age group differed between the two groups. In the retrospective group, the least represented age group was the younger adults aged 18-24. In the main group, the smallest group consisted of individuals aged over 60. This variation in the age distribution highlights different risk profiles and possibly different lifestyles or activities leading to injuries among these age groups. The prevalence of working-age individuals in both groups underscores the significant impact such injuries can have on the workforce and the importance of targeted prevention and rehabilitation strategies for this demographic.

In the main group of our study, the role of the rehabilitator emerged as a central and defining element in the success of the telerehabilitation process. The systematic monitoring of each patient's clinical condition by the rehabilitator was a cornerstone of this approach. This rigorous and continuous monitoring process included the analysis of various key health parameters, such as the range of motion, pain level reduction, and improvement in limb function.

One of the most significant advantages of this approach was the capacity for real-time, remote adjustments to the telerehabilitation protocol. This adaptability ensured that the rehabilitation process remained optimally efficient and effective, tailored to the evolving needs of each patient. Such flexibility is often not feasible in traditional rehabilitation settings, where adjustments may require physical assessments and can be less responsive to immediate changes in a patient's condition.

The outcomes for both the retrospective and primary groups were analyzed using the QuickDASH scale, a tool designed to measure the disability of the arm,

shoulder, and hand. Additionally, we evaluated several other important metrics, including:

- The average time spent by patients on rehabilitation exercises per day.
- The number of patient visits to the medical facility over a period of 3 weeks.
- The total time dedicated by the rehabilitator to each patient during the 3-week period.

These metrics, summarized in Table 1, provided a comprehensive view of the rehabilitation process, including the time commitment from both patients and medical professionals, and the intensity of the rehabilitation activities. This comprehensive evaluation was essential for understanding the effectiveness of the rehabilitation protocols in both groups.

The data presented in Table I offers a comprehensive comparison of the functional results between the retrospective group and the main group, providing valuable insights into the effectiveness of traditional rehabilitation versus telerehabilitation.

Focusing first on the average time spent on rehabilitation exercises per day, we observe a noticeable difference: while the retrospective group dedicated an average of 29±8 minutes daily, the main group invested more time, averaging 42±4 minutes. This significant increase in daily rehabilitation time in the main group ($p<0.005$) suggests that the convenience and accessibility of telerehabilitation may encourage patients to engage more rigorously in their recovery exercises.

Turning our attention to the frequency of medical facility visits over a three-week period, the contrast is striking. The retrospective group reported an average of 12±2 visits, in stark contrast to the main group, which averaged only 4±2 visits. The markedly reduced need for physical visits in the main group ($p<0.005$) highlights one of the key benefits of telerehabilitation: reducing the logistical burden on patients while still providing effective care.

Regarding the total time a rehabilitator dedicated to each patient over the same period, the efficiency of the telerehabilitation model becomes even more evident. The rehabilitators spent considerably less time with each patient in the main group (92±14 minutes) compared to the retrospective group (263±15 minutes), with a significant difference ($p<0.005$). This efficiency could be attributed to the streamlined nature of remote monitoring and guidance.

Finally, the QuickDASH scores on the last day of rehabilitation provide an interesting perspective on patient outcomes. While there was a slightly higher percentage of 'Excellent' outcomes in the main group, the majority of patients in both groups achieved 'Good' functional results. The lack of a significant statistical difference in these outcomes ($p=0.152$) indicates that, despite the reduced in-person contact and lower time commitment from healthcare professionals in the main group, the overall functional recovery was on par with that of the traditional rehabilitation group.

In essence, Table 1 paints a picture of how telerehabilitation can potentially transform patient care, offering an efficient, less burdensome alternative that does not compromise on the quality of patient outcomes. This represents a promising direction in the field of rehabilitation, combining technological innovation with patient-centric care.

DISCUSSION

The findings from our study provide several key insights into the evolving landscape of rehabilitation, particularly when comparing traditional methods with emerging telerehabilitation approaches.

One of the most striking observations is the increased time patients in the telerehabilitation group spent on daily rehabilitation exercises. This suggests that the convenience and accessibility of telerehabilitation may encourage greater patient engagement and adherence to prescribed exercise regimens. The ease of performing exercises in a comfortable, familiar home environment, coupled with the continuous remote support from medical professionals, likely contributes to this increased engagement [4].

The significantly reduced number of visits to medical facilities and the decreased time commitment required from rehabilitators in the telerehabilitation group underscore the efficiency of this model. This aspect is particularly relevant in the context of healthcare resource optimization and reducing the logistical burden on patients, especially those with mobility challenges or residing in remote areas.

The discovery in our study that there was no notable statistical difference in the functional outcomes, as evaluated by QuickDASH scores, between patients undergoing telerehabilitation and those receiving traditional rehabilitation is of significant importance. This equivalence in QuickDASH scores demonstrates that telerehabilitation, despite involving fewer in-person interactions and requiring less time from healthcare professionals, does not diminish the effectiveness of patient recovery. Moreover, this finding points to the broader applicability of telerehabilitation, especially in scenarios where regular clinic visits pose challenges. This could include situations where patients face mobility issues, live in remote areas, or when there are constraints like pandemics that limit physical contact. In such contexts, telerehabilitation not only emerges as

a feasible alternative but also as a potentially preferred method of delivering rehabilitation services [6].

The study also sheds light on the potential of personalizing rehabilitation plans based on real-time monitoring. The ability of medical professionals to remotely adjust rehabilitation protocols in response to patient progress or challenges is a significant advantage, allowing for more dynamic and responsive care. These findings have important implications for healthcare policy and future practice. The integration of telerehabilitation into standard care practices could enhance the efficiency of healthcare delivery, improve patient accessibility to rehabilitation services, and potentially lead to better patient satisfaction due to the convenience and personalization it offers.

While the results are promising, further research is needed to explore the long-term outcomes of telerehabilitation [6], its applicability to different types of injuries or patient populations, and its cost-effectiveness compared to traditional methods. Additionally, understanding the barriers to its adoption and how to overcome them will be crucial for its wider implementation.

Our study indicates that telerehabilitation is not only a feasible alternative to traditional rehabilitation but also an efficient and patient-friendly option that does not compromise on treatment outcomes. Its adoption could be a significant step forward in modernizing rehabilitation services, making them more accessible and tailored to individual patient needs.

As the healthcare landscape continues to evolve, integrating telerehabilitation into standard care could not only enhance the efficiency of healthcare delivery but also improve patient accessibility and satisfaction.

However, this study also opens the door to further research, particularly in exploring the long-term outcomes of telerehabilitation, its cost-effectiveness, and its applicability across diverse patient populations and injury types.

CONCLUSIONS

The findings reveal that telerehabilitation can significantly increase patient engagement in rehabilitation exercises, primarily due to its convenience and accessibility. This mode of rehabilitation not only reduces the need for frequent medical facility visits but also decreases the time commitment required from healthcare professionals, all while delivering functional outcomes comparable to conventional methods.

The ability to tailor rehabilitation plans based on real-time monitoring and adjust them dynamically to the patient's progress or challenges marks a significant advancement towards more personalized and responsive healthcare.

This study points towards a future where rehabilitation services are more adaptable, patient-friendly, and aligned with the growing digitalization of healthcare, promising a more inclusive and accessible healthcare system for all.

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CONTENTS

Mental health of children with special educational needs in the context of long-term crisis challenges: as seen by parents

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ABSTRACT

Aim: To study the peculiarities of the mental health of children with special educational needs after 1.5 years of full-scale war in Ukraine.

Materials and Methods: The mental health of children with special educational needs (SEN) as well as the peculiarities of the impact of hostilities on their emotional and volitional sphere was assessed through the anonymous survey of their parents using the questionnaire developed by the authors (25 questions). The research, which was conducted in 2023 using a Google form, involved 466 parents having children with SEN aged 6 to 10.

Results: It was found that among the surveyed families raising children with SEN, 30.7 % of children were in the combat zone or zone of temporary occupation for a week to a month, 19.1 % – for more than a month; 36.9 % of children experienced relocation, 23.4 % were separated from their parents, 19.7 % witnessed hostilities; 49.4 % of children experienced an unstable psycho-emotional state ("emotional swings") during 1.5 years of war in Ukraine, 40.1 % – restlessness, 38.6 % – anxiety; 23.2 % of parents noted that their children were "hooked" on computer games and social networks, 11.2 % – had problems with sleep, 10.5 % – demonstrated the emergence or increase in cognitive problems.

Conclusions: The negative impact of prolonged stress during the war on the mental health of children with SEN has been revealed, which requires psychological support for such children from parents and psychologists.

KEY WORDS: mental health, children with special educational needs, emotional and volitional sphere, parents, war

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INTRODUCTION

The full-scale war has become a significant challenge for Ukrainians, including children. Part of the population witnessed the hostilities directly, stayed in the temporarily occupied territory, or was forced to relocate, losing their homes and belongings, some saw their homes destroyed or lost their jobs and income as a result of the war. In addition, the vast majority, if not every citizen of Ukraine, currently has relatives, friends, or acquaintances who are fighting or performing other tasks in the combat zone [1, 2]. At the same time, the entire population of Ukraine, including those in relatively safe areas, is at high risk of secondary psychological trauma due to a sense of collective danger during air raids, massive shelling, and their consequences, including power, heat, and water outages. In addition, those Ukrainian citizens abroad are at high risk of experiencing symptoms of acculturation stress and secondary trauma as a result of reading or watching the news, and communicating with other war victims [3, 4]. Not only adults but also children are exposed to these influences. At the same time, children with special educational needs (SEN) are the most vulnerable category due to their developmental characteristics and individual needs [5-7].

The severity of the problem was confirmed at the first stage of our research, conducted in April-May 2022, which was devoted to determining the psychological well-being of children in the acute phase of traumatic stress caused by the full-scale war in Ukraine [8]. This gives grounds to study the problem of mental health of children with SEN in the context of a full-scale high-intensity war with a high component of secondary trauma 1.5 years after the outbreak of hostilities in Ukraine.

AIM

The aim is to study the peculiarities of the mental health of children with special educational needs after 1.5 years of full-scale war in Ukraine.

MATERIALS AND METHODS

The mental health of children with SEN, as well as the study of the peculiarities of the impact of hostilities on their emotional and volitional sphere, was assessed by interviewing their parents using the questionnaire developed by the authors. The survey was anonymous and conducted in May-August 2023. The research involved 466 parents having children with SEN aged 6 to 10 years. The parents who took part in the survey lived in Ukraine or were temporarily displaced from Ukraine.

Research methods: analysis and generalization of literary sources, questionnaire survey, statistical methods. 24 sources from the databases Scopus, PubMed, Web of Sciences Core Collections, Index Copernicus and others were investigated. The survey was conducted according to the author's questionnaire, which contains 25 questions to determine the impact of hostilities across the territory of Ukraine on the mental health of children with SEN. The survey was conducted using the Google form created by the authors (https://docs.google.com/forms/d/1pk4gmeDuFtL3l4VuMZv4oopgWWH2s6SpkgU-xMLqNng/edit?ts=6570b8af). The results of the research were presented in percentages and processed in Microsoft Excel for Windows 10. This research followed the regulations of the World Medical Association Declaration of Helsinki and ethical principles for medical research involving human subjects. Informed consent was received from all respondents who took part in this research.

RESULTS

The survey found that at the time of the survey, 87.8 % of parents were at home with their children, 9.4 % were forced to move abroad with their children, and 2.8 % were temporarily displaced to another region of Ukraine. According to experts, the most negative impact on the mental health of children, especially children with SEN, is the duration of stay within a stressful environment. Thus, it was found that 19.1 % of children with SEN had been in the combat zone or on the temporarily occupied territory for more than one month, 30.7 % of children had been in the combat zone for one to four weeks, 9.7 % had been in the combat zone for 1-7 days, and 38.0 % had not been in the combat zone. It was found that the values of the Ukrainian population changed during the war. Thus, the situation in the country (71.7 %) and the situation in the family (20.8 %) have the greatest impact on the psycho-emotional state of the surveyed parents during martial law; at the same time, economic difficulties affect the psycho-emotional state of only 3.4 % of parents. A similar trend was observed when studying the factors shaping the psycho-emotional state of children during the war: for 42.8 % of children, the situation in the country was a determining factor, for 39.5 % – the situation in the family, for 9.7 % – the situation at school (class). First of all, this is due to the spread of situations of general social tension, which naturally affects various social groups (communities, families, classes, etc.).

The survey also revealed that during the full-scale war in Ukraine, children with SEN had to go through the following: relocation (36.9 %), separation from parents (23.4 %), witnessing hostilities (19.7 %), losing friends (8.2 %), losing loved persons (5.8 %), etc. (Fig. 1). It was found that at home, most children were cheerful (43.1 %) and vigorous (39.7 %), but a significant number of children showed an unstable psycho-emotional state ("emotional swings", 39.7 %), as well as aggression (6.9 %), sadness (4.3 %), fear (3.4 %), detachment and unsociability (1.9 %).

It has been established that during the war in Ukraine, parents of children with SEN most often experienced anxiety (70.8 %), restlessness (41.2 %), fear (40.6 %), "emotional swings" (37.8 %), hope (33.5 %), panic (17.4 %), and emotional pain (17.4 %). And their children most often experienced "emotional swings" (49.4 %), restlessness (40.1 %), anxiety (38.6 %), joy (28.3 %), fear (26.6 %), hope (15.5 %), and sadness (13.9 %) (Table 1). As we can see, the emotional and volitional spheres of both parents and children reacted differently to critical stressful situations provoked by the war. However, negative emotions are dominant.

It was found that most of the time during the war, parents of children with SEN were in the following moods: neutral (47.9 %), unstable ("emotional swings", 32.0 %), depressed (14.2 %); some parents reported being in a good mood (21.5 %). In contrast to their parents, children with SEN, according to their parents, were in a good mood (42.1 %), experienced "emotional swings" (30.3 %), were in a neutral (25.3 %), joyful (19.1 %) or happy (7.9 %) mood. Only 1.5 % of children were in a depressed mood.

Fig 2 shows the changes that have occurred in the mental health of children with SEN after 1.5 years since the beginning of the war in Ukraine. It was found that 23.2 % of children increased the time spent on social networks and playing computer games, 12.2 % became more sensitive and began to show tearfulness, 11.2 % began to sleep poorly at night, and some chil-

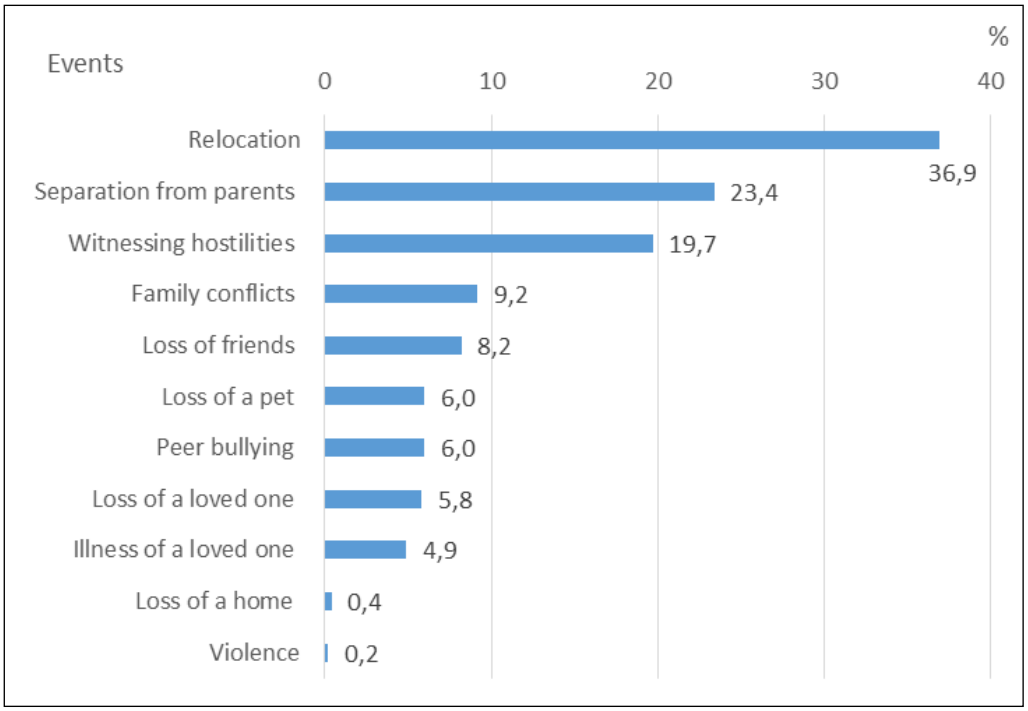

Fig. 1. Events experienced by children with SEN during the war in Ukraine (%).

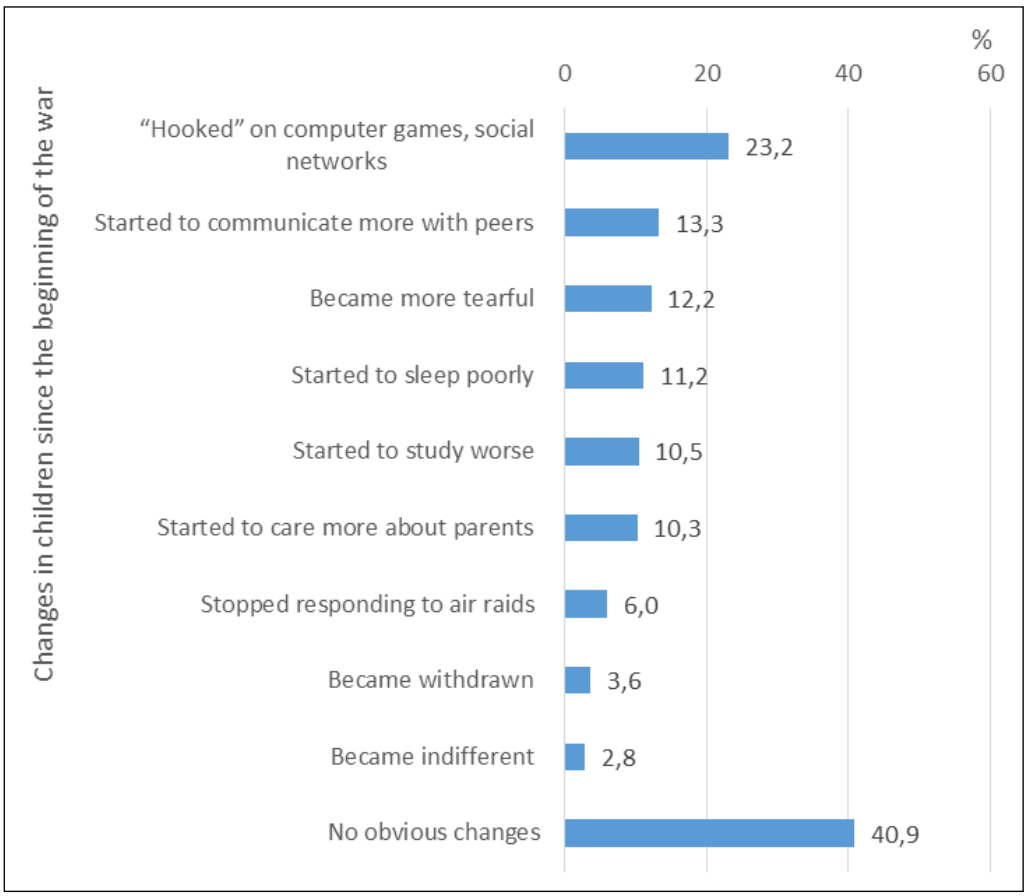

Fig. 2. Changes in the mental health of children with SEN after 1.5 years since the beginning of the war in Ukraine (%).

dren became withdrawn (3.6 %) and began to show indifference (2.8 %). These indicators can be explained by the reassessment of values and the emergence of compensatory mechanisms in children's psyches that are different from those that are relevant in normal peaceful life.

It was also found that over the past year, 23.8 % of parents regularly consulted psychologists for help in working with children with SEN; 25.1 % of parents did so sporadically; 52.3 % of parents did not consult psychologists. At the same time, 23.2 % of children are currently working with psychologists offline, 8.2 %

Table 1. The feelings most often experienced by parents and their children during the war in Ukraine (no more than 3 options were allowed, %)

Feelings experienced by respondents	Interviewed respondents	
	Parents of children with SEN	Children with SEN
Fear	40.6	26.6
Anxiety	70.8	38.6
Restlessness	41.2	40.1
Panic	17.4	10.3
Emotional pain	17.4	3.9
Grief	5.2	0.6
Joy	3.0	28.3
Hope	33.5	15.5
Self-confidence	4.9	9.4
Confidence in the future	9.4	5.4
Despair	9.9	2.1
Sadness	12.9	13.9
"Emotional swings"	37.8	49.4

online; 11.2 % in a mixed mode (offline + online); and 57.5 % of children do not need psychological help.

It has been established that 45.9 % of parents receive the necessary information about psychological assistance and support for children with SEN during consultations with specialists, 27.7 % – from websites and social networks, 23.4 % – from relatives and friends, 21.9 % – from educational and awareness videos, 20.2 % – from specialized literature, 3 % – from television. At the same time, 48.9 % of parents need more information on how to improve their children's mental health and correct their emotional as well as volitional sphere. Moreover, 54.9 % of parents are convinced that to improve their children's mental health, it is necessary to increase the number of classes aimed at developing such mental cognitive processes as memory, attention, and thinking; 47.0 % prefer art therapy (fairy tale therapy, music therapy, etc.); 42.5 % of parents see the prospect of improving the mental health of children with SEN in the development of their speech; 26.2 % – in the development of discipline in children; 25.1 % – in the formation of their psycho-emotional stability. Thus, the results of the survey revealed certain negative changes in the mental health of children with SEN during the war in Ukraine, which requires psychological support for such children from parents and psychologists. The main purpose of such support should be to create a comfortable psychological environment that would help restore the psychoenergetic resources of children with SEN.

DISCUSSION

Ukraine has a psychosocial model for determining special educational needs and, under subparagraph 20 of paragraph 1 of Article 1 of the Law of Ukraine "On Education" (2017), a person with special educational needs is a person who needs additional permanent or temporary support in the educational process to ensure his or her right to education, which significantly expands the number of children who may have special educational needs. Under paragraph 7 of Article 19 of the Law of Ukraine "On Education" (2017), the categories of persons with special educational needs are defined by acts of the Cabinet of Ministers of Ukraine, taking into account international norms and standards. These categories were defined by the Regulation on the Inclusive Resource Center, approved by the Cabinet of Ministers of Ukraine on July 12, 2017, No. 545. Appendix 4 referred to as "Categories (Types) of Special Educational Needs (Difficulties)" provides 5 categories (types) of difficulties, including intellectual, functional, physical, educational, and socio-adaptation/socio-cultural difficulties, which may be based, in particular, on the presence of manifestations of the consequences of psychological trauma. As a result, children with SEN can include a fairly wide group of children, which tends to increase, which maximizes the severity of the problem [5, 6, 9, 10].

According to the survey conducted by Gradus Research Company in April 2022 in Ukraine with 784 parents having children (under 18, n = 1179), 75 % of parents claim that their children show some symptoms of mental trauma. The most common symptom is the so-called "emotional swings" when the mood quickly fluctuates without external causes from very good to extremely bad and vice versa. In addition, every fifth child has sleep disorders, and every tenth child has a decreased desire to communicate, nightmares, and memory impairment [11].

If we turn to the experience of researching the impact of war on the psychological state of the population, including children, we can note the significant impact observed over several years. In particular, scientists [12, 13], using the scale of the impact of events in Sierra Leone, found that 99 % of the population has levels of disorders indicating severe post-traumatic stress disorder (PTSD). Similar findings were reported in a study of Kosovo Albanians, including adolescents over 15 years of age, one year after the war, which found an increase in respondents meeting the criteria for PTSD (25 %) and two years later, when 18 % of respondents still met the criteria for PTSD, although only 2 % of respondents' main complaints were related to mental health problems [14, 15]. The results of a long-term study conducted in Armenia show that the level of post-traumatic stress disorder in children remained high 4.5 years after exposure to severe trauma [16]. At the same time, a similar study, which surveyed 813 school-age children from municipal schools in Pristina, identified three main clusters of stress in these children: 1) lack of recreational and cultural resources; 2) health and mental complaints; 3) school problems [17]. The issue of the consequences of psychological trauma on children who have survived war or terrorism has been raised in the studies of many scientists who focus on long-term changes in the child's social construction of the world [18, 19]. At the same time, scientists [20, 21] note that the factors that should be taken into account whenever assessing the mental health of children and adolescents after psycho-traumatic events include: 1) severity and type of trauma, 2) the need to assess multiple disorders, 3) independent assessment of children's behavior, 4) assessment of family members, especially mothers, 5) functional status, 6) age and developmental differences, 7) existing risk factors, 8) cultural competence. Authors [22-24], based on the analysis of several studies, show a high prevalence of mental health problems among migrants and refugees. In particular, the experience of "culture shock" and "acculturation stress" can aggravate the psychological state of migrants, and lead to repeated stress, nervous breakdown, depression, and anxiety disorders. Thus, a large number of scientific studies have been identified in this area, but despite the 1.5 years of high-intensity war in Ukraine with a high component of secondary trauma, there is a lack of research on mental health issues specifically for children with SEN. There are also no longitudinal studies that would allow comparing the dynamics of mental health of children with SEN at different stages of martial law in Ukraine. The results of our research confirm and supplement the findings of many scientists about the negative impact of prolonged stress during the war on the mental health of children with SEN.

CONCLUSIONS

It was found that among the surveyed families raising children with SEN, 30.7 % of children were in the combat zone or zone of temporary occupation for a week to a month, 19.1 % – for more than a month; 36.9 % of children experienced relocation, 23.4 % were separated from their parents, 19.7 % witnessed hostilities; 49.4 % of children experienced an unstable psycho-emotional state ("emotional swings") during 1.5 years of war in Ukraine, 40.1 % – restlessness, 38.6 % – anxiety; 23.2 % of parents noted that their children were "hooked" on computer games and social networks, 11.2 % – had problems with sleep, 10.5 % – demonstrated the emergence or increase in cognitive problems.

The negative impact of prolonged stress during the war on the mental health of children with SEN has been revealed, which requires psychological support for such children from parents and psychologists. The obtained results also indicate the expediency of conducting long-term studies to research the state of mental health of children with SEN in the coming years and the need to develop programs to restore and maintain the mental health of children with SEN.

PROSPECTS FOR FURTHER RESEARCH

It is planned to investigate the peculiarities of psychological support for children with SEN by pedagogical workers during the war in Ukraine.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Self-assessment of somatic and mental health by instructor-officers under the influence of negative factors of professional activities

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ABSTRACT

Aim: To investigate the impact of negative factors of professional activities in the context of the COVID-19 pandemic and martial law in Ukraine on the somatic and mental health of instructor-officers with different teaching experiences.

Materials and Methods: The research involved 131 instructor-officers with different teaching experiences. Three groups of instructor-officers were formed: Group 1 – instructors with up to 10 years of teaching experience (n = 30), Group 2 – instructors with 10 to 20 years of experience (n = 47), Group 3 – instructors with more than 20 years of experience (n = 54). The self-assessment of somatic and mental health was carried out using a questionnaire developed by the authors.

Results: The negative impact of the factors of professional activities in the context of the COVID-19 pandemic and martial law in Ukraine on the somatic and mental health of instructor-officers was established. More than 50 % of the instructors rated their health as satisfactory, and more than 20 % as poor. The overwhelming majority of instructors reported a slight (over 40 %) and significant (over 30 %) deterioration in both somatic and mental health. Health problems over the past year have interfered with the performance of professional duties for more than 80 % of instructor-officers.

Conclusions: The systematic impact of negative factors can lead to some psychosomatic disorders and diseases in instructor-officers and a decrease in the quality of their teaching activities. This necessitates the search for ways to restore the somatic and mental health of instructor-officers.

KEY WORDS: somatic health, mental health, instructor-officers, negative factors, professional activity

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INTRODUCTION

Specific factors of professional activities in higher education that negatively affect the professional and personal development of the teacher, as well as his/her health, are: multifunctionality of professional activities; large amount of work; intensity of communicative interaction in the field of "person-to-person"; heterogeneity of the audience in terms of intellectual and socio-cultural peculiarities, level of responsibility, general education, orientation of educational and professional motivation, etc. [1, 2]. The analysis of scientific works [3, 4] has shown that one of the prevailing trends in the structure of modern professional activities of instructors of higher educational institutions with specific learning environment (HEIs SLE) in Ukraine is its growing intellectualization and a sharp increase in requirements for quality, speed of mental and psychomotor operations. As noted by scientists [5, 6], instructor-officers spend most of their service time indoors in a forced posture (usually sitting), which convincingly indicates the impact of a significant number of negative factors of professional activities on instructors, including hypodynamia and hypokinesia, the length of the working day and week, nervous and emotional stress, monotony, mental overload and others [7, 8]. In addition, a heavy teaching load, bad habits, and lack of time for recovery do not allow for the required level of somatic and mental health of instructor-officers. The information and emotionally intense pedagogical activities of instructors under the influence of negative factors for a long time lead to a deterioration in both somatic health (muscle detraining, overweight, hypertension, and many other diseases) and mental health (emotional exhaustion, professional burnout, etc.) of instructors in HEIs SLE. The negative impact of professional activities factors on the indicators of somatic and mental health of instructor-officers has become even more acute with the onset of the COVID-19 pandemic and the introduction of martial law in Ukraine and, accordingly, the transition of all Ukrainian HEIs SLE to distance learning.

Table 1. The results of self-assessment by instructor-officers with different teaching experiences of their somatic health (n=131, %)

Question	Answers	Groups of instructor-officers			Chi-square (χ^2) criterion		
		Group 1 (n=30)	Group 2 (n=47)	Group 3 (n=54)	1-2	2-3	1-3
1. Your somatic health is currently...	very good	-	-	-	2.99	2.80	11.12
	good	26.7	17.1	9.3			
	satisfactory	50.0	53.1	55.5			
	poor	23.3	29.8	35.2			
2. How would you rate your somatic health compared to 2 years ago?	slightly better	-	-	-	3.32	1.35	8.51
	almost the same	13.3	10.6	7.4			
	slightly worse	56.6	46.8	42.6			
	much worse	30.2	42.6	50.0			
3. How often have somatic health problems interfered with your professional duties?	not at all	6.7	4.3	-	2.84	9.60	20.96
	almost did not interfere	20.0	12.8	5.6			
	somewhat interfered	46.7	44.7	37.0			
	greatly interfered	26.6	38.2	57.4			
4. Over the last year, have you had any difficulties in performing your professional duties due to your somatic health?	yes	83.3	87.2	92.6	0.93	1.63	4.63
	no	16.7	12.8	7.4			
5. Over the last year, how often have you experienced somatic health disorders?	often	63.3	68.1	74.1	0.51	0.87	2.71
	occasionally	36.7	31.9	25.9			
	never	-	-	-			

1-2 (2-3; 1-3) – the significance of the difference between the indicators of studied groups of instructor-officers by the Pearson's Chi-square criterion.

AIM

The aim is to investigate the impact of negative factors of professional activities in the context of the COVID-19 pandemic and martial law in Ukraine on the somatic and mental health of instructor-officers with different teaching experiences.

MATERIALS AND METHODS

The research was conducted at the National Academy of Internal Affairs (NAIA) and the National Academy of the Security Service of Ukraine (NASSU) (Kyiv, Ukraine) in 2023. The research involved instructor-officers of the NAIA (n = 86) and NASSU (n = 45) with different teaching experiences. Three groups of instructor-officers were formed: Group 1 – instructors with up to 10 years of teaching experience (n = 30), Group 2 – instructors with 10 to 20 years of experience (n = 47), Group 3 – instructors with more than 20 years of experience (n = 54).

