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## CHANGES OF IMMUNE STATUS IN PATIENTS WITH MIXED ANXIETY AND DEPRESSIVE DISORDER AND HERPETIC VIRAL INFECTION

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**Abstract.** *Depression and anxiety are the most common mental disorders worldwide. A number of researchers have described a correlation between immune, limbic and endocrine systems and their role in the development of anxiety – depressive disorder. However, a more detailed examination of this correlation is yet to be performed. This study was conducted to examine immunological disorders' impact on cytomegalovirus (CMV), Epstein – Barr virus and herpes simplex virus antibodies' production; to evaluate antiviral antibodies' level impact on an immune status; to estimate an amount of strong systemic correlation between immunological parameters. Blood samples of 40 patients with Mixed Anxiety and Depressive Disorder were explored, immunological and "infectious" statuses were evaluated. Therefore, the variation in titer of antibodies to cytomegalovirus, Epstein – Barr virus and Herpes Simplex Virus with respect to changes of immunological parameters was detected. Additionally, taking the above into account, many strong correlations between HSV and CMV and immune system (48 and 32 respectively) suggest that there is high – level immunity against these viruses. In contrast, only 3 correlations between Epstein – Barr Virus and immunological parameters indicate that poor immune response is usual to this virus. The strong correlations between HSV and EBV and immune response among patients with proved diagnosis of MADD possibly indicate that mental condition is able to impact on human immune status.*

**Keywords:** *anxiety, depression, immunity, herpes simplex virus, cytomegalovirus, Epstein – Barr virus.*

**Introduction.** According to epidemiologic data, depression and anxiety disorders are the most common mental disorders [9]. The data indicates that the prevalence of anxiety – depressive disorders worldwide is between 4,4 and 20 % among all population (between 350 million and 1,5 billion people) [1]. The new evidence has shown that the number of patients with anxiety and depressive disorders was higher than the number of patients with other mental disorders. The prevalence among all population was about 10 %, and 30% of patients in ambulatory medical institutions [8]. At the same time, more consistent data about Mixed Anxiety and Depressive Disorder's (MADD) prevalence is yet to be researched.

MADD is characterized by bad mood, worries, feeling of impending disaster, death or incurable disease, feeling of anxiety. ICD – 10 classifies this condition as "Mixed anxiety and depressive disorder", code F41.2.

There are several concepts concerning the association between human psyche and human immune system. A significant correlation between immune, limbic and endocrine systems and its role in the development of anxiety – depressive disorder was described by a number of scientists [2]. Furthermore, the data has shown a bidirectional regulation of immune and mental systems. In fact, a chronic stress, known as a predictor of many mental disorders, is associated with a high production of inflammatory mediators (cyto-

kines) and increased risk of infections and chronic total inflammation. Furthermore, an HPA – axis, activated by inflammatory cytokines, triggers a production of kynurenine. Kynurenine is one of the main risk factors of anxiety and depression development [3]. Moreover, neuroinflammation, provoked by the impact of stressors, is detected by many researchers. Thus, the sympathetic system is directly related to HPA – axis functioning [10]. Normally, under the impact of stressors the sympathetic system starts a high production of noradrenaline, which, in turn, stimulates progenitor immune cells and increase granulocytes and monocytes blood level [7]. Modern research technologies allow to study a possible correlation between mental misadaptation and immune and endocrine system [4]. However, a number of current studies are still unable to clarify the interaction of all these factors. Apart from this, the comprehensive description of pathological mechanisms is also necessary. Therefore, further studies are to be performed.

Likewise, current studies are unable to exclude an infectious part of anxiety and depression pathogenesis. Apparently, a significant increase of anxiety and depression manifestation, caused by herpes simplex virus, type 6B (HSV), was reported by colleagues [6]. In addition, an HSV was detected in respiratory tract and olfactory bulbs in brain, known also as immune organ. An olfactory bulbs' enlargement was detected among experimental mice, infected by HVS type 6B. Apart from this, further tail – suspension test, when infected mice stayed immobile, was interpreted as a significant mark of depression [5, 6]. Our research is to study a possible association of anxious and depressive symptoms and immune changes.

All in all, the existing studies have failed to explain an exact association between anxiety and depression and contamination by NVS, Epstein – Barr Virus and CMV. Furthermore, immunological disorders' impact on cytomegalovirus (CMV), Epstein – Barr virus (EBV) and herpes simplex virus antibodies' production was rarely analyzed in previous studies. Thus, the aim of this study is to examine an impact of cytomegalovirus's (CMV), Epstein – Barr virus's and herpes

simplex virus's presence on an immune status and to evaluate a correlation between immunological parameters and virus presence.

**Design and methods.** This study was retrospective and individually randomized. All participants gave written informed consent. We recruited 40 participants, both men and women, aged 18 – 45, from day patient department of Voronezh Regional Clinical Psychoneurological Dispensary, with the diagnosis of Mixed Anxiety and Depressive Disorder (MADD) and with no cardiovascular, respiratory, urinary, endocrine or oncological somatic anamnesis. The anamnesis and complaints were examined. All participants were asked to fill in a Hamilton Depression and Anxiety Rating Scale to prove the psychiatric diagnosis of MADD. We measured blood samples at the Screening Visit of the study to evaluate an immune status (CD3 – cells, CD4 – T – helpers, CD8 – cytotoxic cells, CD19 – B – cells, CD16+56 – N – killers, CD 28 +/- - lymphocytes, CD 25 +/-, CD8+16 – cells; adherent phagocytosis assay) and infectious status (determination of IgG, IgA, IgM of cytomegalovirus, Epstein – Barr virus and herpes simplex virus in blood serum by radial immunodiffusion method) of all participants. We used such approved laboratory materials and gadgets as vacutainer serum tubes 2 ml, vacutainer plasma tubes K3 2 ml, vacutainer hematocrit tubes K2 – EDTA 2 ml, photometer Zenyth 340, Zenyth 340 ST, Zenyth 340 RT, Zenyth 340 S, cytofluorometer NAVIOS. The measurements were consolidated and data-processed by estimation of normality of distribution, determining mathematical expectation and its errors, evaluation of statistically significant correlations.

**Results.** 40 male and female participants, aged 18 – 45, from day patient department of Voronezh Regional Clinical Psychoneurological Dispensary were included in the study. All the patients were diagnosed with Mixed Anxiety and Depressive Disorder (MADD) and had no cardiovascular, respiratory, urinary, endocrine or oncological somatic anamnesis. Three most important components of immune system were evaluated: humoral, cellular and phagocytic. Additionally, the evaluation of immune status (CD3 – cells, CD4 – T – helpers, CD8 – cytotoxic cells, CD19 – B –

cells, CD16+56 – N – killers, CD 28 +/- - lymphocytes, CD 25 +/-, CD8+16 – cells; adherent phagocytosis assay) and infectious status (determination of IgG, IgA, IgM of cytomegalovirus, Epstein – Barr virus and herpes simplex virus in blood serum by radial immunodiffusion method) was completed. The presence of all herpetic viruses was determined among all included patients. Thus, antibodies to all herpetic viruses (CMV, EBV and HSV) were determined in 30% of patients; antibodies to Epstein-Barr Virus were found in 100% of subjects; 60% of subjects were carriers of cytomegalovirus; antibodies to herpes simplex virus were detected in 70% of patients.

Our data indicates, that there are many strong associations between antibodies for HSV and immune cells: a positive statistically significant correlation with CD3+, CD38+ (T-cells) ( $r=0,46$ ); a negative statistically significant correlation with CD3+, CD8+ (T-cytotoxic lymphocytes) ( $r=-0,67$ ); a negative statistically significant correlation with CD8+(T-suppressors) ( $r=-0,37$ ); a negative statistically significant correlation with CD16+(NK-cells) ( $r=-0,37$ ); a negative statistically significant correlation with colony – enhancing factor ( $r=-0,40$ ); a negative statistically significant correlation with phagocytic index ( $r=-0,66$ ); a positive statistically significant correlation with macrophage activity (NBT-Test) ( $r=0,82$ ). Furthermore, the titer of CMV antibodies was negatively significantly correlated CD3+, CD8+ ( $r=-0,37$ ); also, has a negative statistically significant correlation with CD8+ ( $r=-0,54$ ); a negative statistically significant correlation with CD16+(NK-cells)

( $r=-0,71$ ); a negative statistically significant correlation with phagocytic index ( $r=-0,72$ ).

The similar study of possible correlations indicated that antibodies to Epstein-Barr Virus positively significantly correlated with macrophage activity (NBT-Test) ( $r=0,57$ ) as well.

**Discussion.** Our findings demonstrate that the variation in titer of antibodies to cytomegalovirus, Epstein – Barr virus and Herpes Simplex Virus with respect to changes of immunological parameters was detected. The total number of strong correlations between HSV and immunological parameters was 48; the total number of strong correlations between CMV and immune system was 32. On the other hand, the sum of strong correlations between EBV and immune system parameters was only 3. Additionally, taking the above into account, strong correlations between HSV and CMV and immune system (48 and 32 respectively) suggest that there is high – level immunity against these viruses. In contrast, only 3 correlations between Epstein – Barr Virus and immunological parameters indicate that poor immune response is usual to this virus.

**Conclusion.** Our research results allowed to suggest an unspecified association between a human immune system and human mentality. All proved strong correlations between HSV and EBV and immune response among patients with proved diagnosis of MADD possibly indicate that mental condition is able to influence human immune status. However, these are preliminary findings that lead to further research.

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## ИЗМЕНЕНИЯ ИММУННОГО СТАТУСА У БОЛЬНЫХ СО СМЕШАННЫМ ТРЕВОЖНО-ДЕПРЕССИВНЫМ РАССТРОЙСТВОМ И ГЕРПЕТИЧЕСКОЙ ВИРУСНОЙ ИНФЕКЦИЕЙ

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***Аннотация.** Депрессия и тревоги являются одними из самых распространенных психических заболеваний во всем мире. Целым рядом авторов была описана связь между психикой и иммунной системой человека, при этом требуется более подробное изучение роли этой связи. Наше исследование было проведено с целью изучения влияния иммунологических расстройств на образование антител к цитомегаловирусу, вирусу Эпштейн – Барра и вирусу простого герпеса человека, оценки влияния концентрации антивирусных антител на иммунный статус и определения количества сильных внутрисистемных корреляционных связей между иммунными показателями. Мы исследовали образцы крови 40 участников с диагнозом «Смешанное тревожное и депрессивное расстройство». Кроме того, были оценены иммунологический статус пациентов и носительство ими антител к вирусам герпесной группы. В результате была установлена зависимость изменения титров антител к цитомегаловирусу, вирусу Эпштейн – Барра и вирусу простого герпеса человека от нарушения иммунологических показателей. Кроме того, на основе результатов корреляционного анализа, было определено количество сильных корреляционных внутрисистемных связей при изучении иммунной картины инфицирования вирусом простого герпеса человека – 48 связей. Аналогичная оценка связи инфицирования цитомегаловирусом и иммунного статуса говорит о наличии 32 сильных связей. Такое количество сильных связей свидетельствует о формировании напряженного иммунитета в отношении вышеуказанных вирусов. С другой стороны, количество сильных корреляционных связей между инфицированием вирусом Эпштейн – Барра и иммунным состоянием было всего 3, что позволяет говорить о формировании слабого иммунитета к инфицированию этим вирусом.*

*Собранные данные свидетельствуют о существовании связи иммунной системы с психикой человека. Установленные сильные связи между титрами антител к цитомегаловирусу, вирусу простого герпеса человека, вирусу Эпштейн – Барра и выраженностью иммунологических показателей говорят о возможном влиянии психического состояния на иммунный статус человека.*

***Ключевые слова:** тревога, депрессия, иммунитет, вирус простого герпеса, цитомегаловирус, вирус Эпштейн – Барра.*



## SURGICAL 3D NAVIGATION TEMPLATES IN IMMEDIATE DENTAL IMPLANT: EFFECTIVENESS OF APPLICATION

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**Abstract.** *Treatment of edentulism has always been relevant, but the requirements for treatment techniques constantly grow. A few decades ago it was sufficient to compensate the defect of a missing tooth, currently it is necessary to perform prosthetics adequately, aesthetically, atraumatically and promptly. To solve all these problems, modern computer techniques are increasingly being used in dentistry nowadays. The use of 3D printers, intraoral scanners and new treatment options allows performing prosthetics in the area of a missing tooth on the day of extraction [1; 2].*

*Our study demonstrates that treatment of edentulism using tooth extraction and immediate dental implant technique has a number of advantages compared to the classical two-stage technology. In addition, the use of a 3D surgical navigation template significantly improves the accuracy of implant positioning, which leads to reduced complications.*

**Keywords:** *dental implantation, surgical 3D template, surgical navigation template, implantation plan, implantation complications, edentulism treatment.*

**Introduction.** Depending on the sequence of manipulations, there are several schemes for implant treatment of edentulism [1]. The first scheme is conventional consisting of two stages: at the first surgical stage an implant is placed which is followed by an integration period of 3 to 6 months (the second stage). After implant integration, the third surgical stage follows - a gingiva former is inserted; after formation and healing of the gingiva, impressions and prosthetics can be performed.

According to the second scheme, the first stage includes tooth extraction, then a healing period, and in 3-6 months, implantation and installation of a gum former is carried out within one surgical stage, followed by an integration period of 3 to 6 months, and prosthetics. According to the third scheme, the first stage includes tooth extraction, implantation and installation of a gum former within one operation. This is followed by an integration period of 3-6 months and prosthetics.

When comparing the above schemes, it is apparent that the latter scheme is more cost-effective both financially and in terms of time, since it is not necessary to wait several months for implantation after tooth extrac-

tion, respectively, the treatment period is reduced by 3-6 months [3]. Moreover, the manipulation becomes less traumatic by combining three surgical stages into one, the number of incisions and operations is reduced, the fact positively affecting the soft tissues surrounding the implant. When using 3D navigation templates during one-stage implantation, it allows achieving maximum positioning accuracy [4; 5].

**Challenges of dental implants.** Currently one of the most demanding issues of dental implantology is a long period of treatment. In fact, with the technique of delayed implantation, the entire course of treatment (from the moment the tooth is removed to its prosthetics) takes from 3 to 6 months. In addition, atrophic processes are triggered in the periodontal tissues after tooth extraction. Sufficient bone volume is an important condition for reliable attachment of the implant to the bone. Therefore, dental implants in most cases are preceded by the stage of the bone augmentation using bone grafting [6]. It should be noted that the process is different in case of immediate implants: the implant is installed immediately after a natural tooth extraction. However, this method of implantation is pos-

sible only under certain conditions, among which are the state of the dental system and the general somatic health of a patient.

Indications for immediate dental implantation [7]:

1. Tooth dystopia and indications for its removal for the purpose of prosthetics.
2. Periodontitis II and III degree with the vertical bone atrophy.
3. High motivation and desire of a patient for early surgery outcomes.
4. Elimination of the incorrect therapeutic (endodontic) treatment effects.
5. Violation of the integrity of the tooth crown.
6. Tooth injuries without bone damage.
7. Fractures of the tooth root.

Diagnosis and implantation planning are critical factors for achieving high results in implant placement and restoration of integrity and functional activity at the site of the extracted tooth [8]. Diagnostic procedures include radiography, preferably using CT (computed tomography). Based on the diagnosis, the doctor decides on further interventions. The main advantages of single-stage implantation include:

1. Reduced number of interventions and visits.
2. Prompt restoration of the functions of the chewing and speech apparatus;
3. Decreased atrophy of the alveolar process;
4. Restored aesthetics after implantation [2].

As known, the bone tissue undergoes atrophy after tooth extraction and loss of its supporting function and load in this area. At the same time, most of the atrophic processes occur in the first four years of the absence of a tooth. During the first year approximately 25% of the outer cortical plate atrophies, during the next 3 years 40% of the outer cortical plate atrophies. These changes result in the outer cortical plate shift more towards a lingual or buccal position, which manifests itself as an aesthetic defect: the concave hard and soft tissues [9].

In addition to the loss of the bone tissue in width, there is also an atrophy in height. Loss of bone tissue in height leads further to problems such as the limited choice of implant

length. In some cases, in particular with a shallow vestibule of the mouth, atrophy in height leads to a change in the depth of the vestibule. In this case, attachment of mimic muscles directly to the atrophied crest of the alveolar process can be observed. With further implantation these signs can result in ischemia and chronic injury of the soft tissues of the gingival cuff leading to the soft tissues inflammation followed by atrophy and resorption of the bone tissue surrounding the implant (mucositis and peri-implantitis). The worse the conditions before implantation, the greater the likelihood of complications during and after implantation [10].

Currently, there are different types of operations to increase the volume of the bone tissue and to improve the implant treatment outcomes. The most common options are bone grafting in the upper and lower jaws, augmentation with bone blocks, autogenous bone chips, xenogenic bone materials, etc. [6]. Open and closed sinus lifting is most often performed on the upper jaw. In addition, with insufficient bone height in the lower jaw, mobilization and lateralization of the neurovascular bundle in the mandibular canal is carried out. However, due to a large number of neurological complications, such as persistent sensory disturbance in the area of innervation, neuralgia and paresthesia, this operation is less popular among implantologists [5].

Based on the above, it can be concluded that delayed implantation leads to significant bone tissue atrophy, which in turn worsens the implant treatment outcomes creating a shortage of bone volume [10].

**The aim of the study** was to compare clinical outcomes of immediate dental implantation using surgical 3D navigation templates and the "free hand" (FH) technique, and to evaluate effectiveness of the surgical templates application for immediate implantation.

**Materials and methods.** Clinical outcomes of immediate implantation and its long-term results were analyzed in 20 patients aged 28 to 82 years. The patients were divided into two groups. In patients of the first group tooth extraction and immediate implant placement were performed using the "free

hand” technique. In patients of the second group tooth extraction and immediate implant placement were performed using a surgical 3D navigation template. A comparative analysis of the two groups performance included the following criteria: duration of the surgery, invasiveness, positioning accuracy, pain intensity in the postoperative period, degree of primary stability and osseointegration according to ISQ (Implant Stability Quotient - Implant Stability Coefficient) at the time of surgery and in 3-6 months.

**Results.** The results of immediate dental implantation in the first and second groups are as follows. In the second group, with the use of surgical templates, the duration of the operation reduced by 30%, the length of the incision and the area of gingival peeling decreased by 100% (the template allows installing an implant without additional incisions for visualization); this reduced the degree of invasiveness of the surgical intervention and significantly reduced postoperative

pain. In the first group, all patients manifested deviations from the originally planned position. In the second group, deviations from the originally planned position were registered in 30% of patients. ISQ parameters in patients of the first group were lower by 3-17 units compared with patients of the second group, the fact indicating a lower primary stability of the implants. In 3-6 months, patients of the first group had ISQ scores 5-10 units lower than those of the second group. At the same time, in both groups, the ISQ values were above 70 units, which is the evidence of high implant stability.

**Conclusion.** The use of surgical 3D navigation templates increases the efficiency of the immediate dental implant operation, which is supported by the reduced duration of the operation, increased accuracy of implant positioning, decreased invasiveness of surgical intervention, decreased postoperative pain and increased primary stability.