To achieve the aim of the research, the following methods were used: analysis and generalization of literary sources, surveys, and methods of mathematical statistics. 16 sources from the databases Web of Sciences Core Collections, Scopus, PubMed, Index Copernicus and others were investigated. The survey was conducted according to the author's questionnaire (10 questions) to determine the impact of negative factors of professional activities during the COVID-19 pandemic and the legal regime of martial law in Ukraine on the somatic and mental health of instructor-officers (Appendix 1).

The mathematical and statistical method was used to process the experimental data obtained. The compliance of the sample data distribution with the Gauss' law was assessed using the Shapiro-Wilk W test. The reliability of the difference between the indicators was determined using the Pearson's Chi-square (χ^2) criterion. The reliability of the difference was set at $p < .05$. All statistical analyses were performed using SPSS software, version 10.0, adapted for medical and biological research. This this research followed the regulations of the World Medical Association Declaration of Helsinki and ethical principles for medical research involving human subjects. Informed consent was received from all respondents who took part in this research.

Table 2. The results of self-assessment by instructor-officers with different teaching experiences of their mental health (n=131, %)

Question	Answers	Groups of instructor-officers			Chi-square (χ^2) criterion		
		Group 1 (n=30)	Group 2 (n=47)	Group 3 (n=54)	1-2	2-3	1-3
1. How would you rate your mental health at the moment?	very good	-	--		0.75	0.18	1.01
	good	16.7	14.9	12.9			
	satisfactory	46.7	42.5	44.4			
	poor	36.6	42.6	42.7			
2. What changes have occurred in your mental health over the past 2 years?	improved	-	-	-	4.18	2.43	7.48
	not changed significantly	6.7	2.1	-			
	deteriorated	53.3	46.8	51.8			
	deteriorated significantly	40.0	51.1	48.2			
3. Over the past year, how often have your mental health problems interfered with your communication with colleagues, students, and cadets?	not at all	3.3	4.3	9.3	0.64	2.23	4.55
	almost did not interfere	13.3	10.6	7.4			
	somewhat interfered	50.1	46.8	42.6			
	greatly interfered	33.3	38.3	40.7			
4. Over the past year, have you had any difficulties in fulfilling your professional duties due to your mental health problems?	yes	86.7	89.4	90.7	0.34	0.09	0.79
	no	13.3	10.6	9.3			
5. How much time have you spent in the last year...							
feeling full of life?	always	-	-	-	22.73	1.49	13.70
	often	13.3	4.3	7.4			
	occasionally	63.4	40.4	44.4			
	never	23.3	55.3	48.2			
being very irritable?	always	6.7	8.5	9.3	3.71	1.94	0.92
	often	50.0	55.3	51.9			
	occasionally	40.0	36.2	36.9			
	never	3.3	-	1.9			
feeling happy?	always	10.0	-	-	17.18	0.74	14.60
	often	23.3	17.0	18.5			
	occasionally	66.7	76.6	77.8			
	never	-	6.4	3.7			
feeling depressed?	always	-	6.4	3.7	13.11	0.88	10.53
	often	43.3	42.5	42.6			
	occasionally	50.0	51.1	53.7			
	never	6.7	-	-			

1-2 (2-3; 1-3) – the significance of the difference between the indicators of studied groups of instructor-officers by the Pearson's Chi-square criterion.

RESULTS

The results of self-assessment by instructor-officers of HEIs SLE with different teaching experiences of their somatic health under the influence of negative factors of professional activities are presented in Table 1.

It has been found that the vast majority of instructor-officers in the HEI SLE assess their somatic health as satisfactory at the moment (in group 1 – 50.0 %, in group 2 – 53.1 %, in group 3 – 55.5 %). A fairly large proportion of instructors consider their health to be poor – from 23.3 % to 35.2 %, depending on their teaching experience. And only 26.7 % of instructors in group 1, 17.1 % in group 2, and 9.3 % in group 3 rated their somatic health as good. It is worth noting that no instructor from all three study groups rated their somatic health as very good. The comparative analysis of the results of self-assessment of instructors' somatic health showed that there was a significant difference between the indicators of the study groups ($\chi 2 = 2.99$; 2.80; 11.12), which indicates a deterioration in somatic health in instructor-officers with experience of their professional activities under the influence of negative factors.

The comparison of the instructor-officers' current somatic health with that before the COVID-19 pandemic and the war showed a deterioration in the health of instructors of all three study groups. The vast majority of instructors reported a slight (56.6-42.6 %) and significant (30.2-50.0 %) deterioration in health. There were no instructors who reported an improvement in somatic health over the past two years. It was also found that problems with somatic health over the past year interfered with the performance of professional duties for more than 70 % of instructors in group 1, more than 80 % of group 2, and more than 90 % of group 3. At the same time, there was a significant deterioration in the obtained indicators with increasing experience of professional activities of instructors ($\chi^2 = 2.84$; 9.60; 20.96). Moreover, the vast majority of instructors in all three groups (group 1 – 83.3 %, group 2 – 87.2 %, and group 3 – 92.6 %) had some difficulties in performing their professional duties due to problems in their somatic health (they were limited in some actions, spent much more time than usual on their usual work). In addition, all instructor-officers of all three groups often (group 1 – 63.3 %, group 2 – 68.1 %, group 3 – 74.1 %) or occasionally (group 1 – 36.7 %, group 2 – 31.9 %, group 3 – 25.9 %) experienced somatic health problems over the past year.

The analysis of the results of self-assessment of mental health by instructor-officers showed that no instructor from any of the three groups rated their mental health as very good. The majority of instructor-officers consider their mental health to be satisfactory (group 1 – 46.7 %, group 2 – 42.5 %, group 3 – 44.4 %) or poor (group 1 – 36.6 %, group 2 – 42.6 %, group 3 – 42.7 %) (Table 2). At the same time, no significant difference was found between the indicators of instructors depending on their professional experience ($\chi^2 = 0.75$, 0.18, 1.01). However, over the past two years, mental health deteriorated in almost 100 % of instructors in all three groups, and it significantly deteriorated in 40.0 % of instructors in group 1, 51.1 % in group 2, and 48.2 % in group 3. It is important to note that the difference between the indicators of the studied groups is significant ($\chi^2 = 4.18$; 2.43; 7.48), which indicates a deterioration in the mental health of instructor-officers in HEIs SLE under the influence of negative factors of professional activities (Table 2).

We also found out that certain mental health problems interfered with communication (interaction) between most of the instructor-officers and their colleagues, students, and cadets. Such instructors in group 1 accounted for 83.4 % (somewhat interfered – 50.1 %, greatly interfered – 33.3 %), in group 2 – 85.1 % (somewhat interfered – 46.8 %, greatly interfered – 38.3 %), in group 3 – 83.3 % (somewhat interfered – 42.6 %, greatly interfered – 40.7 %). The responses of instructor-officers with different professional experiences to the question of whether they have had difficulties in performing their professional duties over the past year due to mental health were significantly similar ($\chi^2 = 0.34$, 0.09, 0.79) and almost unanimous – 86.7 % of instructors in group 1, 89.7 % of group 2 and 90.7 % of group 3 gave a positive answer. They noted that they spent less time at work, did less than they wanted to, and could not work as usual. The research also found that over the past year, only 13.3 % of instructors in group 1, 4.3 % of group 2, and 7.4 % of group 3 felt full of life. At the same time, the indicators of instructor-officers in groups 2 and 3were significantly worse than in group 1, which indicated a deterioration in mental health among instructors with increasing experience of professional activities under the influence of negative factors. Irritability was often manifested in 50.0 % of instructors in group 1, 55.3 % of instructors in group 2, and 51.9 % of instructors in group 3. 43.3 % and 50.0 % of instructors in group 1, 42.5 % and 51.1 % of group 2, and 42.6 % and 53.7 % of group 3, respectively, often or occasionally felt depressed. Only 23.3 % of instructors in group 1, 17.0 % of group 2, and 18.5 % of group 3 often felt happy. The results obtained indicated the negative impact of negative factors of professional activities in the context of the COVID-19 pandemic and martial law in Ukraine on the somatic and mental health of instructor-officers with different teaching experiences. Instead, the most pronounced changes in the studied

indicators were found in instructor-officers with 10 to 20 years of experience and more than 20 years of teaching experience.

DISCUSSION

Scientists [6, 9, 10] note that the negative impact of the factors of professional activities of instructor officers in HEIs SLE, which occurs over many years, with age leads to a significant decrease in the mental and physical working capacity of instructors, deterioration of health and functioning of the main body systems, and with systematic exposure cause the emergence of various psychosomatic disorders and diseases. According to experts [11-13], physical inactivity or low motor activity results in various disorders of body systems, metabolism, and overweight, which adversely affects health and leads to various diseases. First of all, the cardiovascular system is affected (atherosclerosis, hypertension, coronary heart disease, etc.), and the condition of the musculoskeletal system deteriorates. As a result, there is a phenomenon of detraining (deterioration in functional load bearing). Low motor activity as well as nervous and emotional stress lead to chronic stress. According to scientists, hypertension, atherosclerosis, and obesity currently account for more than 80 % of fatalities in middle-aged and elderly people [14]. Professional burnout or emotional exhaustion, as a reflection of the negative impact of professional factors on the mental health of instructor-officers, is manifested in chronic fatigue (overwork), mood deterioration, sleep disturbance (insomnia), susceptibility to somatic diseases; partial exclusion of emotions in response to some psycho-traumatic actions; personal detachment and reduced satisfaction from the work performed; depersonalization (cynical attitude towards work and its objects/subjects, negative attitude towards colleagues and those who are trained) and reduction of personal achievements (feeling of incompetence and awareness of failure in one's professional field); decreased labor productivity; a tendency to use alcohol or other psychoactive substances to obtain temporary relief, which tends to develop physiological dependence; depression, dismal mood, restlessness, irritability, anxiety, miffiness [15, 16]. The results of our research confirm the conclusions of many scientists about the negative impact of professional activities factors in the context of the COVID-19 pandemic and martial law in Ukraine on the somatic and mental health of instructor-officers and supplement them with a more pronounced negative impact of factors on the health indicators of instructor-officers with more experience in teaching.

CONCLUSIONS

The negative impact of the factors of professional activities in the context of the COVID-19 pandemic and martial law in Ukraine on the somatic and mental health of instructor-officers in the HEIs SLE was established. More than 50 % of the instructors rated their health as satisfactory, and more than 20 % as poor. The overwhelming majority of instructors reported a slight (over 40 %) and significant (over 30 %) deterioration in both somatic and mental health. Health problems over the past year have interfered with the performance of professional duties for more than 80 % of instructor-officers. Irritability and depression were frequently found in more than 50 % of instructor-officers, and only 7-13 % of instructor-officers felt full of life, depending on their professional experiences. It was found that more pronounced changes in somatic and mental health indicators occurred in instructor-officers with 10 to 20 years of teaching experience and more than 20 years of experience compared to instructors with less than 10 years of experience. The systematic impact of negative factors can lead to some psychosomatic disorders and diseases in instructor-officers and a decrease in the quality of their teaching activities. This necessitates the search for ways to restore the somatic and mental health of instructor-officers.

PROSPECTS FOR FURTHER RESEARCH

It is planned to substantiate a program of rehabilitation measures to improve the somatic and mental health of instructor-officers in HEIs SLE.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Changes in somatic and mental health indicators of instructor-officers under stress

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ABSTRACT

Aim: To investigate changes in the indicators of somatic and mental health of instructor-officers in higher educational institutions with specific learning environment under stress.

Materials and Methods: The research involved instructor-officers of the National Academy of Internal Affairs (Ukraine, n = 86) with different teaching experiences: up to 10 years (group 1, n = 22), from 10 to 20 years (group 2, n = 31), over 20 years (group 3, n = 33). The study of somatic and mental health was carried out in September-October 2021 (Stage 1) and in September-October 2023 (Stage 2).

Results: Significantly negative changes in the indicators of somatic and mental health of instructor-officers with different experiences of teaching under stress were found. The most pronounced negative changes were found in the body weight index, vital index, strength index, Martin-Kushelevsky index, and emotional exhaustion of instructors. Among the studied groups of instructor-officers, the greatest changes occurred in instructors with 10 to 20 years of experience and more than 20 years, and the least – in instructors with up to 10 years of experience.

Conclusions: It was found that the professional activities of instructor-officers, which take place under stress, negatively affect both the somatic and mental health of instructors, regardless of their teaching experience. Such activities lead to an increase in body weight, deterioration of the functioning of the main body systems, and increased professional burnout of instructors. This can lead to several psychosomatic disorders and diseases in instructor-officers and a decrease in the quality of their teaching activities.

KEY WORDS: somatic health, mental health, instructor-officers, stress

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INTRODUCTION

The professional activities of higher education teachers are considered to be one of the most informational and emotionally intense [1]. The scientific and pedagogical activities of teachers involve numerous unpredictable communication situations, a high level of responsibility for learning outcomes, and difficulties in determining performance indicators. All this is professional stress, which eventually factors in the professional burnout of teachers [2]. This problem is particularly acute for instructor-officers in higher educational institutions with specific learning environment (HEIs SLE), where future law enforcement officers are trained. The professional activities of instructor-officers in Ukrainian HEIs SLE take place in conditions associated with a large instructional load, a constant increase in the amount of educational information, a high level of responsibility for the results of cadets' and military students' learning, overloading the intellectual sphere of instructor-officers, high nervous and emotional stress, prolonged restriction of motor activity and preservation of a static posture, constant interruption of instructors to perform non-specific tasks of public order protection and line of duty [3, 4]. The above factors lead to a decrease in mental and physical performance, deterioration of the activity of the main body systems, overweight, deterioration of somatic and mental health indicators, and the manifestation of professional burnout syndrome [5-8]. This problem was exacerbated in 2019 with the transition of all Ukrainian HEIs SLE to distance learning due to the rapid spread of coronavirus in the world. The situation worsened even more in 2022 with the introduction of

martial law in Ukraine. Inadequate distance learning due to the forced relocation of most of the HEIs SLE from their permanent locations; the need to suspend training sessions due to constant air alerts or power outages; short training periods associated with the need for early graduation of specialists and other factors have led to even greater stress among instructor-officers and, as a result, increased professional burnout syndrome and reduced the effectiveness of their professional activities. Therefore, it is expedient to study changes in the indicators of somatic and mental health of instructor-officers in HEIs SLE under stress to substantiate a program of corrective and rehabilitation measures to restore their somatic and mental health and overcome professional burnout syndrome.

AIM

The aim is to investigate changes in the indicators of somatic and mental health of instructor-officers in higher educational institutions with specific learning environment under stress.

MATERIALS AND METHODS

The research was conducted at the Department of Legal Psychology of the National Academy of Internal Affairs (NAIA, Kyiv, Ukraine). The research involved instructor-officers of the NAIA (n = 86) of different ages and, accordingly, with different teaching experiences. Three groups of instructor-officers were formed: Group 1 – instructors with up to 10 years of teaching experience (n = 22, 25.6 %, age 33 ± 4.5 years), Group 2 – instructors with 10 to 20 years of experience (n = 31, 36.1 %, age 44 ± 3.7 years), Group 3 – instructors with more than 20 years of experience (n = 33, 38.3 %, age 52 ± 4.1 years). The study of somatic and mental health indicators was carried out in two stages: in September-October 2021 (Stage 1) and in September-October 2023 (Stage 2).

The following methods were used to achieve the research aim: analysis and generalization of literature sources, the methodology for assessing somatic health by professor H. L. Apanasenko, psychodiagnostic testing, and methods of mathematical statistics. 20 sources from the databases Web of Sciences Core Collections, Scopus, PubMed, Index Copernicus and others were investigated. Professor H. L. Apanasenko's methodology for assessing somatic health included the study of body weight index (BWI), vital index (VI), strength index (SI), Robinson index (RI), Martine-Kushelevsky index (MKI), and somatic health level (SHL) [9]. Psychodiagnostic testing was used to assess the mental health of instructor-officers. For this, the "Diagnostics of professional burnout" methodology was used. This methodology consisted of 28 statements, which, in turn, were divided into three components of professional burnout: "emotional exhaustion", "depersonalization", and "reduction of personal achievements": 1) emotional exhaustion is characterized by low emotional background, indifference, and emotional oversaturation; 2) depersonalization is manifested in the deformation of relationships with other people; 3) reduction of personal achievements consists either in the tendency to negatively evaluate oneself, and one's achievements, or in leveling personal dignity, and limiting one's capabilities, etc. Quantitative indicators of professional burnout were calculated according to the key as the sum of points for each component [10]. The level of professional burnout was determined for each component: pronounced (a); insignificant manifestations (b); not observed at all (c).

The mathematical and statistical method was used to process the experimental data obtained. The compliance of the sample data distribution with the Gauss' law was assessed using the Shapiro-Wilk W test. The reliability of the difference between the indicators was determined using the Student's t-test and Pearson's Chi-square (χ^2) criterion. The reliability of the difference was set at $p < .05$. All statistical analyses were performed using SPSS software, version 10.0, adapted for medical and biological research. This research was carried out in accordance with the requirements of the Regulations on academic integrity at the National Academy of Internal Affairs. Also this research followed the regulations of the World Medical Association Declaration of Helsinki and ethical principles for medical research involving human subjects. Informed consent was received from all respondents who took part in this research.

RESULTS

Changes in the indicators of somatic health of instructor-officers with different teaching experiences are presented in Table 1.

The analysis showed that regardless of teaching experience, the dynamics of all studied indices have a similar trend – a significant ($p \leq .05$) deterioration of all indicators during the research period, except the RI, which also deteriorated, but the changes were not significant ($p > .05$). The most pronounced changes were in the BWI of instructor-officers (in Group 1 – 1.54 kg/m^2; in Group 2 – 1.71 kg/m^2; in Group 3 – 1.69 kg/m^2); VI (in Group 1 – 1.81 ml/kg; in Group 2 – 2.65 ml/kg; in Group 3 – 2.47 ml/kg), SI (in Group 1 – 2.23 %; in Group 2 – 2.51 %; in Group 3 – 2.47 %) and MKI (in Group 1 – 17.54 s; in Group 2 – 21.57 s; in Group 3 – 24.21 s). It should be noted that a more

Table 1. Changes in the indicators of somatic health of instructor-officers with different teaching experiences under stress (n=86), Mean±m

Indicators of somatic health	Research stages		Changes	Student's test	
	Stage 1	Stage 2		t	p
Group 1 – instructors with up to 10 years of teaching experience (n = 22)					
BWI, kg/m^2	23.97±0.48	25.51±0.52	1.54	2.18	≤.05
VI, ml/kg	52.58±0.63	50.77±0.59	1.81	2.10	≤.05
SI, %	62.34±0.79	60.11±0.75	2.23	2.05	≤.05
RI, c. u.	92.63±1.27	94.05±1.32	1.42	0.78	>.05
MKI, s	165.30±5.22	182.84±5.53	17.54	2.31	≤.05
SHL, points	4.26±0.39	2.73±0.45	1.53	2.57	≤.05
Group 2 – instructors with 10 to 20 years of experience (n = 31)					
BWI, kg/m^2	25.06±0.38	26.77±0.44	1.71	2.94	≤.05
VI, ml/kg	50.96±0.57	48.31±0.62	2.65	3.15	≤.01
SI, %	60.73±0.84	58.22±0.87	2.51	2.08	≤.05
RI, c. u.	93.36±1.19	94.95±1.25	1.59	0.92	>.05
MKI, s	172.63±4.83	194.20±5.07	21.57	3.08	≤.01
SHL, points	3.91±0.36	2.06±0.39	1.85	3.49	≤.01
Group 3 – instructors with more than 20 years of experience (n = 33)					
BWI, kg/m^2	26.47±0.41	28.16±0.48	1.69	2.68	≤.05
VI, ml/kg	50.53±0.55	48.06±0.59	2.47	3.06	≤.01
SI, %	60.45±0.76	57.18±0.80	3.27	2.96	≤.01
RI, c. u.	93.81±1.24	96.74±1.30	2.93	1.30	>.05
MKI, s	180.51±5.15	204.72±5.28	24.21	3.28	≤.01
SHL, points	3.26±0.31	1.61±0.35	1.65	3.53	≤.01

t – the value of Student's test; p – the reliability of the difference.

detailed analysis of the BWI showed that at the end of the study, 45.4 % of the Group 1 officers were found to be overweight, with 9.1 % of them having grade I obesity. In Group 2, 58.1 % of instructors were found to be overweight and 16.1 % of them had grade I obesity; in Group 3, 57.6 % were found to be overweight and 24.2 % had grade I obesity. The increase in body weight under stress was due to insufficient motor activity of instructors during distance learning, lack of regular physical activity, irrational diet, and bad habits. It is also worth noting that under the legal regime of martial law, the functional capabilities of the respiratory system, cardiovascular system, and strength indicators of instructor-officers significantly deteriorated: the indices by which these body systems were assessed at the end of the research in instructors of all three groups correspond to a low level. The analysis of instructors' somatic health, which was assessed by the methodology of professor H. L. Apanasenko, showed that under stress conditions there was a significant deterioration in the SHL: in Group 1 – by 1.53 points ($p \leq .05$), in Group 2 – by 1.85 points ($p \leq .01$), in Group 3 – by 1.65 points ($p \leq .01$). In general, comparing the amount of changes in the somatic health indicators of instructor-officers under stress depending on their teaching experience, we found that the greatest changes occurred in instructors with 10 to 20 years of experience and more than 20 years, and the least – in instructors with up to 10 years of experience.

The analysis of changes in the mental health of instructor-officers, assessed by the indicators of their professional burnout, showed that in all the studied groups of instructors, there was a significant ($p \leq .001$) deterioration in all indicators: emotional exhaustion, depersonalization, and reduction of personal achievements (Table 2).

The detailed analysis of the results of applying the "Diagnostics of professional burnout" methodology showed that instructors with more experience in teaching tend to reduce sensitivity in their work and the level of emotional background, which indicates emotional exhaustion of the individual. They demonstrate responsibility in their work and good professional skills, but their attitude towards colleagues and military students (cadets) changes in a certain way, they become more critical or even show some indifference. With considerable professional experience (10-20 years or more), instructors show signs of emotional saturation, with in-

Table 2. Changes in the indicators of mental health of instructor-officers with different teaching experiences under stress (n=86), Mean±m

Indicators of mental health	Degree of manifestation	Research stages		Changes	Chi-square criterion	
		Stage 1	Stage 2		χ^2	p
Group 1 – instructors with up to 10 years of teaching experience (n = 22)						
Emotional exhaustion	a	18,2	40,9	22.7	31.97	≤.001
	b	31,8	45,5	13.7		
	c	50,0	13,6	36.4		
Depersonalization	a	13,6	27,2	13.6	15.05	≤.001
	b	22,8	36,4	13.6		
	c	63,6	36,4	27.2		
Reduction of personal achievements	a	9,1	22,8	13.7	16.27	≤.001
	b	13,6	27,2	13.6		
	c	77,3	50,0	27.3		
Group 2 – instructors with 10 to 20 years of experience (n = 31)						
Emotional exhaustion	a	32,3	61,2	28.9	26.23	≤.001
	b	35,4	32,3	3.1		
	c	32,3	6,5	25.8		
Depersonalization	a	21,2	35,5	14.3	14.12	≤.001
	b	27,3	38,7	11.4		
	c	51,5	25.8	24.2		
Reduction of personal achievements	a	19,4	35,5	16.1	8.83	≤.001
	b	22,5	25,8	3.3		
	c	58,1	38,7	19.4		
Group 3 – instructors with more than 20 years of experience (n = 33)						
Emotional exhaustion	a	39,4	63,6	24.2	17.24	≤.001
	b	30,3	27,3	3.0		
	c	30,3	9,1	21.2		
Depersonalization	a	27,3	42,4	12.1	8.32	≤.001
	b	30,3	33,3	3.0		
	c	42,4	24,3	18.1		
Reduction of personal achievements	a	21,2	45,5	24.3	13.30	≤.001
	b	27,3	18,2	9.1		
	c	51,5	36,3	15.2		

a – pronounced manifestations of the indicators; b – insignificant manifestations of the indicators; c – not observed at all; χ^2 – the value of Chi-square criterion; p – the reliability of the difference.

creased negativism and cynicism in their attitudes and feelings toward their colleagues. The attitude toward their professional activities changes significantly, and they underestimate their achievements and successes. Accordingly, the style of behavior and communication may be accompanied by manifestations of disregard for corporate values and rules of interaction in the team. Moreover, in the process of professional activities under stress, all these characteristics of the mental health of instructor-officers tend to deteriorate. At the same time, the most pronounced negative changes were found in instructors with 10 to 20 years of experience and more than 20 years.

DISCUSSION

The pedagogical activities of instructor-officers in HEIs SLE are accompanied by constant stress, which is a nonspecific reaction of the body in response to a very strong external stimulus (excitant) that exceeds the norm [11]. According to scientists [12-14], stress negatively affects all body systems, including the musculoskeletal system, respiratory, cardiovascular, endocrine, digestive, nervous, and reproductive systems. The human body can cope with small doses of stress, but when stress becomes chronic or long-term, it can have serious consequences for both somatic and mental health [15]. Chronic stress causes the body's muscles to be in a constant state of tension, which can cause other body reactions and even

contribute to certain disorders such as headaches, migraines, etc. Stress and strong emotions can manifest themselves in respiratory symptoms such as shortness of breath and rapid breathing. Persistent stress can cause long-term heart and blood vessel problems: a constant increase in heart rate as well as high blood pressure can increase the risk of hypertension, heart attack, or stroke. Stress can also affect the connection between the brain and the intestinal tract, and can cause pain, bloating, and other intestinal discomfort. Moreover, stress can lead to stomach ulcers. Chronic stress can result in long-term nervous exhaustion, which is explained by the fact that the persistent activation of the nervous system affects other body systems and disrupts their functioning [16]. Our research confirms the findings of many scientists that, regardless of professional experience, somatic health indicators of instructor-officers in the HEI SLE deteriorate under stress.

Regarding the negative impact of stress on the mental health of instructors, it should be noted that in the process of teaching activities (in the field of "person-to-person"), the constant impact of stress leads to the professional burnout of instructors. According to scientists [17], professional burnout is a syndrome that develops against the background of chronic stress and leads to the depletion of the emotional energy and creative resources of a working person. Burnout syndrome belongs to the phenomena of personal deformation and is a multidimensional construct characterized by a set of negative psychological experiences, and prolonged and intense interpersonal interactions. Burnout can also be a response to the prolonged stress of interpersonal professional communications [18]. The syndrome of "professional burnout" is characterized by three components: tension, resistance, and exhaustion. According to experts [19, 20], resistance in instructors is the dominant component in the syndrome of "professional burnout", which is characterized by termination of professional duties, reduced interaction with colleagues and students, expansion of the sphere of emotional economy, desire to be alone, and inadequate emotional response. After analyzing the trends of professional burnout in instructor-officers, we found that with 10-20 years of teaching experience or more, the syndrome is more pronounced. They have a lowered emotional background, indifference and emotional saturation, more intense negativism, and cynicism of attitudes and feelings towards the objects of influence: cadets, colleagues, and other participants in professional interaction. Concerning the reduction of personal achievements, over time, instructor-officers, in the context of the specifics of their professional activities, begin to deliberately underestimate their achievements and successes.

CONCLUSIONS

Significantly negative changes in the indicators of somatic and mental health of instructor-officers with different experiences of teaching under stress were found. The most pronounced negative changes were found in the body weight index, vital index, strength index, Martin-Kushelevsky index, and emotional exhaustion of instructors. Among the studied groups of instructor-officers, the greatest changes occurred in instructors with 10 to 20 years of experience and more than 20 years, and the least – in instructors with up to 10 years of experience.

It was found that the professional activities of instructor-officers, which take place under stress, negatively affect both the somatic and mental health of instructors, regardless of their teaching experience. Such activities lead to an increase in body weight, deterioration of the functioning of the main body systems, and increased professional burnout of instructors. This can lead to several psychosomatic disorders and diseases in instructor-officers and a decrease in the quality of their teaching activities.

PROSPECTS FOR FURTHER RESEARCH

It is planned to study changes in the indicators of somatic and mental health of other categories of law enforcement officers under stress.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Influence of maternal cholesterol-enriched diet on chemical composition of teeth enamel in offspring of mice

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ABSTRACT

Aim: To determine the chemical composition of the tooth enamel of two-day-old mice from hypercholesterolemic mothers by energy dispersive X-ray spectroscopy.

Materials and Methods: Forty mature female mice were randomly assigned (n = 20/group) to either a standard chow vivarium diet (control group) or a cholesterol-enriched chow diet (experimental group). After fertilization, pregnancy and birth, on postnatal day 2, the incisor segments of 6 pups form each group were used for energy dispersive X-ray spectroscopy.

Results: Influence of maternal hypercholesterolemic diet on tooth development and mineralization was examined, which revealed changes in enamel chemical composition. First, the results indicate the presence of seven elements (Na, Cl, Ca, P, Mg, S, Fe) in the enamel of both the hypercholesterolemic and normal offspring, but the content of element Ca2+ decreased, the content of elements P5+, Na+, Cl- tended to increase in pups from hypercholesterolemic mice. Second, the initial level of mineralization according to the atomic (%) Ca / P in hypercholesterolemic pups ratio was 1.26, comparing with normal pups where level of mineralization was 1.34. Taking into account that irreversible changes in the structure of the enamel were observed when the Ca / P ratio was below 1.33, we can suggest that the eruption of teeth with an imperfect structure could be because of maternal hypercholesterolemic diet.

Conclusions: Results of this study suggest that hypercholesterolemic diet during gestation and lactation leads to altered enamel mineralization in mice because of changes in chemical composition and may link to the early childhood caries.

KEY WORDS: the tooth enamel mice, cholesterol-enriched diet, chemical composition of teeth enamel

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INTRODUCTION

Nutrition during pregnancy and lactation is perhaps the most influential but often overlooked non-genetic factor in fetal development [1, 2]. A maternal diet containing adequate quantities of micro- (vitamins, macro- and microelements) and macronutrients (proteins, fats, carbohydrates) is a key point for maintaining the health of a pregnant woman and plays an important role in the growth and development of the fetal oral cavity and the teeth [3, 4]. A low-protein diet during gestation-lactation results in impaired odontogenesis that may increase susceptibility of dental anomalies [5]. Studies have suggested that enamel hypoplasia, salivary gland hypofunction and saliva compositional changes may be the mechanisms through which the malnutrition is associated with caries, while an altered eruption timing may create a challenge in the analysis of the age specific caries rates [6]. Not only a deficiency, but also an excess of nutrients can negatively affect the course of pregnancy and fetal organism, as well as the fetal teeth condition in the pre-eruption phase, as it can affect the cellular architecture of the organic matrix and enamel maturation processes [7, 8]. Maternal high-fat diet together with embryonic *Cited2* deficiency significantly reduces the expression of the left-determining gene *Pitx2*, with a dramatic increase in the penetrance of left–right patterning defects, and the appearance of novel defects including cleft palate [9]. Cholesterol intake increases during pregnancy because pregnant women are advised to consume more eggs and other foods rich in cholesterol [10]. However, higher dietary cholesterol from eggs intake during pregnancy was associated with greater risk of gestational diabetes mellitus [11]. The result of a hypercholesterolemic diet, on the one hand, is an increase in the expression of BMP2, which accelerates odontogenesis, on the other hand, a decrease in the expression of the osteocalcin gene leads to insufficient saturation of the tooth hard tissues with hydroxyapatite, which results in the eruption of teeth with low mineralization [12].