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### **ЭФФЕКТИВНОСТЬ ПРИМЕНЕНИЯ ХИРУРГИЧЕСКИХ НАВИГАЦИОННЫХ 3D ШАБЛОНОВ ПРИ ПРОВЕДЕНИИ ОПЕРАЦИИ ОДНОМОМЕНТНОЙ ДЕНТАЛЬНОЙ ИМПЛАНТАЦИИ**

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***Аннотация.** Тема лечения адентии остается актуальной всегда, но с каждым годом требования к методам лечения растут. Если несколько десятилетий назад было достаточно восполнить дефект отсутствующего зуба, то сегодня протезировать при отсутствии зуба нужно правильно, эстетично, атравматично и в максимально короткие сроки. Для решения всех этих задач в стоматологии все чаще применяются современные компьютерные технологии. Применение 3D принтеров, внутриротовых сканнеров и новых методов лечения позволяют протезировать в области отсутствующего зуба уже в день удаления [1; 2].*

*Проведенное исследование показало, что лечение адентии методом одномоментного удаления зуба и денальной имплантации имеет ряд преимуществ по сравнению с классическим двухэтапным методом. Также, применение хирургического навигационного 3D шаблона значительно повышает точность позиционирования имплантата, что приводит к уменьшению процента осложнений.*

***Ключевые слова:** денальная имплантация, хирургический 3D шаблон, хирургический навигационный шаблон, планирование имплантации, осложнения имплантации, лечение адентии.*

## CATARACT: THE REVIEW OF PROBLEMS AND SOLUTIONS

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**Abstract.** Nowadays cataract remains one of the urgent problems that public healthcare needs to address. It is the leading cause of blindness and disability worldwide. Although there is constant research to establish cataract pathogenesis and offer management, the data are insufficient and need critical reflection. The objective of this paper is to examine national and international studies on cataract development and treatment so that to specify approaches addressing cataract issues. The article presents data from literature and systematic reviews, clinical guidelines and protocols concerning epidemiology, risk factors, classification, pathogenesis, and mortality risk of cataracts.

**Keywords:** cataract, risk factors, classification, pathogenesis, and mortality risk of cataracts.

**Introduction.** Blindness remains an urgent problem of modern ophthalmology, as well as one of the main public health problems [1, p. 130]. According to the systematic review and meta-analysis by Joshua R Ehrlich et al., the risk of mortality was higher in people with visual impairments, in contrast to those with normal vision or mild visual impairment [2, p. 418].

According to the World Health Organization, about 2.2 billion people worldwide have visual impairments, and almost half of them could have prevented this pathology [3, p. 144]. According to the All-Russian Public Organization "Association of Ophthalmologists", cataract is considered to be partial or complete opacification of the lens of the eye, commonly developing after 60 years of age and manifested by various degrees of visual impairment up to the complete loss of objective vision [4, p. 7]. Today cataract is the second leading cause among all cases of vision loss, being inferior only to uncorrected refractive errors, which determines its medical and socio-economic significance, along with age-related macular degeneration, glaucoma, diabetic retinopathy, corneal opacity, trachoma. Most people with lens opacity live in low-income countries [5, p. 1495]. However, the data on cataract incidence and prevalence change regularly with the constant growth of epidemiological and public health studies.

Therefore, ophthalmological researchers and clinicians have to be updated with fundamental innovations and practical applications of cataract research. With regard to the above, the objective of this paper is to analyse recent epidemiological research data on cataract so that to compare and contrast the approaches and findings/

**Materials and methods.** The authors used a search for literature data on the epidemiology of cataracts. The literature corpus included recent epidemiological studies, systematic and literature reviews as well as clinical guidelines on cataract treatment and prevention. The methodological techniques involved analysis, synthesis, comparison and interpretation of the concepts and literature findings.

**Results and discussion.** Cataract is one of the leading causes of visual impairment and reversible blindness in the world. The disease occurs in every sixth person over the age of 40 and in most people by the age of 80. According to a number of international studies, cataracts are considered to be the main cause of blindness in middle- and low-income countries [6, pp. 1-23].

The recent literature review shows that there are several classifications that are based either on clinical or epidemiological criteria: they relate to clinical practice, to the use of epidemiological analysis or drug manufacturing for conservative treatment.

The light conductivity of the lens depends on the type of cataract and the localization of opacities. According to the intensity of opacities and the values of visual acuity, the following stages of cataract are distinguished: initial, immature, mature and overripe. Ophthalmologists do not have a single point of view on the issue of diagnosis. Thus, there is an opinion that it is more correct to attribute only those opacities in the lens that cause a decrease in visual acuity [7, p. 474].

In the Russian Federation the prevalence of cataracts is 3.36% for the urban population and 3.63% for the rural population. Apparently, there has been one study conducted in the Russian Federation according to the international standard RAAB, in which the sample was 4044 people aged 50 years. The study made it possible to diagnose cataracts with a decrease in visual acuity to 0.3 in 8.69% of the examined, which is 2.5 times more than official statistics, and women were 2 times more likely to suffer from this pathology than men [8, p. 84].

When studying the dynamics of cataract incidence, the increase in the number of new cataract cases growth has been reported in certain Russian regions and on the national scale. Along with all the achievements of modern ophthalmology, cataract prevalence is permanently high, being the second most common cause of visual impairment worldwide. According to the multicenter research, higher rates of cataract incidence are gender-related and more commonly occurred in women compared to men [9, p. 98].

The research also identified differences in the geographical distribution of cataracts. The findings suggest that the incidence is four times as common in low- and middle-income regions as in their high-income counterparts. According to scientific research by R. Acosta et al. the prevalence of cataracts in Europe, the USA and Australia is significant and ranges from 5% to 30% [10, p. 509] compared to 10.7% in Taiwan, 9.7% in Singapore, 2.2% in Indonesia, and 5.3% in Nepal [11, p. 40]. The proportion of cataracts in Saudi Arabia was 55.1%, 31.1% in Afghanistan, 9.7% in Israel, 34.9% in Syria [12, p. 103]. Among the Chinese population, cataract as a cause of blindness was detected in 41.1% of

patients, and in 49.4% among the visually impaired, while the prevalence of visual impairment and blindness in the age group over 60 years was 73.1% [13, p. 282].

The pathogenesis of cataracts still requires a comprehensive examination and thorough understanding. According to several studies, in cataract development the composition of the intraocular fluid of the anterior chamber of the eye changes, pathological metabolites are formed, which leads to the destruction of the protein of the lens fibers. It was found that the activity of carbonic anhydrase, pyruvate phosphokinase, ATP synthase decreases with cataract; the amino acid and trace element composition changes; the amount of sodium, calcium, zinc, and water in tissues increases, and there is a decrease in potassium, aluminum, soluble proteins, sulfur-containing amino acids, bound c-crystallins, ascorbic acid, riboflavin, and cytochrome. It is still unknown what is the trigger of these changes.

There are several risk factors that affect the development of cataracts. These include age, the presence of diabetes mellitus, the use of glucocorticosteroids for a long time, previous surgical treatment of the eyes. It should be noted that there is a relationship between certain risk factors for cataract development and the type of lens opacities. Thus, risk factors for cortical cataracts are diabetes mellitus, heredity, ionizing radiation (low and high doses), smoking; for nuclear cataracts – diabetes mellitus, heredity, arterial hypertension, previous vitrectomy, smoking, exposure to ultraviolet (hereinafter – UV) rays of the B spectrum; for posterior capsular cataracts – the use of inhaled glucocorticosteroids, ionizing radiation (low and high doses), obesity, eye injuries, previous vitrectomy, retinal pigment degeneration, local and systemic use glucocorticosteroids, for a mixed form - previous vitrectomy, smoking, exposure to UV rays of the B spectrum. Most of the studies concerning the study of risk factors for cataracts are observational. With this in mind, it is not possible to reliably confirm cause-and-effect relationships, because studies are not conducted in a standardized way.

Some research findings demonstrate that almost 80% cases of visual impairment associated with cataracts can be restored after re-

removal of the clouded lens. However, the significant economic costs of this approach should be taken into account. Currently, according to estimates, about 1,750 thousand patients suffer from cataracts in the Russian Federation. The number of cataract extraction operations performed annually covers only a third of the patients in need of such treatment. This indicator varies depending on the subject of the Russian Federation. Surgical treatment for cataracts refers to high-tech types of medical care, which is more accessible to patients in large settlements and cities compared to residents of rural areas [14, pp. 600-612].

The results of a number of studies have shown anxiety and fear in patients before surgery, which in the future may cause refusal or postpone the date of hospitalization. In addition, elderly people may have contraindications for this operation due to the presence of concomitant pathology [15, p. 197].

According to the United Nations Population Division, it is projected that about 50 million people aged 60 will suffer from cataracts by 2025. According to the World Vision Problems Report, about \$24.8 billion needs to be spent to address the problem of insufficient coverage for cataracts and uncorrected refractive errors that could be prevented. These financial investments are needed now, but this

requires additional planning and investment. For example, by 2030, according to WHO estimates, low- and middle-income countries should invest in creating jobs for 23 million medical workers and building more than 415,000 medical facilities. However, appropriate measures have not yet been taken [16, p. 4].

**Conclusion.** Cataract is still an urgent problem that requires systematic analysis and management to assess its contribution to the unfavorable ophthalmological situation in general. For competent management and specialized medical care it is necessary to study the parameters of risk areas, improve the availability of high-tech care, solve the problem of insufficient medical coverage for cataracts, determine financial investments for job creation and professional training of medical workers.

It may be confirmed that the unified approach to classification and diagnosis of cataract has not been developed yet. Although numerous studies on cataract prevention and management have been conducted, they have collected inconsistent evidence to confirm the causal relationships of cataract risk factors in a standardized way, the pathogenesis and the trigger mechanism, which affects the management of ophthalmic care processes.

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## КАТАРАКТА: ОБЗОР ПРОБЛЕМ И РЕШЕНИЙ

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***Аннотация.** На сегодняшний день катаракта остается одной из насущных проблем общественного здравоохранения. Она является основной причиной слепоты и инвалидности во всем мире. Исследования в области этиологии и методов лечения катаракты не теряют своей актуальности, однако их данные и подходы к решению проблем катаракты требуют обобщения и систематизации. Целью настоящей работы является обзор современной научной литературы, а также международных клинических рекомендаций по профилактике и лечению катаракты. В статье обобщаются данные актуальных исследований по эпидемиологии, факторам риска, классификации, патогенезу и риску смертности от катаракты*

***Ключевые слова:** катаракта, факторы риска, классификация, патогенез, риск смерти от катаракты.*

## PREVENTION OF CARIES AND ITS COMPLICATIONS IN THE POPULATION OF A SPECIAL ECONOMIC ZONE: EFFECTIVENESS OF MANAGEMENT AND PRACTICAL ACTIONS

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**Abstract.** *The article highlights the problem of caries prevention in the adult population. It is emphasized that individual prevention of dental diseases contributes to the improvement of the public health, it is carried out through awareness of the role and importance of hygiene procedures and is aimed at eliminating the causes and conditions for the occurrence and development of diseases, and increasing the body's resistance to adverse environmental factors. The authors conducted a study that, in addition to carrying out preventive measures, took into account systemic diseases that directly affect the level of acidity of the oral fluid, as well as the patients' residential occupancies. A complex of measures that registers the main cariogenic factors and predicts the occurrence of a carious process has been developed. The developed options of clinical examination allow tracing the patterns that occur in the surface layers of the enamel after therapeutic and preventive treatment and comparing the effectiveness of individual preventive measures in permanent dentition.*

**Keywords:** *caries, prevention, prevalence, management.*

**Introduction.** Caries prevention does not evoke an adequate response in adults in practical healthcare, the fact evidencing low level of oral hygiene compliance in the Russian population as a whole. With age, there is a significant increase in caries extension: in various regions of Russia the prevalence of dental caries in permanent teeth ranges from 61 to 96% among 12-year-old schoolchildren, and it reaches 100% in adults.

The main goal of individual dental disease prevention is to improve the health of the country's population through the disease awareness and importance of hygiene procedures. Knowledge of oral hygiene products and their proper use allows converting individual oral hygiene procedures into effective preventive and therapeutic ones, but for this, it is necessary to correctly select the appropriate personal hygiene products for each specific patient in accordance with his dental status. This algorithm will allow specialists to better navigate in the development of the "Individual hygienic program for the caries prevention", since on this basis, they will be able to explain indications for the use of specific drugs and the direction of their action, so that patients can use them reasonably and for their intended purpose. The main objectives of

prevention are to eliminate the causes and conditions for the occurrence and development of diseases, as well as to increase the body's resistance to the effects of adverse environmental factors.

Studies related to individual caries and periodontal disease prevention are carried out in many countries; however, there is insufficient literature data to cover the results of these studies.

Significant dental well-being is to be achieved only by providing individual preventive measures. Introduction of a complex of effective measures for caries prevention in temporary and permanent occlusion will significantly improve the dental health level in the country's population. Carrying out preventive measures requires an individual approach considering common diseases, for example, gastrointestinal pathologies, which directly affect the level of acidity of the oral fluid, as well as the conditions of the patients' living environment. Previously, these factors were not analysed as part of caries preventive measures. Insufficient research results, a variety of controversial issues and the need to resolve them prompted us to take up this problem.

**Materials and methods.** The study included 300 people, 152 (50.7%) women and 148 (49.3%) men, aged 18-44 years (that is, with completed mineralization of hard dental tissues), having at least 20 natural teeth with a preserved crown, not exposed to industrial hazards, without severe concomitant pathology. The studies involved patients without a systemic pathology or patients who had initial manifestations of certain diseases (gastritis, colitis, mild dyskinesia, the initial stage of coronary heart disease detected by ECG, the initial stages of hypertension, etc.), but at the time of the examination, there were either no pronounced changes, or the identified changes were within the age norm, i.e. the disease was recorded in the remission stage. Including in research patients with existing health problems allowed creating research conditions as close as possible to those taking place at a dental appointment, and objectively assessing the impact of the patient's individual parameters on his dental status and effectiveness of mass and individual prevention. All patients were divided into two groups: the control group and the experimental group. In the control group, after educating patients on the oral health issues and conducting professional oral hygiene, the patients carried out mass prevention techniques based on the information taken from the media; they were further examined to compare the results. In the experimental group, we developed individual preventive measures for caries prevention. We developed a complex of investigations registering major cariogenic factors and predicting occurrence of a tooth decay process. This included: medical history data; visual inspection of hard tooth tissues; detection of the pH of the oral fluid; detection of the cariogenic effects of dental plaque; detection of the KPU index (KPU - the Russian abbreviation meaning caries-fillings-loss teeth); detection of the CPITN index; detection of oral hygiene status index (OHI-s) according to the Green-Vermillion; detection of KOSRE-test (clinical definition of tooth enamel remineralization rate); clinical macro-histochemistry of gum tissues according to A.A. Kunin; bacterioscopy of the plaque from the tongue and cheeks, the contents of the periodontal sulcus; touch imprint cytology of the oral mucosa; electrometric studies of the

tooth hard tissues; detection of unsatisfactory filling by staining the enamel at the border with the filling material with a 2% solution of methylene blue; clinical assessment of the quality of the filling according to D.M. Karalnik. The data were processed statistically using Statistika 6.0, SPSS-11. For all types of analysis, the representativity of the results obtained was assessed. When testing statistical hypotheses, differences were considered significant at  $p \leq 0.05$ .

**Results and conclusion.** The conducted clinical examination allowed tracing the patterns occurring in the surface layers of the enamel after therapeutic and preventive measures and conducting a comparative assessment of the effectiveness of individual preventive measures in the permanent dentition. A preliminary examination of patients and the search for ways to implement the intended goals and objectives of the study revealed the need for a new integrated system for the detection, management and follow-up treatment of caries-susceptible individuals. The solution to this problem, in our opinion, is introducing into modern dentistry a targeted modified method of clinical examination of caries-susceptible patients consisting of 3 stages: stage 1 - clinical selection - detection of caries-susceptible patients for their succeeding registration; stage 2 - clinical registration - registration of caries-susceptible patients for succeeding observation; stage 3 - clinical observation - conducting individual therapeutic and preventive measures and dynamic monitoring of their effectiveness. Detection of a caries-susceptible cohort at the stage of clinical selection supported results of previous studies and literature data on the significant prevalence of caries. Of 2673 patients, 11.1% (297 people) needed primary caries prevention, 88.9% (2376 people) needed secondary caries prevention. Thus, in all examined patients, there was a need for measures to prevent caries.

It should be noted that 2054 people (76.8%) refused to be involved in the caries prevention program for various reasons, and only 619 patients (23.2%) felt like participating in the proposed program. Moreover, of these 619 patients, 419 people (67.7%), i.e. 2/3 of the total, gave their consent to conduct preventive measures only after a conversation

with a specialist at the Center for Individual Caries Prevention. This fact evidencing urgency of health education interventions that can be effective only when purposefully introduced into the work of specialized structures and carried out by a specially trained, highly professional employee who deals directly with the problem of caries prevention. Thus, the effectiveness of the first stage of medical examination of caries-susceptible patients, equal to the percentage of the number of patients selected during the examination (619 people) to the total number of those examined (2673 patients), was 23.2%. However, the coverage caries-susceptible patients identified during the clinical registration stage (the ratio of caries-susceptible patients detected during clinical registration (300 patients) to the total number of patients with identified cariogenic factors (619 patients)) was 48.5%.

It is noteworthy that of the identified caries-susceptible patients, we were not able to include in the study 307 people (11.5%) who had serious somatic diseases and were administered constant maintenance drug therapy. The general status of these patients being a limitation for participation in this study, is not a contraindication for the participation in an individual caries prevention program in specialized dental institutions. Five patients (0.8%) changed their place of residence, 4 (0.06%) refused medical examination for family reasons, 3 (0.05%) did not attend a specialized examination appointment at the clinical registration stage.

The patients selected and sent for clinical registration were as follows:

- patients with medium, high and very high intensity of caries;
- patients identified during their appointment for periodontal pathology (edema, hyperemia of the gingival mucosa, its bleeding during probing);
- patients with visually determined poor oral hygiene;
- patients who do not have clinical indications, but were eager to participate in an individual caries prevention program.

Then the selected patients were admitted to the second stage of medical examination - clinical registration. During the clinical registration, a comprehensive examination of the patient was carried out using diagnostic

methods for predicting caries and identifying cariogenic factors previously determined by the a priori ranking method.

The results of the targeted examination of patients allowed concluding about the effectiveness of clinical registration and determining the diagnostic error of clinical selection. At the 3rd stage of medical examination - clinical observation - patients were prescribed, in accordance with the indications, active or passive caries prevention interventions aimed at eliminating general and local cariogenic factors, control examinations. When an organ pathology was detected (according to the medical history and / or examination), especially that of the digestive system, the patients were referred to specialists of the relevant profile, a proper diet was prescribed; when dental diseases were detected, patients were referred for individual consultations to health professionals in related specialties (orthodontists, surgeons, orthopedists). Patients with decompensated form of caries ( $KPU \geq 10$ ) were individually prescribed calcium-rich foods, bottled drinking water (with mineralization no more than 0.2 g/l,  $HCO_3$  mg/l,  $Ca^{2+}$  mg/l,  $Mg^{2+}$  mg/l,  $K$  + mg/l, fluorides no less than 0.2 mg/l and no more than 1.0 mg/l, hardness of water no more than 2.0 mg-equ/L). With the improper pH value of the oral fluid, the acid-base balance of the oral cavity was individually corrected using hygiene products with different pH values.

Individual preventive measures compliance was monitored during the control check-ups, if necessary, the prescriptions were corrected. As reported, the developed program of individual caries prevention through clinical examination of caries-susceptible patients helped achieve high efficient clinical outcomes. Individual preventive measures resulted in changes in the increased or decreased pH value of the oral fluid to a neutral level ( $6.9 \leq pH \leq 7.1$ ), cariogenic activity of the plaque decreased by 59%, and the level of oral hygienic status improved by 1.4 times, the fact allowing reducing activity of the cariogenic process by 0.22, according to the increase in KPU. According to the KOSRE-test, an individual caries prevention program caused an 8.2-time increase in tooth caries resistance.

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## ПРОФИЛАКТИКА КАРИЕСА И ЕГО ОСЛОЖНЕНИЙ У НАСЕЛЕНИЯ ОСОБОЙ ЭКОНОМИЧЕСКОЙ ЗОНЫ: ЭФФЕКТИВНОСТЬ УПРАВЛЕНИЯ И ПРАКТИЧЕСКИЕ ДЕЙСТВИЯ

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***Аннотация.** Статья посвящена проблеме профилактики кариеса у взрослого населения. Подчеркивается, что индивидуальная профилактика стоматологических заболеваний способствует оздоровлению населения страны, она проводится через осознание роли и значимости гигиенических процедур и нацелена на устранение причин и условий возникновения и развития заболеваний, а также повышение устойчивости организма к воздействию неблагоприятных факторов окружающей среды. Авторы провели исследование, в котором, помимо проведения профилактических мероприятий, учитывались общие заболевания, непосредственно влияющие на уровень кислотности ротовой жидкости, а также условия зоны проживания пациентов. В процессе работы был сформирован комплекс методов, регистрирующих основные кариесогенные факторы и прогнозирующих возникновение кариозного процесса. Проведенное клиническое обследование позволило проследить закономерности, происходящие в поверхностных слоях эмали после проведения лечебно-профилактических мероприятий и провести сравнительную оценку эффективности индивидуальных мер профилактики в постоянном прикусе.*

***Ключевые слова:** кариес, профилактика, распространенность, лечение.*

## NEGATIVE ASPECTS OF THE COMORBID COURSE OF COPD AND CHF

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**Abstract.** *The paper focuses on challenges in the diagnosis and treatment choice for patients with CHF and COPD. It is underlined that in the pathogenesis of both diseases there are common processes of systemic inflammation, oxidative stress, and endothelial dysfunction. One of the main systemic inflammation markers is highly sensitive C-reactive protein (hs-CRP). The fact that N-terminal pro-brain natriuretic peptide (NT-proBNP) is a standard laboratory biomarker of CHF, but the adverse effect of COPD on the cardiovascular system can also affect its level in blood serum is also stressed. The study was aimed to assess the impact of COPD on the level of NT-proBNP, hs-CRP and the functional status of patients with CHF. The results obtained demonstrate that combination of COPD and CHF amplifies systemic inflammation and myocardial remodeling processes determined by the level of NT-proBNP. A negative effect of COPD on the functional status of patients with CHF with different left ventricular ejection fraction was reported. The results obtained contribute to expansion of the diagnostic capabilities, and prognosis and effectiveness of pharmacotherapy in patients with COPD and CHF.*

**Keywords:** CHF, COPD, NT-proBNP, hs-CRP, 6MWT.

**Introduction.** Nowadays we are observing an increase in the number of patients with chronic heart failure (CHF). CHF decompensation is the main reason for hospitalization in cardiology departments, especially among patients over 65 [1]. New CHF management algorithms made it possible to increase the survival rate; nevertheless, the annual mortality rate of this group of patients is 7%, and severe decompensation reaches 17% [2]. It is also worth noting that the comorbidity of CHF and chronic obstructive pulmonary disease (COPD) significantly worsens the prognosis for such patients.

Difficulties in the diagnosis and treatment choice for patients with CHF and COPD determine the increased scientific interest in the study of the cardiorespiratory state in recent years. Currently available data indicate that COPD affects 25% - 42% of patients with CHF. Such patients are at increased risk of readmission and death [3].

In the pathogenesis of both diseases, there are common processes of systemic inflammation, oxidative stress, and endothelial dysfunction [4]. One of the main systemic in-

flammation markers is highly sensitive C-reactive protein (hs-CRP) that could be identified in the systemic circulation. In turn, N-terminal pro-brain natriuretic peptide (NT-proBNP) is a standard laboratory biomarker of CHF, but the adverse effect of COPD on the cardiovascular system can also affect its level in blood serum.

**The aim of the study** was to assess the impact of COPD on the level of NT-proBNP, hs-CRP and the functional status of patients with CHF with different left ventricular ejection fraction.

**Material and methods.** Participants' recruitment for the study was conducted using the CHF registry of the Voronezh region. From two thousand patients of the register, the study included 240 patients aged from 40 to 70 years with ischemic CHF (of which - 134 men and 106 women, average age  $71.4 \pm 8.4$  years). The patients were divided into two groups: the first group ( $n = 160$ ) - patients with isolated CHF (86 men and 74 women, mean age -  $73.2 \pm 8.8$  years) who had no signs of the lung diseases, the second group ( $n = 80$ ) - patients with a comorbid course of

CHF and COPD, including 48 men (60.0%) and 32 women (40.0%), the mean age is  $67.5 \pm 5.9$  years.

The main criterion for dividing patients into subgroups was the left ventricular ejection fraction, which was measured using echocardiography. Consequently, each of the two groups (with an isolated course of CHF, with a comorbid course of COPD and CHF) was divided into two subgroups. Patients with CHF with borderline ejection fraction (40-50%) and reduced ejection fraction (<40%) were combined into a group of patients with chronic heart failure with reduced ejection fraction (CHF<sub>r</sub>EF) (ejection fraction <50%). Subgroup 1 included 69 patients with an isolated course of CHF<sub>p</sub>EF (EF  $\geq 50\%$ ), subgroup 2 - 91 patients with CHF<sub>r</sub>EF (EF <50%). Subgroup 3 consisted of 36 patients with COPD and CHF<sub>p</sub>EF (EF  $\geq 50\%$ ) and subgroup 4 consisted of 44 patients with COPD and CHF<sub>r</sub>EF (EF <50%).

All participants were examined by a cardiologist and a pulmonologist every week from the moment of inclusion. This was used to control the absence of symptoms of CHF decompensation and COPD exacerbation. After 12 weeks, the study participants underwent 6-minute walk test (6MWT) and standard examination. We used a complex of cardiorespiratory analysis to assess exercise tolerance and 6MWT. The result was expressed in meters and compared with the proper 6-minute walk distance (6MWD (i)). The formula for calculating 6MWD (i) for men:  $6MWD (i) = 1140 - 5.61 \times BMI - 6.94 \times \text{age}$ .

For women -  $6MWD (i) = 1017 - 6.24 \times BMI - 5.83 \times \text{age}$  [5]. In addition to general clinical laboratory studies, enzyme immunoassays of blood were used to determine the levels of NT-proBNP and hs-CRP.

Statistical analysis was carried out using the STATISTICA 10.0. The data normality was assessed using the Shapiro-Wilk and Kolmogorov-Smirnov test. Continuous variables are presented as  $M \pm SD$  (M - mean, SD - standard deviation). Comparison of unrelated groups was performed in the case of normal distribution using Student's t-test. The null hypothesis was rejected at a significance level of  $p < 0.05$ . All quantitative data have a normal distribution.

**Results.** The data obtained show that CHF<sub>r</sub>EF was accompanied by an increased level of NT-proBNP regardless of the presence or absence of COPD (Table 1). However, it should be noted that the combination of COPD and CHF (1512  $\pm$  229 ng / L) in patients of the second group was accompanied by a statistically higher level of NT-proBNP than in patients with isolated CHF 1004  $\pm$  174 ng / L ( $p = 0.042$ ).

The hs-CRP level was measured to assess the severity of endogenous inflammation. In patients with CHF<sub>p</sub>EF the level of hs-CRP was  $3.7 \pm 0.62$  mg / L, while in patients with CHF<sub>r</sub>EF it was significantly lower -  $2.6 \pm 0.59$  mg / L ( $p < 0.001$ ). It was also lower in patients with COPD and CHF<sub>p</sub>EF (third subgroup) ( $4.9 \pm 0.85$  mg / L) then in patients from the fourth subgroup ( $4.4 \pm 0.74$  mg / L.), ( $p < 0.001$ ).

Table 1. Comparison of laboratory parameters in the studied patients

Indicator	Subgroup 1 (CHF <sub>p</sub> EF)	Subgroup 2 (CHF <sub>r</sub> EF)	p1 value	Subgroup 3 (COPD and CHF <sub>p</sub> EF)	Subgroup 4 (COPD and CHF <sub>r</sub> EF)	p2 value
NT-proBNP, ng/L	813 $\pm$ 127	1171 $\pm$ 191	<0.001	1228 $\pm$ 206	1876 $\pm$ 254	<0.001
hs-CRP, mg / L	3.7 $\pm$ 0.62	2.6 $\pm$ 0.59	<0.001	4.9 $\pm$ 0.85	4.4 $\pm$ 0.74	<0.001

Note: data are presented as "Mean  $\pm$  standard deviation"; CHF<sub>p</sub>EF - chronic heart failure with preserved ejection fraction; CHF<sub>r</sub>EF - chronic heart failure with reduced ejection fraction; COPD - chronic obstructive pulmonary disease; hs-CRP - highly sensitive C-reactive protein; NT-proBNP - NT-terminal fragment of natriuretic peptide.

The results obtained during 6MWT in patients with COPD and CHF, regardless of LVEF, were less than in patients with CHF ( $p_1 = 0.04$ ;  $p_2 = 0.03$ ). It can be explained by a combination of both types of breathing disorders in patients with a comorbid CHF and

COPD: obstructive and restrictive. At the same time, in patients with an isolated course of CHF, there are no significant obstructive breathing disorders.

Calculation of the 6MWD / 6MWD (i) ratio allowed us to establish that in patients

with CHF and COPD, this indicator is lower than in patients with CHF, regardless of LVEF. The results are shown in Table 2.

Heart rate (HR) before and immediately after 6MWT did not differ significantly in the subgroups. In addition, the device did not record an excess of submaximal values during the test in the subjects.

The SpO<sub>2</sub> level was the same in the studied subgroups before the start of the test.

When assessing this parameter after the test, significantly lower indicators were recorded in patients with a comorbid course of CHF and COPD, regardless of LVEF. Exercise tolerance was assessed also by using the Borg scale for assessing the severity of dyspnea after 6MWT. In patients with comorbid CHF and COPD, the higher scores were obtained compared to subgroups 1 and 2 (with isolated CHF) (Table 2).

Table 2. Comparison of 6MWT parameters in the studied patients

Indicator	Subgroup 1 (CHFpEF)	Subgroup 3 (COPD and CHFpEF)	p1 value	Subgroup 2 (CHFReEF)	Subgroup 4 (COPD and CHFReEF)	p2 value
6MWD, m	301,5±153,5	264,6±120,6	0,04	251,5±183,5	202,4±130,2	0,03
6MWD, % from the proper	53,0±29,2	47,2±25,6	0,01	48,1±30,5	42,8±22,4	0,02
HR before test, beats / min	76,1±15,2	77,8 ± 17,3	0,18	86,1±15,2	87,8 ± 17,3	0,16
HR after test, beats / min	102,4±17,5	107,3 ± 18,8	0,15	109,4±17,2	115,1 ± 14,8	0,15
SpO <sub>2</sub> before test, %	97,9±2,0	97,5±2,1	0,12	95,2±2,4	94,9±2,6	0,26
SpO <sub>2</sub> after test, %	95,5±3,0	93,3±3,1	0,001	94,1±3,3	91,2±2,5	0,001
Dyspnea according to Borg, points	2,41±0,17	3,22±0,29	0,01	3,83±0,32	5,19±0,37	0,001

Note: data are presented as "Mean ± standard deviation"; 6MWD - distance covered in the six-minute walk test; CHFpEF - chronic heart failure with preserved ejection fraction; CHFReEF - chronic heart failure with reduced ejection fraction; COPD - chronic obstructive pulmonary disease; HR - heart rate; SpO<sub>2</sub> - blood oxygen saturation.

**Discussion.** The manifestation of CHF means unfavourable prognosis for the patient, but early diagnosis makes it possible to more effectively restrain the disease progression.

A number of articles have been published on the effectiveness of determining the level of NT-proBNP in patients with CHF and COPD. There are results that indicate that NT-proBNP is an independent predictor of death in patients with COPD [6]. Conversely, there is evidence that an increase in NT-proBNP allows CHF to be suspected in patients with COPD and should be accompanied by further examination [7]. Similar results were obtained in our study: this biomarker does not lose its diagnostic value in the case of a combined course of COPD and CHF. It was also noted that in patients with a combination of COPD and CHF, the NT-proBNP level was statistically significantly higher than in patients with isolated CHF.

In addition, there are data that indicate an increased risk of CHF in patients with COPD with an increased level of CRP that indicates the processes of endogenous inflammation [8].

Previously, we found that in patients with COPD, a decrease in physical activity is apparently associated not only with lung dysfunction at rest, but also depends on a number of other factors. Thus, in patients with COPD, a decrease in lean body mass is often observed. It is a consequence of systemic inflammation and muscle atrophy due to low physical activity [3]. Therefore, it can be assumed that one of the components that reduce exercise tolerance in such patients is the activation of systemic endogenous inflammation, leading, among other things, to a decrease in muscle mass.

**Conclusion.** Patients with CHFpEF have higher levels of hs-CRP in comparison with patients with CHFReEF. The combination of COPD and CHF amplifies systemic inflammation and myocardial remodeling processes, determined by the level of NT-proBNP, in comparison with the isolated course of CHF. A negative effect of COPD on the functional status of patients with CHF with different LVEF was established, which is manifested by lower 6MWT values, the 6MWD / 6MWD ratio (i). With further study, the results ob-



tained will expand the diagnostic capabilities, as well as assess the prognosis and effectiveness of pharmacotherapy in patients with COPD and CHF.

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## НЕГАТИВНЫЕ АСПЕКТЫ КОМОРБИДНОГО ТЕЧЕНИЯ ХОБЛ И ХСН

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***Аннотация.** Статья посвящена проблемам диагностики и выбора лечения больных ХСН и ХОБЛ. Подчеркивается, что в патогенезе обоих заболеваний присутствуют общие процессы системного воспаления, окислительного стресса и эндотелиальной дисфункции. Одним из основных маркеров системного воспаления является высокочувствительный С-реактивный белок (вч-СРБ). Также обращает на себя внимание тот факт, что N-концевой промозговой натрийуретический пептид (NT-proBNP) является стандартным лабораторным биомаркером ХСН, но неблагоприятное влияние ХОБЛ на сердечно-сосудистую систему может сказываться на его уровне в сыворотке крови. Целью исследования было оценить влияние ХОБЛ на уровень NT-proBNP, вч-СРБ и функциональное состояние больных ХСН. Было установлено, что сочетание ХОБЛ и ХСН усиливает системное воспаление и процессы ремоделирования миокарда, определяемые уровнем NT-proBNP. Отмечено негативное влияние ХОБЛ на функциональное состояние больных ХСН с различной фракцией выброса левого желудочка. Полученные результаты способствуют расширению диагностических возможностей, прогноза и эффективности фармакотерапии больных ХОБЛ и ХСН.*

***Ключевые слова:** ХСН, ХОБЛ, NT-proBNP, hs-CRP, 6MWT.*

## METHODS OF INTRAOPERATIVE CORRECTION OF HEPATIC DYSFUNCTION

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**Abstract.** *The hepatobiliary system pathology remains an urgent problem of modern medicine. The liver regeneration ability largely determines the outcome of surgery and postoperative complications. The aim of the study was to enhance the prevention of postoperative hepatic dysfunction by activating methylation processes. The study involved experimental and clinical phases. In the experimental unit, the best results (15,17% acceleration of liver mass recovery) were observed with intrahepatic administration of cyanocobalamin, and intrahepatic administration of cyanocobalamin with intraperitoneal administration of ademethionine (12,04% acceleration). In clinical conditions, intravenous administration of cyanocobalamin and ademethionine contributed to the normalization of indicators of cholestasis syndrome, hepatic cell insufficiency and inflammation, a decrease in cytolysis, hepatic cell insufficiency. Thus, the proposed method of activation of methylation processes allows to increase the reparative potential of the liver, ensures the restoration of its anatomical and functional integrity, prevents the development of postoperative hepatic dysfunction.*

**Keywords:** *hepatic dysfunction, cyanocobalamin, ademethionine, regeneration, cholecystectomy.*

**Introduction.** Despite the constant improvement of surgical techniques, the pathology of the hepatobiliary system remains an urgent problem of modern medicine [1-4]. The literature data of recent years indicate a steady trend towards an increase in chronic diffuse liver diseases associated with postoperative changes in liver tissue [2]. Surgical interventions on the liver remain among the most difficult in the abdominal surgery section [3, 5]. The ability of liver tissue to regenerate largely determines the outcome of surgery and the risk of postoperative complications [1, 5]. Despite the high level of development of modern medicine, the number of postoperative complications after liver surgery ranges from 18,2% to 71,4%, while liver dysfunction develops in 8,3-14,4% of cases, which indicates the need to influence the rate of regeneration of the remaining liver tissue [3, 4, 6].

A comprehensive study of diseases of the hepatobiliary system is determined by medical and social aspects – their progressive course not only worsens the quality of life, but causes the occurrence of severe complica-

tions leading to disability [3, 5]. Thus, the search for new ways to stimulate the regeneration of liver tissue and improve the functional state of the liver is an actual task of modern medicine.

**The aim of the study** was to improve the prevention results of postoperative hepatic dysfunction by activating methylation processes.

**Materials and methods.** The study was carried out in two blocks – experimental (I) and clinical (II). In block I Wistar rats underwent resection of 70% of the initial liver mass: in Group 1 (n=24) – prevention of postoperative hepatic dysfunction was not performed; in 2 Group 2 (n=24) – 0.9% NaCl solution was administered intrahepally after resection: in Group 3 (n=24) – ademethionine was administered, in Group 4 (n=24) cyanocobalamin was administered; in Group 5 (n=24) – intraperitoneal ademethionine was administered; in Group 6 (n=24) – cyanocobalamin was administered, in Group 7 (n=24) ademethionine and cyanocobalamin intraperitoneally were administered; in Group 8 (n=24) ademethionine intraperitoneal, cyano-

cobalamin intrahepatic were administered. The therapies were discontinued on the 1st, 5th, 7th, 14th day after surgery.

The second block of the study was clinical, and included 2 groups: in the control group (n=15), standard treatment was used in patients after laparoscopic cholecystectomy: in the case group (n=15), standard treatment after laparoscopic cholecystectomy was supplemented with intravenous administration of ademethionine and cyanocobalamin. The result was evaluated using clinical, laboratory, instrumental, morphological and statistical research methods.

**Results.** In the experimental block, we found that intrahepatic administration of cyanocobalamin accelerates the recovery of liver mass by 15,17%, reduces oxidative stress by 1,3 times, increases the concentration of growth factors by 2,1 times, the proliferation index by 7,8 times, compared with the 1st group ( $p < 0,05$ ); intrahepatic administration of ademethionine significantly reduces proliferative activity by 1,2 times, promotes the development of fibrous changes; intrahepatic

administration of cyanocobalamin with intraperitoneal administration of ademethionine accelerates the recovery of liver mass by 12,04%, improves all biochemical parameters and relieves oxidative stress, increases the concentration of growth factors by 1,3 times, the proliferation index rose by 6,4 times, compared with Group 1 ( $p < 0,05$ ).

In clinical conditions we found that intravenous administration of cyanocobalamin and ademethionine in patients after laparoscopic cholecystectomy contributes to the normalization of indicators of cholestasis syndrome, hepatic cell insufficiency and inflammation, a decrease in cytolysis by 2,5-3,9 times, hepatic cell insufficiency by 1,1-1,4 times. In the control group the decrease in biochemical parameters was statistically insignificant.

**Conclusion.** The proposed method of activation of methylation processes allows to increase the reparative potential of the liver, ensures the restoration of its anatomical and functional integrity, prevents the development of postoperative hepatic dysfunction.