AIM

The aim of the study was to determine the chemical composition of the tooth enamel of two-day-old mice from hypercholesterolemic mothers by energy dispersive X-ray spectroscopy. We hypothesized that hypercholesterolemia during gestation and lactation would result in altered mineralization of the enamel.

MATERIALS AND METHODS

ANIMALS AND DIET

Forty mature female mice were purchased and housed in the vivarium of the Bogomolets Institute of Physiology National Academy of Science of Ukraine (Kyiv, Ukraine) in stainless steel cages under controlled conditions (20–24 °C, 50–60% relative humidity, 12-h light–dark cycle) with free access to water. Mice were randomly assigned (n = 20/group) to either a standard chow vivarium diet (24% protein, 11% fat, 48% carbohydrates, 5.5% fiber, 6% vitamin, 5.5% ash) (control group) or a cholesterol-enriched chow diet (a standard chow vivarium diet with the addition of 0,2% Cholesterol (manufactured by Merck, Germany) (experimental group). Female mice were given ad libitum access to their respective diet throughout the study duration. Females in proestrus or estrus phase were mated overnight with male breeders (4 females with 1 male) and separated the following morning. The presence of spermatozoa in the vaginal smear was considered as an indicator of fertilization and first day of pregnancy (gestational *day (GD) 0)*. Pregnant females had spontaneous birth, and day of birth was recorded as day 0 of the mouse's life. Throughout the suckling period the dams remained on their respective diets.

TISSUE COLLECTION

At wearing (postnatal day 2) 6 pups form each group (appearance features were nubs in ear area, visible milk spot and manifesting pigment on skin) were by inhalation overdose of carbon dioxide. CO2 exposure time is recommended 60 minutes for euthanasia of two day old mice (D-2) [13]. The lower jaws were removed and all soft tissue carefully cleaned by dissection. All samples were stored in test tubes (10% streptomycin solution), tightly closed, at a temperature of +2...+4°C. Before the study, the samples were washed with hands wearing rubber gloves in distilled water and passively dried. The incisor segments were used for scanning electron microscopy–Energy dispersive X-ray analysis. The mice used in this experiment were cared for in accordance with the guidelines established by the «Rules and Regulations for Carrying Out Animal Research Work» [14]. All procedures were reviewed and approved by the Private Higher Educational Institution «Kyiv Medical University».

SCANNING ELECTRON MICROSCOPY–ENERGY DISPERSIVE X-RAY ANALYSIS

When jaws were passively dried, the samples were placed in a vacuum apparatus (Ion Sputter JFC-1600, Jeol, Japan) for 5 min until the residual moisture completely evaporated. The samples were affixed to the scanning electron microscopy (SEM) stubs and sputter-coated with a thin layer of Pt (~25 nm), in order to make the material conductive (Fig. 1). examined with a JSM-6100 JEOL SEM operating at 15 kV and 15–20 mm working distance.

SEM analysis was performed by JSM-6100 JEOL SEM under the standard high vacuum mode, operating at 5–10 kV throughout the analysis and 15–20 mm working distance. Measurements took place on 19 areas of enamel in the control group and on 21 areas in the experimental group. The morphology of each sample was imaged with a variety of magnifications. The size of the areas of enamel spectroscopy ranged from 50x50 μm to 250x250 μm.

The chemical composition of the enamel was obtained using an energy dispersive X-ray spectral analyzer INCA Energy 450 (Oxford Instruments Nanoanalysis, UK). EDX analysis was performed at 10 kV and a 10 mm working distance. The count was conducted on the vestibular surface of incisors (19 areas of enamel in the control group and on 21 areas in the experimental group).The elements quantified were Oxygen (O), Natrium (Na), Chlorine (Cl), Calcium (Ca), Phosphorus (P), Magnesium (Mg), Sulfur (S), Ferrum (Fe). All analyzed elements were normalized to the factory calibration provided by Oxford Instruments Aztec/INCA software and an Oxford Instruments X-Max 50 mm^2 detector system. C, O, F, Na, Mg, P, and Ca were calibrated based on $CaCO_3$, SiO_2, MgF_2, albite, MgO, GaP and wollastonite. The element content was calculated as the relative weight percentage of the total element content (100%).

STATISTICAL ANALYSIS

Statistical analysis of the digital data was performed using Excel 2000 and Origin 7.0. Results were expressed mainly as means +/− standard error of the mean. Probability distribution of mean ($P<0.05$) was calculated using Student's t-test.

Table 1. Offspring characteristics of experimental and control groups

Groups	Gestation length, days ± SD	Average litter size, ± SD	Male/female (ratio)	Birth weight ± SE, g	Body length at birth ± SE, mm	Survival rate at 2 PNDs
Experimental, n=20	18.9 ± 0.6*	7.21 ± 1.1*, n=144	74/70 (1.06)*	1.22 ± 0.01*	25.00 ± 0.16*	95 %*, n=137
Control, n=20	19.0 ± 0.3	7.14 ± 2.7, n=142	75/67 (1.12)	1.28 ± 0.01	24.93 ± 0.13	97 %, n=139

1. SD standard deviation
2. PND – postnatal days
3. *p ≥ 0.05.

Table 2. Chemical (elemental) composition of D-2 mouse teeth enamel by the EDX method of the control group

	Chemical element	The number of examined samples	Number of samples containing a chemical element		Qualitative composition of samples, %
			abs	%	
Atomic	O	19	19	100	61.65
	Na	19	19	100	1.15
	Cl	19	19	100	0.31
	Ca	19	19	100	21.82
	P	19	19	100	14.35
	Ca/P				**1.34**
	Mg	19	1	5,26	0.89
	S	19	1	5,26	0.36
	Fe	19	9	47,37	0.45
Weight	O	19	19	100	41.82
	Na	19	19	100	1.13
	Cl	19	19	100	0.47
	Ca	19	19	100	36.55
	P	19	19	100	19.28
	Mg	19	1	5,26	0.92
	S	19	1	5,26	0.5
	Fe	19	9	47,37	1.06

RESULTS

OFFSPRING PHENOTYPE

Each dam was between 6–9 pups with an average size of 7.2 ± 1.2 in experimental group and 7.1 ± 2.7 in control group (means ± standard deviations). There were no other significant differences in the following parameters between the pups of experimental and control groups: gestation length, survival rate, average litter size, male/female ratio, birth weight, and birth body length (Table 1).

SEM-EDX ANALYSIS

Fig. 1. shows the photo of enamel surface on the vestibular area of incisor of a two-day-old mouse, that was made by scanning electron microscopy.

Characteristic X-ray spectra were obtained on the vestibular area of incisor of a two-day-old mouse with the help of an energy dispersive X-ray spectrum analyzer (Fig. 2).

Different distribution of the trace elements concentration in tooth enamel was revealed using energy-dispersive spectral X-ray diffraction analysis. In the enamel of the experimental and the control groups were found seven elements – Na, Cl, Ca, P, Mg, S, Fe. It was found that the chemical elements Ca2+, P5+, Na+, Cl- were found in 100% of the samples in the control group when studying the chemical composition of the D-2 mouse teeth enamel using the EDX method (Table 2).

Elements Mg2+, S were found in 5.26% of the samples, Fe3+ – in 47.37%. The Ca2+ content was 36.55%, the P5+ content was 19.28%. The initial level of mineralization according to the atomic (%) Ca / P ratio was 1.34. It was found that the chemical elements Ca2+, P5+, Na+, Cl- were found in 100% of the samples in experimental group, which received a diet with an increased content of Cholesterol (Table 3).

DISCUSSION

In this study, influence of maternal hypercholesterolemic diet on tooth development and mineralization was

Fig. 1. A section of the tooth enamel (vestibular surface of incisor) of a two-day-old mouse (D-2), obtained by SEM where the chemical (elemental) composition was measured.

Table 3. Chemical (elemental) composition of D-2 mouse teeth enamel by the EDX method of the experimental group

	Chemical element	The number of examined samples	Number of samples containing a chemical element		Qualitative composition of samples, %
			abs.	%	
Atomic	O	21	21	100	61.64
	Na	21	21	100	1.23
	Cl	21	21	100	0.33
	Ca	21	21	100	20.29
	P	21	21	100	16.08
	Ca/P				**1.26**
	Mg	21	3	14,29	0.92
	S	21	3	14,29	0.36
	Fe	21	11	52,38	0.47
Weight	O	21	21	100	41.86
	Na	21	21	100	1.20
	Cl	21	21	100	0.50
	Ca	21	21	100	34.51
	P	21	21	100	21.14
	Mg	21	3	14,29	0.92
	S	21	3	14,29	0.50
	Fe	21	11	52,38	1.12

examined, which revealed changes in enamel chemical composition. We found out few findings that warrant further discussion. First, the results of this study indicate the presence of seven elements (Na, Cl, Ca, P, Mg, S, Fe) in the enamel of both the hypercholesterolemic and normal offspring, but the content of element Ca2+ decreased, the content of elements P5+, Na+, Cl- tended to increase in pups from hypercholesterolemic mice. Second, the initial level of mineralization according to the atomic (%) Ca / P in hypercholesterolemic pups ratio was 1.26, comparing with normal pups where level of mineralization was 1.34 (at the lower limit (1.33), that suggests that the enamel of the teeth of mice that have just erupted is immature). Taking into account that irreversible changes in the structure of the enamel were observed when the Ca / P ratio was below 1.33 [5], we can suggest that the eruption of teeth with an imperfect structure could be because of maternal hypercholesterolemic diet during gestation and lactation.

Although previous work suggests that maternal high-fat diet during pregnancy and lactation can alter fetal cholesterol metabolism and predispose adult offspring to metabolic abnormalities [15, 16] , no investigation has assessed the relationship between maternal hyper-

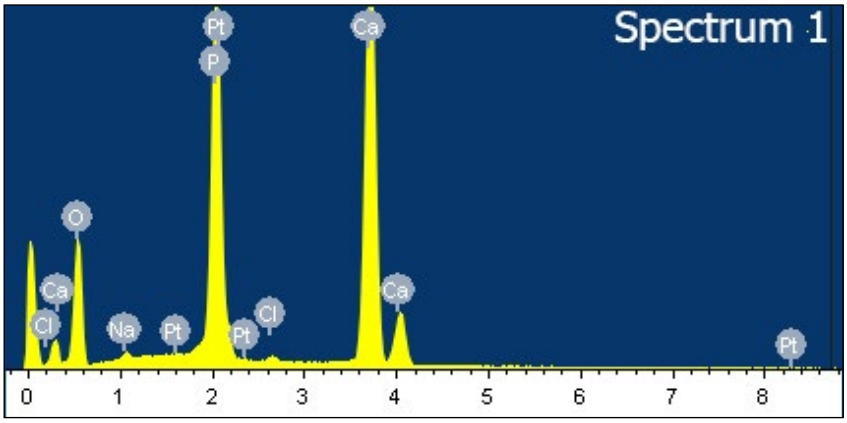

Fig. 2. X-ray characteristic spectrum of the tooth enamel surface (vestibular surface of incisor) of a two-day-old mouse (D-2 mouse) obtained using an energy dispersive X-ray spectrum analyzer.

cholesterolemia and chemical composition of tooth enamel. In our study we have found that a hypercholesterolemic diet during pregnancy and lactation is associated with enamel maturation violation.

The study of the chemical composition of the surface layers of enamel is relevant due to the fact that the variability of the elemental composition of teeth allows to detect metabolic disorders in the process of tooth development and after eruption [17]. The large amounts of free fatty acids, diglycerides, cholesterol and phospholipids as intrinsic components can influence on enamel maturation [18]. A limited number of studies reported significant associations between molar incisor hypomineralization and pre- and perinatal factors such as maternal illness and medication use in pregnancy [19] There are data in the literature that the intensity of caries of temporary teeth in children is affected by the amount of sweet food consumed by a pregnant woman [20]. Evidence suggests that cholesterol intake increases during pregnancy, so maternal hypercholesterolemia could be one of the factor that leads to hypomineralization of the enamel and in its turn manifested in early caries [21].

CONCLUSIONS

In summary, results of this study suggest that hypercholesterolemic diet during gestation and lactation leads to altered enamel mineralization in mice because of changes in chemical composition. Based on the rise of cholesterol intake during pregnancy and the early childhood caries because of the eruption of teeth with an imperfect structure mechanism of maternal hypercholesterolemia influence on enamel maturation needs further investigation.

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ORIGINAL ARTICLE

CONTENTS

Possibilities of predicting adverse cardiovascular events based on the analysis of clinical and instrumental research methods, as well as sST2 in patients after myocardial infarction

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ABSTRACT

Aim: To determine the possibility of predicting adverse cardiovascular events based on the analysis of clinical and instrumental research methods, as well as sST2 in patients after myocardial infarction.

Materials and Methods: The study included 64 patients who suffered an acute myocardial infarction and underwent PCI with balloon angioplasty and stenting of the infarct-related vessel in the acute period. The predictors of adverse cardiovascular events were assessed events during 1 year of observation. Indicators of echocardiography and coronary angiography were assessed and concentrations sST2.

Results: A worse prognosis was associated with intermediate ejection fraction (EF) (odds ratio (OR)=3.981, $p<0.05$), left aneurysm ventricle (LV) (OR=29.5, $p<0.05$), high concentrations of sST2 (OR=1.017, $p<0.05$) and scores on the Syntax scale (OR=1.001, $p<0.05$).

Conclusions: In patients who underwent percutaneous coronary intervention for myocardial infarction, adverse outcome during the next 2 years is associated with coronary and echocardiographic parameters, as well as biochemical indicators of myocardial stress and fibrosis. HF patients with intermediate EF, LV aneurysm, high sST2 concentrations, and high Syntax scores have the worst prognosis.

KEY WORDS: sST2, myocardial infarction, predicting adverse cardiovascular events, left ventricular ejection fraction, arterial hypertension

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INTRODUCTION

Acute myocardial infarction (MI) remains one of the most common causes of morbidity, disability and mortality in the population of developed countries. Despite the significant expansion of the technical capabilities of early myocardial reperfusion using percutaneous coronary intervention (PCI) in patients with acute MI, the frequency of repeated adverse cardiovascular events still remains high [1]. A fairly common complication after an MI is the development of heart failure (HF). The inability of the heart to provide full pumping function significantly worsens the short-term and long-term prognosis of such patients [2, 3]. Verification of predictors of repeated adverse cardiovascular events in patients after MI is an important direction in modern cardiology. Thanks to the formation of a group of high-risk individuals who need more careful monitoring, it is possible to influence their condition in time to prevent the appearance of serious complications. sST2 is one of the promising biological markers for predicting the course of coronary heart disease (CHD) and HF in particular [4,5]. The morphological basis of MI is acute thrombosis of the coronary artery due to the destruction of an unstable atherosclerotic plaque [6]. The course of MI is associated with damage to the structure of cardiomyocytes due to a sharp lack of oxygen, an increase in the hemodynamic load on the part of the myocardium that was not affected, as well as fibrosis and subsequent remodeling of the left ventricle (LV) [7]. The described pathophysiological processes change the morphological structure of the myocardium and negatively affect the contractile function of the LV. All this contributes to the progression of HF after MI. A member of the interleukin-1 receptor family, the growth-stimulating factor expressed by gene 2 (ST2), is a marker of myocardial biomechanical stress and fibrosis. A number of publications highlight its diagnostic and prognostic value in HF [8,9] and various forms of coronary heart disease [10,11]. At the same time, works focused on the comprehensive assessment of traditional clinical-instrumental and laboratory indicators and new biomarkers in predicting clinical outcomes in patients in the remote period of MI remain limited.

AIM

The aim was to determine the possibility of predicting adverse cardiovascular events based on the analysis of clinical and instrumental research methods, as well as sST2 in patients after myocardial infarction.

MATERIALS AND METHODS

After obtaining written consent to conduct a comprehensive examination, in accordance with the principles of the Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, as well as the relevant laws of Ukraine, 64 patients who suffered an acute myocardial infarction no earlier than 12 months before and no later than 24 months relative to the moment of inclusion in the study, for which they underwent PCI with balloon angioplasty and stenting of the infarct-related vessel in the acute period. Written informed consent was obtained from all participants. Diagnosis and treatment of patients were carried out in accordance with current recommendations [12]. Exclusion criteria were acute coronary syndrome, acute disorders of cerebral blood circulation, chronic kidney disease IV-V stage, liver failure, blood diseases, oncological diseases, pregnancy and breastfeeding, acute and chronic inflammatory diseases of the heart and its lining (endocarditis, myocarditis, pericarditis). , atrial/ventricular fibrillation/flutter, II-III degree AV-blockade, neuropsychiatric pathology, severe course of coronary artery disease complicated by cardiogenic shock, severe heart failure with HF<40%. The participants of the study were interviewed and underwent a physical examination, transthoracic echocardiography (EchoCG) with assessment of the main parameters: LVEF according to Simpson's method, pressure in the pulmonary artery (BP). The data of coronary angiography were analyzed : the number of coronary arteries (CA) and hemodynamically significant stenoses, score on the Syntax scale . A study of general and biochemical blood tests was carried out with the determination of standard parameters. The glomerular filtration rate (GFR) was calculated based on the creatinine level using the CKD-EPI equation (Chronic Kidney Disease Epidemiology Collaboration). The concentration of the soluble ST2 receptor (sST2) was determined by quantitative enzyme-linked immunosorbent assay. Presage ® ST2 Assay EIA Test kits were used to determine s ST2 Kit REF # BC-1065E, manufactured by CRITICAL DIAGNOSTICS 3030 Bunker Hill St. Suite 117A San Diego.

After 12 months of follow-up, the achievement of the endpoints of the study was recorded, which included repeated MI, unstable angina, HF decompensation, stroke, and cardiovascular death.

Statistical processing of the obtained results was carried out using the STATISTICA-10 computer program and a package of statistical functions of the Microsoft-Excel program on a personal computer, using the variational-statistical method of analysis. The quantitative indicators obtained in the study were first checked for the type of their distribution according to the method of A. M. Kolmogorov – M. V. Smirnov and H. Lilliefors and S.S. Shapiro – M. Wilk 's W test. Since all of them did not correspond to the law of normal distribution, to present measures of central tendency (Measures of Central Tendency) chose the median value (Me) and the interquartile range (LQ-UQ). Accordingly, to test the null hypothesis, the non-parametric test of the H.B. Mann – D.R. Whitney U test was used, values $p < 0.05$ were considered probable. Categorical variables are presented as absolute values (n) and percentages (%), and Pearson's χ^2 test was used to compare them. To identify predictors of adverse outcome, parameters with significant between-group differences were included in univariate logistic regression analysis with determination of odds ratio (OR) and 95% confidence interval (CI). The prognostic efficiency of the indicators was evaluated based on the results of the ROC analysis with the calculation of the area by the ROC curve – area under curve (AUC).

RESULTS

The study included 64 patients with MI and primary PCI (mean age 52.4±7.6 years, 100% men) who were treated at the myocardial infarction department No. 2 of the Ivano-Frankivsk Regional Clinical Cardiology Center. HF with preserved ejection fraction (EF) was diagnosed in 64.1% of participants, HF with intermediate EF – in 35.9%. Q-wave MI was verified in 70.3% of cases. 78.1% of patients had hypertension, diabetes mellitus (DM) – 45.3%, excess body weight (BMI) or obesity – 75%, confirmed chronic kidney disease (CKD) (<60 ml/min/1.73 m^2) – 7.8%, tobacco smoking – 64.1%. According to coronary angiography, in 73.4% of patients, 1-vessel nature of the lesion of the coronary blood flow was detected, in 3.1% – significant stenosis of the trunk of the coronary artery.

According to the results of the echocardiogram, LVEF was 52% (45–60), 6.25% of patients had an LV aneurysm, and 53.1% had increased systolic pulmonary artery pressure. Most patients had dyslipidemia: low-density lipoprotein (LDL) – 3.7 mmol/l (2.8–4.3), high-density lipoprotein (HDL) – 1.0 mmol/l (0.8–1.4). The following sST2 concentrations were determined in the patients: 38.1 ng /ml (30.5-49.5), respectively.

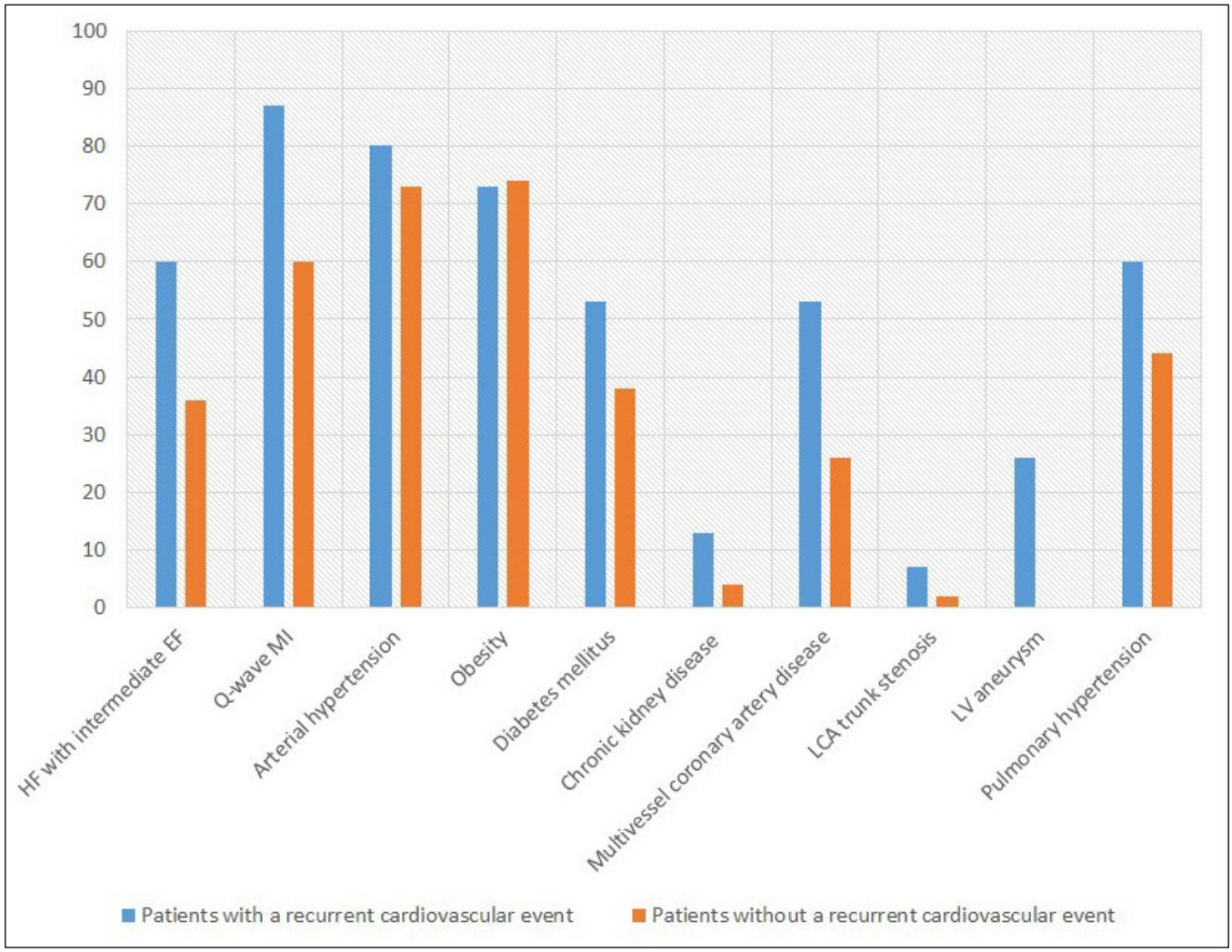

Fig 1. Clinical and instrumental characteristics of patients depending on the occurrence of repeated cardiovascular events (% of observations).

15 (23.4%) participants reached the end points of the study during the 12-month observation period, contact could not be established with 2 (3.1%). In the following, data are presented for the 62 patients who did not drop out of the study. The structure of repeated cardiovascular events: unstable angina – 10 cases, HF decompensation – 3, fatal outcome – 2.

Regardless of the observed result, the patients turned out to be comparable in age and gender, the therapy used – the subjects were prescribed antiplatelet and hypolipidemic agents, beta-blockers, ACE inhibitors, nitrates (for all indicators $p>0.05$). Study participants with adverse cardiovascular events during the observation period were distinguished by a high prevalence of HF with intermediate LVEF ($\chi^2=6.5$, $p<0.05$), the presence of a formed LV aneurysm ($\chi^2=17$, $p<0.05$). Patients who reached the endpoints more often had hypertension, Q-wave MI, impaired carbohydrate metabolism, multivessel coronary artery disease, stenosis of the LV trunk, increased pressure in the pulmonary artery. However, statistically significant differences were not achieved according to these parameters (for all $p>0.05$). Patients also had similar rates of CKD prevalence. The corresponding clinical and instrumental characteristics are presented in fig. 1.

According to the quantitative indicators of the evaluation of the coronary blood flow and the structural and functional state of the myocardium, more pronounced changes were observed in patients with an unfavorable outcome compared to participants in whom no repeated events were noted during the observation period: they had a higher score on the Syntax scale and lower LVEF (Table 1).

During the observation period, 11 myocardial revascularization operations were performed – stenting of coronary arteries in a planned manner. The frequency of interventions in the studied groups was similar ($\chi^2=0.9$, $p>0.05$).

Patients who reached endpoints were characterized by higher levels of sST2 , but showed similar parameters of renal function and lipid metabolism to patients without recurrent events (Table 1).

Table 1. Instrumental and laboratory indicators depending on the achievement of the endpoints of the study

Indicator	Reaching endpoints		p
	Yes (n=15) Me (LQ-UQ)	No (n=47) Me (LQ-UQ)	
Syntax scale , points	23.5 (14.7-35.5)	14.0 (7.0-22.5)	<0.05
Left ventricular ejection fraction, %	47.3 (42.8-54.3)	52.0 (48.5-61.5)	<0.05
Myocardial mass index of the left ventricle, g/m ^{2}	126.8 (98.3-148.5)	116.9 (100.1-135.4)	>0.05
Pulmonary artery pressure, mm Hg.	31.0 (27.0-39.0)	29.0 (26.0-34.0)	>0.05
sST2 , ng /ml	54.0 (38.8-62.6)	35.1 (30.2-41.9)	<0.05
Glomerular filtration rate, ml/min/1.73m2	75.0 (64.0-88.5)	81.0 (72.0-89.0)	>0.05
LDL, mmol/l	2.9 (2.7-4.5)	3.2 (2.9-4.2)	>0.05
HDL, mmol/l	0.9 (0.8-1.1)	1.1 (0.8-1.3)	>0.05

Table 2. Instrumental and biochemical predictors of unfavorable prognosis

Predictor	χ^2	OR	95% CI	p
HF with intermediate LVEF	6.2	3.981	1.231-12.987	<0.05
Aneurysm of the left ventricle	9.1	29.5	3.210-265.176	<0.05
Left ventricular EF	4.2	0.897	0.789-0.991	<0.05
Syntax scale	5.9	1.001	0.901-1.102	<0.05
sST2	14.1	1.017	0.982-1.205	<0.05

According to univariate logistic regression analysis, the clinical-instrumental and biochemical predictors of the development of adverse cardiovascular events during the next 12 months of follow-up in patients after MI with primary PCI include HF with intermediate EF, formation of LV aneurysm, LV EF, Syntax score, sST2 concentration (Table 2).

Determining the contribution of these indicators to the assessment of the prognosis in this cohort, it should be noted that the highest ratio of the chances of developing cardiovascular complications was found for LV aneurysm. However, the CI for LV aneurysm is in a very wide range, which is probably due to the small number of observations of this feature in the group without recurrent events.

Biomarker sST2 has the highest value of χ^2 (criterion of significance of regression coefficients), which indicates its prognostic power.

ROC-analysis confirmed the prognostic efficiency of predictors determined by the results of univariate regression analysis (for all indicators p>0.05). sST2 had the following AUC values: 0.792 (95% 0.678-0.966, p<0.05).

DISCUSSION

In the presented prospective study with a 12-month follow-up period, we performed a comparative assessment of the prognostic value of clinical-instrumental and laboratory parameters, including a modern biomarker of myocardial stress and fibrosis – sST2, in 64 patients with MI and primary PCI. Despite the active study of the contribution of traditional and new indicators to improve prognosis and reduce risk in patients with cardiovascular diseases [13, 14], most of the work in this field has considered the possibility of using sST2 in acute situations.

We should also mention the RAP of Weir et al. [15], who evaluated the relationship between the level of sST2 in blood plasma and changes in left ventricular ejection fraction (LVEF) 12 and 24 weeks after an acute myocardial infarction (MI). Plasma sST2 levels are known to increase immediately after MI and are associated with lower LVEF before hospital discharge and adverse cardiovascular events. The average level of sST2 decreased from 263.3 pg /ml at admission to the hospital to 140.0 pg /ml after 24 weeks (p<0.001) and was significantly correlated with LVEF. The level of sST2 was positively associated with the infarct volume index at admission to the hospital and after 24 weeks and was significantly higher in patients with a higher degree of transmuralization of the infarct and the presence of microvascular lesions. Thus, determination of sST2 after MI helps in predicting medium-term recovery of LV functional capacity.

In our work we analyzed the value of clinical, echocardiographic, and biochemical indicators in determining the outcome of patients in the remote period of MI.

According to the obtained results, along with traditional risk factors, sST2 was also predictor of adverse cardiovascular events.

STUDY LIMITATIONS

The main limitation of the study was the relatively small number of examined patients. This fact could affect the accuracy of the obtained statistical results and requires additional verification on larger groups of patients. However, it was shown that information on the dynamics of indicators of instrumental research methods in patients is suitable for use in clinical trials.

PROSPECTS FOR FURTHER RESEARCH

sST2 remains an understudied biomarker in cardiology. Its further study in order to find new characteristics and possibilities of use in clinical practice remains an urgent challenge for scientists.

CONCLUSIONS

In patients who underwent percutaneous coronary intervention for myocardial infarction, adverse outcome during the next 2 years is associated with coronary and echocardiographic parameters, as well as biochemical indicators of myocardial stress and fibrosis. HF patients with intermediate EF, LV aneurysm, high sST2 concentrations, and high Syntax scores have the worst prognosis.

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ORIGINAL ARTICLE

CONTENTS

Clinical and laboratory assessment of the state of periapical tissues in systemic lupus erythematosus

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ABSTRACT

Aim: To evaluate changes in clinical and laboratory parameters in patients with SLE depending on the severity and activity of the disease.

Materials and Methods: The study included 50 patients with SLE of different age groups, 10 men and 40 women.

Results: Systemic lupus erythematosus (SLE) is a chronic disease that belongs to the group of rheumatic diseases and is characterised by autoimmune tissue damage. Chronic inflammatory periodontal diseases remain one of the most common dental pathologies. Chronic gingivitis and periodontitis in SLE are described as one of the earliest and most striking symptoms of the disease. Approximately the same trend was found in patients with SLE depending on the degree of clinical and laboratory activity of the disease. Patients with minimal, 1 degree of activity (characterized by the longest duration of SLE) showed the greatest decrease in bone mineral density (up to 2.25 points), and patients with higher activity had a significantly shorter duration of SLE and, accordingly, a smaller decrease in bone mineral density: in patients with 2 degrees of activity (1.79 points), with 3 degrees of activity (1.94 points).