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## СПОСОБЫ ИНТРАОПЕРАЦИОННОЙ КОРРЕКЦИИ ПЕЧЕНОЧНОЙ ДИСФУНКЦИИ

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**Аннотация.** Патология гепатобилиарной системы по-прежнему остается актуальной проблемой современной медицины. Способность печеночной ткани к регенерации во многом определяет исход оперативного вмешательства и риск возникновения послеоперационных осложнений. Целью настоящего исследования являлось улучшение результатов профилактики послеоперационной печеночной дисфункции путем активации процессов метилирования. Исследование выполнено в двух блоках – экспериментальном и клиническом. Изучено влияние различных способов введения цианокобаламина и адеметионина на развитие послеоперационной печеночной дисфункции. В экспериментальном блоке наилучшие результаты наблюдались при внутripеченочном введении цианокобаламина, что ускоряет восстановление массы печени на 15,17%, и внутripеченочном введении цианокобаламина с внутривентральным введением адеметионина, что ускоряет восстановление массы печени на 12,04%. В клинических условиях внутривенное введение цианокобаламина и адеметионина способствовало нормализации показателей синдрома холестаза, печеночно-клеточной недостаточности и воспаления, снижению показателей цитолиза, печеночно-клеточной недостаточности. Таким образом, предложенный способ активации процессов метилирования позволяет повысить репаративный потенциал печени, обеспечивает восстановление ее анатомической и функциональной целостности, предупреждает развитие послеоперационной печеночной дисфункции.

**Ключевые слова:** печеночная дисфункция, цианокобаламин, адеметионин, регенерация, холецистэктомия.

## MALIGNANT NEOPLASMS OF THE HEAD AND NECK IN THE ADULTS OF VORONEZH REGION: CURRENT NOSOLOGICAL STATISTICS, TRIGGERS AND PREVENTION

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**Abstract.** Tumors of visible localizations of the head and neck are significant in the structure of oncological morbidity. In the early stages, they respond well to surgical treatment, targeted and radiation therapy; in the later stages, there is a high degree of trauma, disability and mortality. The objective of the study was to identify parameters of oncogenic risks for their further implementation as applications for mobile devices computer programs. The study involved adults diagnosed with oncopathologies. The information was collected by anonymous survey; the authors have also specified the gradation of the most common localizations. The main findings of the study were presented as prevention guidelines and recommendations available to all Russian citizens. Questionnaires and programs on modern platforms were introduced to detect the studied factors and early symptoms of oncological diseases, thus contributing to preventive medicine concept and increasing the efficiency of healthcare.

**Keywords:** incidence of head and neck malignant neoplasms; medical and social factors of malignant neoplasms; questioning patients; preventive healthcare.

**Introduction.** According to the published data from the Global Cancer Statistics 2020 study, about 19.3 million new cases and almost 10 million deaths from cancer were recorded in 2020 worldwide [1]. At the same time, according to Cancer Journal for Clinicians there are changes in the statistics of oncological diseases. Oncology statistics 2020-2021 provides new data on cancer incidence in 185 countries. The specialists from the International Agency for Research on Cancer report that the number of new cases has reached 19.3 million and the number of deaths has reached 10 million [2].

Insufficiently effective measures for the early cancer detection in the population are the cause of a significant proportion of late (III-IV) stages of the initially diagnosed disease. Therefore, the timely diagnosed tumor is considered to be one of the criteria for providing quality of oncological care for the population, which ensures the effectiveness of treatment, and therefore the quality and life expectancy of patients; this, in turn, results in a reduction in the cost of palliative care and disability costs, and a reduction in non-recoverable losses of human resources due to

an increase in the rate of premature mortality from cancer to 52.6%.

According to WHO, the number of newly diagnosed cases reached 16 million in 2020 [3]. Presumably, according to experts from the World Cancer Research Foundation the number of cancer cases will increase by 30% by 2030 [4]. Globally, the increased absolute number of sick people is the result of both an increased number of the population and its aging. The reason for the increased number of cancer patients are environmental and lifestyle factors that are carcinogenic in nature, which are widely spread in the world and especially in developing countries.

More than 30,000 new cases of malignant neoplasms of the head and neck are registered annually in Russia. Thus, approximately 15 thousand patients die from this pathology every year. About 60-70% of patients starting treatment have III-IV stage of the disease, and 80% of them have regional metastases [5].

In 2020, 120 billion rubles were allocated for the implementation of the federal program "Fight against cancer", which occupies a leading position in the structure of financial support for socially significant diseases and

accounts for 56% of total funding. It was found that most of the cancer patients are of working age (from 30 to 60 years). And recently, the tendency to patients rejuvenating has been determined. According to the latest data there is also a high level of postoperative disability, up to 60-70%, the fact inevitably reducing the quality of life of the population.

The overall mortality in patients during the first year after being diagnosed reached 40.3% in the Russian Federation - this evidences insufficient oncological alertness of physicians at outpatient appointments, low awareness of the population about the factors contributing to the development of laryngeal tumors, and lack of wide access to specialized medical care.

In this regard, the main problems that complicate the effectiveness of therapy are the late detection of the disease and the features of the process (rapid growth and metastasis). These facts support the significance, importance and relevance of early diagnosis of these pathologies.

The selected medical and social issues demonstrate concentration of medical, psychological, social, demographic, economic aspects of the disease and determine negative social risk factors: loss of family, friends, work, livelihood, etc. health assessment, development of functional routing algorithms for patients with a high risk of cancer in the early stages of the disease. Also, the prevention program we have developed will allow monitoring the correction of oncofactors in patients over time.

It should be noted that this study has not been previously conducted for our region, which confirms the relevance of integrating statistical control over the regional verification of this pathology and introducing a program for its prevention in all sections of healthcare.

**Material and methods.** The study involved 420 adults (men and women of different ages, with confirmed malignant neoplasms of the head and neck) receiving treatment in oncological hospitals. The study also included adults without malignant neoplasms and diseases (n=420) examined by general practitioners and surgeons, head and narrow specialists (dermatologists, dentists, maxillo-

facial surgeons, otorhinolaryngologists, endocrinologists, etc.) for complaints in the head and neck areas during entry medical examination, who developed oncopathologies under extended examination, and people undergoing routine medical examination, occupational health checks.

All patients underwent an anonymous examination on the basis of healthcare facilities: outpatient clinics, including district hospitals, interregional outpatient cancer care centers, inpatient facilities, organization of regional healthcare management. There were 55 points in the questionnaire related to attitude and financial situation, harmful production factors of life, image and quality, mode and place of work, living conditions and other things. In the case of cancer patients, there were included questions to detect oncogenic triggers before and after illness.

In the course of the study, we used the data from the e-register of patients with malignant neoplasms of the head and cancer, findings obtained by primary care physicians, polyclinic and their interaction with narrow groups of hospital authorities and health authorities at the local level. The study also included 500 medical histories of the disease, clinical audits for 10 years.

**Results.** The study demonstrated that the number of patients diagnosed with malignant neoplasms of the head and neck increased during the survey in healthcare facilities due to the implementation of our project, and remote examination methods and analysis of liability to these diseases using the created computer and telephone programs contributed to a reduction in the time spent to collect anamnesis of oncogenic factors.

Medical history records from the archive of Voronezh oncological hospital reflecting the statistical parameters of oncological morbidity of the head and neck in the adult population per 100 thousand people were generated and analysed. The data obtained were as follows:

Oral cavity 2011 - 23.1, 2019 - 29.7;  
Throat 2011 - 10.1, 2019 - 12.7;  
Esophagus 2009 - 7.7, 2019 - 9.8;  
Larynx 2009 - 28.7, 2019 - 31.1;  
Thyroid gland 2009 - 78.6, 2019 - 120.5;  
Skin melanoma 2009 - 44.5, 2019 - 66.9;

Skin (except melanoma) 2009 - 236.5, 2019 - 310.4;

Oral cavity 2011 - 28.8, 2019 - 34.4;

Throat 2011 - 38.8, 2019 - 49.7;

Esophagus 2009 - 30.9, 2019 - 30.2;

Larynx 2009 - 16.7, 2019 - 21.6.

Relevant triggers that cause oncological diseases, according to the World Health Organization, all-Russian study findings and our survey, were identified and compiled, classification by nosologies was made and their gradation according to the frequency of occurrence was determined as follows:

Skin (melanoma): PCBs, solar radiation, UV protection device, mechanical damage.

Skin (malignant neoplasms): arsenic and inorganic arsenic compounds, azathioprine, coal tar distillation, coal tar pitch, cyclosporine, methoxsalen plus ultraviolet, mineral oils, raw or lightly processed, shale oils, solar radiation, soot, light radiation,  $\gamma$ -radiation, mechanical damage.

Oropharynx: acetaldehyde associated with the use of alcoholic beverages, alcoholic beverages, betel cancer due to tobacco use, betel cancer without tobacco use, smokeless tobacco use, tobacco smoking, intense radiation,  $\gamma$ -absorption, constant consumption of hot food.

Oral cavity, lips and tongue: alcoholic beverages, betel cancer due to tobacco use, betel cancer without tobacco use, human papillomavirus type 16, smokeless tobacco use, tobacco smoking.

Larynx: acid mists, inorganic, alcoholic beverages, asbestos (all forms), tobacco smoking.

Thyroid: radioiodins, including iodine-131 (exposure in childhood and adolescence), x-rays, gamma radiation, diet and malnutrition, hypovitaminosis.

Salivary gland: external radiation, gamma radiation.

Tonsils: papillomavirus type 16, upper digestive system, acetaldehyde associated with human consumption of alcoholic beverages, candida.

Nose and sinuses: production of isopropyl alcohol using high acid, leather dust, nickel compounds, radium-226 and its decay products, radium-228 and its decay products, tobacco smoking, wood dust.

Nasopharynx: Epstein-Barr virus, formaldehyde.

**Discussion.** The dynamics of the incidence of head and skin tumors in the published statistics of Western countries and the Russian Federation remains steadily external. The level of disability and mortality from such diseases, despite ongoing therapeutic and diagnostic measures, remains colossally high in many cases due to insufficiently developed disease prevention and monitoring.

Oncological alertness of primary care physicians and public awareness of the consequences of long-term exposure to oncogenic risk factors and the first symptoms of the disease remain low. Due to the fact that we applied modern feasible methods of organizing healthcare to optimize the work of specialists and developed the direction of self-identification of microsymptoms, we made the population more aware of this topic, the quality of detection of head and neck tumors became better.

The study published epidemiological and statistical features of patients with malignant neoplasms of the head and neck. The level, structure and dynamics of morbidity have been studied, which will undoubtedly significantly contribute to the development of practical healthcare. Data on the incidence of cancer of the lip and oral cavity have been demonstrated: 354,864 people fell ill, 177,384 died worldwide; 10,827 fell ill, 10,040 died in Russia; after being diagnosed 41.5% of patients die from pharyngeal cancer, 34.2% of patients died from cancer of the oral cavity, 23% of patients died from cancer of the larynx.

The results of repeated surveys demonstrated that patients with malignant neoplasms of the head and neck changed their lifestyle and excluded the influence of aggressive oncogenic factors in 65 % of cases after the treatment and the studied methodological aids for prevention of oncological diseases. Patients without these pathologies responded to the recommendations in 15% of cases when they were re-interviewed and questioned.

Since our data includes information about Voronezh regional oncological hospital patients, they are highly significant in terms of analyzing patient cohorts treated in various



healthcare facilities in the Voronezh region. Thus, in cases where subjective parameters are to be considered, treatment outcomes can be influenced by various oncogenic factors, as well as social factors. Therefore, detection and observation of these triggers in diseased individuals and their correction during ongoing therapy, better compliance between the doctor and the patient, and the developed optimal patient routing algorithms will be beneficial achievements for public health.

This research study highlights the issues that require constructive changes in the approach to cancer diagnosis in the near future. Confirming statistical data have been obtained that the proportion of patients with microsymptoms of the initial stages of the disease during routine examination remains underestimated, and passing a survey and questioning in the created modules provides greater verification of diseases. In this connection, we offer our program, project modules and preventive recommendations for wide use in other regions of the country.

**Conclusion.** The study has provided statistical correlation of morbidity for 10 years in healthcare facilities of Voronezh and the Voronezh region, the data being compared with the all-Russian ones.

The leading medical and social oncogenic factors have been identified. We have created prognostic models that allows assessing the dynamics of morbidity. Most importantly, algorithms for preventive measures have been compiled and methodological recommendations for patients have been prepared, a questionnaire has been developed for medical workers to assess the tendency to develop ne-

oplasms, help recognize the first symptoms and monitor their dynamics and control, develop correct routing for further verification of health factors or cancer diagnosis.

The study demonstrated that the number of patients diagnosed with malignant neoplasms of the head and neck increased during the survey in healthcare facilities due to the implementation of our project, and remote examination methods and analysis of liability to these diseases using the created computer and telephone programs contributed to a reduction in the time spent to collect anamnesis oncogenic factors.

All these will increase the level of disease prevention, significantly reduce the incidence rate, the number of cases of temporary incapacity for work, disability and mortality of the population of the region, and, conversely, will increase the early detection of serious nosologies leading in the statistics of morbidity and mortality.

This is the first study to analyze the incidence of malignant neoplasms of the head and neck in our region. Based on questionnaires and surveys, a unique database including patients of all age groups was created; it considers the features of patients with detected oncopathologies, which helps develop the approach to the treatment of these patients. The above will contribute to better management of Department of Health resources.

The implementation of the study results will allow practical preventive healthcare authorities of the Voronezh region to improve diagnostics and treatment of head and neck malignant neoplasms and contribute to a higher level of cancer prevention.

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## ЗЛОКАЧЕСТВЕННЫЕ НОВООБРАЗОВАНИЯ ГОЛОВЫ И ШЕИ У ВЗРОСЛЫХ ВОРОНЕЖСКОЙ ОБЛАСТИ: СОВРЕМЕННАЯ НОЗОЛОГИЧЕСКАЯ СТАТИСТИКА, ТРИГГЕРЫ И ПУТИ ПРОФИЛАКТИКИ

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***Аннотация.** Значительное место в структуре онкологической заболеваемости занимают опухоли видимых локализаций головы и шеи. На ранних стадиях они хорошо поддаются хирургическому лечению, таргетной и лучевой терапии; на поздних стадиях отмечается высокая степень травматизма, инвалидности и летальности. Целью настоящего исследования является определение параметров для оценки риска развития рака головы и шеи для последующего использования в качестве приложения для мобильных устройств и компьютерных программ. Для отбора параметров были использованы опросы онкологических пациентов, уточнена градация наиболее частых локализаций. Результаты исследования представлены в виде профилактических рекомендаций для жителей российских регионов. Внедрены опросники и программы на современных платформах для выявления изучаемых факторов и ранних симптомов онкологических заболеваний.*

*Участие в разработанной программе формировало осознанное отношение к болезни, повышало приверженность к лечению и улучшало прогноз заболевания. Реализация таких проектов соответствует современной концепции профилактической медицины и повышает эффективность оказания медицинской помощи населению.*

***Ключевые слова:** заболеваемость злокачественными новообразованиями головы и шеи; медико-социальные факторы злокачественных новообразований; опрос пациентов; профилактическое здравоохранение.*

## RADIOMICS FOR DIAGNOSTIC PROCESS AND COMPREHENSIVE TREATMENT IN GLIOBLASTOMA: CLINICAL CASE

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**Abstract.** *The paper highlights diagnostic and therapeutic options for glioblastoma. Glioblastoma is known to be a neuroepithelial malignant with an aggressive clinical course and extremely adverse prognosis. It is pointed out that contrast-enhanced magnetic resonance imaging (MRI) is the “gold standard” in glioblastoma diagnostics. Special attention is paid to radiomics that presents a multi-stage process involving image acquisition and pre-processing, segmentation, feature extraction and selection, and advanced statistics using machine learning algorithms. The aim of the study is to investigate objective numerical control options of pathological process dynamics and monitoring of the comprehensive glioblastoma treatment effectiveness in a particular patient according to the informative parameters of MR-images. Primary confirmation of objectifying diagnostic and treatment process in patient with glioblastoma according to the indicated statistical parameters of T2-weighted images was obtained. Further research should be aimed at the use of radiomics for planning, monitoring treatment of glioblastoma, predicting clinical outcomes.*

**Keywords:** *glioblastoma, radiomics, magnetic resonance imaging, radiotherapy, lesion.*

**Introduction.** Glioblastoma is a neuroepithelial malignant, predominantly astrocytic brain tumor with an aggressive clinical course and extremely adverse prognosis [1, 2, 3]. According to the Central Brain Tumor Registry of the United States (CBTRUS), the incidence of glioblastoma is 14.7% among all central nervous system tumors and 47.7% among all malignant brain tumors [4].

Glioblastoma overall survival median is 14.6 months after standard treatment, including combination of surgery, radiotherapy and chemotherapy [1, 3, 4]. Various molecular genetic characteristics of glioblastoma in individual patients, as well as intratumoral heterogeneity, explain the relatively low effectiveness of standard treatment methods [1, 3, 4], which creates a problem in providing quality oncological care and indicates the need to develop a personalized approach to the diagnosis and treatment of glioblastoma.

Contrast-enhanced magnetic resonance imaging (MRI) is the “gold standard” in glioblastoma diagnostics. Due to the hyperpermeability of the immature tumor vessels, extravascular accumulation of contrast agent occurs with a shortening of T1-time and hyperintensive signal in T1-weighted images [2, 3]. On MR-images, glioblastoma characteristically appears as a fuzzy-contoured heterogenous structure lesion containing regions of unequal contrast agent accumulation surrounding the necrotic tumor center, which is hypointensive (dark) on T1-weighted MR-images [2, 3, 4]. Necrosis, the hallmark of glioblastoma, is associated both with the presence of thrombosed vessels and with high rate tumor cell proliferation, which leads to a mismatch between accelerated oxygen consumption and blood supply deficiency.

Perifocal vasogenic edema, signs of hemosiderin inclusion (hemorrhages in the tumor

structure), mass-effect (deformation or displacement of adjacent structures) are also common features of glioblastoma MR-imaging, which reflect the structural tumor characteristics itself, as well as its microenvironment [3].

Since MR-images reflect structural tumor lesions that are inextricably linked with impaired metabolism of normal tissues, their quantitative assessment and informative parameters of MR-images can improve the intratumoral heterogeneity determination and studying the pathophysiological and molecular genetic mechanisms of a particular tumor [5, 6, 7].

Radiomics is a multi-stage process that includes image acquisition and pre-processing, segmentation, feature extraction and selection, and advanced statistics using machine learning algorithms [5, 6, 7, 8]. There are a lot of methods for describing and analyzing the object features in radiomic images: geometric characteristics analysis, local brightness differences analysis, statistical characteristics of textures analysis, etc. As a result, up to hundreds of features are extracted from one MR-image. Finally, the identified informative features, combined with clinical outcomes, are used as input data for classificational or prognostic models construction [5, 8, 9, 10].

**The aim of the study** is to investigate objective numerical control possibility of pathological process dynamics and control of the comprehensive glioblastoma treatment effec-

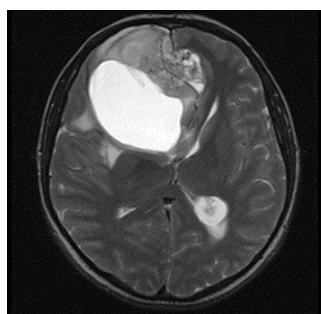
tiveness in a particular patient according to the informative parameters of MR-images.

**Material and methods.** Authors used clinical data of a patient underwent chemoradiotherapy course for glioblastoma in the Radiotherapy Department No.1. of Voronezh Region Budgetary Healthcare Institution “Voronezh Regional Clinical Oncological Dispensary” in 2021. Presented MRI-studies were performed in the Department of Diagnostic Radiology of the same hospital using magnetic resonance tomographs Philips Ingenia 1.5T and Philips Ingenia Ambition 1.5T. MR-images analysis was carried out at the Moscow State Technical University named after N.E. Bauman using the Matlab 2021 application package.

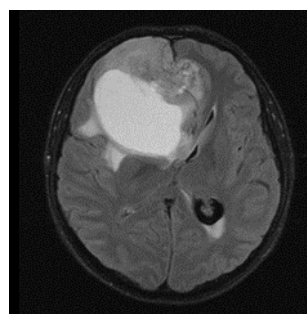
*Clinical data.* Patient S., born in 1986, diagnosed with glioblastoma G4 of the right frontal lobe. Histological diagnosis No. 22854 dated 09/20/2021: Glioblastoma G4.

MRI dated 09/12/2021 (before surgical treatment):

Description: in the right frontal lobe, a large cystic-solid lesion is determined, with a pronounced mass-effect, extending to the temporal lobe. The total dimensions are 8.7x6.7x7.8 cm. The lesion compresses brain ventricular system; left lateral ventricle posterior horn is dilated. Median structures dislocation is 1.7 cm to the left. The right hemisphere sulci are narrowed. *Conclusion:* MR-picture of the right frontal lobe tumor (more likely, oligodendroglioma).



T2\_tra



T2\_tirm tra dark fluid

Figure 1. MRI before surgical treatment.

Patient S. was being treated at Neurosurgical department since 09/13/2021 to 09/29/2021 with the diagnosis: cystic-solid right frontal lobe tumor. Edema, dislocation of brain structures. Surgical treatment performed on 09/15/2021 included microsurgical

removal of intracerebral right frontal lobe tumor with intraoperative ultrasound scanning.

MRI dated 10/20/2021 (after surgical treatment):

*Description:* in the right frontal lobe spreading to the left frontal lobe, a post-

operative cavity with hemosiderin deposits measuring 51x49x28mm is determined. The walls of the post-op cavity unequally accumulate contrast agent. Perifocal edema appears measuring 53x68x40mm. Parasagittally along the posterior and inferior contours of the post-

op cavity in the right frontal lobe, there is an altered MR-signal lesion in FLAIR-weighted images, measuring 17x36x33 mm, pushing the left frontal lobe. *Conclusion:* glioblastoma G4, condition after surgical treatment. MR-picture of residual tumor.

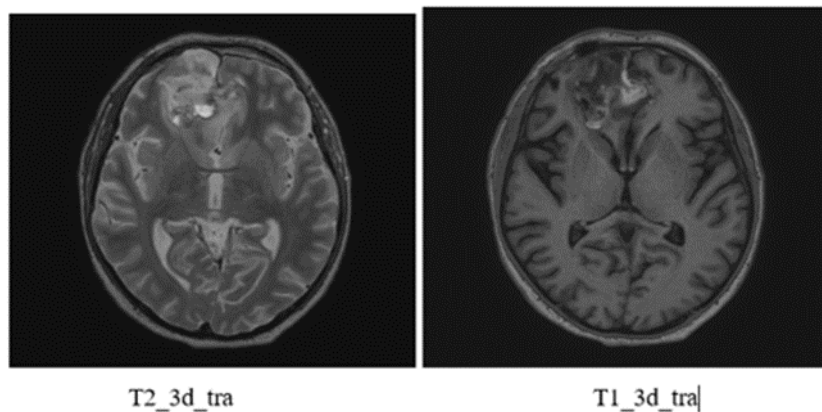


Figure 2. MRI after surgical treatment

In the Department of Radiation Therapy No.1. patient S. underwent chemoradiotherapy from 11/01/2021 to 12/17/2021, specifically a 33-day-course of IMRT-radiation therapy on the right frontal lobe residual tumor tissue on Varian Halcyon linear particle accelerator

with single focal dose 1.8 Gy and total focal dose 59.4 Gy. Chemotherapy: Temozolomide in capsules, 140 mg per day, a total of 4620 mg for the entire period of treatment; Dexamethazone 12 mg intramuscular daily.

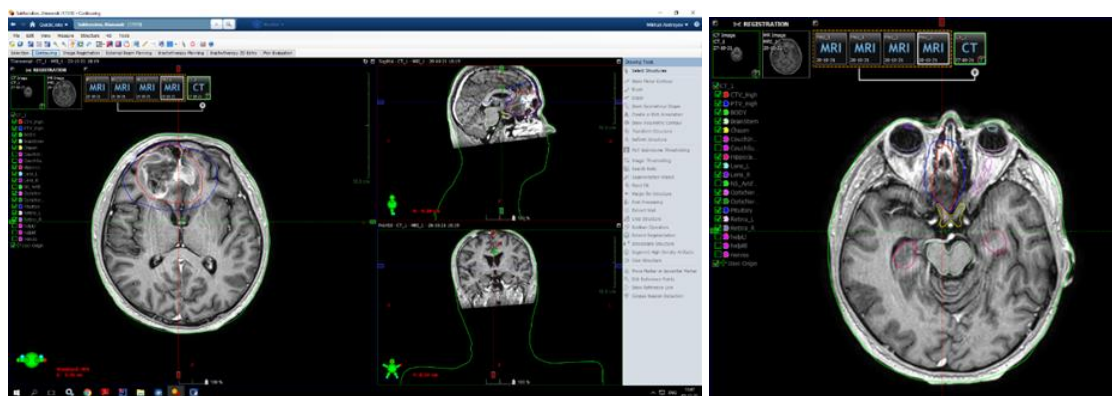


Figure 3. Radiotherapy planning: clinical target volume (CTV) and planning target volume (PTV) contouring in axial T1-contrast-enhanced-weighted images

*MRI dated 01/21/2022 (after comprehensive treatment):*

*Description:* in previously determined localization in the right frontal lobe with spread to the left frontal lobe, a post-op cavity with hemosiderin deposits measuring 48x45mm (previously 52x52mm) is determined. There is a less pronounced heterogeneous accumulation of contrast agent. A perifocal changes region remains 59x54 mm (previously 62x51 mm). Parasagittally along the posterior and

inferior post-op cavity contours in the right frontal lobe, a region of altered MR-signal on FLAIR T2-weighted images with dimensions of 24x11mm (previously 26x17mm) remains, pushing the left frontal lobe. *Conclusion:* condition after surgical treatment, chemoradiotherapy. The MR-picture of residual tumor in the right frontal lobe, in comparison with the study dated October 20/ 2021, shows a slight decrease in all previously determined changes size.



Figure 4: MRI after chemoradiotherapy.

*Data analysis.* As an initial stage of the study, T2-weighted MR-images recorded before surgery, after surgery, and after chemoradiotherapy course were analyzed. As informative lesion signs on images, the statistical characteristics of brightness local distribution of the lesion images were analyzed, which are described by statistical texture parameters [11]:

- the intensity average value in the region (hereinafter referred as the average value);

- the intensity standard deviation in the region (hereinafter referred as the standard deviation);

- texture smoothness;

- the third moment characterizing asymmetry of the intensity histogram;

- entropy [11].

Figure 5 shows examples of analyzed images. Affected regions are highlighted in red, transitional regions in blue, and normal tissue regions in green.

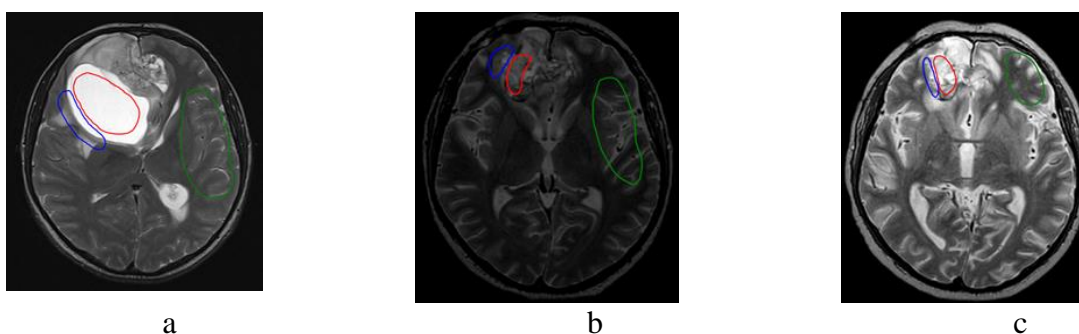


Figure 5. Examples of analyzed MR-images: a) before operation; b) after operation; c) after comprehensive treatment.

The results of texture parameters calculations are presented in tables 1-3.

Table 1. Statistical textural parameters of homogeneous lesion regions

Parameter	Before operation	After operation	After complex treatment
Mean	1218.3±37.4	641.2±52.2	631.3±47.4
Standard deviation	33.8±21.3	106.3±21.2	84.2±23.0
Smoothness (x10-6)	0.37±0.49	2.73±1.01	1.78±1.02
Third Moment (x10-4)	-1.10±2.44	-0.23±1.15	-0.27±0.74
Uniformity	0.017±0.004	0.005±0.001	0.006±0.001
Entropy	6.24±0.42	7.91±0.31	7.65±0.24

Table 2. Statistical texture parameters of transition regions

Parameter	Before operation	After operation	After comprehensive treatment
Mean	826.2±65.5	527.4±51.0	484.3±23.4
Standard deviation	301.9±61.8	119.9±15.8	112.3±17.3
Smoothness (x10-6)	22.1±9.0	3.4±0.9	3.0±0.9
Third Moment (x10-4)	4.73±2.01	0.62±1.83	-0.07±1.19
Uniformity	0.0027±0.0008	0.0039±0.0007	0.0040±0.0005
Entropy	8.97±0.35	8.25±0.24	8.18±0.14

Table 3. Statistical textural parameters of normal tissue regions

Parameter	Before operation	After operation	After comprehensive treatment
Mean	303.6±24.9	327.9±30.7	298.1±29.9
Standard deviation	49.6±12.8	71.0±21.9	62.9±21.9
Smoothness (x10-6)	0.81±0.23	1.28±0.64	1.03±0.58
Third Moment (x10-4)	0.46±0.49	1.19±0.84	0.73±0.75
Uniformity	0.0081±0.0026	0.0066±0.0026	0.0081±0.0032
Entropy	7.28±0.39	7.63±0.49	7.37±0.52

**Results.** As a result of texture parameters values analysis, the statistical significance of differences in the standard deviation, smoothness, and the third moment of affected, normal tissue and transition regions intensity on T2-weighted MRI images recorded before surgical treatment, after surgical treatment, and after a full course of chemoradiotherapy was established. Thus, as a result of clinical case analysis, the primary confirmation of objectifying diagnostic and treatment process in patient with glioblastoma according to the

indicated statistical parameters of T2-weighted images was obtained.

**Conclusion.** The goal of further research in this direction is the use of radiomics for planning, monitoring treatment of glioblastoma, for predicting clinical outcomes, as well as predictive analysis of comprehensive treatment response, which would help open up prospects for the precision (personalized) oncological care development in patients with glioblastoma.

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## КЛИНИЧЕСКИЙ СЛУЧАЙ ПРИМЕНЕНИЯ РАДИОМИКИ ДЛЯ ОБЪЕКТИВИЗАЦИИ ПРОЦЕССА ДИАГНОСТИКИ И КОМПЛЕКСНОГО ЛЕЧЕНИЯ ПРИ ГЛИОБЛАСТОМЕ

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***Аннотация.** В статье освещаются диагностические и терапевтические возможности для лечения глиобластомы. Известно, что глиобластома является нейроэпителиальным злокачественным новообразованием с агрессивным клиническим течением и крайне неблагоприятным прогнозом. Отмечается, что магнитно-резонансная томография (МРТ) с контрастным усилением является «золотым стандартом» в диагностике глиобластомы. Особое внимание уделяется радиомике, которая представляет собой многоэтапный процесс, включающий получение и предварительную обработку изображений, сегментацию, извлечение и выбор признаков, а также расширенную статистику с использованием алгоритмов машинного обучения. Цель исследования — изучить возможности объективного численного контроля динамики патологического процесса и мониторинга эффективности комплексного лечения глиобластомы у конкретного пациента по информативным параметрам МР-изображений. Получено первичное подтверждение объективизации лечебно-диагностического процесса у больного с глиобластомой по указанным статистическим параметрам T2-взвешенных изображений. Дальнейшие исследования должны быть направлены на использование радиомики для планирования, контроля лечения глиобластомы, прогнозирования клинических исходов.*

***Ключевые слова:** глиобластома, радиомика, магнитно-резонансная томография, радиотерапия, очаг поражения.*



## PALLIATIVE CARE FOR THE CHILDREN OF VORONEZH REGION

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**Abstract.** *Palliative care for children is a medical service that develops separately from adult palliative care. The purpose of this study is to analyze the medico-social structure of palliative care for children of Voronezh region. Data were collected from 47 medical institutions of Voronezh region. It included the number of children, the area of residence, social status, diagnosis. The method of nutrition and respiration of the child, the need for oxygen therapy, artificial ventilation, psychological and social assistance were also evaluated. It was revealed that the largest number of palliative patients was detected in the Left-Bank district. According to the structure of the detected palliative pathologies, non-oncological diseases prevail in children of the Voronezh region. Also, acquired neurological diseases are most common – cerebral palsy and congenital anomalies of brain development. Oncological diseases in children, according to our data, occupy a small proportion (4%). In the Voronezh Region, depending on the probability of a fatal outcome, irreversible but not progressive conditions with severe disability and the patient's exposure to complications prevail, which requires the organization of a multidisciplinary approach to palliative therapy, the introduction of new diagnostic methods and rehabilitation measures.*

**Keywords:** *palliative care, children, palliative pathology, Voronezh region, pediatrics, oncology.*

**Introduction.** At the moment palliative care for children is a unique and independently developing palliative service. Palliative care for children is aimed at improving the quality of life of a child with severe chronic diseases in which the rehabilitation potential is reduced or absent. The International Children's Palliative Care Network (ICPCN) annually registers more than 8 million children worldwide born with genetic diseases and birth defects who will need palliative care in the future [1]. In Russia, 182089 children need primary palliative pediatric care, and 81950 children need specialized care. In the structure of diseases of children in need of palliative care, non-oncological diseases prevail in Russia and account for 93%, these include congenital malformations and genetic diseases - 42%, diseases of the cardiovascular system – 23%, diseases of the neonatal period – 12%, and other diseases account for 16%. Malignant neoplasms in the structure of palliative pediatrics account for 7% [2,3]. In 2009, the European Palliative Care Association identified 4 groups of patients in need of palliative pediatric care:

1. Life-threatening conditions or diseases for which curative treatment is possible, but it may be ineffective.

2. Diseases in which long-term intensive treatment is aimed at prolonging life and allows for normal activity, but premature death is possible.

3. Progressive conditions without curative treatment options, the therapy of which is palliative from the moment of diagnosis.

4. Irreversible, but not progressive conditions with severe disability and the patient's exposure to complications [4].

Palliative care for children of all four groups is based on a multidisciplinary approach, which is aimed at relieving physical symptoms that violate the quality of life of a child and preventing complications of an incurable disease.

**The aim of the study:** to analyse the structure of palliative care for children of Voronezh region.

**Material and methods:** Data were collected from 47 medical institutions providing medical care to children: 15 children's polyclinics in Voronezh and Novovoronezh and

32 central district children's hospitals in the period from September 2021 to December 2021. The criteria for inclusion in the study were: the child age from 0 to 18 years, the need for palliative care help. Data were obtained on the number of children in need of inpatient and outpatient palliative care, the area of residence, the social status of the family, the main and concomitant diagnoses. The method of feeding the child (independent, probe or through a gastrostomy), the method of breathing the child (independent, tracheostomy or hardware artificial lung ventilation), the need for additional oxygen therapy, artificial lung ventilation, the need for

psychological and social assistance were also evaluated. All the data obtained were depersonalized, and a register of palliative pathology of children of Voronezh Region was created on their basis. Methods of nonparametric statistics were used to analyze the data obtained.

**Results.** Information was collected about 356 children of Voronezh region receiving palliative care. Among children with palliative pathology, 35.1% live in the city of Voronezh, and 64.9% in Voronezh region. The distribution of children with palliative pathology by districts is presented in the table.

Table 1. The district structure of palliative care for the children of Voronezh region

District	Number of children	%	District	Number of children	%
Anninsky	4	1,1	Ostrogozhsky	7	2
Bobrovsky	9	2,5	Pavlovsky	13	3,7
Bogucharsky	2	0,6	Paninsky	1	0,3
Borisoglebsky	14	3,9	Petropavlovsky	2	0,6
Buturlinovsky	8	2,2	Povorinsky	3	0,8
Verkhnemamonsky	1	0,3	Podgorensky	6	1,7
Verkhnekhavsky	4	1,1	Ramonsky	10	2,8
Vorobyevsky	5	1,4	Rossoshansky	23	6,5
Gribanovsky	6	1,7	Semiluksky	9	2,5
Kalacheevsky	6	1,7	Talovsky	4	1,1
Kamensky	3	0,8	Ternovsky	3	0,8
Kantemirovsky	9	2,5	Khokholsky	9	2,5
Kashirsky	5	1,4	Ertilsky	11	3
Liskinsky	16	4,5	Railway	24	6,7
Nizhnedevitsky	2	0,6	Comintern	24	6,7
Novovoronezh	3	0,8	Levoberezhny	36	10,1
Novousmansky	18	5	Leninsky	8	2,2
Novohopersky	12	3,4	Central	7	2
Olkhovatsky	3	0,8	Soviet	26	7,3

The average age of children receiving palliative care is 10 [7;11], girls - 41%, and boys - 59%. According to the structure of palliative states, non-oncological diseases prevail in Voronezh region and account for 96% of all pathologies. Of these, acquired neurological diseases prevail and account for 69.9%, congenital malformations and genetic diseases - 24.1%, other diseases - 2%. Palliative oncological pathology accounts for 4% among children of Voronezh region.

A detailed analysis of acquired neurological pathology revealed that epilepsy as an independent disease occurs in 2% of children receiving palliative care, spinal muscular atrophy - in 4.8%. The leading positions are

occupied by cerebral palsy and brain damage due to injuries, strokes, meningoencephalitis - 93.2%. At the same time, 106 children suffer from combined comorbid pathology: cerebral palsy and epilepsy.

In the structure of pathologies of congenital malformations and hereditary diseases of Voronezh region, the leading place is occupied by brain malformations (microcephaly, hemiatrophy, hydrocephalus, cysts, encephalomalacia) and account for 45.3%, Duchenne myodystrophy and other unspecified myodystrophy - 22%. Metabolic diseases account for 8.1% and are distributed as follows: adrenoleukodystrophy - 4.6%, leucinosis - 2.3%, neuronal ceroid lipofuscinosis - 1.2%.

There are 5.8% of chromosomal abnormalities which include Down syndrome – 2.3%, and Wolf-Hirshhorn syndrome, Patau syndrome, Edwards syndrome by 1.1%, respectively. Children who have hereditary diseases and receive palliative care in the Voronezh Region account for 7%: cystic fibrosis accounts for 3.5%, Rett syndrome – 2.3% and Foam-Shoiker syndrome - 1.1%. Hereditary ataxias account for 2.3% and are divided into Louis-Bar syndrome and Friedreich ataxia by 1.1%, respectively. Other malformations in children account for 8.1%: 2.3% for isolated congenital heart defects, spinal cord abnormalities (Spina bifida), malformations of the facial skeleton and 1.1% for malformations of the anterior abdominal wall (gastroschisis).

When analyzing the structure of neoplasms of children receiving palliative care, tuberous sclerosis prevails and amounts to 28.6%. Neuroblastoma, medulloblastoma and acute lymphoblastic leukemia account for 14.3%, respectively. Neurofibromatosis, glioblastoma, ovarian tumor and rhabdomyosarcoma account for 7.1%, respectively.