Conclusions: In patients with acute SLE, the maximum value of the Muhlemann-Cowell index was 2.31 points, in patients with subacute SLE – 1.89 points, and in patients with chronic SLE – 1.58 points. CPITN values increase inversely with the nature of the course of SLE, which is associated with the duration of the underlying disease.

KEY WORDS: systemic lupus erythematosus, periodontitis, gingivitis, vasculitis

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INTRODUCTION

Chronic inflammatory periodontal diseases remain one of the most common dental pathologies, the effectiveness of treatment of which is still low [1, 2]. Despite the generally recognized role of microbial factors and occlusal disorders in their development, somatic disorders are one of the important aggravating factors of periodontal disease [3]. Especially relevant is the problem of diagnosing dentogenic pathology among patients with chronic somatic diseases of autoimmune genesis, whose adequate immune responses change dramatically [4, 5].

Systemic lupus erythematosus is a chronic disease that belongs to the group of rheumatic diseases and is characterized by autoimmune tissue damage, mainly connective tissue and blood vessels, with the development of necrosis, hemorrhage, and thrombosis of various soft tissue areas, including the oral cavity [6].

Chronic gingivitis and periodontitis in SLE are described as one of the earliest and most prominent symptoms of the disease, but the literature remains controversial regarding the features of periodontal pathology in SLE: some authors [7] speak of the long-term integrity of the periodontal tissues and the development of a process similar to periodontal disease, while others [8] describe early necrotic changes in the periodontium and associated tooth loss in patients with SLE. In SLE, severe immune, rheological, and degenerative disorders in tissues develop early enough, which negatively affects the periodontal condition [9].

In this regard, a number of issues related to the detailed characterization of periodontal pathology in SLE, their relationship with general immune homeostasis in the systemic lupus process, as well as the impact of SLE on the condition of the periradicular tissues of the oral cavity have not been sufficiently reflected in studies [10].

AIM

To evaluate changes in clinical and laboratory parameters in patients with SLE depending on the severity and activity of the disease.

MATERIALS AND METHODS

The study included 50 patients with SLE (10 men, 40 women) of different age groups from 20 to 55 years (mean age was 38.8±7.6 years). All patients were treated in the rheumatology department of the named A. Novak ZRCH.

The comparison group consisted of 30 patients who sought treatment for periodontal diseases and had no somatic pathology (11 men, 19 women, mean age 37.1+7.3 years). The age and sex distribution of the control group corresponded to that of patients with SLE. All selected patients met the diagnostic criteria for SLE.

According to the nature of the underlying disease, patients with SLE were distributed as follows: acute course – 9 (18%) patients, subacute – 10 (20%), chronic course – 31 (62%). By the degree of SLE activity: I degree – 16 (32%), II degree – 19 (38%), III degree – 15 (30%) patients.

All patients underwent a comprehensive clinical and laboratory examination using general and special methods. General methods, including clinical examination of organs and systems, radiography of the TMJ and hand joints to determine the radiological stage of the disease, laboratory tests to determine the degree of activity of the process.

To determine the degree of general inflammatory activity of the disease, all patients underwent determination of hemoglobin, leukocytes, immunoglobulins, ESR in peripheral blood, biochemical and immunological parameters.

Immunological studies of blood serum were performed to determine the titer of rheumatoid factor from the latex test, cryoprecipitins, complement, antibodies to nucleoprotein, anti-DNA, antinuclear factor, and antistreptolysin.

Standard dental examinations were carried out according to the generally accepted methodology. Complaints, medical history, general status, and dental examination data were recorded. During the external examination, attention was paid to the condition of the skin (presence of hyperemia, edema), facial configuration and expression. Particular attention was paid to the symmetry of the face in the position of central occlusion. In the presence of areas of swelling or deformation in the study area, their location and skin color were determined. The examination of the oral cavity began with an examination of the mucous membrane.

Attention was paid to the presence of edema, hyperemia, infiltration, erosion, ulcers, scars. The examination of the dentition took into account the location of defects in the teeth or crowns, the presence of extracted teeth, periodontal preservation, tooth mobility, bite condition, occlusal dysfunction, and other deformities of the hard and soft tissues of the face. When examining the periodontium, attention was paid to the color, shape, consistency of the gingival papillae and marginal gingival margin, the presence of exudation, hypertrophy, ulcers, the degree of tooth mobility, exposure of the necks and roots of the teeth, and the presence of gingival pockets. The location and nature of dental plaque was determined.

Special research methods included a set of objective indicators characterizing the condition of teeth and periodontal tissues (for the convenience of mathematical processing of the results, numerical expressions using indices were used). The intensity of dental caries in the examined patients was assessed using the CPV index, the condition of the periodontal tissues – using the Green-Vermillion hygiene index, the CPITN index of the need for periodontal disease treatment, the Russel periodontal index, the Silness-Loe gingivitis index, and the Muhlemann-Cowell bleeding index.

The reliability of the results was evaluated according to the Student's t-test as follows: the arithmetic mean – M, standard deviation and standard error of the arithmetic mean – m, Student's coefficient were calculated. The value of $p<0.05$ was taken as a significant difference.

The databases collected by us, containing information on the characteristics of patients and research results, were subjected to statistical processing using Jamovi 2.2.5 program.

The statistical processing determined the compliance of the studied indicators with the normal distribution. The arithmetic mean, standard deviation, standard error, skewness, Pearson and Spearman correlation coefficients were calculated.

Absolute and relative differences in a number of dynamic indicators were calculated, as well as the above parameters for absolute and relative differences.

Statistical hypotheses when comparing samples under conditions of normal distribution were tested using the Student's t-test, paired Student's test, and in other cases, the Fisher's exact test, Kolmogorov-Smirnov test, and other non-parametric criteria.

Correlation and regression analyses were conducted using a number of specialized packages for processing statistical information on ordinal, rank and nominal scales. The correlation coefficients exceeding the absolute value of 0.30 were considered statistically significant.

RESULTS

SLE is a chronic, often lifelong disease with a polymorbid component and numerous clinical symptoms, a number of which have a significant impact on the peri-

Fig. 1. Pathological elements on the skin of the face in SLE (rosaceous symmetrical hyperemic spots).

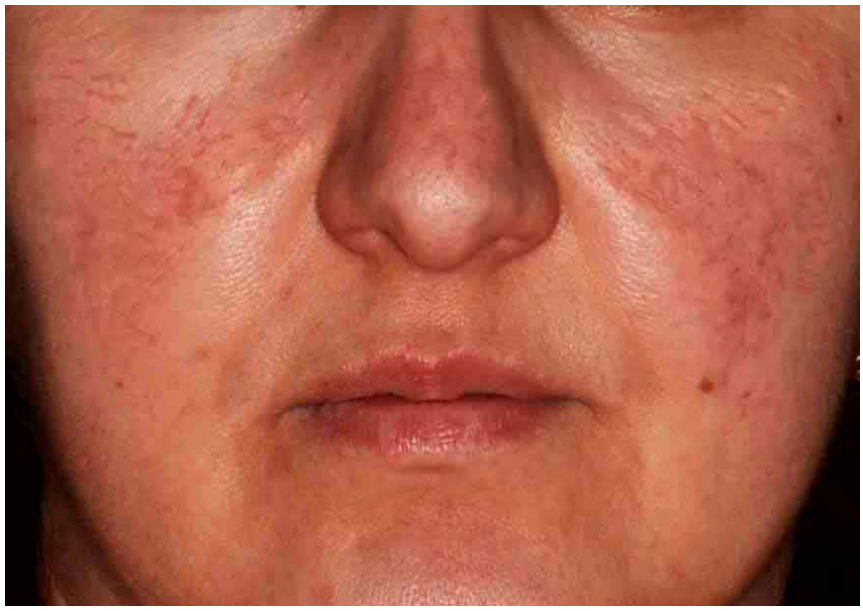

Fig. 2. Symmetrical skin lesions in SLE (telangiectasias, hyperemic spots, rosacea).

odontium. The average age of the examined patients did not reveal any differences depending on the nature of the course and the degree of clinical and laboratory activity of SLE; most patients were aged 28-45 years. The mean age of patients with acute course of SLE was 41.2±10.3 years, with subacute course – 34.4±10.2 years, with chronic course – 39.5±9.6 years.

SLE has a vivid clinical picture involving the maxillofacial area, where the symptoms are clearly visible, quite evident and can be verified by doctors. The skin of the face with SLE usually shows foci of dermatitis in the characteristic "butterfly" shape – these are hyperemic spots or pronounced telangiectasias with elements of vasculitis (Fig. 1, Fig. 2).

In the mouth, vasculitis is manifested by various pathological elements: spots, papules, and sometimes ulcers (Fig. 3). Thus, there is often a focus of congestive hyperaemia along the midline of the hard palate (enanthema), which is sometimes accompanied by erosion and ulceration.

Periodontal lesions in SLE (Fig. 4, Fig. 5) in the initial stages of the disease are represented by catarrhal gingivitis, which is characterized by acute (and then chronic) inflammation. As a rule, the marginal gingiva of one or both dentitions is affected. Clinically, the pathological process in the initial stage often manifests itself in the form of bright hyperemia and swelling of the gingival margin, somewhat reminiscent of hypertrophic gingivitis (edematous form).

Patients complained of pain, discomfort, sometimes burning sensation in the gums, bad breath, bleeding gums when eating or brushing teeth. In the case of

Fig. 3. Symmetrical spots in SLE on the palatal mucosa.

chronic SLE lasting at least 5 years, the bright hyperemia of the marginal gingival margin and interdental papillae was replaced by a stagnant cyanotic tint, and was thickened (as in roller-like thickening). Later, the process progressed as periodontitis with the formation of periodontal pockets, destruction of the tooth-gingival attachment and increased tooth mobility. In severe cases, tooth displacement in the dentition and occlusion disorders were observed.

In patients with SLE, the clinical picture of periodontitis was often aggravated by multiple manifestations of vasculitis, telangiectasia, and petechiae. In the area of these elements, patients had a particularly severe course of periodontitis. As a rule, the presence of large subcutaneous and submucosal hemorrhages, petechiae, ecchymoses in patients with SLE was combined with the presence of antiphospholipid syndrome, which often aggravates the course of SLE and is characterized by significant hemodynamic disorders. Large areas of hemorrhage and vasculitis sometimes involve large areas of the body.

The aggravating factors also include frequent trophic disorders in the distal parts of the body (especially the hands and feet). When located in the area of the hands, this significantly impaired the function of the hands, which affected the level of oral hygiene and, of course, worsened the level of oral hygiene, the accumulation of dental plaque and complicated the course of periodontal pathology.

In patients without adequate therapy, periodontal destructive phenomena rapidly increased, which were complemented by necrotic elements of vasculitis, multiple petechiae, and ulcers. With the progression of the underlying disease, the destruction of the gingival ligament and increased tooth mobility occurred. The clinical picture of inflammatory and dystrophic changes was combined with destructive changes in the bone tissues surrounding the tooth, characterized by the presence of deep bone "pockets" in the long course of the disease and causing tooth loss. This is consistent with the data of a group of authors [11, 12] who described early tooth loss in SLE.

When discussing clinically significant factors of SLE that affect the severity of periodontal pathology, we note, first of all, mineral metabolism disorders: a decrease in bone mineral density in patients with SLE was inversely proportional to the activity of the underlying disease. Thus, in patients with acute SLE, the mean value of bone mineral density reduction was 1.76 points; it was approximately the same in the subgroup of patients with subacute SLE (1.66 points), and in patients with chronic SLE, a significantly greater reduction in bone mineral density was found (up to 2.17 points); the data obtained are likely to be explained

Fig. 4. Catarrhal gingivitis in SLE.

Fig. 5. Catarrhal gingivitis in SLE, marginal gingival involvement.

by the longer duration of SLE, during which a greater decrease in bone mineral density occurs. Patients with a chronic course are still distinguished by a prolonged course of the underlying disease.

The analysis of the results of the oral cavity assessment in patients with SLE is presented in Table 1.

Approximately the same trend was found in patients with SLE depending on the degree of clinical and laboratory activity of the disease. Patients with minimal, 1 degree of activity (characterized by the longest duration of SLE) showed the greatest decrease in bone mineral density (up to 2.25 points), and patients with higher activity had a significantly shorter duration of SLE and, accordingly, a smaller decrease in bone mineral density: in patients with 2 degrees of activity (1.79 points), with 3 degrees of activity (1.94 points).

We analyzed the features of periodontal status in the examined patients with SLE. It was found that the values of the CPITN index increased in inverse proportion to the nature of the course of SLE, which is also probably associated with the duration of the underlying disease: in patients with acute SLE, the average value of the CPITN index was 1.69 oral sextants, with subacute course – 1.82 sextants, with chronic course – 2.56 sextants. The same trend was noted in the analysis depending on the degree of clinical and laboratory activity: in patients with grade 1, which is usually characterized by the longest course, the average value of the CPITN index was 2.57 sextants, with grade 2 activity – 2.37 sextants, with grade 3 – 1.91 sextants.

The Russel index values did not show a pronounced dependence on the nature of the course of SLE or the degree of clinical and laboratory activity, amounting to: in acute SLE – 3.17 points, in subacute course – 2.72 points, in chronic course – 3.24 points; in grade 1 clinical and laboratory activity of SLE – 2.87 points, in grade 2 – 3.42 points, in grade 3 – 3.02 points.

We also did not find significant differences in the analysis of Lo-Silence index values depending on the

Table 1. Index assessment of the hygienic and clinical condition of periodontal tissues in patients with SLE depending on clinical and laboratory characteristics of the underlying disease

Characteristics of the SPS	Medium age, years	Degree osteopenia interalveolar partitions, points	Average CPITN index, sextants	Average Russel index, points	Average Green-. Vermillion index, points	Average Loe-Silence index, points	Average Muhlemann-. Cowell bleeding index, points
Nature of the course of SLE							
- acute (n=10)	41.2±10.3	1.76±0.05	1.69±0.06	3.17±0.05	1.55±0.01	2.01±0.05	2.31±0.05
- subacute (n=9)	34.4±10.2	1.66±0.064 *p=0.0014	1.82±0.054 * p=0.0001	2.72±0.08 * p=0.0001	1.47±0.023 * p=0.0001	1.55±0.07 * p=0.0001	1.89±0.018 * p=0.0001
- chronic (n=31)	39.5±9.6	2.17±0.012 **/*** p=0.0001	2.56±0.015 **/*** p=0.0001	3.24±0.07 ** p=0.005 ***p=0.0001	1.79±0.014 **/*** p=0.0001	1.65±0.034 **/*** p=0.0001	1.58±0.015 **/*** p=0.0001
The degree of clinical and laboratory activity of SLE							
1 (n=16)	37.2±8.9	2.25±0.013	2.57±0.01	2.87±0.05	1.61±0.010	1.68±0.01	1.69±0.015
2 (n=19)	40.4±9.2	1.79±0.02 * p=0.0001	2.37±0.03 * p=0.0001	3.42±0.06 * p=0.0001	1.85±0.018 * p=0.0001	1.72±0.015 * p=0.0001	1.61±0.03 * p=0.0001
3 (n=15)	38.4±9.5	1.94±0.021 **/*** p=0.0001	1.91±0.018 **/*** p=0.0001	3.02±0.08 **/*** p=0.0001	1.54±0.015 **/*** p=0.0001	1.68±0.012 *** p=0.0001	2.07±0.02 **/*** p=0.0001

* - statistical significance between acute and subacute or grade 1 and 2 of ACS; ** - statistical significance between acute and chronic or grade 1 and 3 of ACS; *** - statistical significance between subacute and chronic or grade 2 and 3 of ACS.

nature of the course and the degree of activity of the underlying disease: in patients with acute SLE, the mean Lo-Silness index value was 2.01 points, in patients with subacute and chronic course – significantly less (1.55 and 1.65 points), and when comparing the degree of clinical and laboratory activity, we found practically no significant differences: In the subgroup with grade 1 activity, the mean value of the Loeh-Silness index was 1.68 points, with grade 2 – 1.72 points, with grade 3 – 1.68 points.

DISCUSSION

It is characteristic that the influence of the activity of the underlying disease on the level of oral hygiene in patients with SLE has not been established: For example, in patients with acute course of SLE, the average value of the hygiene index was 1.55 points, with subacute course – 1.47 points, with chronic course – 1.79 points; with 1 degree of clinical and laboratory activity – 1.61 points, with 2 degree of activity – 1.85 points, with 3 degree of activity – 1.54 points. Similar data also have reported in overview of Z Rutter-Locher et al. [7].

A directly proportional relationship between the activity and nature of the course of SLE and the values of the Muhlemann-Cowell bleeding index was established. Thus, in patients with acute SLE, the maximum value of the Muhlemann-Cowell bleeding index was 2.31 points, with subacute course – 1.89 points, with chronic course – 1.58 points. Such trends noted before M. Martínez-García et al. [3]. The same correlation was noted too with the degree of clinical and laboratory activity of SLE: in patients with minimal, 1 degree of activity, the mean value of the Muhlemann-Cowell bleeding index was 1.69 points, with 2 degree of activity – 1.61 points, with 3 degree of activity – the maximum value (2.07 points).

Thus, the data obtained show that the severity of periodontal damage in SLE depends more on the duration of the underlying disease than on its activity: It is the long-term course of SLE that has a more unfavorable effect on the periodontium, not its activity (probably due to the fact that the collagen structures of the periodontium are destroyed by a long-term pathological process, but the activity of the pathological process is much less important – the periodontium is quite resistant to many pathological processes, but it cannot withstand the long-term factor). In addition, an interesting fact was noted B. Sojod et al., (2021) about the direct correlation between the values of the Muhlemann-Cowell bleeding index and the degree of SLE activity – the latter indicates the

prevalence of vasculitis in the picture of periodontal pathology in SLE [8]. The severity of vasculitis, respectively, directly depends on the characteristics of the underlying disease (the nature of the course, the degree of clinical and laboratory activity, a number of laboratory parameters).

CONCLUSIONS

1. In patients with acute SLE, the maximum value of the Muhlemann-Cowell index was 2.31 points, in patients with subacute SLE – 1.89 points, and in patients with chronic SLE – 1.58 points.
2. The influence of the activity of the underlying disease on the level of oral hygiene in patients with SLE was not established: thus, in patients with acute SLE, the average value of the hygiene index was 1.55 points, with subacute course – 1.47 points, with chronic course – 1.79 points; with 1 degree of clinical and laboratory activity – 1.61 points, with 2 degree of activity – 1.85 points, with 3 degree of activity – 1.54 points.
3. CPITN values increase inversely with the nature of the course of SLE, which is associated with the duration of the underlying disease.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Impact of meeting housing needs on human health

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ABSTRACT

Aim: To identify the impact of meeting the housing needs on human health, which must be taken into account when developing the health care policy for the country's population.

Materials and Methods: The system of general scientific and special research methods was used during the research. The materials of the work were: statistical data; standards and recommendations regarding sanitary living conditions; court case-law; reports in mass media; scientific sources; regulatory legal acts of Ukraine.

Conclusions: Sanitary and hygienic conditions of living in housing provide for the formation of a human life environment, where there is no harmful effect of its factors on human health and there are opportunities to ensure normal and to restore impaired body functions. Each person is responsible for maintaining own sanitary and hygienic living conditions in the housing. Sanitary and hygienic living conditions of a person must be considered through the principle of reasonableness and safety of public health.

KEY WORDS: human rights, health care, sanitary standards, housing, housing policy, living conditions

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INTRODUCTION

The urgent areas of the society's development strategy are the provision of human / public health and meeting the housing needs. The relationship between the quality, safety and availability of housing on the one hand and the health, well-being of people on the other is well known, because housing can simultaneously be both an element of human protection and the main source of harm and risk to the health [1]. Both scholars and ordinary residents pay attention to the relationship between meeting the housing needs and human health. The latter express concern and try to take various measures against poor-quality housing and its impact on people's health and city functioning [2]. At the same time, attention is not always paid to such mutuality at the level of political decisions. Thus, the Strategy of Human Development, approved by the Decree of the President of Ukraine dated from June 2, 2021 No. 225/2021 has no areas for preserving public health at the expense of the development of the system for providing housing needs. The document only emphasizes the uncertainty of housing perspectives for internally displaced persons [3]. Depriving a person of own housing as a result of war has a negative impact both on a person's social protection, as well as physical and mental health.

The issue of economic poverty is urgent for the population of Europe. A third of the population on the European continent lives on the edge of poverty, and more than half of them live in cold apartments. 45% of the population does not heat their homes enough to save money. Europe's population suffered from energy poverty is almost three times more often live in damp, unhealthy buildings. However, living in unheated house affects the health. People who cannot maintain thermal comfort in their apartments during the winter period are twice more often complain on health problems. Almost every third resident of underheated house has such problems in Poland. However, houses affect the health of their residents not only because of poor living conditions. Thus, single-family houses with low energy standards and outdated heating systems (about 40%) do not always use environmentally friendly materials for heating. They are responsible for the formation of smog and poor air quality in Poland [4].

Many somatic health problems arise as a result of the direct or indirect influence of living conditions. Thus, health is affected by construction materials, equipment,

dimensions and design of the apartment. Let's consider the example with Legionella pneumophila. The Bellevue Stratford Hotel in Philadelphia hosted the Pennsylvania American Legion Veterans Convention in 1976, which resulted with the death of 29 members and 5 hotel employees. 221 people had severe pneumonia at that time. Joseph McDade proved that the cause of this mass disease was a previously unknown microorganism that was formed in the air conditioner of a hotel room. The researcher called it Legionella pneumophila (legionnaires disease) [5]. The given example emphasizes the relationship between living conditions and human health. It must be taken into account when improving the legal provision of health care protection for both a specific person and for public health in general.

AIM

The purpose of the article is to identify the impact of meeting the housing needs on human health, which must be taken into account when developing the health care policy for the country's population.

To achieve this purpose, the authors have set forth the following objectives: to identify the impact of the sanitary and hygienic suitability of the housing on human health; to establish the significance of the human role in maintaining sanitary living conditions in the housing; to reveal the levels of the housing needs and their impact on human health; to suggest strategic areas of the governments' health care policy in the aspect of meeting the housing needs.

MATERIALS AND METHODS

The following materials were used while conducting the study of the impact of meeting the housing needs on health care: EU and Ukrainian legislation, mass media reports, statistical data on living conditions in Ukraine, Poland, Germany, court cases on living conditions of individuals in Ukraine, literary sources in the fields of jurisprudence, health care and economics.

The system of general scientific and special methods of scientific research was used to solve the set objectives. The dialectical method became the basic one that made it possible to establish the essence of the research problem, the nature and types of the housing needs, the importance of the housing for both human and public health. The impact of meeting the housing needs on human health was emphasized by the axiological method, which made it possible to identify value categories in scientific research. Its use made it possible to distinguish values in the researched phenomenon. Methods of analysis and synthesis were used to reveal the relationship between the availability of the housing and adequate living conditions and human health. The differences in the legal regulation for providing the housing needs in different countries have been revealed due to the comparative and legal method. The statistical method was used to analyze statistical data on the spread of global, energy poverty, housing provision. The formal and logical method made it possible to reveal the peculiarities of regulatory legal regulation for meeting the housing needs, in particular for health care.

REVIEW AND DISCUSSION

The need to identify the impact of housing availability and living conditions on human health stems from the provisions of the document entitled "Sustainable Development Goals", adopted at the UN Sustainable Development Summit on September 25, 2015, for the period up to 2030. 17 Global Sustainable Development Goals, which are an urgent call to action for all countries, are its core element. Thus, addressing poverty and other disadvantages must be implemented alongside strategies that improve health and education, reduce inequality and stimulate economic growth. In particular, the third goal involves ensuring a healthy life and promoting well-being for all people [6]. It is well-known fact that a person spends part of life at home, and therefore living conditions have a direct impact on a person's health situation. Thus, these conditions include: established housing dimensions (minimum living space for a person); quality of building materials; indoor air quality; availability of housing and municipal services; noise level; characteristics of the territory where housing is located, etc.

According to the data of the European Union Agency for Fundamental Rights (FRA), the majority of Ukrainians do not plan to return to Ukraine. Thus, during the survey respondents aged 16+ were asked about their plans for the future. 35% of respondents said that they plan to return home, and 37% would like to stay in their host country. 23% have not decided on their plans yet, and about 4% plan to move elsewhere [7]. Mostly, people do not want to return due to the difficult socio-economic conditions of living in Ukraine, particularly housing conditions.

The issue of returning Ukrainian refugees is one of the debated, because its solution depends both on legal, and political, socio-economic factors. To accomplish this, it is necessary, first of all, to create safe and sufficient conditions for human habitation, to bring them in line with living standards in EU countries. At the same time, it is necessary to solve not only the issue of en-

suring the safety of living, which is caused by the war, but also to improve the quality of living conditions in housing. We are analyzing living conditions in Ukraine and some EU countries.

As of 2021, 46.3% of Ukrainian population lived in separate apartments, 49.3% – in individual houses. Herewith, one room was occupied by: four people and more 8.8%; three persons – 25.8%; two persons – 34.7%. On average, one person accounts for: up to 7.5 m^2 – 7.1%; up to 9.0 m^2 – 5.0%; from 9.01 m^2 to 13.65 m^2 – 22.9%; from 13.66 m^2 to 20.0 m^2 – 27.4%; from 20.01 m^2 to 25.0 m^2 – 12.1% [8].

There is other data in the Republic of Poland. Thus, the housing stock of Poland increased by 40% in 2022. On average, one person in Poland has 31 square meters of living space, according to HREIT, based on data from the Central Statistical Office. The latest figures are 3 meters higher than 5 years ago and 8 meters higher than in 2002. Improvement of new building construction is due to the attraction of individual funds and individual construction [9].

There were about 43.1 million apartments in residential and non-residential buildings, including dormitories in 2021 in Germany. The average living space per apartment in 2021 was 92.1 square meters. Living space per capita (the total allowable area of rooms belonging exclusively to a residential unit) in Germany increased from 46.1 square meters to 47.7 square meters within the period from 2011 up to 2021. It is about 2.5 million apartments more than in 2011 (+6.0%). The actual used residential area was significantly increased by 7.3% during the same period. One of the reasons for that is the ever-increasing supply of houses and large apartments, even though households are getting smaller on average and single-person households become more common [10].

Analyzing the given data, it can be stated that living conditions in Ukraine are lower than in EU countries. At the same time, the provision of housing conditions in Ukraine, aimed at supporting health care is achieved through the establishment of sanitary requirements set forth for housing. Modern sanitary requirements for housing in Ukraine were developed in the 80s of the XX century. They were established for different types of housing depending on climatic conditions, in particular, the minimum sanitary area per person was 9 $м^2$.

Modern legislation of Ukraine on housing requirements and living conditions has been significantly updated. Part 4 of the Art. 7^2 of the Law of Ukraine "On Building Regulations" establishes that the main requirements for buildings and constructions are to ensure mechanical resistance and stability, fire safety, hygiene, health and environmental protection, safety and accessibility during operation, protection against noise and vibration, energy saving and energy efficiency, sustainable use of natural resources. Thus, residential buildings must be designed and built in such a way that they do not pose a threat to the safety of residents or neighbors during the entire life cycle and do not have a significant impact on the quality of the environment or on the climate during their construction, operation and demolition, in particular, as a result of any of the following factors: release of toxic gas; release of hazardous substances into the air inside or outside the premises [15]. The specified requirements are provided in details in the Law of Ukraine "On the Public Health Care System"[12]. Thus, the Art. 31 of the Law states that residential premises in terms of area, design, lighting, insolation, microclimate, air exchange, air condition, as well as noise, vibration, ionizing and non-ionizing radiation levels must meet the requirements defined by state health and sanitary regulations and rules in order to ensure safe and harmless living conditions, regardless of the duration of such living.

The following state sanitary rules related to housing currently exist in Ukraine:

1) State sanitary rules for planning and real estate development of settlements. They established that complex engineering infrastructure, which includes centralized systems of water supply and sewage, heat-, gas- and energy supply, sanitary cleaning and other types of engineering equipment and urban land improvement ensuring the environmental protection and favorable conditions for population living, should be provided in settlements in accordance with the current building norms and regulations [13].

2) State sanitary norms of permissible noise levels in the premises of residential and public buildings and on the territory of residential buildings [14];

3) State sanitary standards and rules for maintaining the territories of populated areas [15].

Establishing sanitary requirements for housing is a modern necessity for ensuring human health. Thus, the COVID-19 pandemic has formulated a number of problems regarding the right to safe housing, namely: the lack of sanitary requirements during the construction of housing in some countries has led to overcrowded living; free penetration of the virus through ventilation systems became one of the factors of the spread of the disease [16]. Housing affects human health through: the size, indoor air quality, safety, accessibility, neighborhoods and area characteristics. Such topical issues as thermal and hygrometric comfort, lighting, noise protection, water supply, and waste disposal have a strong impact on both the psychological and physical health of residents [17].

The Polish Law "Prawo budowlane" [18] establishes that a building (in particular, residential real estate) must meet the following requirements: 1) load-bearing capacity and stability of the construction, fire safety, noise protection, energy saving and thermal insulation and other requirements that are enshrined in the Annex I to the Regulation of the European Parliament and of the Council of European Union No. 305/2011 of 9 March 2011 which lays down harmonized conditions for the marketing construction products and replaces Products Directive 89/106/EEC [19]; 2) operation of the construction object according to its purpose. It is about the supply of water and electricity, removal of sewage, rainwater and waste, the possibility of accessing telecommunication services, etc.; 3) the ability to maintain a proper technical condition and have the necessary conditions for the use of communal facilities and multi-apartment housing construction by the disabled; 4) labor protection; 5) protection of the population in accordance with the requirements of civil protection; 6) protection of objects that are in the register of monuments; 7) appropriate location on the building site; 8) compliance with and respect for the legitimate interests of third parties, including providing access to public roads; 9) safety and health of persons staying in the construction premises (the Art. 5 of the Law) [20]. The above requirements include the presence of sanitary living principles in housing, which are laid during the construction of the housing. At the same time, housing that has been built before the establishment of modern construction standards does not meet the relevant sanitary standards that would ensure safe living conditions.

The Preamble of Regulation (EU) No 305/2011 of the European Parliament and of the Council of European Union of 9 March 2011 which lays down harmonized conditions for the marketing construction products and replaces Products Directive 89/106/EEC determines that the rules of Member States require that construction works be designed and executed so as not to endanger the safety of persons, domestic animals or property nor damage the environment. Member States have introduced provisions, including requirements, relating not only to safety of buildings and other construction works but also to health, durability, energy economy, protection of the environment, economic aspects, and other important aspects in the public interest (clause 4 of the Preamble). When assessing the performance of a construction product, account should also be taken of the health and safety aspects related to its use during its entire life cycle (clause 15 of the Preamble) [19]. The requirements related to the safety of people and the surrounding environment emphasizes the importance of developing sanitary and hygienic living conditions in housing at the level of a separate state.

Summarizing, we can state that housing must meet sanitary living standards. Sanitary and hygienic conditions of living in housing provide the creation of an environment for human activity, where there is no harmful effect of its factors on human health and there are opportunities to ensure normal and restoration of impaired body functions. These conditions are the integral element of housing suitability, which provides a safe and healthy environment for human habitation. It must be taken into account that living in housing is interconnected with the living of other people. Because of that, the privacy rules of living in housing may be limited by the requirements of safe living, in particular sanitary, hygienic conditions of living. Rules for safe living in housing should be established at the level of the state (basic sanitary living conditions), local self-government agencies (depending on the state of the climate, topography, sanitary and epidemiological situation of a particular area, etc.), individual family, person.