According to the groups of patients in need of palliative pediatric care identified by the European Association of Palliative Care in Voronezh region:

- life-threatening conditions or diseases for which curative treatment is possible, but it may be ineffective account for 5.9%, these include patients with neoplasms, severe malformations, chronic heart failure, chronic kidney disease;

- diseases in which long-term intensive treatment is aimed at prolonging life and allows for normal activity, but premature death is possible – 10.7% and include cystic fibrosis, neurodegenerative diseases, spinal muscular atrophy, myodystrophy;

- progressive conditions without curative treatment options, the therapy of which is palliative from the moment of diagnosis – 2%, these include mucopolysaccharidoses and metabolic diseases;

- irreversible, but not progressive conditions with severe disability and the patient's

susceptibility to complications are the most numerous group and account for 81.4% (cerebral palsy, genetic disorders, congenital and acquired brain/spinal cord injuries, epilepsy).

When analyzing the data obtained, it was revealed that all children need outpatient palliative care, and 71.3% of children additionally need inpatient palliative care. At the moment, 7% of children are fed with a probe, 4 children (1.1%) have a gastrostomy and nutrition occurs through it, all other patients (91.9%) feed themselves. When analyzing the method of breathing, it was revealed that 96.1% breathe independently, and 3.6% of children have a tracheostomy tube installed. Additionally, 2.2% of children need oxygen therapy, and 1.7% of patients need artificial ventilation at home. At the same time, 2% of all palliative patients are fed by the probe method and at the same time they have a tracheostomy installed.

**Conclusion.** Based on the data obtained, it was revealed that directly in the districts of the city of Voronezh, the largest number of palliative patients was detected in the Left-Bank district. Perhaps the fact that 35 manufacturing enterprises operate on the territory of the Levoberezhny district plays a role. According to the structure of the detected palliative pathologies, non-oncological diseases prevail in the children of Voronezh region, which is compared with statistical data for Russia. Also, acquired neurological diseases are most common – cerebral palsy and congenital malformations, in particular brain malformations. Oncological diseases in children, according to our data, occupy a small share (4%), whereas according to WHO, about 34% of the adult population worldwide with oncological diseases need palliative care [5]. In Voronezh region irreversible but not progressive conditions with severe disability and the patient's exposure to complications prevail, which requires the organization of a multidisciplinary approach to palliative therapy, the introduction of new diagnostic methods and rehabilitation measures.

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## ПАЛЛИАТИВНАЯ ПОМОЩЬ ДЛЯ ДЕТЕЙ ВОРОНЕЖСКОЙ ОБЛАСТИ

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***Аннотация.** Паллиативная помощь детям представляет собой отдельно развивающуюся службу паллиативной помощи. Цель данного исследования – проведение структурного анализа паллиативной помощи пациентам-детям Воронежской области. Были собраны данные 47 медицинских учреждений Воронежской области. Получены сведения о количестве детей, районе проживания, социальном статусе, диагнозе. Также оценивался способ осуществления питания и дыхания ребенка, необходимость в кислородотерапии, искусственной вентиляции легких, психологической и социальной помощи. Выявлено, что наибольшее число паллиативных пациентов находится в Левобережном районе. По структуре выявляемых паллиативных патологий у детей Воронежской области преобладают неонкологические заболевания. Также наиболее часто встречаются приобретенные неврологические заболевания – детский церебральный паралич и врожденные аномалии развития головного мозга. Онкологические заболевания у детей занимают малую долю (4%). В Воронежской области в зависимости от вероятности летального исхода преобладают необратимые, но не прогрессирующие состояния с тяжелой инвалидностью и подверженностью пациента осложнениям, что требует организации мультидисциплинарного подхода к паллиативной терапии, внедрению новых методов диагностики и реабилитационных мероприятий.*

***Ключевые слова:** паллиативная помощь, дети, паллиативная патология, Воронежская область, педиатрия, онкология.*

## X-RAY WITH TOMOSYNTHESIS AS AN ALTERNATIVE DIAGNOSTIC TOOL FOR ABNORMALITIES OF VARIOUS ETIOLOGIES

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**Abstract.** *The paper highlights tomosynthesis as a novel diagnostic tool in various pathologies, including chest organ disorders. It allows obtaining a certain number of layered images of the patient's study area in one pass of the X-ray tube, thus, improving the detectability. It is emphasised that high-quality tomograms can help to study the nature and features of small limited pathological processes of the main, lobular, zonal, segmental and subsegmental bronchi, lymph nodes of the lungs and mediastinum. The fact that the capabilities of tomosynthesis is comparable in some cases with the data of digital chest X-ray and MSCT is stressed. The aim of the study performed was to reveal the diagnostic value of chest radiography with tomosynthesis in the diagnosis of oncological diseases of various etiologies. The study included medical records of 82 patients of Voronezh oncological regional hospital. The results obtained allow concluding that tomosynthesis combines the advantages of CT, but at a lower radiation dose and cost, eliminates the main disadvantage of standard R-graphy - the overlap of objects in the image, avoids additional costly imaging methods with increased radiation exposure.*

**Keywords:** *tomosynthesis, oncological pathology of various etiology, chest organs.*

**Introduction.** Recently, there has been a growing interest in thoracic diagnostics with tomosynthesis application, which allows obtaining a certain number of layered images of the patient's study area in one pass of the X-ray tube. It improves the detectability and clarifies the characteristics of pathological changes in the chest organs detected in CR, and at the same time has a relatively low radiation load [1].

In the process of the intervention, a certain number of images of the studied area are produced in one pass of the X-ray tube. As a result, an average of 53 tomograms are obtained in the frontal plane. When using tomosynthesis for the study of small intrapulmonary foci, the sensitivity and specificity are about twice as high as with traditional radiography, and the dose load is less than with CT. This allows firstly, "unloading" the CT department, and secondly, seeing a more accurate picture of pathological changes compared with the conventional radiography.

Tomosynthesis allowed in some cases excluding the presence of a pathological process and identify additional changes, namely: signs of limited small-focal dissemination,

destruction of lung tissue, a symptom of "bronchial amputation" and "air bronchography", focal shadows, signs of rib damage, etc. In case of pneumonia, the vehicle reports additional data clarifying the extent and localization of infiltration.

According to a 2013 study by A. Terzi et al., tomosynthesis can be used as a screening method in diagnostics lung cancer in risk groups. Only high-quality tomograms can help to study the nature and features of small limited pathological processes of the main, lobular, zonal, segmental and subsegmental bronchi, lymph nodes of the lungs and mediastinum [2].

Lee et al. in 2015 compared the capabilities of tomosynthesis in determining calcification of the walls of the aortic arch with the data of digital chest X-ray and MSCT. The study showed the advantage of tomosynthesis over digital chest X-ray in identifying pleural plaques characteristic of asbestos [3].

Layer-by-layer examination can play a crucial role in identifying not only the primary cancer, but also the metastatic process. Back in 2012, H. N. Jung in his study determined the sensitivity of tomosynthesis in de-

termining lung metastases in patients with colorectal cancer and also revealed the superiority of tomosynthesis over CR. With the help of tomosynthesis, 83% were noted, and with CR – 27% of the foci of their total number detected with MSCT [4].

Thus, tomosynthesis can be used in the assessment of metastatic lung damage with different localization of the primary focus. Tomosynthesis allows identifying individual small shadows of metastases in metastatic tumors that are invisible when using other methods of X-ray examination.

Thus, it is possible to use 4 options of tomosynthesis to improve the detection of pulmonary foci:

- 1) as an additional technique to the CR instead of BP;
- 2) as a clarifying technique after the identified focus in CR;
- 3) as a method of tracking and monitoring previously identified formations;
- 4) screening of risk groups.

The layered examination of the normal and pathologically altered lungs occupies a special place among other numerous, well-developed and evidenced-based methods of lung investigation.

Therefore, the **aim of the study** was to reveal the diagnostic value of chest radiography with tomosynthesis in the diagnosis of oncological diseases of various etiologies.

**Materials and methods.** The study included diagnostic findings of 82 patients who were admitted to Voronezh oncological hospital in February 2022: 30 women, 52 men, aged 36-85. All patients had oncopathology of various etiologies; they were administered R-graphy of the chest with tomosynthesis to specify the diagnosis. Visualization was performed with a Shimadzu apparatus. Alternative methods of instrumental examination of chest organs - ultrasound, CT, MRI - were not used.

**Results.** Malignant neoplasms of the mammary gland were diagnosed in 17 patients: in 7 of them, R-graphy of the chest with tomosynthesis revealed R-signs of subtotal/total exudative pleurisy, in 10 of them pneumofibrosis of the upper/lower lobes of the lung was observed. In 13 patients, the

main diagnosis was a benign neoplasm of the breast. Visualization of the chest showed single focal compaction of the lung parenchyma, focal/diffuse-focal fibrosis.

Malignant neoplasm of the bronchi was diagnosed in 9 male patients. Imaging revealed R-signs of subtotal/total exudative pleurisy. 15 patients had benign neoplasms of the skin, in 17 patients the main diagnosis was a benign neoplasm of the pancreas. Their X-ray images showed pneumofibrosis, focal fibrosis; X-ray data for mts of the chest organs were not revealed. Benign neoplasms of bones and articular cartilage were diagnosed in 9 patients; no X-ray data for mts were found on their images. Small-focal lesions of bone structures (mts?) were observed.

One patient was referred to the hospital with complaints of dysuria; since 2013 he was observed by a urologist with prostatic hyperplasia. The examination plan included R-graphy of the chest with tomosynthesis. The picture showed rough fibrous bands, areas of compaction of the stranded structure of the lung tissue and pleura, calcifications; in the left lung in S6, areas of compaction up to 2.4x0.5 cm with cords to the costal pleura and root; domes of the diaphragm are deformed by adhesions; formation on the head of the left lung up to 4.2x3.8 cm with a bumpy contour. A conclusion was made about post-tuberculous changes in the lungs and the formation of the head of the left root (Susp centr. c-r).

**Conclusion.** Tomosynthesis combines the advantages of CT, but at a lower radiation dose and cost. This method allows multiple sections to be reconstructed from a single image, thus providing improved visibility of anatomical structures. Tomosynthesis eliminates the main disadvantage of standard R-graphy - the overlap of objects in the image, which can lead to misdiagnosis. It avoids additional imaging methods with increased radiation exposure and high cost.

R-graphy is the main tool in the diagnosis of chest organ diseases. R-graphy with tomosynthesis allows to accurately and quickly visualizing the anatomical structures, making a diagnosis, prescribing treatment, which is vital for cancer patients.

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## РЕНТГЕНОГРАФИЯ С ТОМОСИНТЕЗОМ КАК АЛЬТЕРНАТИВНАЯ ДИАГНОСТИЧЕСКАЯ ОПЦИЯ ПРИ ПАТОЛОГИЯХ РАЗЛИЧНОЙ ЭТИОЛОГИИ

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***Аннотация.** В статье рассматривается томосинтез как новый метод диагностики при различных патологиях, в том числе при заболеваниях органов грудной клетки. Этот метод позволяет получить определенное количество послойных изображений исследуемой области за один прием, тем самым повышая выявляемость. Подчеркивается, что качественные томограммы позволяют изучить характер и особенности мелких ограниченных патологических процессов главных, долевого, зональных, сегментарных и субсегментарных бронхов, лимфатических узлов легких и средостения. Обращается внимание на тот факт, что возможности томосинтеза в ряде случаев сопоставимы с данными цифровой рентгенографии органов грудной клетки и МСКТ. Целью проведенного исследования явилось выявление диагностической значимости рентгенографии органов грудной клетки с томосинтезом в диагностике онкологических заболеваний различной этиологии. Был проведен анализ медицинских карт 82 пациентов Воронежского областного онкологического диспансера. Полученные результаты позволяют сделать вывод, что томосинтез сочетает в себе преимущества КТ, но при меньшей дозе облучения и стоимости, устраняет основной недостаток стандартной Р-графии - перекрывание объектов на изображении, позволяет избежать дополнительных затратных методов визуализации с повышенной лучевой нагрузкой.*

***Ключевые слова:** томосинтез, онкологическая патология различной этиологии, органы грудной клетки.*

## BIOMARKERS OF KIDNEY INJURY IN CHILDREN WITH LEUKEMIA AFTER ANTICANCER THERAPY

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**Abstract.** *The paper deals with the problem of kidney injury in children with leukemia after anticancer therapy. It is stated that cancer incidence has a steady growing trend all over the world, including the children population of Russia. It is reported that a significant proportion of childhood cancer survivors suffer serious late complications, including heart failure, neurotoxicity, nephrotoxicity, growth failure, hormonal disorders, and secondary cancers. Therefore, current research is focused on the problems of early diagnosis even in the "asymptomatic" period of the disease. Special attention is paid to early diagnosis of kidney disorder in children with leukemia who have received anti-cancer treatment. The aim of research was to study the markers of kidney damage after completion of polychemotherapy and radiation therapy. The results obtained demonstrate that in the first two years after completion of anticancer therapy children with acute lymphoblastic leukemia (ALL) had an increased level of urinary kidney damage-1 molecule (KIM-1). It is highlighted that further long-term follow-up studies are necessary to assess the significance of the urinary KIM-1 and cystatin C in the blood serum and their relationship to kidney damage after anticancer treatment in childhood.*

**Keywords:** *leukemia, children, anticancer therapy, nephrotoxicity, biomarkers, kidney damage, CKD.*

Cancer incidence has a steady growing trend all over the world, including the children population of Russia. Implementation of the National Project "Healthcare" (the federal project "Fight against Cancer"), significantly improved results of anticancer treatment and accompanying support in children. The project has also resulted in a wider introduction of anticancer drugs into clinical practice, progress in studying the molecular biological features of the disease, search for the main immunological, cytogenetic and molecular targets for epigenetic therapy, contribute to the survival of patients with cancer [1-4]. Up to 40% of childhood cancer survivors suffer serious late complications, including heart failure, neurotoxicity, nephrotoxicity, growth failure, hormonal disorders, and secondary cancers [5]. Cancer survivors are at risk for early and late renal side effects, including CKD and kidney failure, impaired (estimated) GFR, proteinuria, hypomagnesaemia, hypophosphatemia, impaired tubular phosphate reabsorption, and hypertension. The prevalence of long-term renal outcomes ranges from 0 to 84% [6]. Green DM. et al. 2021

found that 2.1% of 2753 adult childhood cancer survivors diagnosed  $\geq 10$  years ago had stage 3-5 CKD according to the KDIGO 2012 criteria [7]. Anticancer chemotherapy is associated with nephrotoxic side effects that affect long-term consequences, and their study is of particular relevance [8]. Late complications not only seriously impair the quality of life of patients and cause higher rates of hospitalization, but in 15% of cases become the direct cause of patient death [9-11]. Therefore, current research is focused on the problems of early diagnosis even in the "asymptomatic" period of the disease. Early diagnosis of kidney disorder in children with leukemia who have received anti-cancer treatment is essential in prevention of development and progression of chronic kidney disease. Currently the new diagnostic approach is the assessment of kidney function using new biomarkers that are more sensitive and specific in relation to the functional state of the kidneys compared to blood creatine. The presence of markers of kidney damage is possible in the early stages from the onset of the development of the pathological process to establish the level of



manifestation of the nephron. It is worth noting that biomarkers are detected in children with severe early injury and recovery before proteinuria or serum creatinine reveal irreversible expansion and disappearance of the nephron [12]. The aim of our research was to study the markers of kidney damage after completion of polychemotherapy and radiation therapy.

**Methods.** We examined 39 children with acute lymphoblastic leukemia (ALL) after anticancer therapy (22 boys and 19 girls) aged  $10,7 \pm 3,7$  years. They received anticancer therapy according to approved treatment protocols. The examination period from the end of anticancer therapy ranged from 2 weeks to 6,5 years. The patients were divided into 3 groups: Group I - patients with a period of 2 weeks to 2 years from completion of the therapy; Group II - patients with a period of 2 years to 4 years from completion of the therapy, and Group III - patients with a period of 4 to 6.5 years from completion of the therapy. The control group included 50 children (25 boys and 25 girls) at the age of  $10,7 \pm 4,8$  years of I-II health groups. All children in the control group had estimated glomerular filtration rate (eGFR)  $> 90$  ml / min / 1,73 m<sup>2</sup>, urine tests and kidney ultrasound data were normal, SDS BMI was from -1 to +1. Formulas based on serum creatinine and cystatin C concentrations (CKiD U25 using age-dependent coefficient) were used to calculate eGFR. Lipocalin associated with neutrophilic gelatinase (NGAL),  $\beta$ 2-microglobulin ( $\beta$ 2-m), kidney damage-1 molecule (KIM-1), interleukin 18 (IL-18), in blood serum - cystatin C were studied by ELISA method. The results were presented as a median and interquartile range [IQR]. Comparison between groups was performed using the Mann-Whitney U test.

**Results.** Children of Group I had the level of urinary KIM -1 - 323.19 pg / ml [150.43-888.55], which was significantly higher according to the control group: 162.35 pg/ml [95.85-253.95],  $p=0.009$ . Urinary  $\beta$ 2-m /UCr - 0.85 mkg / mg [0.35-7.55], urinary IL -18 /UCr - 26.36 pg/mg [17.32-39.05] were even lower than in control group;  $\beta$ 2-m /UCr - 4.63 mkg/mg [1.75-9.43],  $p=0.035$ , IL-18 /UCr - 44.86 pg/mg [35.03-58.15],  $p= 0.018$ . All uri-

nary markers in children from Group II and Group III did not differ from those in the control group. The level of cystatin C in blood serum in all three groups of patients was higher than in the control group 0.47 mg/l [0.43-0.53]: 1-st group - 0.62 mg/l [0.54-0.86],  $p<0.001$ ; 2-nd group - 0.6 mg/l [0.48-0.64],  $p=0.024$ ; 3-d group - 0.57 mg/l [0.51-0.63],  $p=0.004$ .

**Discussion.** The influence of anticancer treatment, especially radiotherapy and nephrotoxic agents such as ifosfamide and cisplatin, on kidney function is well known in patients with ALL treated in childhood. Bárdi E. et al., 2004, found that the level of serum cystatin C remains elevated after the end of specific therapy [13]. In a study by Grevtseva E., 2017, children were identified with persistent elevated levels of cystatin C and interleukin-18 in the blood serum after the end of specific therapy [14]. Zubowska et al., 2013, studied the role of IL-18, IMT-1, and beta2-microglobulin in the detection of chronic kidney disease in cancer patients after the end of treatment. The author concluded that beta2-microglobulin and especially IL-18 can be used as early markers of chronic damage to the proximal tubules in children after chemotherapy [15]. Latoch E et al., 2021, evaluated urinary beta2-microglobulin levels in children with leukemia. The authors found a significantly higher concentration of beta2-microglobulin in the urine in children with a longer follow-up period (more than 5 years after treatment) [16]. In another study by the same authors, it was shown that children 5 years after the end of treatment had higher levels of KIM-1, NGAL compared with those whose time from the end of therapy did not exceed 5 years at the time of the study [17].

But there are studies demonstrating that in children with ALL these markers remain normal after anticancer therapy. Krawczuk-Rybak M et al. reported that after the completion of specific therapy, renal function in children returned to normal, despite previous use of nephrotoxic drugs. Cystatin C in blood serum, beta2-microglobulin and cystatin C in urine after the end of specific therapy were the same in the analyzed and control group of healthy children [18]. Kaya Z et al. concluded that renal toxicity for low-risk ALL resolves

slowly, leaving almost no significant late nephrotoxicity in survivors [19].

In the current study we tried to find out whether biomarkers are elevated in survivors of childhood ALL patients compared to control group.

There are several limitations of this study. It was a single-center analysis, with a relatively small number of patients. We did not evaluate the levels of biomarkers before the start of treatment, during exposure to chemotherapy or at the end of therapy. The strengths of our research include the homogenous group of acute lymphoblastic leukemia survi-

vors, relatively long follow-up time and no ethnic diversity.

**Conclusions.** In the first two years after completion of anticancer therapy children with ALL had an increased level of urinary KIM -1. The level of cystatin C in the blood serum after completion of the polychemotherapy and radiation therapy remains elevated during 6 years. Further long-term follow-up studies are necessary to assess the significance of the urinary KIM-1 and cystatin C in the blood serum and their relationship to kidney damage after anticancer treatment in childhood.

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## БИОМАРКЕРЫ ПОВРЕЖДЕНИЯ ПОЧЕК У ДЕТЕЙ С ЛЕЙКОЗАМИ ПОСЛЕ ОКОНЧАНИЯ ПОЛИХИМИОТЕРАПИИ

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*Аннотация.* Статья посвящена проблеме поражения почек у детей с лейкозом после противоопухолевой терапии. Установлено, что заболеваемость раком имеет устойчивую тенденцию роста во всем мире, в том числе и среди детского населения России. Сообщается, что значительная часть выживших после рака в детстве страдает серьезными поздними осложнениями, включая сердечную недостаточность, нейротоксичность, нефротоксичность, задержку роста, гормональные нарушения и вторичный рак. Поэтому современные исследования сосредоточены на проблемах ранней диагностики даже в «бессимптомном» периоде заболевания. Особое внимание уделено ранней диагностике патологии почек у детей, больных лейкозом, получающих противоопухолевое лечение. Целью исследования было изучение маркеров поражения почек после завершения полихимиотерапии и лучевой терапии. Полученные результаты свидетельствуют о том, что в первые два года после завершения противоопухолевой терапии у детей с острым лимфобластным лейкозом (ОЛЛ) повышен уровень молекулы мочевого повреждения почек-1 (КИМ-1). Подчеркнута необходимость дальнейших долгосрочных катамнестических исследований для оценки значимости мочевого КИМ-1 и цистатина С в сыворотке крови и их связи с поражением почек после противоопухолевого лечения в детском возрасте.

**Ключевые слова:** лейкоз, дети, полихимиотерапия, нефротоксичность, биомаркеры, повреждение почек, ХБП.

## LONG-TERM OUTCOMES OF TREATMENT FOR PATIENTS WITH LOCALLY ADVANCED HIGHLY DIFFERENTIATED THYROID CANCER

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**Abstract.** *An analysis was made of 52 outpatient records of patients with locally advanced thyroid cancer who received treatment at the VOKOD Health Center in the period from 2012 to 2017. All 52 patients were referred for radioiodine therapy. Moreover, a relapse of the disease was detected in 3.8% of cases, the appearance of regional metastases in 30.7%, and the generalization of the process in 15.4%. The stabilization of the process was observed in 45.6% of cases.*

**Keywords:** *thyroid gland, papillary cancer, radioiodine therapy*

**Relevance.** Thyroid cancer as a nosological form is currently one of the most frequently diagnosed in modern oncology. Due to the fact that recently there has been a significant increase in this pathology, especially among young people, the study of thyroid cancer is highly relevant [1-3]. Therefore, the problem of diagnosis and the choice of further treatment of thyroid cancer is particularly acute. The progressive development of modern science opens up new prospects for identifying individual characteristics of differentiated forms of thyroid cancer and choosing an individual approach to each patient. The treatment plan for highly differentiated (papillary and follicular) thyroid cancer involves surgical intervention, which is often supplemented with radioiodotherapy, radioiodotherapy involves the procedure of destruction of residual thyroid tissue with radioactive iodine after surgical treatment [7, 8]. The use of radioactive iodine occupies one of the leading places in the diagnosis and treatment of thyroid cancer metastases. Most often, the areas of distant metastasis of thyroid cancer are the lungs [4, 5]. Due to the selective accumulation of I-131 in metastatic foci, with minimal radiation load on the patient, and the absence of serious complications, this method of therapy allows not only to achieve stabilization, improvement of the patient's condition, but also to lead to a complete cure [6, 9, 10].

Tasks: 1. To determine the relapse-free survival of patients; 2. To estimate the num-

ber of cases of stabilization and generalization of the process.

**Objective:** to analyze the results of treatment in patients with thyroid cancer over the past 5 years.

**Materials and methods.** The analysis of 52 outpatient records of patients with locally advanced thyroid cancer, with courses of radioiodotherapy, who were treated at the VOCOD Medical Center in the period from 2012 to 2017, was carried out. The patients underwent surgery - thyroidectomy in 19.2%, thyroidectomy with fasciofutular excision of the neck tissue - in 25%, primary hemithyroidectomy was performed in 1 case, and primary subtotal resection of the thyroid gland in 2 cases. All 52 patients were referred for radioiodotherapy due to the local spread of the process. Evaluation of the results of treatment was carried out on the basis of a number of studies: ultrasound of the thyroid gland and lymph nodes of the neck, scintigraphy of the whole body, ultrasound of the abdominal cavity and chest X-ray. When analyzing outpatient patient records, it was determined that the number of sick women (43 people) significantly prevails over the number of men (9 people). It was decided to divide all patients into 2 large groups: patients who were treated with radioactive iodine once, and patients who were treated with radioactive iodine two or more times. The first group included 34 people, among whom there were 16 persons under the age of 45 (all with stage 1 of the disease). In the second group of pa-

tients, 18 people were counted, 11 persons under 45 years of age (8 with the first stage, 3 with the second). Separately, a group of patients who died due to the generalization of the process was taken out, there were 2 of them. The analysis of pathohistological findings among patients of both groups revealed a significant advantage of papillary cancer (42 cases) over follicular and papillo-follicular (2 and 4, respectively). The number of patients who completed treatment with radioactive iodine in September 2017 is 42 people (31 in the first group and 11 in the second). Another course of radioiodotherapy is planned for 10 people (all representatives of the 2nd group).

**Results and their discussion.** Analyzing the relapse-free survival, 21 people were counted in the first group, in whom metastases and relapses were not detected after surgery either before or after radioiodotherapy. Almost all relapses (1 case) and metastases (7 cases) were recorded after primary subtotal

resection (5 out of 6 cases). Two patients were diagnosed with the 2nd cancer in the period between surgical treatment and the beginning of radioiodotherapy. In the second group, 2 people were recorded without relapses and metastases. Relapse was recorded in the 1st person, before the start of radioiodine therapy, he was subsequently diagnosed with a second cancer. Metastases in the left neck were detected in 9 people, both before the start of radioiodine therapy and during treatment. Metastases to the lungs were detected in 3 people, in one-in the left mediastinum.

#### **Conclusions.**

1. Out of 52 patients, relapse of the disease was detected in 3.8% of cases;
2. The appearance of regional metastases in 30.7%, generalization of the process in 15.4%;
3. Stabilization of the process from 52 patients was observed in 45.6% of cases.

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**ОТДАЛЕННЫЕ РЕЗУЛЬТАТЫ ЛЕЧЕНИЯ БОЛЬНЫХ  
МЕСТНОРАСПРОСТРАНЕННЫМ ВЫСОКОДИФФЕРЕНЦИРОВАННЫМ  
РАКОМ ЩИТОВИДНОЙ ЖЕЛЕЗЫ**

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***Аннотация.** Произведен анализ 52 амбулаторных карт пациентов с местно распространённым раком щитовидной железы, которые получали лечение в БУЗ ВО «ВОКОД» в период с 2012 по 2017 год. Все 52 пациента были направлены на радиойодтерапию. При этом рецидив заболевания был обнаружен в 3,8% случаев, появление регионарных метастазов в 30,7%, генерализация процесса в 15,4%. Стабилизация процесса наблюдалась в 45,6% случаев.*

***Ключевые слова:** щитовидная железа; папиллярный рак; радиойодтерапия.*

## MODERN OPTIONS FOR PRESBYOPIA CORRECTION IN PATIENTS WITH COVID-19

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***Abstract.** This review discusses current options of pharmacotherapy in the treatment of patients with age-related refractive disorder – presbyopia - combined with COVID-19 viral infection. Various treatment options are currently being developed to correct presbyopia, but all of them involve either eyeglass correction, or surgical intervention with application of intraocular lenses. Drug therapy in this case is preferable, since it is less cost-effective, and patients comply more readily to this type of treatment. The application of myotics for presbyopia correction, as well as the combinations of myotics and other drugs for additive treatments and side effects reduction are well documented; however, there is no sufficient data on the results of such treatment. Currently, pyrenoxine, being a component of Catalin-eye drops, has been studied in this regard. It prevents the appearance of quinoid compounds in the lens, which lead to a decreased lens elasticity and, accordingly, to the development of presbyopia. The use of Catalin-eye drops in patients with COVID-19 is especially relevant, since this virus appears to be a predictor of metabolic disorders development. It is necessary to further study Pyrenoxine as a substance that effectively reduces risks of presbyopia development.*

***Keywords:** presbyopia, quinoid compounds, drug treatment, pyrenoxine, myotics.*

### **Mechanisms of presbyopia development.**

Presbyopia is a refractive error, which is defined as a violation of near vision. This condition is typical for all people over 55 and is obviously associated with aging of the body. In 2011, there were 1.272 billion cases of presbyopia worldwide [1]. In addition, the global prevalence of presbyopia is projected to increase to 1.8 billion by 2050 [2]. The potential productivity burden of uncorrected or insufficiently corrected presbyopia was estimated at \$ 25.367 billion, or 0.037% of the world's gross domestic product in 2011 [1]. Presbyopia affects not only near vision, that is, at a distance of 20 to 40 cm from the eyes, but also intermediate vision, that is, at a distance of 50 to 100 cm from the eyes. Regularities of structural and functional changes in the organ vision in presbyopia remains unclear, the root cause of presbyopia is unknown, and the mechanisms leading to loss of accommodation are not defined.

Accommodation is a mechanism that allows the eyes to adjust their refractive power to focus on close objects. There are three main processes involved in accommodation. They are (1) contraction of the ciliary muscle,

which in turn reduces zonular tension and leads to an increase in lens thickness, (2) constriction of the pupil, and (3) convergence of both eyes. A common cause of presbyopia is lens compaction, which restricts the accommodation of the lens.

**Options of presbyopia correction.** Treating and correcting presbyopia is still challenging, as there are no medications or procedures that can produce perfect vision at all distances without risk. Currently, there are several treatment options for presbyopia: optical correction, including bifocal or progressive glasses, monofocal or multifocal contact lenses, corneal or intraocular surgical procedures, and pharmacological treatment. Optical correction with eyeglasses, such as monofocal, bifocal or multifocal lenses, are common options due to an easy and non-invasive access. However, eyeglasses are perceived by many patients as uncomfortable.

Multifocal contact lenses can be an alternative to glasses, but they can cause discomfort or inconvenience in some patients, especially in those who have no experience of wearing contact lenses. Surgical options, corneal or intraocular, are of increasing inter-



est, as they are based on the most modern technologies. Corneal surgery, such as corneal monovision, corneal insertions, collagen shrinkage, or multifocal LASIK, has been one of the common methods of correcting presbyopia. They have demonstrated success in improving near vision, but there are drawbacks, such as reduced middle or far vision, reduced contrast sensitivity, dysphotopsia, or refractive regression. Due to this, some patients still need eyeglasses after the procedures.

Pharmacological treatment of presbyopia has been studied in recent years based on various drugs and different treatment regimens. Pharmacological treatment, in theory, may offer the advantage of having a condition without glasses with a lower risk of irreversible eye complications compared to surgery. In November 2021, the U.S. Food and Drug Administration approved pilocarpine hydrochloride, a 1.25% ophthalmic solution (AGN-190584), as an eye drop for the treatment of presbyopia [3]. Inducing miosis may not be an ideal solution for treating presbyopia, since miosis itself is not a physiological condition of the eye. After the approval of 1.25% ophthalmic solution pilocarpine in the United States, patients experienced the drug application with different effects. According to initial data from online sites, some patients reported that the drug improved their myopia for approximately two hours, while others did not notice any differences compared to their initial condition [4].

Finally, Tsuneyoshi Y, Higuchi A, Negishi K, Tsubota K. demonstrated that pyrenoxine is effective in treating presbyopia by slowing down the development of lens opacities and preserving its elastic properties [5].

**Presbyopia and COVID-19.** According to D. M. Dockery et al. (2020), data on eye damage in COVID-19 are underestimated, since emergency and hospital doctors usually do not pay attention and do not record eye symptoms that seem insignificant for the patient's general condition [6]. However, according to Kazuno Negishi, Masahiko Ayaki, stress and rapid digitalization associated with strict infection control and quarantine during a pandemic COVID-19 may be contributing factors to the development of presbyopia [7]. Long waiting times for surgery are also asso-

ciated with anti-epidemic measures and restrictions that are currently related to COVID-19 pandemic [8].

M. Kovalevskaya et al. demonstrated that the level of peroxiredoxine in the lacrimal fluid of patients with cataracts is reduced [9]. Pyrenoxine-eye drops have been reported to reduce optical density in the layers of the cortical lens and under the posterior capsule in humans [10]. It has also been reported that higher lens density impairs contrast sensitivity [11]. Correlation of nuclear cataract lens density using Scheimpflug images with the lens opacity classification system and visual function and the near visual function of presbyopia is improved by increasing contrast [12]. The above facts give rise to the need for prescribing drug therapy in the form of eye drops containing pyrenoxine to elderly and senile patients who have undergone COVID-19. As stated, this fact will prevent a decrease in the elastic properties of the lens and, accordingly, presbyopia.

**Catalin.** The mechanism of action of Catalin (pyrenoxine)-eye drops is based on competitive inhibition of quinoid substances and pre-protection of the SH group of lens proteins from oxidation. In the study evaluating the effectiveness of cataractogenesis prevention in patients with epiretinal membrane after vitrectomy, it was demonstrated that a pyrenoxine-based drug is highly effective in preventing the development of cataracts in this group of patients [13]. Tsuneyoshi et al. have demonstrated that pyrenoxine is effective in the treatment of presbyopia by slowing down the development of opacities of the lens and preserving its elastic properties [5]. Catalin-eye drops are effective in protecting the lens from oxidative stress, especially in the early stages of cataract development [14].

Catalin-eye drops containing pyrenoxine were first registered in Japan in 1958 by Senju Pharmaceutical and are currently used in more than 20 countries around the world. The effectiveness of Catalin has been proven in both clinical and laboratory studies. J. Kociecki et al. conducted a study which included 72 patients over 40 with the initial stage of age-related cataracts and visual acuity of at least 0.5%. Of these, 35 patients received Catalin instillations, 37-placebo [15]. Results

were evaluated in 3, 6, 12, 18, and 24 months using densitometric measurements of lens transparency on an anterior segment analyzer EAS-1000 (Nidek, Japan). Catalin-eye drops in the treatment of patients with presbyopia are the most effective means that slows down the decrease in the elastic properties of the lens. The cumulative effect of the drug was observed in 18 months of treatment. Catalin-eye drops are well tolerated by patients even for long-term application. Detailed observation of patients who used Catalin manifested the intensity of opacities decreased by 3.9%, while in the control group, the intensity of opacities increased by 4.6% [15].

**Conclusion.** Studies of drugs that could affect age-related changes in refraction are conducted in various areas. Over the past few decades, research has focused on pharmacological strategies to prevent and decelerate progression of presbyopia using Pyrenoxine. Adequate tolerability of the drug is important for patients of all age groups, and side effects are extremely rare. High therapeutic efficacy and safety with long-term use allow recommending Catalin-eye drops for prevention of presbyopia progression. Further research on the use of pyrenoxine are required.

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## СОВРЕМЕННЫЕ МЕТОДЫ ВОЗДЕЙСТВИЯ НА РАЗВИТИЕ ПРЕСБИОПИИ У ПАЦИЕНТОВ С ПЕРЕНЕСЁННЫМ COVID-19

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***Аннотация.** Данный обзор освещает современные возможности фармакотерапии в лечении пациентов с возрастным нарушением рефракции - пресбиопией, развившейся на фоне перенесённого инфицирования вирусом COVID-19. Различные методы лечения разработаны в настоящее время для коррекции пресбиопии, однако все они подразумевают использование очковой коррекции, а также оперативное вмешательство с постановкой интраокулярных линз. Медикаментозная терапия в данном случае является предпочтительной, поскольку предполагает минимальное количество материальных затрат, а также комплаентность пациентов к такому виду лечения. Достоверно известно о применении миотиков для лечения пресбиопии, а также комбинаций миотиков и других препаратов для достижения аддитивных методов лечения и снижения риска развития побочных эффектов, однако данные о результатах такого лечения отсутствуют. В настоящее время исследовано вещество Пиреноксин, которое входит в состав глазных капель Каталин. Оно предотвращает появление хиноидных соединений в хрусталике, которые приводят к снижению эластичности хрусталика и, соответственно, к развитию пресбиопии. Особенно актуально применение глазных капель Каталин у пациентов с перенесённым COVID-19 как предиктором развития метаболических нарушений. Необходимо продолжить исследование Пиреноксина как вещества, эффективно снижающего риски развития пресбиопии.*

***Ключевые слова:** пресбиопия, хиноидные соединения, медикаментозное лечение, пиреноксин, миотики.*

## IMPLEMENTIERUNG VON FERNUNTERRICHT IM KONTEXT VON COVID-19 IN RUSSLAND UND IN DEUTSCHLAND

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**Zusammenfassung.** Die Verbreitung von Covid 19 wurde für Universitäten festgelegt, um neue Bildungstechnologien in den Bildungsprozess einzuführen, die eine qualitativ hochwertige Bildung bieten und Bedingungen schaffen sollten, um die Ausbreitung von Covid zu stoppen. Bildungseinrichtungen waren gezwungen, elektronische Technologien und Fernunterricht in den Bildungsprozess einzuführen, was sowohl positive als auch negative Seiten hatte. Fernunterricht hat sowohl in Russland als auch in westlichen Ländern seine eigenen Besonderheiten.

**Schlüsselwörter:** neue Bildungstechnologien, Fernstudium, Bildung, Online-Lernen, Fernunterricht, Fernunterrichtstechnologien.

**Einführung.** Die Verbreitung von COVID-19 hat Gesundheitsfachkräfte im Zusammenhang mit der schnellen Diagnose und medizinischen Versorgung von Patienten vor Herausforderungen gestellt, und für medizinische Universitäten die Notwendigkeit, Fernunterricht einzuführen. Der Begriff „Distance Education“ wurde erstmals 1892 an der University of Wisconsin in der Liste der Fernstudiengänge verwendet [1] und spiegelte die Besonderheiten des Fernunterrichts (Fernstudium) wider, d.h. Ausbildung am Wohnort außerhalb der Bildungseinrichtung. Es sei darauf hingewiesen, dass der Fernunterricht zuerst in Russland als Institut für Fernunterricht organisiert wurde und dann andere Länder dem Beispiel Russlands folgten. Bis Mitte der 1970er Jahre. dieser Begriff definierte die Korrespondenzform der Bildung [2].

Neben dem Begriff „Fernunterricht“ wird in der fremdsprachigen Literatur und pädagogischen Praxis auch der Begriff „Fernunterricht“ verwendet, der den eigentlichen Lernprozess widerspiegelt, darunter das Unterrichten „Lehren“, das in Zusammenarbeit mit einem Lehrer durchgeführt wird, und das Selbststudium „Lernen“. Dennoch werden in der ausländischen Literatur die Begriffe „Distance Education“, „Distance Learning“ und „Distance Teaching“ als Synonyme verwendet [3].

Die Begriffe „Bildung“, „Ausbildung“, „Lernen (Lehren)“ haben unterschiedliche

Bedeutungen. Und in dieser Hinsicht umfasst der Begriff "Bildung" als Ergebnis der Ausbildung und Ausbildung einer Person, die sich in der Bildung eines Systems von Wissen, Fähigkeiten und Fertigkeiten sowie der Bildung persönlicher Qualitäten ausdrückt. In diesem Fall bedeutet der Begriff "Fernunterricht" eine Ausbildung, die unter Verwendung von Ferntechnologien (Fernunterricht) erworben wurde.