Healthy living in the housing is not always supported at a family level. For example, when identifying circumstances that may lead to deprivation of parental rights in Ukraine, the child's living conditions are taken into account. Thus, one of the court's decisions describes the following improper living conditions for children, which were discovered by specialists of the regional center for social and psychological rehabilitation of children during their visit to the family: unsanitary conditions, lack of bed linen, heating and hot water; cockroaches, bedbugs, dirt and mess in the rooms; non-working refrigerator and bathroom; lack of space for children's studies, activities and games; unusable dishes; lack of daylight in the rooms, etc. [20]. Another court decision describes a situation when a mother tried to take a disabled child from a center for social and psychological rehabilitation of children. After all, during the examination of the child's living conditions, it was established that there is no electricity and gas in the apartment building, there is no way to heat water and cook food; the premises are not heated in winter period; the residence needs repair [21].

Analyzing these and other court cases, it can be established that appropriate and safe living conditions for health depend on the social status of a person, economic opportunities to maintain sufficient conditions for living in the housing. The maintenance of the necessary sanitary living conditions is influenced by the state housing policy, the socio-economic status and the state of health of an individual. Thus, people with health problems, in particular, with a disability status or mental health disorders, including alcoholism, drug addiction, cannot independently meet their own housing needs, the needs

of their family and children. We note that apartments are bought by people who have a stable state of health and income. Therefore, it is necessary to take into account that not every person can maintain the proper living conditions. This provision must be taken into account when developing housing legislation. At the same time, it is necessary to take into account the balance of mutual interests. Thus, if a person does not maintain proper sanitary living conditions, it can affect not only his / her living conditions, but also the living conditions of other people. Here is an example that one of the authors of this article faced. Thus, a person with disabilities and low incomes was cut off sewers in the summer of 2023 in one of the central districts of Kharkiv. As a result, this person was forced to pour own feces from the window of the apartment onto the pedestrian sidewalk. Therefore, the state of sanitary and hygienic living conditions must be considered through the principle of reasonableness and safety of public health, giving it priority over economic interests.

Depending on the availability of meeting the housing needs, the standard of living of society can be determined. Housing need has several types. Depending on the reason for its occurrence, it can be primary, which originates because of the lack of housing for a person (for example, as a result of the destruction of a house; in other cases, when housing loses the ability to meet the conditions of safe living; in case of loss of housing due to fraudulent actions, illness, etc.) and derived one, which arises as a result of a change in life circumstances (for example, moving, expanding the family, the desire to change living conditions, etc.). The housing need may also vary depending on the state of vulnerability of a person. It is about the housing need of: a child; women who found themselves in difficult life circumstances; persons who have experienced domestic violence; internally displaced persons; refugees; persons receiving temporary asylum; persons with disabilities; unemployed.

The primary housing need is the most dangerous for health situation. If a person does not have housing that can provide conditions for meeting the primary needs of a person, then there is a threat to a person's existence as a biological being. If we are talking about the derived housing need, there is a subjective feeling of satisfaction or dissatisfaction with housing as a result of comparing the available housing with the cultural norms of living in a specific society and in a specific time period. The inconsistency of these norms with real living conditions causes awareness of the housing problem and prompts a person to take specific actions to satisfy it [22].

The primary housing need is related to the right to human life and health protection. The lack of housing or its destruction makes a person to be in the state of dangerous existence. In order to overcome this situation, most countries are developing social housing systems. At the same time, those mechanisms do not always work. Thus, there were only 1,098 social housing apartments and 1,997 temporary housing apartments in Ukraine in January 2021. Unfortunately, a significant part of such housing was on temporarily occupied territories with the beginning of the full-scale war [23].

The situation of social housing in Ukraine is extremely unsatisfactory. Social housing stock was practically not built in the state, which negatively affected meeting the housing need during the war. Non-systematic actions were taken to overcome it. Thus, preparatory works for the construction of eight apartment buildings for patients of the national rehabilitation center "Nezlamni" began in Lviv in June 2023. The uniqueness of this project is that the newly constructed housing stock will belong to the city, which can use it for different needs with the change of circumstances. 90% of wounded civilians and soldiers treated at the "Nezlamni" center are residents of other cities. Depending on the situation (the type of injury and the type of needed treatment) they will be able to live there from six months up to one year.

It is rightly noted in the scientific literature that housing conditions significantly affect the health of both an individual and the community [24]. The most optimal way for the state (from a financial and time point of view) to provide the population with housing is the construction of temporary buildings and towns [25]. At the same time, it is impossible to overcome the primary housing need at the expense of temporary housing. The experience of other countries emphasizes that it is necessary to involve government programs to meet the housing needs, in particular, direct subsidies provided to local authorities for the purpose of building cheap apartments, which are then rented out; various forms to support non-governmental organizations engaged in social construction (subsidies, various types of benefits, etc.); benefits, exemptions, etc., addressed directly to people with low incomes who are trying to get their own apartment [26].

Derived housing need is related to human health care. It is detailed in accordance withdependin on the housing's compliance with technical and sanitary requirements. Thus, the number of people living in one room has a direct impact on human health. For example, the spread of infectious and viral diseases increases due to the crowding of people. Poor housing conditions such as leaking water, poor ventilation, dirty carpets and pest infestations can lead to an increase in mold, mites and other allergens related to poor health. However, not everyone can create safe and sufficient conditions for a person to live in the housing, maintain a proper state of living conditions that would ensure the health of the people who live there.

Therefore, the acquisition of sufficient housing from the point of view of ensuring human health protection for a certain part of the population of Ukraine is only a dream.

In terms of sustainable development of mankind, the issue of developing the general system of affordable housing, which can ensure the support of human health, is especially relevant. At the same time, it is necessary to take into account the impact of different types of housing needs on human health.

It can be argued that there is a direct relationship between the satisfaction of housing needs, a person's sanitary living conditions and the health. It emphasizes the reciprocity of human rights, namely the right to life, health care and housing. Taking this into account, we offer the following strategic areas of the governments' health care policy in the aspect of meeting the housing need: development of state and municipal housing programs; formation of the system of conditions for the sufficient housing; expansion of social housing construction; support of low-income people in the field of adequate housing (benefits, provision of social housing, write-off of debts for housing and municipal services, etc.); continued updating of sanitary and hygienic living conditions in the housing.

CONCLUSIONS

On the basis of the conducted research, we can suggest the following conclusions:

1. Sanitary and hygienic living conditions in the housing stipulate the creation of a human living environment, where there is no harmful effect of its factors on human health and there are opportunities to ensure normal and restoration of impaired body functions. These conditions are the integral element of housing suitability, which provides a safe and healthy environment for human habitation.
2. Each person is responsible for maintaining own sanitary and hygienic conditions of living in the housing. Maintaining such conditions has a positive effect on a person's health situation, his / her family and neighbors. However, not every person can maintain proper living conditions, therefore the state of sanitary and hygienic living conditions must be considered through the principle of reasonableness and safety of public health, giving it the priority over economic interests.
3. It has been suggested to distinguish two types of meeting the housing needs: primary and derived. The primary housing need is related to human right to life, protection of human health. Derived housing need is related to human health care. Housing that does not meet the technical and sanitary conditions of suitability can negatively affect a person's health. The derived housing need in contrast to the primary one emphasizes the condition of unsatisfactory residence in the housing.
4. In terms of sustainable mankind development, the governments of countries should elaborate strategies for the development of health care in the aspect of meeting the housing needs, in particular, to develop state and municipal housing programs. Such strategic documents should determine and establish the conditions for adequate housing, expansion of social housing construction, support for low-income persons (allowances, provision of social housing, write-off of debts for housing and municipal services, etc.), further updating of sanitary and hygienic living conditions in the housing.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Modern view on the problem of acute pleural empyema surgical treatment

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ABSTRACT

Aim: data study on the results of treatment of acute non-specific purulent-destructive pleura diseases with the purpose of further improvement of its results on the basis of improvement of diagnostics, identification of factors of disease prognosis and by implementing differential tactics of surgical treatment with the use of minimally invasive interventions.

Materials and Methods: We have studied modern literary sources on the topic of current trends in the treatment of acute pleural empyema and its complications. The studied material is summarized and presented in the form of a literature review in this article.

Conclusions: These issues cannot be considered to be completely solved and require further study. Everything mentioned above dictates the search of new effective methods of the treatment of the mentioned pathology and proves the relevance of the theme. The outlined information highlights the necessity of improvement of surgical tactics in patients with pleural empyema.

KEY WORDS: surgical treatment, acute purulent-destructive lung and pleura diseases, acute pleural empyema.

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INTRODUCTION

According to the literature number of patients with acute destruction of the lungs equals to more than 68.4% of total number of inflammatory diseases of the chest cavity and mediastinum [1].

According to some authors' data acute pathology of lungs becomes chronic with 11 – 40%, leads to partial invalidism of 30 – 40%, permanent disability of 7.1 – 9.7%. Mortality with purulent-destructive lung and pleura diseases is 7.2 – 28.3%, and with its gangrenous forms, it is 23.4 – 74.1% [2].

Specific gravity of complicated forms of abscesses pneumonia has increased within recent years from 15.8% to 43.6% [3].

In order to improve the quality of treatment of patients with purulent-destructive lung and pleura diseases and their surgical complications an important practical role is played by objective formation of risk groups of developing complications and forecasting of the dynamics of the disease. Successful solution of this problem is related mostly to highly informative early diagnostics, reliable determination of the severity of the disease, as well as creation of multidirectional classification of inflammatory lung and pleura diseases [3].

Notwithstanding the fact that at the moment various methods of diagnostics of non-specific purulent-destructive lung and pleura diseases have been widely implemented into clinical practice, a range of issues related to examination of these patients has not been outlined in the literature wide enough.

Among the methods of early diagnostics of acute destruction of lungs and pleura according to the literature sources the most informative are X-ray and ultrasound research methods [4].

However ultrasound examination capabilities in examination of patients with purulent-destructive lung and pleura diseases have not been studied well enough. In the Ukrainian and foreign literature there are single messages concerning this issue.

According to the literature [5] the task of ultrasound scanning is to diagnose the parietal formations, pleurisy, echinococcus, lung cancer and tumors of the pleural cavity.

The data concerning application of ultrasound study to scan intrapulmonary formations, interpleural edema, preoperative examination of patients who underwent video thoracoscopy and postoperative dynamic monitoring of patients, has not been outlined thoroughly enough [6].

Some authors indicate the impossibility of lungs examination through the air in the alveoli [7].

The problem of classification of acute non-specific purulent-destructive lung and pleura diseases is still under discussion. A wide range of classifications of acute destruction of lungs and its surgical complications has been put forward [7].

The offered classifications define clinical and radiological symptoms of the disease, the degree of endogenous intoxication, compensatory capabilities of the body, but they do not let to forecast the development of intrapleural purulent complications. In the literature we have not found the classification which could include all the criteria mentioned above in combination.

Pleural empyema is frequent and dangerous complication of inflammatory diseases of the lungs, chest injuries and surgical interventions on the organs of the chest cavity [3, 8].

The relevance of the problem has been promoted by increase of frequency of pathological conditions development complicated by pleural empyema. Within the last decade there has been steady increase of incidence of acute pneumonia, which in 4% cases is complicated with development of pleural empyema [9].

In the structure of injuries and wounds the specific weight of chest wounds remains high and equals to 6 – 12%. Pleural empyema complicates the course of closed chest injuries in 2.9 – 5.2% of observations, wounds caused by cold weapon – 1.7% – 5.4% [7, 10]. With gunshot wounds of chest frequency of pleural empyema increases to 21.7% [10].

The number of thoracic operations has increased, including traumatic interventions which are performed on patients with locally advanced and complicated forms of lung cancer. After such interventions pleural empyema develops in 2.5 – 6.5% of cases [11]. After operations for purulent-destructive diseases of the lungs pleural empyema occurs in 4.8 – 28% of patients [11].

Treatment of pleural empyema involves use of surgical aid aimed at drainage and rehabilitation of the purulent cavity, impact on pathogens of the infectious process and correction of functional disorders of organs and systems. Each of the mentioned directions is still being discussed as for the choice of the most effective method of treatment. During surgical interventions in patients with pleural empyema complications develop in 6.4 – 29.5 % of patients [12].

At lung resection or pneumonectomy against the background of purulent-destructive process, the mortality rate reaches 30% [13].

In connection with this there is necessity to increase effectiveness of conservative and minimally invasive methods of treatment. Effectiveness of video thoracoscopic operations has been proven in numerous studies [5].

Although as experience is gained and summarized further clarifying of indices to carry out video thoracoscopic operations, optimal terms of their conducting is needed. The possibilities of combined use of video thoracoscopic sanitation and proteolytic enzymes have not been studied.

For the time being thoracic surgery has a wide range of tools to eliminate the failure of the trunk of the main bronchus [14].

But the tactics of management of the cavity after elimination of the fistula is quite controversial. Modern surgery has a wide range of minimally invasive methods with the help of which one can eliminate the inflammatory process in the pleural cavity of vast majority of patients [15].

But the expressiveness of residual changes and danger of progress of pleurogenic lung cirrhosis dictates the necessity of creation of monitoring system for patients in the long term [16].

Among the absolutely indicated methods of therapy of purulent septic pathology extracorporeal detoxification takes one of the first places. It is used in complex with surgical sanitation of the purulent focus, rational antimicrobial therapy, transfusion and infusion therapy and immunomodulation [17].

Extracorporeal detoxification is used ever more often with patients in critical conditions and if there are no contradictions it becomes obligatory component of intensive therapy of 73% patients with sepsis [18].

Among methods of extracorporeal detoxification in treatment of non-specific purulent-destructive lung and pleura diseases plasmapheresis and plasmasorption take the leading position [19], but the regime of application, technical peculiarities of conducting, impact on course and prognosis have not been studied sufficiently.

In spite of great success reached within the recent years in pulmonology and thoracic surgery the problem of treatment of acute purulent-destructive diseases of the pleura cannot be considered finally solved and require further development. It is caused by a set of objective and subjective reasons in particular such as wide spread of antibiotic-resistant microflora and allergization of population. Carefully collected anamnesis, patients' examination, study of lung functions indicators, data of

laboratory and X-ray studies, performing of serological, immunological and allergic tests do not always allow to identify the cause of pleurisy and are often not sufficient to identify its etiology. In spite of wide range of the offered methods of treatment of acute purulent-destructive diseases of lungs and pleura study of the long-term results of all types of treatment shows that they do not guarantee 100% success. All of it dictates the search of new effective methods of treatment of the named pathology and proves the actuality of the theme. The outlined information indicates the necessity of improvement of surgical tactics, etiotropic and immunostimulating therapy in patients with pleural empyema.

AIM

Data study on the results of treatment of acute non-specific purulent-destructive pleura diseases with the purpose of further improvement of its results on the basis of improvement of diagnostics, identification of factors of disease prognosis and by implementing differential tactics of surgical treatment with the use of minimally invasive interventions.

MATERIALS AND METHODS

We have studied modern literary sources on the topic of current trends in the treatment of acute pleural empyema and its complications. The studied material is summarized and presented in the form of a literature review in this article.

REVIEW AND DISCUSSION

PATHOGENETIC FEATURES OF PLEURAL EMPYEMA, THE PROBLEM OF CLASSIFICATION AND DIAGNOSTICS

Surgery and therapy of purulent diseases of the lungs and pleura have undergone a difficult way from the past and it has not been finished today yet. During many centuries doctors have been trying to find the most adequate methods of treatment of lung abscesses [20].

Only at the turn of XIX-XX centuries treatment of lung abscesses gained a steady scientific basis and started rapid development. In pathogenesis of purulent diseases of lungs the most important role belongs to pneumonia against the background of the oppressed immunity, causative agent of which is staphylococcus and non-spore-forming anaerobes (identified in 62.83% of patients) [20].

For the time being more than 80 types of toxins that cause purulent processes in the lungs and pleura have been described and it is believed that acute pulmonary-pleural suppurations are polymicrobial infection in the form of anaerobic-aerobic associations of microorganisms among which the leading role belongs to non-spore-forming anaerobic pathogens, staphylococcus aureus, gram-negative aerobic bacillus microflora [18].

In pathogenesis of bacterial destruction of the lung great importance is given to disruption of the patency of bronchial branches with the formation of atelectasis, as well as to the poor blood circulation in bronchial and pulmonary vessels with development of ischemia of bronchopulmonary structures and subsequent necrosis [21].

The most pronounced disorders of final pulmonary structures are observed at the 2-3 week of the disease [22].

Clinical picture in the advanced phase of purulent pleurisy is characterized by symptoms of purulent resorptive fever, with three factors underlying it:

suppuration, absorption (resorption) of products of decay of tissue and microbial activity and loss of the body, inevitable with purulent inflammation. The severity of these symptoms and the seriousness of condition of a patient can vary – from moderately expressed to the most severe, they do not always strictly correlate with the size of empyema cavity and the amount of pus in it [4, 12].

It is extremely difficult to bring the patient out of the state of purulent-resorptive exhaustion and the prognosis is poor. Meanwhile pleurisy is the most frequent complications of pneumonia; it develops with more than 60 diseases [23].

Although type of pleural effusion does not have decisive diagnostic value nevertheless after dividing it into exudate and transudate one can imagine the spectrum of etiological affiliation [12].

There is no unified classification of pleural empyema. The classifications used in clinic include the basic factors:

1) pathogenetic forms,
2) peculiarities of infectious agent;
3) volume of the pleural cavity lesion;
4) presence of complications of pleural empyema and the pulmonary process in the form of bronchial fistulas or destruction of the lung tissue;
5) the degree of irreversible morphofunctional changes of pleura and lungs [7].

By prevalence they classify total empyema that occupies the entire pleural cavity from the dome of the diaphragm and extended empyema in which the empyema is limited to two or three anatomical walls of the pleural cavity. By localization empyemas are classified into parietal, apical and basal ones [24].

The presence of inflammatory process considerably changes the radiographic picture, quite often complicating the diagnosis of empyema. Sometimes it is not easy to identify the localization of purulent cavity, – in the lung or in the pleura, especially if there are several cavities. Later with the formation of multichamber accumulations of effusion their visualization is possible during computer tomography of the chest organs [25].

Certain benefit for correct diagnostics of presence of cavities and bronchopleural fistulas may be gained from injection of a contrast agent into the cavity – pleurography [23].

Radiological method of research underlying the diagnosis also cannot reveal all peculiarities needed for a clinician. Changes revealed on the X-ray of chest organs require clarification: if there is only damage to the lung parenchyma or the pleural cavity is involved in the pathological process [26].

Quite often pleural cavity with empyema is divided into separate chambers, which is almost impossible to identify during ordinary radiological research. According to the X-ray examination of the chest organs the problem of existence and nature of the empyema cavity cannot always be solved via application of a thick layer of mooring and compaction of lung tissue [26].

Ultrasound diagnostics is very informative when treating empyema. Ultrasound allows identifying even a small amount of pleural fluid. Identification of the pathological process in the pleural cavity states the problem in front of a doctor to identify its nosological affiliation [27].

Clinical manifestations can be confirmed with the help of pleural puncture and effusion studies. It allows to identify the amount of exudate, its nature, bacterial, cytological and biochemical composition, to differentiate the symptom of swarta from the presence of exudate and sometimes raise the question of indications for surgical intervention [27].

It is believed that diagnostic puncture is indicated for patients with the thickness of the liquid layer on radiographs in the position of lying on the side of more than 10 mm or there is an ossified pleural effusion, revealed with the help of ultrasound [28].

Cellular composition of pleural fluid presented with polymorphonuclear leukocytes (neutrophils, eosinophils, basophils), lymphocytes and other mononuclear cells (mesothelial and plasma cells, macrophages). Leukocyte exudate formula differs little from the one in blood but it changes in case of pathology. Domination of eosinophils in the pleural fluid of more than 10% is characteristic for posttraumatic hemothorax, tuberculosis, fungal pleurisy, parasitic infection, doctor-induced pleurisy, more rarely malignant disease [28].

With neutrophilia of pleural effusion, in general one should suspect pneumonia, pulmonary embolism (PE), pancreatitis, peritonitis. With mononuclear cells domination, in particular lymphocytes, one should exclude tuberculosis, malignant etiology of effusion, PE [29].

One of the biochemical markers is an enzyme of the class of hydrolases – adenosine deaminase (ADA). ADA rate of more than 45 units/ml is typical for tuberculosis and rheumatoid arthritis. Authors believe [30], that extreme activity of ADA (250 units/ml and above) should increase suspicion of lymphoma or pleural empyema. Normally the level of amylase in pleural fluid does not exceed the reference limit of that in serum [16].

The level of pleural amylase increases in acute pancreatitis, metastatic effusion and esophageal rupture. Cytological examination of pleural exudate takes special place in diagnostics of infection and determining of etiology of pleural effusion [31].

Sensitivity and specificity of exfoliative cytology for diagnostics of exudative pleurisy vary greatly according to etiological reasons. Reliability of cytological examination of pleural effusion varies from 64 to 96% [9].

Researches of authors [30] showed, that combination of cytology with clinical data, including laboratory (biochemical blood analysis, ADA), radiological (CT, PET, MRI) methods of examination, general sensitivity reaches 80.9% with exudative pleurisy of various etiology.Application of modern immunomorphological methods along with classical morphological techniques allows overcoming many difficulties in the study of exudate fluids. Comparative analysis of cytological and immunocytochemical (ICH) methods in detection of dissemination by serous membranes has shown that sensitivity of cytological examination equals to 62% with specificity of 95%, and sensitivity of ICH-examination increases to 93% in case of specificity increase to 99% [30]. For correct research it is necessary to choose the right combination of antibodies which are to be used. For approximately 20% of all patients it is not possible to diagnose only by the results of pleural effusion study [30].

For this reason within the two recent decades video thoracoscopy (VTS) has gained a wide spread in the world as the final stage of diagnosis in the absence of morphological verification of the diagnosis of exudative pleurisy. VTS with biopsy provides high efficiency of differential diagnostics of pleural effusions of various etiology, which according to different authors makes 95.5–100% [21].

VTS allows collecting under visual control the amount of material necessary for immunohistochemical analysis of the most changed areas of the pleura. Frequency of complications is limited to 5-9% [21].

At different stages of evolution of disease there is important problem of necessity of puncture or drainage of the pleural cavity. In case of pleural empyema their strict differentiation is necessary. The experience accumulated for today allows setting a question if puncture is diagnostic or therapeutic method. Practice and analysis of literature prove that unjustified persistent treatment with punctures, late use of pleural cavity drainage often lead to complications of purulent process in the lung. Study of the cellular composition of the pleural fluid is necessary stage in the patients' examination however it does not solve all the problems [32].

The main disadvantages of the closed transthoracic biopsy carried out to identify the nature of the disease lie in the fact that it is carried out blindly (there is no visual control of collection of material from lesions) and it concerns only parietal pleura [27].

When closed transthoracic biopsy is carried out sometimes pneumothorax may occur (from 5 to 17% cases) [5]. Among other complications they describe: occurrence of subcutaneous emphysema, hemothorax, injury to the kidney, liver, spleen [5].

Diagnostic bronchoscopy became obligatory during examination of patients with pleural effusion of unclear genesis and patients with hemoptysis or clinical signs of bronchial obstruction. With a significant collapse of the lung, it is possible to note the convergence of the segmental bronchi, loss of their tone, sometimes swelling of the mucous membrane and an increase in its folds [33].

Bronchoscopy is of great importance to exclude internal bronchial pathology, which may be the cause of pneumonia development and complicate it with purulent pleurisy. First of all it concerns central lung cancer, foreign bodies in the bronchi and other more rare diseases of bronchial system. Especially important is the fact that bronchoscopy allows to identify the form of endobronchitis and justify the indications for sanitation of the tracheobronchial tree [33].

Nevertheless, in spite of variety of methods, identification of etiological properties of pleural effusion presents certain difficulties and to some extent depends on experience, practitioner's intuition and diagnostic capabilities of the medical institution, and finally the most informative is targeted biopsy conducted under supervision of a thoracoscope [34].

PECULIARITIES OF SURGICAL METHODS OF TREATMENT OF PATIENTS WITH PLEURAL EMPYEMA

The basic and decisive moment of treatment of pleural empyema is elimination of the purulent focus in the lungs and pleura. Existing methods of surgical treatment of pleural empyema are targeted at evacuation of purulent contents from the pleural cavity and foci of lung destruction can be classified into two types: open – with the use of thoracotomy and closed or methods of "minor surgery" – without thoracotomy [32].

"Minor surgery" methods in treatment of pleural empyema include pleural punctures, introduction of catheter into the cavity, closed drainage by passive and active aspiration, pleural lavage, diagnostic and operative thorascopy, temporary occlusion of the bronchi [32].

In order to increase efficiency of treatment of patients with pleural empyema at the present stage they consider being actual combination of methods of "minor" surgery depending on indications for use of particular methods and chosen treatment algorithm. One of contemporary methods of minimally invasive surgery of patients with pleural empyema with bronchopleural fistula is temporary occlusion of the bronchi and video assisted thoracoscopy (VATS) [32].They studied method of temporary occlusion of the bronchi and its efficiency in patients with pleural empyema [13].

Polish bronchologist R. Rafmski [35] is rightfully considered to be the originator of modern temporary occlusion of the bronchi; in 1965 he was the first to apply artificial closure of the bronchus carrying peripheral fistulae. In 1968 he announced about straightening of a collapsed lung by the method of bronchial obturation with 11 children who suffered from acute infectious lung destruction complicated by pyopneumothorax and he called this method "temporary sealing of the bronchus". Later researches proved that at the cost of creating temporary atelectasis of the affected lobe of the lung with the help of temporary bronchus occlusion (TBO) it is possible to restore the tightness of the bronchial tree and straighten the healthy parts of the lung [33].

At the moment method TBO is applied at a great contingent of adult patients with spontaneous and traumatic pneumothorax, and also for intraoperative blockade of the bronchus of the affected area of the lung with the goal of preventing pathological contents from entering the opposite bronchus [36].

Nevertheless the TBO is most widely used in patients with acute infectious destruction of the lungs complicated with pyopneumothorax, giant lung abscesses [36].

Mechanism of positive effect of temporary occlusion of the bronchi the course of the purulent-destructive process in the lung with pyopneumothorax is as follows.

- A stable vacuum in the pleural cavity is created as a result of its disconnection with the bronchial tree by the obturator.

- The residual pleural cavity is eliminated at the cost of straightening and increasing the volume of the healthy part of the lung, shift of the mediastinum, reduction of intercostal space and raising of diaphragm.
- It contributes to the emptying and obliteration of foci of destruction in lung tissue in condition of temporary atelectasis of the affected parts of the lung with constant active aspiration of contents from the pleural cavity.
- It prevents bronchogenic dissemination of purulent infection, separating heathy sections of the lungs.
- Favorable conditions are created for closure of bronchopleural fistulae as a result of the formation of adhesions between the visceral and parietal pleura, formation of limited fibrothorax.

The total effect of TBO on the body of a patient depends on the ration of negative and positive aspects of the method impact, general condition of a patient and it is individual in many aspects. Some general patterns can be traced in the development of functional changes in the body of a patient, therefore 4 phases of course of the postocclusion period are identified [27].

1 phase – primary response to the occlusion, it lasts for 1-2 days and can proceed with development of both positive and negative changes of the main indicators of breathing and blood circulation;

2 phase – adaptation, lasts for about a week and is characterized with gradual improvement of general condition of the patients, stabilization of the main indicators of breathing and blood circulation;

3 phase – occurs 7-17 days after the start of occlusion and is characterized with development of inflammatory changes in the lungs and bronchi;

4 phase – traced to 21-24 days, at this period general condition stabilization occurs as well as subsidence of inflammatory changes in the lungs against the background of purulent bronchitis.

The identified peculiarities of post occlusive period dictate the necessity of differentiated approach to the choice of methods of complex conservative therapy depending on the phase. To TBO advantages many authors refer its direct positive impact on the general condition of the patients [36].

After applying temporary occlusion of the bronchus in the first 2-3 days the body temperature is normalized, shortness of breath decreases, purulent discharge form the pleural cavity stops, the patients physical activity increases. Decrease of phenomena of respiratory failure occurs as a result of sealing of the bronchial tree of the affected lung and disappearing of the syndrome of "bronchial reset", fast straightening of unaffected areas of the lung and their inclusion into the function of breathing, removal of intoxication syndrom [18].

TBO affects positively hemodynamics of a small circle of blood circulation and central hemodynamics. According to the data of some authors, after occlusion of bronchi and straightening of healthy parts of the lung there is considerable decrease in anatomical blood shunting in the small circle of blood circulation (more than 2.5 times), pressure in the pulmonary artery decreases or normalizes at once. With occlusion of common bronchus normalization of the function of external respiration (breathing rate was controlled, the minute volume of breathing decreased to 20%, the vital capacity of the lungs increased) and pulmonary gas exchange (the use of oxygen increased in combination with an increase in its consumption by 20-30%, rate of $PaCO_2$ and PaO_2 normalized) occur within first 24 hours; after occlusion of the main bronchus respiratory rate increases, gas exchange disorder follows the mechanism of intrapulmonary shunting with decrease of oxygen consumption. Changes of central hemodynamics after obturation of the common bronchus were characterized by increase in stroke volume and an increase in the minute volume of blood circulation, simultaneously after occlusion of the main bronchus stroke volume decreased and maintenance of minute volume of blood circulation was achieved with the help of increased tachycardia [22].

Thus authors emphasize that patients with occlusion of the main bronchus are in less beneficial functional conditions, this requires additional intensive measures to support cardiodynamics and pulmonary gas exchange. In spite of many years of application of TBO in treatment of pleural empyema with bronchopleural connections (BPC) indications and contraindications as for its use have not been defined clearly. In the literature publications data concerning them is scattered and sometimes has controversial nature. The majority of authors believe that direct indication for use of TBO in patients with pyopneumothorax is impossibility of straightening a collapsed lung by active aspiration and massive discharge of air through drainage [36].

In the presence of a bronchial fistula with a bronchial discharge coefficient of more than 0.25 drainage of pleural cavity is inefficient and such patients are shown endobronchial occlusion [37].

Coefficient of bronchial discharge has been defined by the author by the ratio of the volume of air passing through the bronchial fistula to the volume of inhaled air. They have worked out and approved non-invasive method of determining the degree of lung leakage by the amount of aspirated air from the pleural cavity per unit of time with strictly dosed vacuum [37].

At the first degree of lung leakage alternating active and passive drainage of the pleural cavity with

simultaneous intrapleural administration of solutions irritating to the pleura for the purpose of pleurodesis is quite effective. At the second degree of lung leakage in patients with pyopneumothorax, spontaneous pneumothorax authors consider to be relevant using of TBO of the damaged lobe of the lung with further active drainage of pleural cavity. The third degree of lung leakage is an indication for thoracotomy with suturing or resection of the damaged lung. They inform about rather high efficiency of TBO application to treat acute postoperative pleural empyema in pulmonary failure and failure of the bronchial stump after lung resections. Before the use of temporary occlusion of the bronchi all patients should undergo complex treatment aimed at stabilizing the destructive process in the lungs, rehabilitation of the bronchial tree and pleural cavity, decrease in the severity of intoxication and pulmonary heart failure, increase of immunological reactivity of the body [36]. Feasibility of TBO applying combined with active aspiration through previously installed drains in the pleural cavity is admitted by all the authors, as far as these methods of treatment complement each other and in complex they minimize their drawbacks. Drainage of the pleural cavity is the most widespread effective and rational method of treatment of pleural empyema. Indication for this method of treatment is pyopneumothorax of any length, this complicates gangrenous forms of acute infectious destruction of the lungs, acute pleural empyema with brochopleural connections, tension pyopneumothorax, postoperative pleural empyema with bronchopleural fistulae, chronic pleural empyema with bronchopleural fistulae, failure of the puncture method of treatment during 5-7 days. Majority of surgeons prefer active aspiration content from the pleural cavity [38]. Active aspiration creates conditions for active straightening of a collapsed lung, encourages decrease of intoxication and is a measure of prevention of bronchogenic dissemination of purulent infection. The degree of rarefaction necessary to expand the lung largely depends on the duration of existence of pyopneumothorax, size of bronchopleural connections and degree of lung collapse. Many authors propose to complete active aspiration with conduction of flow, fractional, flow-fractional lavage of empyema cavity, even with the use of automated systems of managing this process [38]. Effectiveness of drainage methods of treatment increases at sanitation of the empyema cavity with antibiotics, antiseptic solutions and lavage of the pleural cavity with the introduction of inhibitors of proteolysis and fibrinolysis. To accelerate the process of cleaning and biochemical (enzymatic) decortication of the lungs proteolytic and fibrinolytic enzymes are successfully used [28].

According to the data of majority of authors the effectiveness of application of closed methods of drainage with active aspiration varies from 47.8% to 81.3%, 16.8% – 32% cases turn into chronic form with mortality up to 19% [39].

The main reason of insufficient effectiveness of drainage methods is presence of bronchopleural fistulae, which not only prevents lung straightening and supports the purulent process, but also limits possibility of washing of pleural cavity. This drawback is eliminated by using TBO [36].

Effectiveness of TBO method is provided by many factors. But the problem of the level and correction of the influence on the result of treatment with TBO method has not been finally solved. One of the most important of them is identification of localization of "failed" bronchus. Visual search of mouth of failed bronchus during bronchoscopy has been applied [36]. To identify localization of bronchial fistulas first of all data from various X-ray studies is used: analysis of X-rays of the patient's chest, conducted before the lung collapse; use of bronchography with water-soluble radiopaque substances; conducting of pleurography, computer tomography. The most efficient at the existing occlusion technique is obturation of the lobar, two lobar or intermediate bronchus. Isolated occlusion of segmental bronchi, as a rule, turns out to be not effective enough. Application of occlusion of main bronchus can be the method of choice only in the cases when using of other methods of treatment is impossible due to the severity of the patient's condition and conducting occlusion of more distal parts of the bronchial tree is technically impossible or ineffective. Occlusion of the main bronchus is more difficult for patients to tolerate and the results of treatment are much worse. Meanwhile some authors claim about favorable results of treatment of pyopneumothorax patients with occlusion of the main bronchus, they indicate its lower effectiveness comparing to the occlusion of lobar bronchi [39].

Effectiveness of TBO method depends on quality of the material used for occlusion. R. Rafinski in 1965 for obturation of the bronchus used emulsion containing 20 parts of talc in 40% iodopolypol solution, – sulfadimezin emulsions in 40% iodolinol solution, and [40] – iodopolyvinol. There are reports about obturation of peripheral bronchopleural fistulae which was carried out with adhesive cyanoacrylate compositions by means of selective catheterization of the bronchi under X-ray television control. Nevertheless application of cyanoacrylate compositions for temporary occlusion of bronchi at pyopneumothorax has not been used widely. The problem of necessary terms of occlusion has been outlined in the literature controversially.

In the first works published in our country 7-10 days were considered to be optimal timing. Nevertheless as the treatment results showed this timing of TBO of adult patients with pyopneumothorax turned out to be insufficient to receive a stable therapeutic effect [36].

According to some authors the term of occlusion should not exceed 21-24 days, as far as increase of occlusion duration does not improve results of patients' treatment and can lead to irreversible morphological changes in the lungs. Term of TBO should depend on the general condition of a patient, level of intoxication and on the severity of inflammatory changes in the occluded part of the lung [36].

In case of moderate changes authors advise to apply continuous technique with retamponade in 7 days [38].

In case of pronounced changes in the occluded part it is recommended to apply intermittent method. Thus one can reach a considerable duration of occlusion.

Indication for obturator removal is considered to be straightening of lungs with complete cessation of air flow from pleural drains during 5-6 days; reduction and cleaning of the pleural cavity with its size stabilization during 5-6 days; ineffectiveness of temporary occlusion of bronchus [38].

Thus basing on the analysis of known literature a pressing necessity of further improvement of methods of temporary occlusion of the bronchi emerges. In the literature there are no clear criteria of assessment of results of treatment. Immediate results of treatment with TBO application are assessed by combination of clinical, radiological and endoscopic data. Thus analysis of literary publications shows that temporary occlusion of bronchi has found wide application in patients with empyema of the pleura with bronchopleural connections. Nevertheless, in spite of considerable experience of its application a lot issues are still unsolved. The problem of indication for use of TBO in the treatment of pleural empyema has not been finally solved, as well as possible safe and effective methods of search of bronchopleural messages, terms of occlusion. The problem of necessary conditions for effective application of TBO has not been considered. Further development of treatment and preventive measures aimed at prevention of complication during its application is necessary. There are practically no works on TBO application in the combined surgical treatment and analysis of its effectiveness.

Creation of endovideo equipment and emergence of new endoscopic instruments has widened the borders of thorascopic instruments – up to

lung and esophagus resections, removal of mediastinal tumors, treatment of spontaneous pneumothorax and hemothorax [37]. However, video thorascopy during pleural empyema has not received recognition and wide practical appliance. Publications devoted to this issue are quite rare [37, 38]. The place of video thorascopy in the complex treatment algorithm of patients with pleural empyema has not been clearly identified, and the indications for application have not been developed. According to some authors video thorascopy at pleural empyema provides an opportunity to assess the morphological changes in parietal and visceral pleura, lung surfaces, identify by direct and indirect signs presence and localization of broncho-pleural connections, to see the expressiveness of purulent-fibrin overlays, diagnose radiologically invisible intrapleural osmosis, sequestrations, foreign bodies and confirm spread and stage of pleural empyema [36].

Application of therapeutic techniques under thorascope control, such as removal of pus, fibrin, necrotic masses from the pleural cavity, partial or complete decortication of the lung, sanitation and adequate drainage as well as removal of brochopleuaral connections with complete straightening of the lung allows in most cases to cure acute pleural empyema and avoid its transition into chronic one [33].

First reports have appeared in the literature on possibility of application of video thoracoscopy during treatment of chronical pleural empyema with treatment of its cavity with ultrasound, high-energy and low-energy laser. As well as during drainage methods application there are still problems with endoscopic sanitation of the pleural cavity in patients with bronchopleural connections [33].

In spite of numerous methods of bronchopleural connections elimination during video thoracoscopy, such as electrocoagulation of their mouths, application of medical glues, stitching devices, welding with high-energy laser radiation, the problem of their elimination remains relevant [22]. Their low effectiveness is related to the fact, that all the manipulations are conducted in conditions of purulent-necrotic process, which encourages incapability of "welded" tissues, cutting through the inflamed lung tissue and rejecting the adhesive seal [34].

In the literature reports on combination of video thoracoscopy with TBO are rarely seen. During pleural empyema with bronchopleural connections of medium and large caliber with compliant lung it is recommended to combine video thoracoscopy with TBO [36].

Thus video thoracoscopy during treatment of patients with pleural empyema is highly informative diagnostic and highly effective therapeutic method. But it effectiveness decreases considerably with lung leak syndrome caused by the presence of functioning bronchopleural connections. In this situation using of video thoracoscopy in combination with TBO is pathogenetically justified, expedient and perspective.

CONCLUSIONS

Summing the data of the literature it should be noted that within recent years minimally traumatic methods of surgical treatment found wide application in the practice of clinics, which deal with the problems of thoracic surgery. It is especially relevant during treatment of postoperative pleural empyema including those with bronchial fistulas. The problem of using physical methods of treatment with aim of increasing effectiveness of surgical treatment of patients with pleural empyema remains relevant. The available information tells about high effectiveness of methods of «minor» surgery when treating closed pleural empyema and not entirely satisfactory results of treatment of acute and chronic pleural empyema with bronchopleural connections. That is why feasibility of finding new and improving known gentle methods of treatment of pleural empyema, their place identification in the algorithm of combined surgical treatment does not cause any doubts.

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CONFLICT OF INTEREST

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REVIEW ARTICLE

CONTENTS

Diffuse familial adenomatous intestinal polyposis in childhood: current state of the problem and case report

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ABSTRACT

Aim: To explore the prevalence, clinical characteristics, and diagnostic aspects of diffuse familial adenomatous polyposis in childhood. This objective is accomplished through an extensive review of recent literature, and the presentation of case report from our clinical practice.

Materials and Methods: We analyzed 75 scientific papers, the findings of which have been documented in the PubMed database. Our search criteria included keywords such as «diffuse familial adenomatous intestinal polyposis,» «children,» and «diagnosis.» Then we conducted a second-stage analysis that involved a detailed review of a practical case – the medical records of inpatient Kh.V. who had been diagnosed with familial adenomatous polyposis.

Conclusions: The analysis of the literature data is consistent with the findings from our clinical observations of familial adenomatous polyposis in a patient with complicated family anamnesis. It is worth noting that clinical features do not significantly differ across various types of polyposis. In cases of suspected familial adenomatous polyposis in adolescents, genetic testing is crucial.

KEY WORDS: Child, polyps, diagnosis, therapeutics

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INTRODUCTION

Diffuse FAP is a rare hereditary systemic disease that predominantly impacts children [1]. This condition is characterized by the formation of numerous polyps and microadenomas in the large intestine [2, 3]. Notably, diffuse familial adenomatous polyposis plays a pivotal role in carcinogenesis among adult patients, warranting close attention from clinicians, including pediatricians and family doctors, to closely monitor the disease progression [4, 5].

In the literature, there are references to the cumulative impact of various environmental and genetic factors on patients with FAP. This interplay is believed to contribute to significant inter- and intra-family variations in the colorectal phenotype during the tumor development process [6]. It is worth noting that research in this field is ongoing despite the sporadic nature of this pathology.

AIM

This study aims to explore the prevalence, clinical characteristics, and diagnostic aspects of diffuse familial adenomatous polyposis in childhood. This objective is accomplished through an extensive review of recent literature and the presentation of the case report from our clinical practice.

MATERIALS AND METHODS

In pursuit of our research objectives, we meticulously analyzed 75 relevant scientific papers, the findings of which have been documented in the PubMed database. Our search criteria included keywords such as «diffuse familial adenomatous intestinal polyposis,» «children,» and «diagnosis.» Additionally, we conducted a second-stage analysis that involved a detailed review of a practical case – specifically, the medical records of inpatient Kh.V. who had been diagnosed with the condition mentioned above.

REVIEW AND DISCUSSION

The study of familial adenomatous polyposis has a rich history, dating back to 1726 when it was initially described by Menzelio. In 1882, B. Gripps further contributed to the understanding of this disease and established its familial nature. A significant milestone occurred in 1925 when St. Mark's Hospital in London

created a registry of 1238 individuals from 510 families with a preliminary diagnosis of diffuse familial polyposis [7].

In 1975, H. Bussey conducted more in-depth research on the disease, offering a detailed description of the clinical and pathomorphological aspects [7]. The year 1986 marked a breakthrough when researchers first described the genetic basis of familial adenomatous polyposis. In 1991, the APC gene responsible for the development of intestinal familial adenomatous polyposis was identified [7].

Some researchers have also investigated the rare hereditary forms of polyposis, including familial adenomatous polyposis, Cowden syndrome, Li-Fraumeni syndrome, MUTYH-associated polyposis, juvenile polyposis syndrome, and Peutz-Jeghers syndrome [2]. However, it is important to note that there is still a shortage of comprehensive data on this topic, indicating a need for further research in this area.

Today, it is firmly established that diffuse familial adenomatous polyposis primarily exhibits an autosomal dominant mode of inheritance and accounts for approximately 1% of colorectal cancer cases within the population [2]. This disease is closely linked to mutations in the highly penetrant tumor suppressor gene (TSG) known as the Adenomatous Polyposis Coli (APC gene), responsible for regulating cell proliferation in the gastrointestinal mucosa. The APC gene is located on the 5th chromosome (5q21-22; OMIMNM_000038.5), and there are over a thousand known mutations in this gene, all of which are documented in the international database of genetic mutations – the Human Gene Mutation Database [2].

It's essential to note that individuals carrying mutations in the APC gene face a near 100% risk of developing diffuse familial polyposis and colon cancer [8]. Furthermore, these patients also have an elevated risk of other tumor processes, particularly gastroblastoma, duodenoblastoma, and hepatoblastoma. This underscores the significance of close clinical monitoring and intervention in these cases [9].

Undoubtedly, comprehensive genetic testing and health monitoring for adolescents with FAP are crucial for early diagnosis and the prevention of malignancy resulting from detected pathomorphological changes. However, it's worth acknowledging the challenge of precisely identifying the genetic subtype of this pathology. This difficulty arises from the fact that approximately 30% of children either lack a family history burdened by the condition or possess spontaneous de novo mutations in the APC gene [10].

It is essential to emphasize that the identification of specific pathogenic APC variants and understanding the correlations between genotype and phenotype play a vital role in monitoring the health and managing family members who may be at risk due to a compromised immune system or a history of colorectal cancer.

CASE REPORT

A boy named Kh. V., born in 2006, was admitted to the specialized department of the CNE "Ivano-Frankivsk RCCH IFRC". He reported experiencing periodic cramping, spastic abdominal pain, which tended to occur more frequently after meals. This pain was often associated with defecation, did not radiate, and was accompanied by occasional heartburn. He also mentioned experiencing episodes of nausea, unstable bowel movements occurring 6 to 8 times a day, severe bloating, decreased appetite, fatigue, weakness, nasal congestion, and conjunctivitis.

MEDICAL HISTORY

These complaints had been troubling him for the past 2 months and had gone untreated, which led to his admission to the Ivano-Frankivsk Regional Children's Clinical Hospital for further examination and treatment.

LIFE HISTORY

The boy's growth and development were by his age. He was born full-term via normal delivery and was up to date with his vaccinations. He had no known allergies and had a notable family history on his paternal side, with both his grandmother and father having a history of familial adenomatous polyposis.

OBJECTIVE FINDINGS

The boy's body weight was 69 kg, and his general condition was moderately severe. His constitution was normosthenic. His skin appeared pink and clean, with atopic dermatitis observed on the cheeks and dryness noted on the elbows. Normal skin turgor was observed, and his sclerae were normal. In the oral cavity, the tongue was thickly coated with white-grey plaque and appeared dry. Submandibular, and anterior cervical lymph nodes were palpable. Respiratory examination revealed vesicular breathing without wheezing, with a respiratory rate of 18 breaths per minute. In the pharynx, there was hyperaemia of the posterior wall, and nasal breathing was slightly difficult.

Cardiovascular assessment revealed audible, rhythmic, and clear heart sounds, with a heart rate of 78 beats per minute. The heart limits were within the

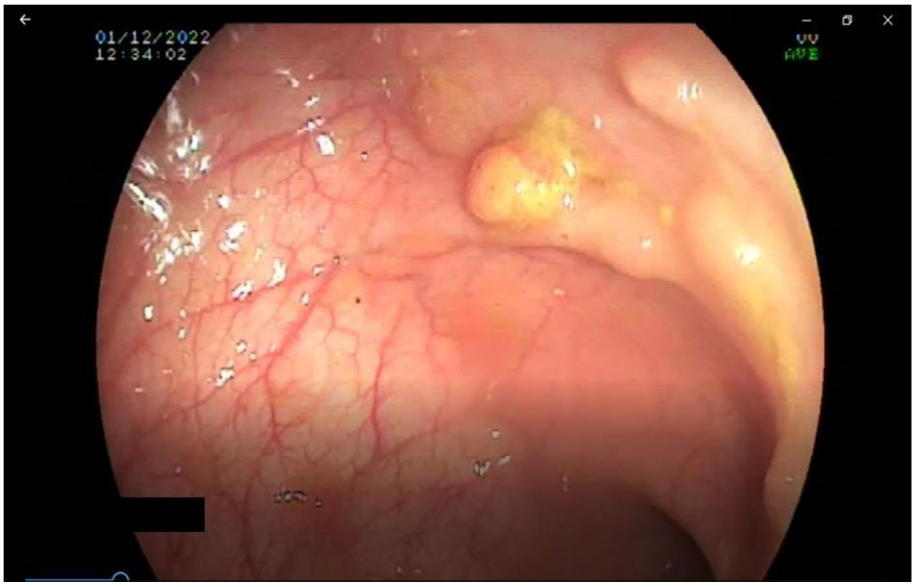

Fig. 1. Colonoscopy of the patient Kh.V.

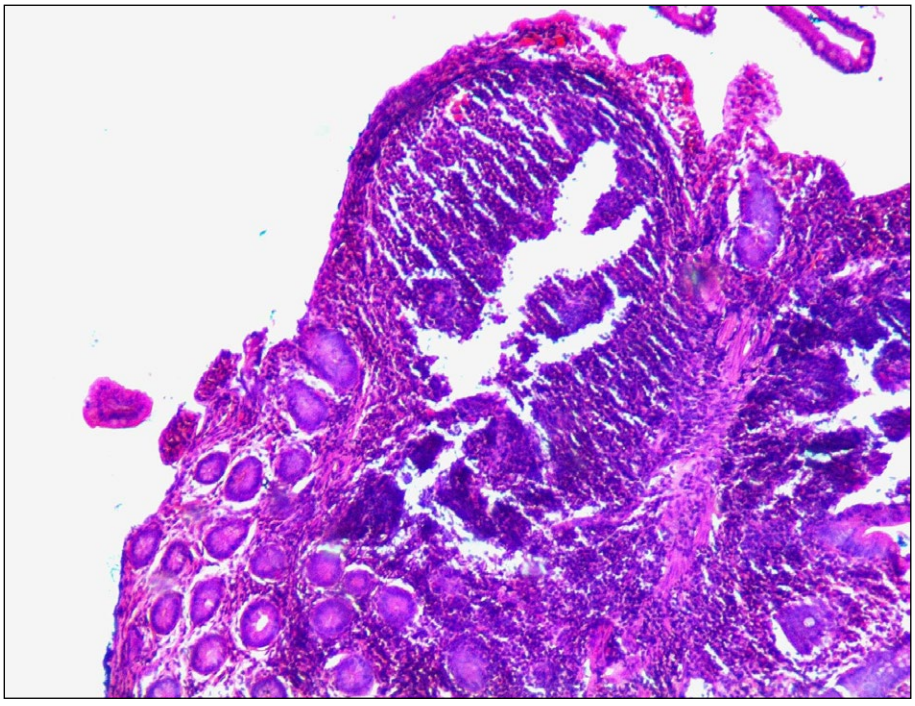

Fig. 2. Biopsy findings in the intestinal mucosa of the patient Kh.V. (H&E stain, x 100 magnification).

age-appropriate range. Upon abdominal examination, the abdomen was soft upon palpation, but tenderness was noted in the epigastric, and umbilical regions, as well as both retroperitoneal areas. The abdomen was distended. The liver, and spleen were not palpable. Segments of the intestine were distended, and spasmodic in both the ileum. Stools occurred 6 to 8 times a day, and they were hard and lumpy.

LABORATORY TESTS AND INVESTIGATIONS

Complete blood count: Hb -158 g/l, erythrocytes 5,23x10^{12}, CI 0,91, leukocytes 7,86x10^{9}, eosinophils 2%, bands 4%, segmented 64%, lymphocytes 20%, monocytes 10%, platelets 214x10^{9}, ESR 4,76.

Biochemical blood assay: ALT 32 U/l, AST 69 U/l, TSB 19.42 µmol/l, direct bilirubin 3.49 µmol/l, indirect bilirubin 15.93 µmol/l, thymol test 1.43 U, total protein 70.0 g/l, BUN 5.2 mmol/l, creatinine 93 µmol/л, amylase 54 (normal range 0–90), glucose 4.7 mmol/l.

Urinalysis: specific gravity 1024, protein – scarce, color – yellow, transparent, pH 6.0, mucous +, leucocytes 3 to 4 per high power field, epithelium 7 to 9 per high power field.

C-reactive protein: 32.4 mg/l (normal range <5). Saccharomyces cerevisiae IgA 0.09 (<1.0), Saccharomyces cerevisiae IgG 0.04 (<1.0).

Fecal calprotectin: 738.0 mcg/g (<50).

Blood type: A (II), Rh+ positive.

Coagulation studies: aPTT 28.2, PT 10.9 sec, PTI 101%, QuicK index 89%, INR 0.99, fibrinogen 2.77 g/l.

Ova stool exam: ova are not detected, no blood in stools.

Esophagogastroduodenoscopy No.524: erosive exudative erythematous reflux esophagitis, catarrhal, and stagnant gastroduodenopathy, along with increased acid production. There are small polyps in the sub-cardiac region. Indirect signs of hepatobiliary dysfunction. pH 1–2.0.

Colonoscopy data are shown below (Fig. 1.).

Colonoscopy report No. 26: During the colonoscopy, an examination of the large intestine up to, and including the dome of the cecum, and the terminal ileum was conducted. The intestine was found to be fully passable. Throughout the large intestine, remnants of turbid, yellow-colored flush water were observed, which were subsequently washed, and removed. Peristalsis was noted as preserved.

The folding of the intestine was maintained, and conformed to anatomical norms. The folds were moderately thickened, and could be unfolded by the introduction of air. In the terminal ileum, rounded folds were present, without thickening. The mucous membrane appeared pink, finely villous, and featured multiple rounded polypoid formations, ranging in size from 0.5 x 0.5 to 1 x 1 mm.

Within the cecum, an oval-shaped appendix pupil was observed, and the ileocecal angle was found to be lip-shaped, and closed. The mucous membrane of the examined sections of the large intestine displayed a shiny, elastic, pink appearance throughout, with areas of erythema, predominantly more pronounced in the left parts of the colon. The vascular pattern of the intestine was preserved, with regular contours, although some blurring was noted in the sigmoid colon.

In the colon, with the majority located in the rectum, and sigmoid colon, multiple rounded polypoid lesions were observed. These lesions had a broad base, and varied in size, ranging from 1 x 0.5 x 0.5 mm to 4 to 5 x 3 x 2 mm. Most of these lesions appeared pink in color, while some were bright red. The anal canal was found to be free-flowing, with pink mucosa. Additionally, there were moderately expressed anal papillae.

Abdominal ultrasound: The liver is positioned typically, protruding 1 cm below the costal arch. The liver parenchyma displays normal echogenicity. Hepatic veins are not remarkable. Bile ducts are slightly thickened. The portal vein measures 9 mm, with unobstructed blood flow, and the choledochus is not dilated.

The gallbladder is ovally shaped, with a volume of 29 cm^3 after oral liquid consumption. The gallbladder wall is not thickened, and its content appears heterogeneous with sediment. The pancreas is visible in its entirety, exhibiting a heterogeneous structure with multiple hyperechogenic inclusions. The parenchyma is isoechogenic. The spleen is of normal size, featuring a homogeneous structure and an additional lobe. Kidneys are typically located with even, and clear contours. Differentiation of the cortical, and medullary layers is preserved. The collecting system of kidneys is not widened, and appears thickened. In the stomach, there is a significant amount of residual content, and the stomach wall measures 4.1 mm, with signs of flatulence. Paraumbilical lymph nodes have a diameter of 8 to 10 mm. The bladder has a volume of 40 cc with sediment.

Thyroid ultrasonography: The thyroid gland is normally positioned, and not enlarged. The isthmus width is 4 mm. The right lobe has a volume of 5.4 cm^3, and the left lobe has a volume of 4.3 cm^3. The echo structure of thyroid gland appears heterogeneous due to the presence of small follicles with calcifications. The blood supply exhibits moderate intensity in the Doppler spectral sonography. The total thyroid volume is 9.7 cm^3, which falls within the normal range of 5.58 to 12.44 cm^3.

ECG: Wandering atrial pacemaker, abnormal ventricular repolarization. Sinus rhythm, with a heart rate ranging from 56 to 68 beats per minute, bradycardia. Increased ECG voltage observed in the left chest leads.

Chest X-Ray No. 16155: not remarkable.

Sinus X-Ray No. 16156: subtotal opacification of paranasal sinuses bilaterally.

The obtained intestinal biopsy data are shown in Fig. 2.

Biopsy of the intestinal mucosa No. 1468-75:

1. The specimen consists of fragments of the small intestine mucosa. Submucosal lymphoid infiltration is evident in certain sections. The crypts remain intact. This finding may be indicative of Crohn's disease, and necessitates clinical correlation and ongoing monitoring of biopsy changes over time.

2. Fragments from the colon mucosa show polypoid hyperemia, and focal proliferation of glandular epithelium, which aligns with familial adenomatous polyposis.

Consultation by a surgeon: No signs of acute surgical condition were observed during the examination.

Consultation by an ophthalmologist: allergic conjunctivitis.

ENT consultation: acute sinusitis. Recommended: antibiotic therapy, glucocorticosteroid nasal sprays (Etacid), nasal decongestant (Nasivin), H1-blockers (Cetrine).

Genetic testing: 19CN003493 mutation of the APC gene was detected.

Treatment: mesalazine, proton pump inhibitors, probiotics, antibiotics, mucolytic drugs, nasal irrigation, hepatoprotective drugs, glucocorticosteroid nasal sprays, H1-blockers.

RECOMMENDATIONS

Follow-up by a paediatric oncologist, gastroenterologist, and surgeon;

Genetic testing of the polyp biopsy specimens (planned visit in the out-patient setting);

Plan for hospitalization one year from now (including esophagogastroduodenoscopy and colonoscopy);

Salofalk 1000 mg three times a day and 500 mg in the evening for one month, with potential long-term use, subject to dose adjustment;

Probiotics (Enterol 250) at a dosage of 1 cap. two times a day for two weeks;

Faecal calprotectin in one month;

Complete blood count, and liver function tests (AST, ALT) in two weeks for follow-up, and once a month thereafter;

Decoction of flaxseed: one tablespoon three times a day before meals for three months;

Hepatoprotective drugs (Ursofalk) 500 mg at bedtime for three months;

Sea Buckthorn Oil: one teaspoon twice a day before meals for three months;

Sanatorium treatment during periods of remission (Morshyn and Myrhorod);

Treatment effectiveness: The patient is discharged with improvement.

As commonly noted in scientific literature, adenomas in the intestine typically manifest during the second decade of life, with clinical symptoms becoming apparent around the age of 16, and their prevalence increases in the third decade [2, 11]. Given the natural progression of intestinal processes, colorectal cancer may emerge in this patient cohort around the age of 40 [2, 11, 12]. It is important to recognize that both the development of colorectal cancer, and the formation of adenomas in the intestine are parallel pathological processes that do not necessarily contradict each other [13].

Recent scientific research has revealed specific correlations between the severity of clinical symptoms in familial adenomatous polyposis and specific mutations in the APC gene. This genetic insight aids in identifying distinct subtypes of FAP [14].

Moreover, more than 70% of FAP patients may exhibit not only intestinal manifestations but also extraintestinal symptoms, which can align with certain syndromes. These include Gardner syndrome, Turcot syndrome, and attenuated FAP [8, 13]. For example, Gardner syndrome presents with intestinal polyposis alongside dental abnormalities, osteomas, and soft tissue tumors. Turcot syndrome is characterized by both: intestinal polyps similar to those in FAP, and central nervous system tumors. Other forms of polyposis share clinical similarities with FAP and attenuated adenomatous polyposis but differ significantly in terms of the number of polyps (ranging from 10 to 100), and the age of symptom onset, which is typically later. Specifically, attenuated familial adenomatous polyposis is characterized by the presence of single intestinal polyps, usually around 30 to 35 in number, with approximately 8% of them occurring in the proximal intestine.

A review of the existing literature indicates that patients with FAP exhibit varying phenotypes, and the associated extraintestinal manifestations can significantly differ, with their occurrence observed in about 40% of cases. Our current understanding of this condition aligns with the prevailing notion that colorectal cancer had been the leading cause of mortality in FAP patients for many years. However, this trend is gradually changing due to enhanced surveillance, early diagnosis, and preventive surgical interventions.

Notably, desmoid tumors, and tumors in the upper digestive tract pose greater risks in terms of malignancy and mortality [14, 15].

When examining the spectrum of polyposis syndromes, it becomes apparent that patients with multiple adenomatous polyps are more likely to exhibit signs of FAP or its variants. Less frequently, patients may have attenuated familial adenomatous polyposis or MYH-associated polyposis (MAP) [2, 10].

For individuals suspected of having a polyposis syndrome, genetic testing is recommended. If no APC gene mutation is detected, further evaluation should include MYH gene testing to assess the potential development of MAP. According to the literature, approximately 10 to 20% of patients who do not carry an APC gene mutation exhibit biallelic MYH gene mutations [10]. This particular form of polyposis is extremely challenging to clinically differentiate from FAP or attenuated familial adenomatous polyposis. The condition is characterized by the presence of small intestinal polyps, ranging from 10 to 100. Notably, this variant of polyposis is associated with older age of onset, autosomal recessive inheritance, and typically lacks a family history of colorectal carcinoma symptoms. Duodenal polyps can be detected in approximately one-fifth of patients with this syndrome [7, 8], but there is no heightened risk of developing other cancer types associated with it.

It's important to highlight that the patient under our observation experienced clinical symptoms at a specific age of 16 years, aligning with the data found in the literature [2, 16]. Additionally, the patient had a family history of the condition. Given that the clinical symptoms in both of our cases were relatively mild, and not highly distinctive, the results of colonoscopy and intestinal biopsy played a crucial role in confirming

the diagnosis FAP. As mentioned earlier, other forms of intestinal polyposis generally present with clinical symptoms at a later age, fewer polyps within the intestinal mucosa, or in combination with other syndromes.

When comparing the clinical case we described with similar cases in the literature, we identified both common and distinct features.

All these cases share a common characteristic of being sporadic, and typically presenting with relatively mild clinical symptoms due to their later onset. The age at which symptoms manifest can vary among cases. For example, in contrast to our study, one case reported in the literature involved a 10-year-old boy with an early onset of clinical symptoms at just one year of age. Additionally, some cases have no family history of the disease or colorectal cancer, unlike the cases we observed.

CONCLUSIONS

1. Familial adenomatous polyposis in childhood is a rare hereditary precancerous disease characterized by an autosomal dominant mode of inheritance. It is primarily caused by pathogenic germline variants in the adenomatous polyposis tumor suppressor (APC) gene, which leads to colorectal cancer in 1% of cases.
2. The analysis of the literature data is consistent with the findings from our clinical observations of familial adenomatous polyposis in a patient with complicated family anamnesis. It is worth noting that clinical features do not significantly differ across various types of polyposis, making them insufficient as the primary diagnostic criterion.
3. In cases of suspected FAP in adolescents, genetic testing is crucial to confirm the diagnosis of familial polyposis, and to refine diagnostic and therapeutic strategies.

FUTURE RESEARCH PROSPECTS

Addressing the feasibility of laparoscopic prophylactic colectomy in the examined patient.

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REVIEW ARTICLE

CONTENTS

Implementation of the classification of medical devices of Ukraine in international approaches

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ABSTRACT

Aim: To study the level of compliance of the National Classifier of Ukraine «Classifier of Medical Devices of Ukraine NC 024: 2023» with international approaches to the classification and use of medical devices.

Materials and Methods: National Classifier of Ukraine «Classifier of Medical Devices of Ukraine NC 024: 2023» and the international nomenclature of medical devices Global Medical Device Nomenclature. Methods: bibliosemantic, of content analysis and of structural-and-logical analysis.

Conclusions: In the course of the study, full compliance of the national classifier of medical devices of Ukraine NC 024: 2023 with the GMDN system was established.

KEY WORDS: Ukraine, medical devices, classification, international approaches, compliance.

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INTRODUCTION

In Ukraine, planned work is underway to implement the classification of medical devices in accordance with international approaches. Thus, on the basis of the relevant Directives of the European Union [1,2], the Cabinet of Ministers of Ukraine approved the Technical Regulations on Medical Devices [3], the Technical Regulations on Medical Devices for in vitro Diagnostics [4], the Technical Regulations on Active Implantable Medical Devices [5], which became mandatory for use in the country on July 1, 2015. In order to put medical devices into circulation and/or operation on the territory of Ukraine, it is necessary to undergo a conformity assessment procedure for these devices and affix a national mark of conformity. In particular, the circulation and use of medical devices in Ukraine is allowed in case of confirmation of their compliance with one of the three specified medical technical regulations.

The first national classifier of medical devices in Ukraine was approved in 2019. Subsequently, it was improved and the classifier NC 024:2023 is currently in force [6].

Taking into account that the purpose of implementing the classifier of medical devices at the national level is the effective application of the European approach to the identification of medical devices in Ukraine, which is a step towards the European integration of the health care system of Ukraine and will simplify the entry of Ukrainian medical devices into foreign markets, we analyzed the compliance of methodological approaches and terminology used in the national classifier of medical devices NC 024: 2023 of Ukraine and GMDN.

GMDN – is a system of universally recognized international descriptors used for the identification of medical devices; a system of product names used for diagnosing, prevention, monitoring, treatment, or alleviation of human illnesses and injuries [7].

AIM

The aim was to study the level of compliance of the National Classifier of Ukraine "Classifier of Medical Devices of Ukraine NC 024: 2023" with international approaches to the classification and use of medical devices.

MATERIALS AND METHODS

MATERIALS

National Classifier of Ukraine "Classifier of Medical Devices of Ukraine NC 024: 2023" and the international nomenclature of medical devices Global Medical Device Nomenclature.

METHODS

Bibliosemantic, of content analysis and of structural-and-logical analysis.

Table 1. A fragment of the National Classifier of Medical Devices of Ukraine «Classifier of Medical Devices NK 024:2023»

Code	English name	Definition in English
34175	Acupuncture needle, single-use	A sterile, long, slender, sharply-pointed instrument used to stimulate peripheral nerves in order to produce surgical anaesthesia, relieve pain, and to promote other therapeutic effects. It is widely used in complementary therapy. This is a single-use device.
34178	Invasive breast implant sizer, single-use	A sterile surgical instrument intended to be placed intraoperatively in a surgically-prepared mammary pocket to provide a volume measurement for the appropriate selection of a breast implant (mammary prosthesis). The device is typically a balloon-like elastomer pouch with tubing that is placed in the pocket, filled to an optimal volume, and then removed. This is a single-use device.
35362	Chemical/physical sterilization process indicator	A sterilization indicator designed to respond with a characteristic chemical or physical change to one or more of the physical conditions within the sterilizing chamber. This is a single-use device.
35368	Auditory stimulator	A mains electricity (AC-powered) device that applies sound stimuli (e.g., pure tones, speech) to a patient's acoustic system. It is typically used as a component of several types of devices such as audiometers, auditory evoked-potential recording systems, and auditory function screening devices.
35380	Tendon stripper	A hand-held manual surgical instrument designed to excise a length of ligament, tendon or fascia for use as a living graft. It typically consists of a handle and a semicircular shaped trough that terminates in a sharp cutting edge. It is typically made of high-grade stainless steel. This is a reusable device.

For the application of these materials and methods during the study, permission was obtained from the ethical commission of Uzhhorod National University. Protocol dated 08.02. 2023 № 6/2.

REVIEW AND DISCUSSION

In the course of the study, it was found that the National Classifier of Ukraine "Classifier of Medical Devices NC 024: 2023" is designed to identify instruments, apparatus, devices, gadgets, materials or other products related to medical devices. It should be noted that the Classifier of Medical Devices NC 024:2023 is an adapted translation of part of the list of medical devices included in the GMDN nomenclature and supplemented with medical devices that are not included in the GMDN nomenclature, but are used in Ukraine.

When creating the national classifier of Ukraine "Classifier of medical devices NC 024: 2023", hierarchical, ordinal, five-digit classification methods were used. Information about a medical device in the national classifier is presented in the form of a 5-digit numerical code GMDN (Code) is cross-referenced with the exact wording of the term (Term Name) and Definition (Definition). This can be seen in the following example: "Code (GMDN Code): 10729. Term (GMDN Term Name): «Central venous catheter». Definition: (GMDN Definition): "A sterile, flexible tube intended to be introduced into a neck or thoracic vein and often advanced into the superior vena cava for various infusion/aspiration procedures (i.e., non-dedicated) including the intravenous administration of nutrients, fluids, chemotherapeutic agents or other drugs, and blood sampling or delivery; it may also be used to monitor venous pressure. The proximal end of this central venous catheter (CVC) is typically fixed to the patient for long-term use. It may include supportive devices associated with introduction (e.g., guidewire, introducer); it is not primarily intended for extracorporeal blood therapies such as haemodialysis. This is a single-use device".

Each of the items of the classifier on a medical device consists of five parts: code, name of the device in Ukrainian, description of the device in Ukrainian, name of the device in English, description of the device in English.

A fragment of the National Classifier of Medical Devices of Ukraine is presented in the table 1. It should be noted that when determining the subject of procurement, the National Classifier NC 024:2023 is used together with the National Classifier of Ukraine SC 021:2015 "Unified Procurement Dictionary" [8].

In the course of the study by comparison, it was found that the National Classifier of Ukraine "Classifier of Medical Devices of Ukraine NC 024: 2023" [6] is harmonized with the international nomenclature of medical devices Global Medical Device Nomenclature [7], which is used in 70 countries of the world, in particular, in most countries of Europe and the United States. Currently, the nomenclature is used by about 7500 manufacturers, it includes about a million items [9]. The GMDN nomenclature is recommended for use by the International Forum of Medical Device Regulators (IMDRF) and is actually the only platform for identifying medical devices and international industry information exchange [9].

CONCLUSIONS

In the course of the study, the full compliance of the methodological approaches, structure and terminology used in the development of the National Classifier of Ukraine "Classifier of Medical Devices of Ukraine NC 024: 2023" with those of the GMDN system was established.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

The use of *Botulinum toxin* in various urological conditions

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ABSTRACT

Aim: The objective of this review paper is to comprehensively analyze and summarize the current understanding and clinical applications of *Botulinum toxin* in the field of urology.

Materials and Methods: The materials and methods for this review paper involved an extensive literature search on the use of *Botulinum toxin* in urology. Multiple online databases such as PubMed, Web of Science, and Google Scholar were utilized to gather peer-reviewed articles, clinical trials, and relevant books published within the last decades. A few articles used in the review come from before 21 century because the information is essential to fully describe the topic. Studies were selected based on their relevance to the topic, with a focus on those that reported on the clinical applications of *Botulinum toxin* in urology – we use information from other review papers, clinical trials and research papers. To expand the database, we have looked through the literature not only in English but also other languages. Thanks to this method we were able to compare the results from different countries and scientific groups all over the world. Data extracted from these sources were then analyzed and synthesized to provide a comprehensive overview of the subject matter.

Conclusions: In conclusion, *Botulinum toxin* has shown significant promise and utility in the field of urology. Its ability to effectively relax muscles has led to its application in a variety of urological conditions, including NDO, OAB, BPS/IC, DSD, BPH, CPP, and PE. The effectiveness and safety of *Botulinum toxin* have been demonstrated in numerous studies, providing a robust evidence base for its clinical use. However, further research is needed to optimize the administration methods, dosage, and treatment protocols. Additionally, more randomized controlled trials are required to establish the long-term safety and efficacy of *Botulinum toxin*, especially for conditions for which the current data is limited. Overall, *Botulinum toxin* represents a valuable tool in the urologist's armamentarium and is likely to continue to be an area of active research and development in the future.

KEY WORDS: chronic pelvic pain, *Botulinum toxin*, overactive bladder, detrusor overactivity, bladder pain syndrome

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INTRODUCTION

Botulinum toxin (*BoNT*) is a neurotoxic protein produced by the bacterium *Clostridium botulinum*. It's widely recognized for its use in cosmetic treatments, but its potent neuromodulating properties have also found numerous applications in the field of urology. By inhibiting acetylcholine release at the neuromuscular junction, *BoNT* can effectively relax muscles, making it a powerful tool in the management of various urological conditions.

AIM

The objective of this review paper is to comprehensively analyze and summarize the current understanding and clinical applications of *BoNT* in the field of urology. We aim to provide an overview of its use in various urological conditions, discuss its effectiveness, and highlight its potential future implications. The information presented in this paper is based on a thorough review of existing literature, including peer-reviewed articles, clinical trials, and relevant books.

MATERIALS AND METHODS

The materials and methods for this review paper involved an extensive literature search on the use of *BoNT* in urology. Multiple online databases such as PubMed, Web of Science, and Google Scholar were

utilized to gather peer-reviewed articles, clinical trials, and relevant books published within the last decades. A few articles used in the review come from before 21 century because the information is essential to fully describe the topic. Studies were selected based on their relevance to the topic, with a focus on those that reported on the clinical applications of *BoNT* in urology – we use information from other review papers, clinical trials and research papers. To expand the database, we have looked through the literature not only in English but also other languages. Thanks to this method we were able to compare the results from different countries and scientific groups all over the world. Data extracted from these sources were then analyzed and synthesized to provide a comprehensive overview of the subject matter.

REVIEW AND DISCUSSION

MECHANISM OF ACTION OF *BoNT*

BoNT blocks the transmission of impulses from the nerve ending to the muscle, affecting the process of the nerve ending releasing the neurotransmitter acetylcholine from the vesicles. Vesicular transport is essential for the functioning of all human cells. In the cell itself, the mechanism for delivering vesicles to the cell surface or organelles is provided by the Golgi complex, endoplasmic reticulum, and lysosomes. Directed transport is accomplished by recognition and binding by SNARE proteins embedded in membranes. For nerve cells that have numerous and functionally different contacts with other cells, the mechanism of targeted transport of intracellular vesicles is extremely important. For example, such a system is necessary for the release of a neurotransmitter and the transmission of a nerve impulse from a neuron to a muscle. The neurotransmitter is transported to the nerve ending to the presynaptic membrane, where it is stored and released when the neuron is excited by fusion of the vesicle with the presynaptic membrane. *BoNT* disrupts this binding by blocking the release of the neurotransmitter acetylcholine by motor neurons [1-3].

BoNT IN NEUROGENIC DETRUSOR OVERACTIVITY (NDO)

NDO is a urodynamic diagnosis and one of the most common manifestations of a neurogenic bladder, which may be a consequence of nerve conduction disturbances due to spinal injury, multiple sclerosis and many other neurological diseases and their consequences [4]. During a urodynamic study, pathological increases in detrusor pressure are recorded during the filling phase of the bladder, violating the basic rule of safe functioning of the bladder, namely maintaining low pressure during filling. Abnormal pressure surges or early increases can lead to impaired continence or vesicoureteral reflux, which can impair kidney function. High-amplitude contractions are especially dangerous: it is believed that a rise in detrusor pressure above 40 cmH2O clearly causes vesicoureteral reflux.

Most studies on the use of *BoNT* for neurogenic bladder dysfunction, manifested by NDO, were carried out in groups of patients with spinal cord injury and multiple sclerosis. For these patients, it is extremely important to recognize any type of NDO and take steps to eliminate it or reduce its severity. Back in 1991, a medical center in the USA studying spinal cord injuries found that, regardless of the presence of concomitant detrusor sphincter dyssynergia (DSD), NDO leads to complications in 50% of patients [5].

The effectiveness and safety of BoNT administration for NDO was studied in the DIGNITY (Double-Blind Investigation of Purified Neurotoxin Complex in Neurogenic Detrusor Overactivity) study conducted several years ago. The program consisted of 2 phase III studies. The study included patients with NDO associated with multiple sclerosis (Expanded Functional Status Scale score ≤6.5) and spinal cord injury below Th1 level. All patients had urinary incontinence due to NDO lasting more than 3 months and with 14 or more episodes of incontinence per week. The observation group included patients both receiving antimuscarinic therapy on a continuous basis and without it. All patients were able or were trained to perform clean intermittent catheterization (CIC) [6]. Patients who received BoNT therapy experienced a clinically significant improvement in quality of life compared to patients who received placebo. With repeated courses of treatment (maximum 5), the achieved values remained stable [6].

For NDO, the standard dose is 200 IU of BoNT, diluted in 30 ml of 0.9% sodium chloride solution. The drug is injected at 30 points, 1 ml of solution into each [7].

BoNT IN OVERACTIVE BLADDER (OAB)

OAB is described as a syndrome that is characterized by a feeling of urgency in relation to urination, with or without the presence of urgency-associated urge urinary incontinence (UUI). Approximately 12% to 17% of the population is impacted by this particular syndrome. Patients diagnosed with OAB who have undergone a duration of three months using one or more distinct antimuscarinic agents, frequently without sufficient therapeutic efficacy and/or incapability to withstand

the adverse reactions of the medication, are classified as refractory OAB patients [8-10]. *BoNT* injections are advocated as the established therapeutic regimen for managing refractory OAB in accordance with the guidelines outlined by the European Urology Association (EUA) and American Urology Association (AUA) [11,12].

Published studies by Nitti et al, Tincello et al, Onem et al and Mangera et al on the usage of BoNT in OAB show a significant decrease in daily frequency, urgency and incontinence episodes. There was also the improvement in the parameters measured urodynamically. The only side effect that was expressed in bigger scale compared to placebo in those articles were urinary tract infections episodes [13-16].

The EUA guidelines have demonstrated that the administration of 100 IU *BoNT* into the bladder wall surpasses the effectiveness of a placebo in relation to UUI and the enhancement of quality of life. There is no indication of reduced efficacy with repeated injections. Nevertheless, it is imperative to highlight that patients should be duly informed regarding the potential occurrence of urinary system infections and the potential need for CIC [9].

For OAB, the standard dose is 100 IU of BoNT, diluted in 10 ml of 0.9% sodium chloride solution [7].

BoNT IN BLADDER PAIN SYNDROME/ INTERSTITIAL CYSTITIS (BPS/IC)

BPS/IC can be characterized as a collection of symptoms that are distinguished by the absence of infection and other identifiable pathologies. These symptoms encompass urgency, frequent urination, discomfort in the bladder or pelvic area, as well as a sensation of pressure [17]. *BoNT* has shown promise in the treatment of BPS/IC. It has been found to have therapeutic effects in reducing bladder pain and improving urinary urgency in BPS/IC patients [18]. *BoNT* has its effect in the central nervous system and the bladder wall, with pain control and reduction of urinary urgency achieved through mast cell stabilization, modulation of TRPV (transient receptor potential cation channel subfamily V) and PGE2 pathways, and other mechanisms. Different methods of *BoNT* administration have been explored, including intravesical instillation, hyperthermia, intravesical hydrogel, and lysosomes [19]. Bladder instillation of *BoNT* in combination with electromotive drug administration has shown promising results as a novel approach for BPS/IC treatment [20]. Studies have also shown that intravesical instillations of Sapylin after *BoNT* injection can produce better clinical outcomes than *BoNT* alone in BPS/IC patients [21]. Intratrigonal injection of *BoNT* has been found to be an effective and safe long-term treatment for BPS/IC patients refractory to conservative forms of treatment.

OTHER UROLOGICAL CONDITIONS

Among other urological conditions that might be managed with *BoNT* are DSD, benign prostatic hyperplasia (BPH), chronic pelvic pain (CPP) and premature ejaculation (PE).

Studies have shown that combined injections of *BoNT* into the detrusor and external urethral sphincter muscles can reduce detrusor and urethral pressures without increasing post-void residual ratio and diaper pad use [22]. This treatment option may be beneficial for spinal cord injury patients with DSD who want to preserve spontaneous voiding [23]. Detrusor injection of *BoNT* leads to a greater improvement in autonomic dysreflexia, possibly due to decreased detrusor pressure and increased compliance [24]. However, patient satisfaction may not increase due to side effects such as exacerbated incontinence and urinary urgency.

Several studies have shown promising results in the use of *BoNT* for BPH-induced lower urinary tract symptoms (LUTS) [25,26]. *BoNT* injections into the prostate tissue have been shown to induce smooth muscle relaxation and gland atrophy, leading to a decrease in prostate volume and improvement in LUTS [27,28]. However, the optimal route of administration, effective dose, and volume of injections still need further investigation. It is also important to consider confounding factors such as placebo effect and underlying medical conditions when evaluating the efficacy of *BoNT* for BPH.

BoNT has been investigated as a potential treatment for PE. Studies have explored the use of *BoNT* in the treatment of PE, including primary PE and PE-related distress. The injection of *BoNT* into the bulbospongiosus muscle has shown promising results in improving intravaginal ejaculatory latency time and various aspects of sexual satisfaction, such as ejaculation control and sexual satisfaction scores. However, the current data on the efficacy and safety of *BoNT* in the treatment of PE are limited, and more randomized controlled trials are needed to establish its long-term safety and efficacy [29,30].

CONCLUSIONS

In conclusion, *BoNT* has shown significant promise and utility in the field of urology. Its ability to effectively relax muscles has led to its application in a variety of urological conditions, including NDO, OAB, BPS/IC, DSD, BPH, CPP, and PE. The effectiveness and safety of *BoNT* have been demonstrated in numerous stud-

ies, providing a robust evidence base for its clinical use. However, further research is needed to optimize the administration methods, dosage, and treatment protocols. Additionally, more randomized controlled trials are required to establish the long-term safety and efficacy of *BoNT,* especially for conditions for which the current data is limited. Overall, *BoNT* represents a valuable tool in the urologist's armamentarium and is likely to continue to be an area of active research and development in the future.

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CONFLICT OF INTEREST

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CASE STUDY

CONTENTS

Atypical course of incarcerated post-traumatic diaphragmatic hernia

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ABSTRACT
The article focuses on the instrumental imaging methods which greatly enhance the possibilities when arriving at correct and quick diagnosis of acute surgical pathology. Analysis of clinical and anamnestic data of the disease course and the results of instrumental research methods made it possible to arrive at clear clinical diagnosis, determine the indications for surgical treatment in this specific clinical case. The use of modern visualization methods while examining the patients prevents errors in diagnosis and helps to determine the optimal treatment tactics.

KEY WORDS: post-traumatic diaphragmatic hernia, acute pancreatitis, differential diagnosis

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INTRODUCTION

Abdominal pain is the leading symptom in most acute and chronic diseases of the abdominal cavity. Considering the nature of pain, its localization, intensity and other symptoms, it is possible to suspect certain pathology. However, in case of atypical course of diseases, the symptoms may be false, not typical, which can result in clinical errors in diagnosis and treatment tactics. Therefore, it is often not possible to arrive at clinical diagnosis based only on the clinical presentation [1–4].

In the clinical picture, a diaphragmatic hernia is accompanied by a painful symptom in patients. Also the symptoms include dysphagia, belching, nausea, vomiting, difficulty breathing, etc. Pain is usually localized in the epigastric area or behind the sternum, in the right or left hypochondrium, depending on the hernia location. The same symptoms can be present in other diseases of the abdominal cavity. Gastric volvulus or incarcerated hernia is associated with the intense pain, which can simulate acute surgical diseases, namely, acute pancreatitis, acute cholecystitis, perforated ulcer, etc [5–8].

CASE REPORT

A 20-years-old female patient presented to the district hospital acutely unwell with the complaints of constant pain in the left hypochondrium irradiating to the left half of the back, urges to vomit, dry mouth, general weakness. The initial diagnosis included «Left-sided renal colic. Chronic pancreatitis in the stage of exacerbation». We did not use modern instrumental examination methods due to the lack of certain conditions in the hospital. Thus, the symptomatic conservative treatment was provided (infusion therapy, antispasmodics, painkillers). But the patient's condition became worse. She was referred to the surgical department of the regional hospital with a diagnosis «Acute pancreatitis».

On admission to the hospital (according to the records in the inpatient card), the general condition of the patient was determined as moderate severe, the patient was active. Physical examination revealed the pale pink skin, muffled heart tones, heart rate – 100 beats/min., BP – 100/60 mmHg. On auscultation: breathing was practically not heard on the left side, it was vesicular on the right one. The abdomen was soft, painful in the epigastric area, both right and left hypochondrium, more painful in the left one. Soft elastic 15x10 cm mass was detected on palpation of the left side, in the infracostal area.

Laboratory tests data. Complete blood test: Hb – 143 g/l, erythrocytes – $4.2x10^{12}$/l, leukocytes – $11.6x10^{9}$/l, rod nuclear – 10%, segment nuclear – 70%, eosinophils – 1%, basophils – 1%, lymphocytes – 13%, monocytes – 5%. Urinalysis: specific gravity – 1016, reaction – acidic, protein – traces, glucose – absent, erythrocytes – 24-26 in the field of vision, leukocytes – 2-3 in the field of vision, bacteria – absent. Biochemical blood test: total protein – 52 g/l, potassium – 4.4 mmol/l, sodium – 155 mmol/l, urea – 5.7 mmol/l, creatinine – 102 μmol/l, total bilirubin – 22.3 μmol/l. Coagulogram: prothrombin

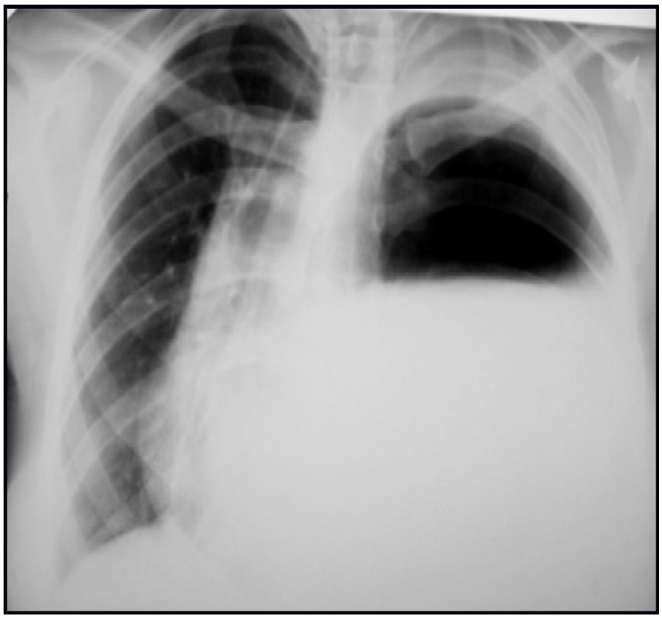

Fig. 1. X-ray of the patient's chest.

index – 96.6%, fibrinogen – 3.1 g/l. Urinary amylase according to Wohlgemuth – 32 units, blood glucose – 3.6 mmol/l. Based on the data of laboratory tests, it was impossible to confirm any diagnosis.

ECG data: heart rate – 105 beats/min, electrical axis of the heart was shifted to the left by 69 degrees. ECG revealed the intracardiac conduction disorder and enlargement of the left atrium. Considering the data obtained, a myocardial infarction (anterior and lateral lower) was suspected. But the patient's condition did not correspond to the clinical presentation.

Abdominal ultrasound findings: liver – the right lobe was 12.5 cm, the left lobe – 2.9 cm, was not enlarged, homogeneous in structure. Gallbladder was oblong – 6.2x2.6 cm, wall – 0.26 cm with septal bile sediment. Choledochus – 0.4 cm, pancreas was not visualized, right and left kidneys were in typical position, parenchyma – moderately echogenic. Ultrasound examination revealed a great amount of gastric content, small amount of free fluid in the left half of the abdomen. Formation of increased echogenicity16.2x10.0 cm in size, uniform in structure was detected in the left hypochondrium above the stomach (similar to spleen). The spleen was not visualized in a typical position; a great amount of free fluid between the intestine loops could be observed. Conclusion: formation in the abdominal cavity, ascites.

On admission, a chest X-ray was provided to the patient (Fig. 1.).

Radiological findings showed intense opacity in the left half of the thoracic cavity, the level of fluid up to the 3rd rib and free air above it. Lung tissue on the left was not traced. The medial shadow was shifted to the right, squeezing the right lung. X-ray of the abdominal organs did not reveal free air and fluid levels. The presentation of the tense left-sided pneumo-hydrothorax was observed.

The clinical presentation did not correspond to examination data. The patient underwent radiography of the gastrointestinal tract for differential diagnosis, which detected accumulation of contrast agent in esophagus, as well as minor traces up to 4 cm from the cardia in stomach. Conclusion: radiological signs of diaphragmatic hernia were present.

The confirmation of the clinical diagnosis involved 3D spiral computer tomography of the thoracic cavity with modeling (Fig. 2).

CT scan showed a significantly dilated stomach with small omentum, small intestine loops and partly colon loops on the left side of the thoracic cavity. Small amount of fluid content and edema of the mesentery were also visualized. The left crus of the diaphragm was not clearly visible. The left lung was completely collapsed and lost pneumatization. The organs of the mediastinum were sharply shifted to the right. The right lung was compressed and pneumatized within normal range. The liver had normal size and shape, the paren-

Fig. 2. 3D spiral computer tomography of the thoracic cavity with modeling.

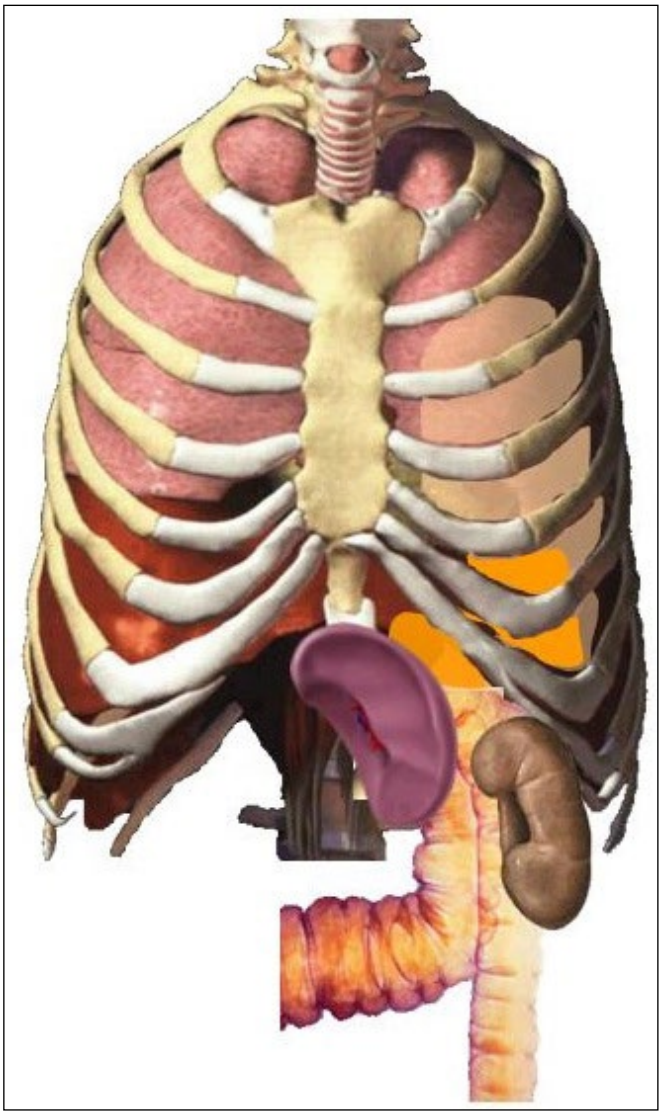

Fig. 3. Diagnosis «Post-traumatic diaphragmatic left-sided hernia with gastric and colon incarceration and upward displacement of the spleen and left kidney».

chymal density was homogeneous. The pancreas had homogeneous density and compressed in the caudal projection. Kidneys and adrenal glands had normal shape and position, homogeneous. Conclusion: CT scan detected the signs of rupture in the left dome of the diaphragm.

When working with the retrospective investigation of the medical history, we determined that 3 months ago the patient had a domestic injury (a fall from the height of 3 meters with the damage to the left half of the chest). She did not seek medical help and did not have any significant complaints. Her condition was stable.

The data of additional imaging techniques made it possible to arrive at the diagnosis «Post-traumatic diaphragmatic left-sided hernia with gastric and colon incarceration and upward displacement of the spleen and left kidney» (Fig. 3).

The surgery was performed under general anesthesia according to absolute indications. It included upper midline laparotomy, diaphragmotomy up to 8 cm, elimination of incarceration and gastric and colonic volvulus. Incarcerated in the diaphragm organs were placed into the abdominal cavity. The viability of the organs was preserved, constriction mark on the stomach and colon did not have the signs of necrosis of their walls. Plastic surgery of the diaphragm was carried out applying patient's own tissues with duplicature; a transnasal probe was introduced into the stomach and the initial part of the small intestine as well as the drainage of the left pleural cavity and abdominal cavity with tubular drains. It should be noted that the narrowing area on the stomach and colon was not peritonized during the operation.

The postoperative management included analgesia, correction of water and electrolyte balance, perioperative antibiotic prophylaxis. The patient was activated on the 2nd day, enteral nutrition was started on the 3rd day.

General or local complications were absent. The treatment course lasted from April 13 to May 4, 2022. The patient was discharged from the hospital on the 10th day after the surgery. Follow up after 1 year: did not have complaints, worked in previous specialty, satisfactory quality of life.

The causes of post-traumatic hernia are rupture of the diaphragm and its layering when inertial injuries of the chest and abdomen occur. Such hernias are more often left-sided. Post-traumatic diaphragmatic hernias are quite rare and occur in 0.8-7% of thoracoabdominal trauma cases [9–11].

According to the literature data, the time after trauma to the formation and clinical manifestations of post-traumatic diaphragmatic hernias can range from a few weeks to 50 years. In more than 50% of cases, hernias may not have clinical manifestations, and symptoms appear after the occurrence of complications [1–4].

The atypical course of surgical diseases usually does not allow arriving at a clinically clear diagnosis and determining the tactics and methods of treatment. The use of modern imaging techniques helps to avoid errors in clinical diagnoses and determines the optimal treatment tactics for patients [6–10].

Diagnosis of hernia, in addition to the analysis of the clinical picture and anamnesis data, includes radiography with the introduction of contrast material, esophagoscopy and research of the contractile activity of the esophagus (manometry). In the event that the hernia is asymptomatic and does not cause discomfort, treatment will be aimed at choosing monitoring tactics and lifestyle correction. Thus, the patient should eat properly, avoiding overeating, not lie down immediately after eating, control body weight, etc. [12–14].

In addition, it is possible to carry out drug therapy, first of all, with the addition of gastroesophageal reflux disease (for example, prokinetics, proton pump inhibitors, antacids). The absence of results after conservative therapy and the severe course of the diaphragmatic hernia require surgical intervention followed by suturing of the hernial gate, ligature of the esophageal ligaments, fixation of the stomach in the abdominal cavity but also carrying out fundoplications according to one of the methods (fundoplication according to Nissen) [7–9].

CONCLUSIONS

The combination and analysis of clinical and anamnestic data of the disease course and the results of instrumental research methods made it possible to arrive at clear clinical diagnosis, determine the indications for surgical treatment in this specific clinical case. The use of modern visualization methods while examining the patients prevents errors in diagnosis and helps to determine the optimal treatment tactics.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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CASE STUDY

CONTENTS

Vertebral metastasis of hepatocellular carcinoma secondary to viral hepatitis B: case report of 2 patients

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ABSTRACT

Bone metastases from liver cancer are rare. We report two cases of bone metastases revealing HBV-induced HCC. A 26-year-old african man presented with 4 months of low back pain in the context of general deterioration. Examination revealed a lumbar spinal syndrome and hepatomegaly. Abdominal ultrasound revealed a multinodular liver, and a CT scan of the spine revealed osteolytic lesions. Biological tests revealed a hepatic cytolysis syndrome, hepatic cholestasis and hepatocellular insufficiency. Alpha foetoprotein levels were elevated and hepatitis B serology was positive. We adopted the diagnosis of HCC of viral B origin with bone metastasis. The second case involved a 44-year-old African man admitted for 10 days with back pain. Examination revealed a spinal syndrome, paraplegia and hepatomegaly. A thoracic-abdominal-pelvic CT scan revealed typical HCC lesions and osteolytic lesions on the ribs, pelvis and vertebrae. The biology revealed a biological inflammatory syndrome, hepatic cytolysis, a hepatocellular insufficiency syndrome and a cholestasis syndrome. Alfa-feto proteins were elevated and HBV serology was positive. The diagnosis of bone metastasis of HCC secondary to HBV infection was accepted.

KEY WORDS: vertebral metastasis, hepatocellular carcinoma, viral hepatitis B, Burkina Faso

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INTRODUCTION

Digestive cancers are not very osteophilic tumours, and bone metastases occur late in their development [1]. Hepatocellular carcinoma (HCC) is a very common cancer worldwide, although its geographical distribution is heterogeneous. The highest incidence is seen in sub-Saharan Africa and East Asia. Chronic hepatitis B virus (HBV) infection is strongly implicated in these regions [2-3]. In the vast majority of cases, bone involvement in HCC is found in the context of polyvisceral metastatic disease [1-3]. The most common site of metastasis is the lung, followed by lymph nodes and the kidneys. However, bone metastases are very rare [4].

We report two cases of bone metastases revealing HCC in Burkinabe patients with HBV infection discovered during hospitalisation.

CASE REPORT

FIRST OBSERVATION

Mr B. M., a 26-year-old student, non-alcoholic, with no history of jaundice and no other particular pathological history, was admitted with hyperalgesic, incapacitating low back pain that had been present for 4 months, in an apyretic context and with an altered general condition consisting of asthenia, anorexia and weight loss estimated at 11%, without notion of trauma or abdominal pain. On admission, the examination revealed an altered general condition, normal consciousness, moderate malnutrition, and a low lumbar spinal syndrome; there was no radicular syndrome. There was gross hepatomegaly with a hard, even-surfaced liver arrow measuring 14 cm, with a sharp lower edge. The rest of the examination was normal. On imaging, abdominal ultrasound revealed a suspicious-looking multinodular cirrhotic liver (Fig.1). Computed tomography (CT) of the spine revealed osteolytic lesions of the vertebral bodies of L3 and L5, osteolysis of the right pedicle of L5 and a moderate fracture of the vertebral body of L3 (Fig.2). The biology revealed cytolysis with aspartate aminotransferase (ASAT) at 440 U/L and alanine aminotransferase (ALAT) at 88 U/L, hepatic cholestasis with gamma GT at 596 U/L, hepatocellular insufficiency with a prothrombin rate (PT) at 47.9%; there was no cytopenia or biological inflammatory syndrome. The alpha-foetoproteine assay came back very high at 332,100 ng/ml and the prostate-specific antigen (PSA) normal at 0.85 ng/ml. Hepatitis B serology came back positive. We were unable to continue our histological investigations due to the absence of technical facilities for liver biopsy and bone sampling. The diagnosis of HCC of viral B origin with bone metastasis was highly probable given the clinical arguments, the lesions on

Fig. 1. Abdominal ultrasound showing a multinodular cirrhotic liver.

imaging and the biological disorders. The patient was treated with morphine for pain, nursing and rehydration, but died 5th days later of hypovolaemic shock during hospitalisation.

SECOND OBSERVATION

Mr C. H. was a 44-year-old shopkeeper, married and a non-drinker. He was admitted to the rheumatology department with hyperalgesic back pain of inflammatory origin, which had been progressing for about ten days in an apyretic context and with a deterioration in his general condition. Examination revealed WHO stage 3 general, normal consciousness and stable haemodynamic parameters. There was a thoracic and lumbar spinal syndrome, proportional paraplegia with motor strength rated at 2/5 in both lower limbs, and no radicular syndrome or sublesional syndrome. Examination of the abdomen revealed global hepatomegaly, with a hepatic arrow measuring 16 cm, with a regular surface and a sharp lower edge, as well as HACKETT type 2 splenomegaly. The rest of the examination was unremarkable. On imaging, the thoraco-abdomino-pelvic CT scan revealed several hypodense liver nodules enhanced by arterial contrast (Fig.3). It also revealed osteolytic lesions in the ribs, pelvis and vertebrae associated with T8 and L2 vertebral fractures (Fig.4). He had no other secondary locations. The biology revealed a biological inflammatory syndrome with a C reactive protein (CRP) of 78 mg/l, hyperleukocytosis of 11500/mm3, predominantly neutrophilic, and no anaemia. There was also hepatic cytolysis with transaminases elevated to 3 times normal, a hepatocellular insufficiency syndrome with a low PT of 32.9% and a cholestasis syndrome with gamma GT elevated to 3 times normal. Alfa foeto protein was elevated to 3097 ng/ml and PSA was normal. HBV serology came back positive. The diagnosis of bone metastasis from HCC secondary to HBV infection was highly probable given our clinical picture, despite the absence of histological evidence, which was not available in our context. The patient was initially treated with tramadol based analgesics, followed by morphine and nursing. The immediate course was marked by a deterioration in general condition, and the patient died on the 6th day of hospitalisation as a result of hypovolaemic shock.

HCC is one of the main causes of cancer-related deaths in many parts of the world. It represents a public health problem because it is the 4th cancer that causes the greatest number of deaths [5]. Chronic HBV infection is the leading cause of HCC in East Asia and in most sub-Saharan African countries, as shown by our two observations, and rarely HCV, as in the two cases reported in Togo [5-8]. The age of onset of HCC varies widely throughout the world. In Japan, HCC tends to appear later in life. In North America and Europe, the median age of onset is over 60 years. [5, 8]. In Africa, on the other hand, the median age

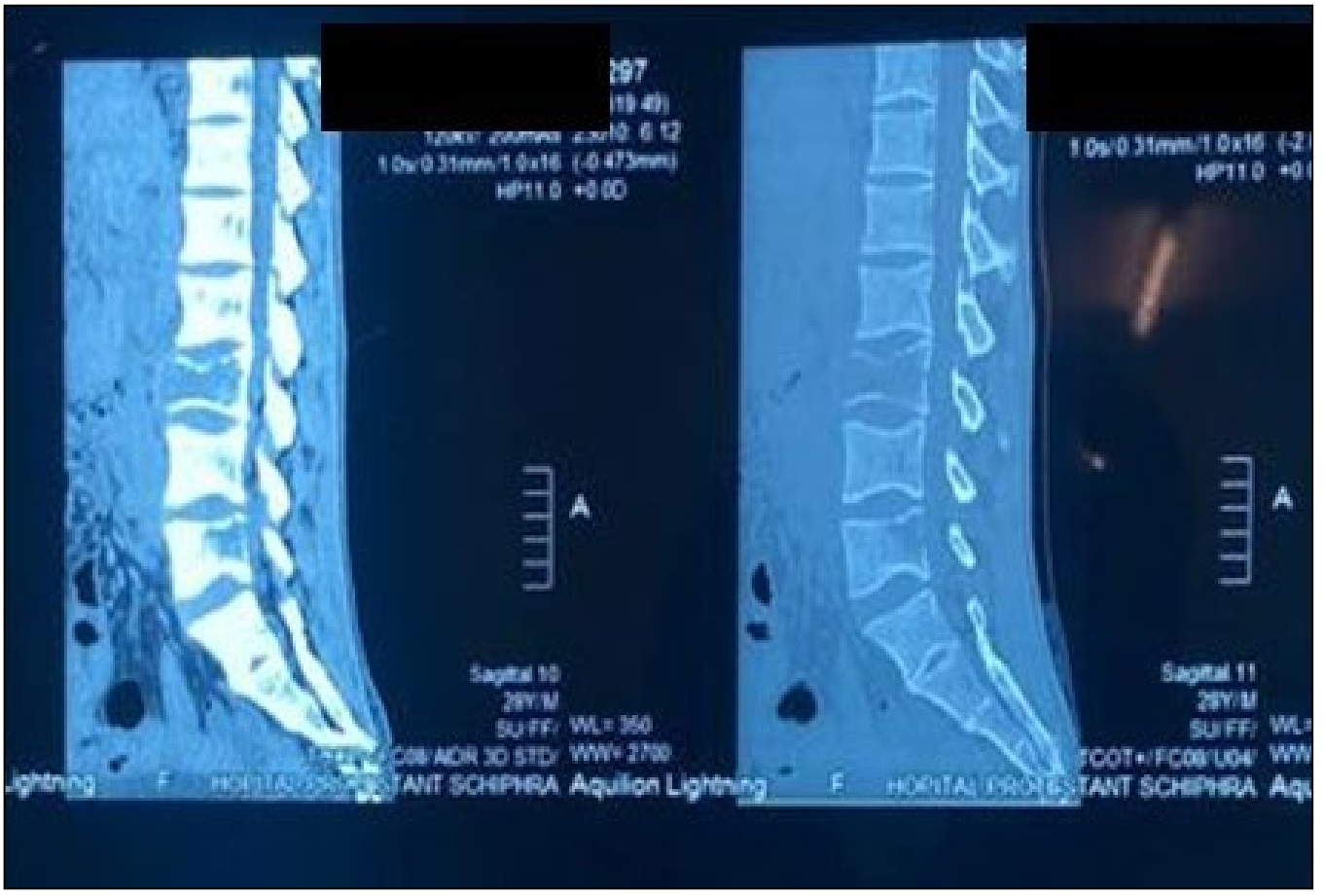

Fig. 2. CT scan of the spine showing multistage vertebral osteolytic lesion.

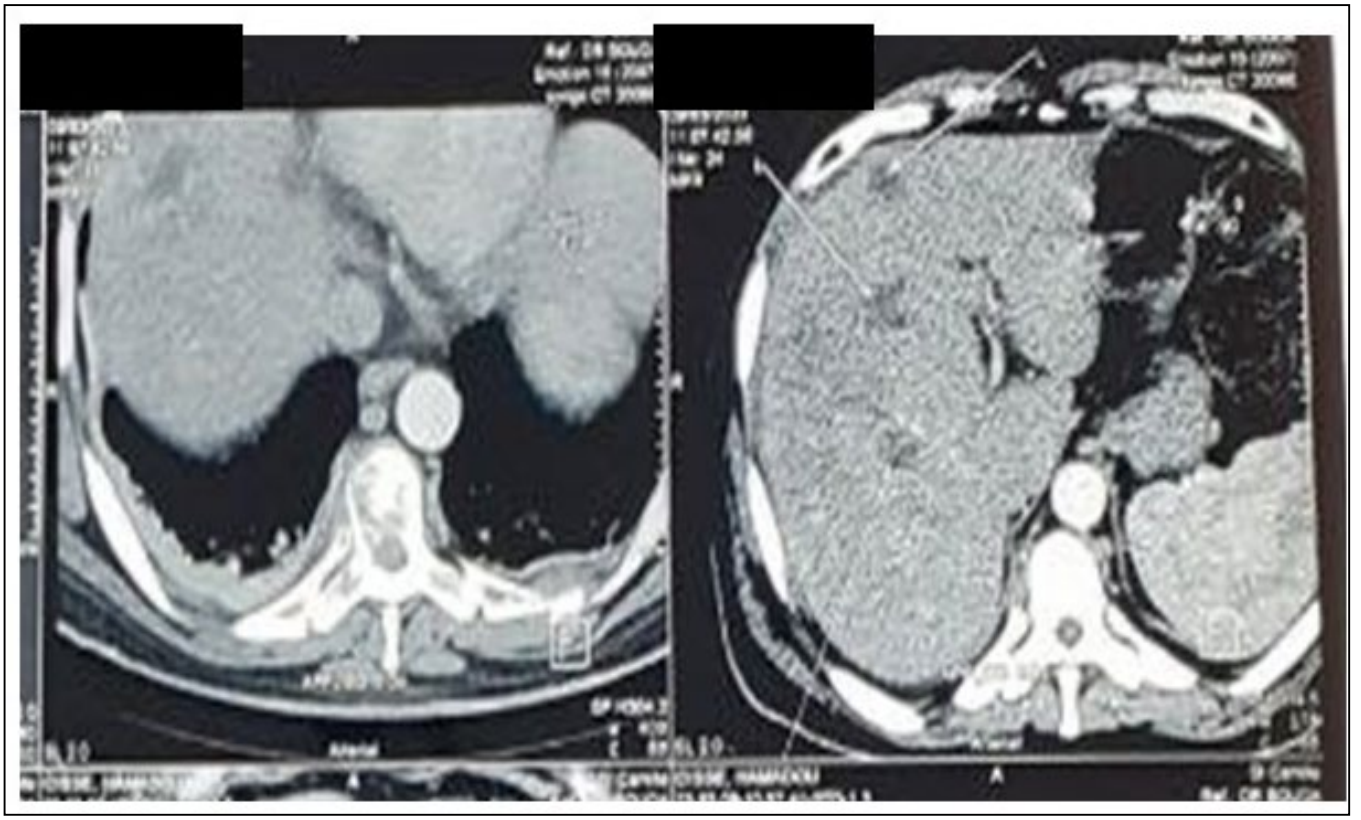

Fig. 3. Abdominal CT scan showing liver nodules.

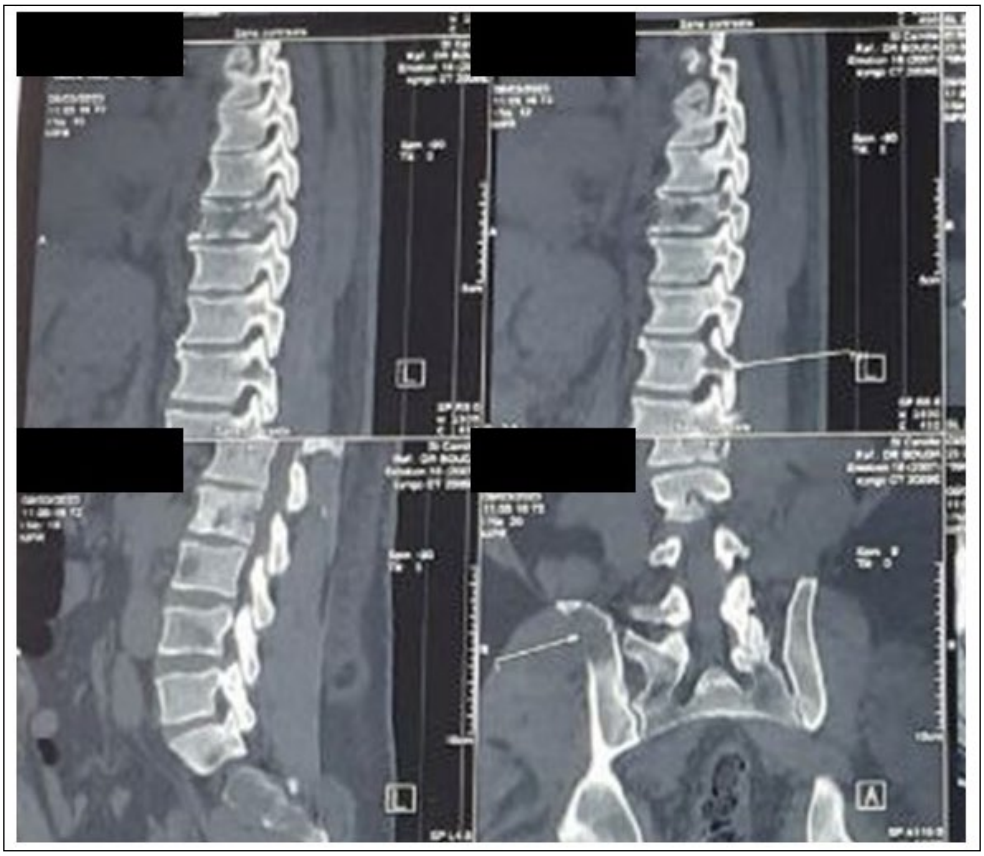

Fig. 4. CT scan of the spine showing osteolytic lesions of the vertebrae and pelvis.

of diagnosis is 45 years with extremes as shown by our two observations [7]. It was particularly early in our first patient, who was diagnosed at the age of 26 with a secondary bone site. The median age of discovery of bone metastases in Asian patients is 65 years, which is much higher than in our patients [9]. Our two patients were men, as in the cases reported in Togo, since HCC is more common in men, accounting for 72% of cases and 85% of bone metastases. [7, 9]. Bone metastases are increasingly reported in the literature, but the revealing bone symptomatology remains exceptional because our patients consulted only for osteoarticular and not digestive symptoms. [10-12]. At the onset, hepatomegaly was found in 9 out of 11 cases with a bone metastasis in Maillefert's review as in our cases with a hard hepatomegaly with a sharp lower border characteristic of HCC [12]. Bone metastases on X-ray and CT scan are frequently osteolytic lesions and in the absence of a biopsy for histological proof, their typical presentations allow the diagnosis to be evoked with a strong presumption [6, 10, 12, 13]. The diagnosis of HCC in the absence of histological evidence is made in the presence of a contrast-enhancing nodule at arterial time with a washout at portal time [5, 14]. The prognosis for HCC with bone metastasis is poor, with a median survival time of 6.2 months. [4]. The modified TOKUHASHI prognostic score was 7 and 4 respectively in our 2 observations, indicating a life expectancy of less than 6 months. [13]. As with all extrahepatic HCC metastases, only palliative treatment can be proposed. From a pharmacological point of view, Sorafenib was indicated for our patients in their advanced stage, but its unavailability in our context reduces the therapeutic alternatives [5].

CONCLUSIONS

HCC revealed by bone metastases is rare. However, it should be considered when a patient with chronic hepatopahy presents with bone pain at any age. The diagnosis must be made quickly, as treatment options are limited.

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Ethical Approval and Consent to participate: we obtain consent of patients.

CONFLICT OF INTEREST

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LETTER TO EDITOR

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THE ONLY ONES IN EUROPE

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In the 19th Century great development in science, including medicine, has been observed. Poland, however, for 123 years had limited contact with international medicine, especially under Russian Partition. It was also difficult to inform the West about our successes and revelations in medicine. Professor's A. Leśniowski's Colitis is a great example, as he was a man from nowhere for the Western Europe, as stated by M. Kawalec.[1)] Those were the hard years of exiles to Siberia and two world wars, followed by 44 years of Soviet supremacy and falsifying history.[2)]

All this made Polish medicine function in an independent country for only 20 years before 1989. During the tragic era of World War II, 50% of physicians were killed (over 6000 out of 12000 alive in 1939). The only memorial plaque dedicated to those killed has been embedded by Polish Medical Association into the wall of Ujazdowski Hospital in 1989. Each year on September 1st they are remembered by physicians.[3)]

Medical Universities hold lectures on Polish medicine history, teaching students about the times since King Augustus Poniatowski until the modern times. Museums play a major role in spreading knowledge about culture, history and national heritage. Poland can be dubbed a state of museums. There are museums of buttons, axes or Christmas Tree baubles.[4)]

According to the Central Statistical Office, in 2017 museums in Poland had 37,5 million visitors, (by 3,2 % more than in 2016). Still, among **981** museums, there is **no museum of medicine**.[5)] Yes, we are the only European state to not have such museum!!! At the same time the Ministry of Culture and National Heritage states, that it supervises and finances as many as 985 museums.[6)]

I would like to underline that Polish Medical Association greatly respects the Ministry of Culture and National Heritage, despite creating the Institute of Theater in surgical hall of former Ujazdowski Hospital contrary to our many-decade-long efforts to found a museum of medicine there. There was also a ministerial plan to use the hall of Central Medical Library for another institute… this time the Institute of Dance.[7)] In 2018 Central Statistical Office stated that there are 188 theaters and 949 hospitals in Poland. Well… Medicine sometimes becomes particularly important and noticeable, for example during the pandemic, but not when talking of such piece of trivia as museum of medicine. When I have become a member of the Polish Medical Association in 1970 I have already raised the problem of the lack of museum of medicine in Poland, which would be open to public. There are museums within structures of several medical universities, but they are not publicly accessible (with the exception of the House of Kraków Medical Society, Radziwiłłowska 2 street, with beautiful stained-glass window by Stanisław Wyspiański).

This marked the beginning of my never-ending journey to found the museum of medicine in the hall of former Ujazdowski Hospital in Warsaw, Jazdów 1a street.[8)] There have been countless visits and dozens of letters sent. So far these enrich our archive. Sadly… no positive decision came.[9)] Some policymakers before 2015 were more interested by the already existing „museum of Polish devils" then by museum of medicine.

I would like to underline with pleasure, that many individuals support our efforts to found the National Museum of Medicine. Among them is the First Lady, earlier we have been supported by the late President of Poland Lech Kaczyński, remembered with enlightenment, by President of Warsaw Stanisław Wyganowski, by Mazowsze Governor Bohdan Jastrzębski and by Minister of Health Zbigniew Religa. So far my effort is not worth more than a common button, which I may hand over to the museum of buttons, located in Łowicz. Still, I believe that I will make it through to see the POLISH NATIONAL MUSEUM OF MEDICINE. I am young at heart, and I have been applying for founding this museum for merely 50 years.

[1)]Antoni Leśniowski described the ileitis as early as 1903, while B. Crohn did so 29 years later. Still, Western

physicians credit the latter with the name of this condition. Magdalena Kawalec-Segond, in an elaborate article notices, that „Partitions were so destructive for Poland, because if one wills to become someone, one may not come from nowhere; Antoni Leśniowski was from nowhere for the World" (TVP Tygodnik, issue 65). Similarly, the sedimentation of blood described by Edmund Biernacki in 1894 is worldwide called the Westergren method, described 25 years later. Also Jakub Jodko-Narkiewicz described the so-called „aura" in 1896. Soviet Siemion Kirlian did so 34 years later, but the propaganda credits him with the first description. In December 1805 the first Polish medical association was founded in Vilnius, initiated by Jędrzej Śniadecki. It was first in this part of Europe, and even the first on our invader's – Tsarist Russia – territory. The second one was founded in Petersburg in 1901, also initiated by Polish physicians.

[2)]Dr. Piotr Szarejko, spent many years searching the archives and the Great Soviet Encyclopedia for the materials to his multi-volume work „Polish Physicians of the 19th Century" („Lekarze Polscy XIX wieku"). He found out that about 20 Polish physicians had their nationality changed to Russian.

[3)] As former KGB major Oleg Zakirow states, NKVD had murdered 25000 Polish officers between 1940 and 1945. Among them were over 850 physicians. The only memorial plaque commemorating them was embedded into the wall of surgical hall of former Ujazdowski Hospital on 50th Anniversary of II World War outbreak. See: „DZIEJE.PL. Portal Historyczny PAP". Update: 14.07.2016, Published: 01.09.2013 Wiadomości., and also: Jerzy Woy-Wojciechowski „Moje towarzystwo", published by Domena, 2015.

Plaque commemorating physicians murdered by NKVD in Katyń is in The Church of The Holy Cross, Krakowskie Przedmieście street in Warsaw (the first chapel on the right).

[4)] Among hundreds of museums there are the following: Buttons in Łowicz, Unusual Bicycles (Gołąb near Lublin), Bread (Radzionków), Axes (Orzechówka), Fairytales (Czarnków), Christmas Tree Baubles (Nowa Dęba), Bedtime Cartoons (Rzeszów), Bells (Jastrzębie-Zdrój), Grand Pianos (Ostromecko), Dolls (Pilzno and Troszyn), Soap and Dirt (Bydgoszcz), Scissors (Tarnogród), Polish Song (Opole), Beekeeping (Czerwonka, Kamianna. Stróże), Gingerbread (Toruń), Toys (Karpacz, Kudowa Zdrój, Toruń), Twirls (Poznań).

[5)] WE HAVE 921 MUSEUMS IN POLAND (as of 2018 official statistics): 180 regional, 171 historical, 91 of art, 72 interdisciplinary, 63 military, 63 of technology and science, 60 other, 55 biographic, 37 ethnographic, 35 open-air, 32 of archaeology, 28 of martyrdom, 28 of nature, 15 geological, 10 of interiors, 9 of literature. Total of 921.

[6)]According to 23.09.2020 data, the Ministry of Culture and National Heritage finances 895 museums, therein: 11 national, 15 regional, 55 biographic, 14 ethnographic, 50 open-air ethnographic, 26 open-air technology museums, 13 other museums and open-air museums, 42 historical, 43 of nature, geology and geography, 16 of art, 39 in palaces, castles and mansions, 64 sacral and religious, 68 military, 75 other.

[7)]Author has been granted „Distinguished Worker of Culture" medal as early as 1966. Ministry of Culture would receive annual invitations to the ceremony of honoring physicians with Gloria Medicinae medal. This resulted in creating (16 years later, in 2005) the Gloria Artis medal. Inquiry sent to the Ministry of Culture for the support of creating the museum of medicine in surgical hall of former Ujazdowski Hospital ended in founding the Institute of Theater (!) there. The explanation was that the hall in „on the royal tract" (Polish Medical Association also inquired for the creation of museum of medicine in the lobby of the Grand Theater in Warsaw, which is not on the tract).

[8)]SELECTED INFORMATION REGARDING UJAZDOWSKI HOSPITAL. Ujazdowski Hospital functioned between 1807 and 1947. In the inter-war period, a high school of military physicians was there. On the wall of surgical hall, there is a plaque dedicated to Gen. Karol Kaczkowski, the Chief Physician of 1831 Uprising. Since 1989 there is also a plaque commemorating 6000 physicians (over 50% of all) killed during the latest war. There were books written about the history of Ujazdowski Hospital (Halina Odrowąż-Szukiewicz – "Rzeczpospolita Ujazdowska") and it appeared in films (Bogdan Kezik – "Szpital Ujazdowski", Warsaw 2001). The historic hall of former Ujazdowski Hospital (Aleje Ujazdowskie 6a street, Warsaw) with its old-print department of Central Medical Library would be an ideal place for a museum. The area of former Ujazdowski Hospital has 0,75 ha, a fragment of parcel number 6 in precinct 5-06-12 which is 5,1 ha large and is at disposal of Centre for Contemporary Art, located in Ujazdowski Castle and being a State Treasury property. For over 50 years Warsaw authorities have vowed to help Polish Medical Association in founding the NATIONAL MUSEUM OF MEDICINE in one of former Ujazdowski Hospital halls. In 1998 Governor of Warsaw region Bohdan Jastrzębski vowed to hand over the hall at Jazdów 1 street for the sake of founding the museum. His death made completing the formalities impossible. The last visit at the office of Governor of Mazowsze Konstany Radziwiłł with an inquiry to support founding museum of medicine in former Ujazdowski Hospital hall took place on June 8th, 2020.

[9)]Selected data regarding efforts to found the museum of medicine. 1970. Idea to create museum of medicine in former Ujazdowski Hospital (Jazdów 1a street). 1971. Dr. Maria Rozwadowska and dr. Jerzy Woy–Wojciechowski visit eng. Biegański, head architect of Warsaw to obtain hall of former Ujazdowski Hospital for the museum of medicine. 1973. Director of National Museum prof. Jan Lorentz suggests that the museum should be created in hospital in Wilanów (Biedronki 6 street). 1981. Janusz Gąsiorowski – chairman of accommodation affairs in the National Capital Council denies handing the hall of former Ujazdowski Hospital over. 1990. Visit at the office of Stanisław Wyganowski, President of Warsaw, who greatly supported our efforts. 2000. Visit at the office of Deputy Governor A. Pietkiewicz (who supported). 2004. Polish President A. Kwaśniewski orders the Minister of Culture Waldemar Dąbrowski to organize Museum of Medicine in the surgical hall of Ujazdowski Hospital. After restoration Minister of Culture creates the Institute of Theater there!!! 2005. Visit at the office of Minister of Health Zbigniew Religa (great support). 2007. Visit at the office of Polish President Lech Kaczyński (great support). 2008. Meeting with senator Krystyna Bochenek (wife of cardiac surgeon); inquiry for the Polish Senate to support our efforts. 2010. Visit at the office of Supreme Medical Chamber president Maciej Hamankiewicz. (who supported). 2012. J. Woy-Wojciechowski presents 49 years of efforts to Healthcare Commission of Polish Senate. 2017. Letter with inquiry to support 48 years of effort to create National Museum of Medicine was sent to Jarosław Kaczyński, chief of Law and Justice party. 2020. Visit (June 6th) at the office of Mazowsze Governor Konstanty RADZIWIŁŁ with an inquiry to support 50 year long effort to found the National Museum of Medicine. Letter was sent to Minister of Culture, prof. Gliński. 2021. Follow-up letter was sent to Minister of Culture, prof. Gliński with inquiry to support founding Museum of Medicine. As in the year 2020, left with no answer.

Dear colleagues,

On May 30, 2024, a scientific and practical conference with international participation ***"Organisational and Clinical Aspects of Patient-Centred Approach to Treatment and Rehabilitation in Modern Conditions"*** will be held. The organisers of the conference are the State Institution of Science "Scientific and Practical Center of Preventive and Clinical Medicine" State Administrative Department, the National Academy of Medical Sciences of Ukraine, the Ukrainian Military Medical Academy and the Public Organisation "Ukrainian Association of Healthcare Management".

Publication of articles and abstracts in the professional journal **"Clinical and Preventive Medicine"** (SCOPUS) (Kyiv, Ukraine) (http://cp-medical.com/index.php/journal).

The programme issues of the conference:

1. Interdisciplinary aspects of medical and non-medical methods of rehabilitation of military personnel-combatants.
2. Topical issues of rehabilitation of civilians who have suffered as a result of the impact of stress and physical destructive factors of war.
3. Organisational and clinical aspects of the use of various rehabilitation types in modern practice of internal medicine.
4. Comorbidity in military personnel: the current state of the problem (topical issues of diagnosis, treatment and rehabilitation).
5. Theoretical and applied aspects of reflexotherapy in the complex rehabilitation of military personnel and civilians who have suffered as a result of war.
6. Features of the application of complex rehabilitation programmes in patients with acute cerebrovascular accident.
7. Modern approaches to the treatment and rehabilitation of patients with pathological changes caused by coronavirus infection (COVID-19).
8. Features of medical rehabilitation of patients with pain syndromes of different localisation.
9. Organisational and clinical aspects and perspective directions of medical rehabilitation after surgical interventions.
10. Clinical approaches to the treatment and rehabilitation of patients with mine-blast trauma.
11. Modern principles of perioperative management of patients and rational anaesthetic accompaniment in surgical practice.
12. Topical questions of rehabilitation at different stages and levels of medical care.
13. Problematic issues of interprofessional and long-term rehabilitation in primary health care.
14. The current state of integration of rehabilitation into primary health care.
15. Experience in implementing European training standards in the system of training medical personnel in the field of health care.

Media partners of the conference:

1. ALUNA Publishing House (Warsaw, Poland).
2. Journal "Clinical and Preventive Medicine" (SCOPUS) (State Institution of Science "Scientific and Practical Center of Preventive and Clinical Medicine" State Administrative Department, Kyiv, Ukraine).