Bei der Umsetzung des Fernunterrichts werden die folgenden Grundsätze umgesetzt:

- Der Lernprozess baut hauptsächlich auf der eigenständigen kognitiven Aktivität des Schülers auf;
- Die kognitive Aktivität des Schülers muss aktiv sein;
- Fernunterricht sollte studierendezentriert sein.

Durch die vollständige Umstellung auf Online-Lernen hat sich in letzter Zeit der Umfang des Lehrstoffs geändert, der Prozess der Einführung verschiedener E-Learning-Methoden hat sich stark beschleunigt und die bisher bekannten digitalen Technologien und technischen Lösungen selbst wurden auf ihre Angemessenheit getestet ihre Anwendung bei einem deutlich gewachsenen Publikum, das gleichzeitig Zugang zu diesen Ressourcen erhielt. Im Gegensatz zu anderen Fachgebieten hat das Lehren an medizinischen Universitäten jedoch seine eigenen Besonderheiten und Schwierigkeiten und erfordert auch die

besondere Aufmerksamkeit der Lehrer, da es hier um die qualitativ hochwertige Ausbildung zukünftiger Fachärzte geht, von denen die Gesundheit ihrer zukünftigen Patienten abhängen wird.

Um jedoch die Ausbreitung der neuen Coronavirus-Infektion COVID-19 zu verhindern, haben die medizinischen Universitäten auf die Durchführung aller Bildungsprogramme der Hochschulbildung (Facharzt, Residenz, Aufbaustudium), der sekundären Berufsbildung und der zusätzlichen Berufsbildung umgestellt. Bildung erfolgt ausschließlich unter Verwendung von engl. E-Learning und Distance-Learning-Technologien (Fernunterrichtstechnologien).

Teil 1 von Artikel 16 des Bundesgesetzes vom 29. Dezember 2012 Nr. 273-FZ „Über Bildung in der Russischen Föderation“ enthält die folgende Definition von E-Learning (EL). EL ist die Organisation von Bildungsaktivitäten unter Verwendung von Informationen, die in Datenbanken enthalten sind und bei der Durchführung von Bildungsprogrammen und Informationstechnologien verwendet werden, technische Mittel, die ihre Verarbeitung gewährleisten, sowie Informations- und Telekommunikationsnetze, die die Übertragung der angegebenen Informationen über Kommunikation gewährleisten. Linien, die Interaktion von Studierenden und Lehrern [4]. Unter Fernunterrichtstechnologien werden Bildungstechnologien verstanden, die hauptsächlich unter Verwendung von Informations- und Telekommunikationsnetzen mit indirekter (ferner) Interaktion zwischen Studierenden und Lehrern implementiert werden.

Um die Ausbreitung von SARS-CoV-2 zu verhindern, genehmigte staatliche medizinische Universität in Woronesh die „Vorschriften über die Verwendung von E-Learning, Fernunterrichtstechnologien bei der Durchführung von Bildungsprogrammen der Hochschulbildung und weiterführende Berufsausbildung an der Universität vom 25. Dezember 2020 Nr. 1141, wonach die grundlegende Technologie für die Organisation des Bildungsprozesses an der Universität unter Verwendung von E-Learning und Distance-Learning-Technologien.

Die Internettechnologie ist die Verwendung von global und lokal basierten Compu-

ternetzwerken, um die Studierende den Zugang zu Informationsressourcen und die Bildung einer Reihe von methodischen, organisatorischen, technischen und Software-Tools für die Implementierung und Verwaltung des Bildungsprozesses zu ermöglichen, unabhängig vom Standort [5].

**Ergebnisse.** Unter den Bedingungen der Einhaltung von Anti-Epidemie-Maßnahmen wird das Fernlernsystem zur Umsetzung des Bildungsprozesses verwendet, der ein struktureller Bestandteil der elektronischen Informations- und Bildungsumgebung der Universität ist.

Die Basis der Distance-Learning-Technologien (des Fernstudiums) ist:

- LMS MOODLE (Learning Management System Modular Object-Oriented

- Dinamic Learning Environment - ein Kursmanagementsystem ist eine modulare objektorientierte dynamische Lernumgebung), in der Studierende getestet werden, die Möglichkeit haben, die dort hinterlegten Materialien (Wörterbücher, Nachschlagewerke, Alben, Atlanten, Illustrationen, visuelle Hilfsmittel. Dieses System verfügt über integrierte Analysen, mit denen Sie die Leistung der Schüler verfolgen und Schüler identifizieren können, die besonderer Unterstützung bedürfen.

- Software (Webanwendung) für die Kommunikation der Teilnehmer am Bildungsprozess im Format von Webinaren und Web-Meetings "WEBINAR (WEBINAR)". Um im WEBINAR-System zu arbeiten, plant der Lehrer ein „Meeting“. In der sich öffnenden Registerkarte werden das Unterrichtsthema, das Datum, die Gruppennummer sowie der Arbeitsplan für den Unterricht angezeigt. Als nächstes werden alle notwendigen Ressourcen geladen. Der Link zum Webinar wird an die Gruppe gesendet. Um am Unterricht teilnehmen zu können, müssen sich die Schüler anmelden: Geben Sie den vollständigen Namen, den Kurs und die Gruppennummer an. Während des Unterrichts erfolgt die Kontrolle über die Anwesenden durch Einschalten der Kameras und Identifizierung mit vollem Namen.

Bei der Durchführung von Bildungsprogrammen unter Verwendung von E-Learning und Distance-Learning-Technologien gewährt

die Universität jedem Studenten einen individuellen unbegrenzten Zugang zu den Lern-technologien der Universität von jedem Punkt, an dem Zugang zum Informations- und Telekommunikationsnetz "Internet" besteht, sowohl auf dem Gebiet der Universität als auch außerhalb während der gesamten Studienzeit.

Doch wie sieht es mit der Umstellung auf Fernunterricht in Deutschland aus, denn das europäische Land ist einer der führenden Hersteller von Hightech-Produkten in vielen Branchen auf dem Weltmarkt? Wissenschaftler stellen fest, dass Deutschland seltsamerweise nicht bereit für den Übergang zu einem Fernunterrichtsformat war. Dies lag sowohl an der großen Dokumentenflut als auch an der Position von Eltern, die glauben, dass Computer und Wi-Fi-Netzwerke sich nachteilig auf die Gesundheit von Kindern auswirken [8]. Darüber hinaus schränken deutsche Bundesvorschriften die Verwendung von Software ein, die in anderen Teilen der Welt erfolgreich im Bildungsbereich eingesetzt wird. Lehrern ist es strengstens untersagt, Cloud-Dienste, soziale Plattformen, Mikroblogging oder Tools zum Teilen von Dokumenten zu verwenden, die außerhalb der EU anlegen, denn sie keinen Konformität der Technologien mit den EU-Anforderungen haben Deutschland ist stolz darauf, die strengsten Datenschutzgesetze der Welt zu haben [8].

Das Recht der Lehrkräfte auf freie Wahl der Unterrichtsmittel, einschließlich der Nutzung digitaler Hilfsmittel, ist in den Wissenschaftsfreiheiten im Grundgesetz verankert. Deshalb haben einige Universitäten trotz staatlicher Förderung auf Druck der Professoren den Unterricht verschoben. Hier waren die Hauptargumente: Gesundheitsschädigung, Bildungsabbau und fehlender Zugang für alle Beteiligten. Andere Universitäten hatten aufgrund der Nichteinhaltung von EU-Standards, des Fehlens von Tools für Videokonferenzen, des eingeschränkten lizenzierten Zugriffs auf elektronische Bibliotheken und der langwierigen bürokratischen Verfahren zur Lösung technischer Probleme dieselben Probleme bei

der Nutzung verschiedener Programme. In Deutschland übernahm man schnell den weiter gefassten Begriff engl. Remote Teaching, der dabei half, scharfe Ecken zu glätten [9]. An manchen Hochschulen beschränkte sich die Auswahl an Lehrformen mit digitalen Technologien auf die Präsentation von Vorlesungen und Literatur als digitale Option für den Unterricht.

**Schlussfolgerung.** In dieser Situation ist der Vorteil des Fernstudiums:

- Zugänglichkeit (Beseitigung der Notwendigkeit, den Unterricht gemäß dem festgelegten Zeitplan zu besuchen, Verhinderung sozialer Kontakte von Menschen in einer schwierigen epidemiologischen Situation);
- Sichtbarkeit (Darstellung visueller Informationen);
- Fehlende Kosten (Reduzierung der Kosten für Verpflegung, Unterkunft usw.);
- Flexibilität (jederzeit Zugriff auf Material);
- Bequemlichkeit für Studenten mit Behinderungen;

Zu den Nachteilen des Fernunterrichts gehören:

- Logistik (Lernplattform nicht durch Computer unterstützt, fehlendes Internet in ländlichen Gebieten, schlechte Internetverbindung);
- Psychologische Merkmale der Bildung (es gibt keinen Lehrer in der Nähe);
- Arbeitsintensität der Trainingsunterstützung;
- Mangel an Spezialisten, um qualitativ hochwertige pädagogische und materielle Unterstützung zu schaffen;
- Psychisches Unbehagen des Lehrers.

Das Fernlernsystem wird im Ausbildungssystem des medizinischen Personals zusammen mit der traditionellen Form verwendet. Die Entwicklung des Fernstudiums schreitet in einem kolossalen Tempo voran, was eine sorgfältige didaktische Auseinandersetzung, die Entwicklung von Methoden zur Wissensbeherrschung und die Analyse der Prioritäten von Einflussfaktoren erfordert.

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### РЕАЛИЗАЦИЯ ДИСТАНЦИОННОГО ОБУЧЕНИЯ В УСЛОВИЯХ COVID-19 В РОССИИ И ГЕРМАНИИ

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***Аннотация.** Распространение Covid-19 вызвало необходимость внедрения в учебный процесс новых образовательных технологий, которые должны обеспечить качественное образование и создать условия для предотвращения распространения пандемии Covid-19. Образовательные учреждения были вынуждены использовать электронные технологии в процессе дистанционного обучения, что имело как положительные, так и отрицательные стороны. Целью настоящей работы стал анализ влияния дистанционных технологий на состояние здоровья обучающихся. В результате показаны преимущества и недостатки дистанционного обучения в аспекте здоровья обучающихся, а также выявлена специфика влияния дистанционных технологий в России и странах Европы.*

***Ключевые слова:** новые образовательные технологии, дистанционное обучение, образование, онлайн-обучение, дистанционное образование, дистанционные образовательные технологии.*

## GESUNDHEITSPROBLEME VON KINDERN UND JUGENDLICHEN MIT AKNE

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**Zusammenfassung.** Der Artikel spiegelt den Prozess der Ausbreitung von Akne in verschiedenen Ländern und auf dem Territorium der Russischen Föderation bei Kindern und Jugendlichen wider. Man untersucht die Gesundheitsprobleme im Zusammenhang mit Akne bei Kindern und Jugendlichen. Es wird Relevanz des Akneproblems und den Einfluss auf den psychischen Zustand der Kinder und Jugendlichen betont.

**Schlüsselwörter:** Akne, psychologische Zustand, Kinder und Jugendlichen, Alter, Weltgesundheit.

**Relevanz.** Die Weltgesundheit steht heute vor einer großen Herausforderung, die Gesundheit von Kindern und Jugendlichen zu verbessern. Die Probleme im Zusammenhang mit der Gesundheit von Kindern, insbesondere von Jugendlichen, wurden der Weltgemeinschaft nicht immer offengelegt, in den meisten Fällen nicht verstanden und in einigen Fällen sogar ignoriert. Jugendliche stehen im Mittelpunkt von allem, was wir erreichen wollen, und im Allgemeinen der Schlüssel zur erfolgreichen Umsetzung der Strategie für den Zeitraum bis 2030, betonte in seinem Vortrag der Generaldirektor der WHO [1].

Es ist notwendig, sich auf pubertäre Kinder und Jugendliche mit Akne konzentrieren. Laut J. Leyden sind 85 % der 12- bis 24-Jährigen, 8 % der 25- bis 34-Jährigen und 3 % der 35- bis 44-Jährigen an Akne erkrankt. Im Jugendalter leiden Jungen und Mädchen zu etwa gleichen Anteilen an Akne, während an Spätakne - überwiegend Frauen [2].

Der Zweck der Arbeit ist es, die Ausbreitung der Akne zu analysieren und Probleme im Zusammenhang mit Akne in den Ländern der Welt und auf dem Territorium der Russischen Föderation bei Kindern und Jugendlichen zu identifizieren.

Beim Studium ausländischer Quellen wurde festgestellt, dass die Meinungen westlicher und russischer Dermatologen die gleichen Merkmale der Akneerkrankung interpretieren - dies ist eine chronisch entzündliche Erkrankung der Talgdrüsenfollikel [3]. Akne ist Ergebnis eines komplexen Zusammenspiels ver-

schiedener pathogenetischer Faktoren zu nennen [4, 5]. In den westlichen Industrieländern und auch in Deutschland leidet in dieser Zeit ein großer Teil der jugendlichen Bevölkerung an Akne. Epidemiologische Daten zur Häufigkeit bei Jugendlichen reichen von 50% bis 95% [6]. In allen Ländern der Welt werden die gleichen klinischen Symptome unterschieden, wie zum Beispiel: Seborrhoe, Komedonen und Pusteln. Und einhellig sprechen sie von einem langfristigen chronischen Krankheitsprozess, dessen Behandlung mehrere Jahre dauern kann [7].

Weltexperten in Russland und im Ausland haben die Meinung, dass genetische Faktoren eine Schlüsselrolle bei der Entstehung der Krankheit spielen [8].

In der modernen Welt haben die Kinder echte psychologische Probleme. Unter Berücksichtigung sozialer Veränderungen, bei denen das Aussehen die Lebensqualität der Menschen beeinträchtigt, können die Folgen von Akne selbst zu sozialer Phobie, Missbildungen der Gesichtshaut aufgrund von Narbenbildung führen. Missbildungen, Angstzustände, Unsicherheit in sich selbst erhöhen Reizbarkeit, Vereinsamung, Misserfolge im beruflichen Umfeld, bis hin zu Depressionen, Schlafstörungen, sowohl im Kindes- als auch im Erwerbsalter [9, 10].

Bei Akne sollte die Behandlung auf zwei verwandte Zustände gerichtet sein. Einer ist das körperliche Erscheinungsbild und der andere ist die psychologische Wirkung, die Akne auf Teenager hat.



Wenn es um die Hautpflege geht, klagen Aknepatienten über übermäßige Fettigkeit. Eine Befeuchtung ist daher in der Regel nicht erforderlich. Das Quetschen von Akne führt zum Bruch des Follikels und zu einer schwereren knotigen Entzündung der Akne. Ölfreies Make-up ist erlaubt. Ein ölfreier Sonnenschutz ist ein Muss, denn Sonnenbrand verursacht Schwellungen der Epidermis und die Ausbreitung von Akne. Die Verwendung übermäßiger Mengen an Sonnenschutzmitteln und Make-up verschlimmert Akne [11].

Experten zufolge gibt es derzeit viele therapeutische Missverständnisse in der Behandlung von Akne, die damit zusammenhängen, dass die Ursachen der Akne nicht identifiziert wurden, unterschiedliche Ätiologien haben: bei den meisten Jugendlichen ist dies nicht auf pathologische Hormonspiegel zurückzuführen, viele Frauen haben Akne „hormoneller Natur“ [11].

So haben beispielsweise Experten sowohl in Russland als auch im Ausland keine gemeinsame Meinung über die Auswirkungen der Ernährung auf den Zustand von Patienten mit Akne. Einige Forscher argumentieren, dass es starke Beweise dafür gibt, dass die Ernährung Akne verschlimmern kann, für andere sind sie nicht so zuverlässig und schlüssig [12, 13, 14].

Einige Forscher glauben, dass Patienten ihre Gesamtkalorienaufnahme ausgleichen und raffinierte Kohlenhydrate, Milch, Milchprodukte, Proteinzusätze, gesättigte Fette und Transfette einschränken sollten. Sie empfehlen eine paläolithische Ernährung, die mit Gemüse und Fisch angereichert ist. [12, 13].

Viele Forscher meinen, dass drei Hauptnahrungsmittelklassen – Kohlenhydrate, Milch und andere Milchprodukte und gesättigte Fette, einschließlich Transfette – sowie ein Mangel an mehrfach ungesättigten Omega-3-Fettsäuren mit dem Auftreten und der Ausbreitung von Akne in Verbindung stehen. Die Rolle von Gamma-Linolensäure (einer Omega-6-Fettsäure), Ballaststoffen, Antioxidantien, Vitamin A, Zink und Jod muss noch aufgeklärt werden (diätinduziertes Insulin und insulinähnlicher Wachstumsfaktor 1 (IGF-1) überlagern sich auf erhöhte IGF-1-Spiegel während der Pubertät und beeinflussen die Homöostase der Talgdrüsen [13, 15].

In China wurde 2012 eine Studie mit 17.345 Personen aus 6 Großstädten durchgeführt, um unter anderem Risikofaktoren für die Prävalenz von Akne und die Beziehung zwischen Akne und der Lebensqualität der Patienten zu bestimmen. Die Ergebnisse dieser Studie zeigten, dass Akne häufiger unter Rauchern und Trinkern auftrat, sowohl bei erwachsenen Patienten als auch bei Jugendlichen. Es wurde jedoch kein Zusammenhang zwischen dem Verzehr von fettigen/würzigen Lebensmitteln und einer erhöhten Prävalenz von Akne gefunden [16].

Es ist interessant festzustellen, dass in einer chinesischen Studie, die die Lebensqualität von Patienten mit Akne untersuchte, die Ergebnisse ähnlich waren. Von 1399 Probanden mit Akne gaben 30,8 % an, dass Akne einen negativen Einfluss auf ihre Lebensqualität hatte, während andere keine Auswirkungen hatten. 79,7 % der Studienteilnehmer behandelten Akne als „natürliches“ Phänomen und nur 17,2 % betrachteten sie als Krankheit. Nur 33,5 % behandelten ihre Akne (darunter 39,0 % Frauen, 29,6 % Männer) [16].

Auch Kurt Gebauer stellt in seiner Arbeit fest, dass bei Jugendlichen Enthusiasmus und Therapietreue im Vordergrund stehen. Es ist ratsam, sich daran zu erinnern, dass diese Patientengruppe den größten Teil ihrer Gesundheitsberatung von Gleichaltrigen oder aus dem Internet bezieht. Sie schätzen den Rat qualifizierter Mediziner – Allgemeinmediziner, Dermatologen – nicht so hoch ein wie ihre Eltern [11].

**Schlussfolgerungen.** Unter Berücksichtigung des oben Gesagten kann festgestellt werden, dass die epidemiologische Situation bei Akne in verschiedenen Ländern ähnlich ist und Spezialisten aus verschiedenen Ländern Europas, Asiens und Russlands die gleichen Probleme bei der Behandlung von Patienten mit Akne haben. Somit ist Akne eine weit verbreitete Erkrankung und hat einen gesellschaftlich bedeutsamen Einfluss auf Kinder und Jugendliche, indem sie ihr Verhalten, ihre Gefühle und Emotionen beeinflusst und ihre Lebensqualität erheblich beeinträchtigt. Es gibt nur sehr wenige Studien, die die Prophylaxe als wirksames Mittel zur Verhinderung der Prävalenz von Akne betrachten. Es ist notwendig, weitere Forschun-

gen fortzusetzen, die darauf abzielen, die Risikofaktoren für Akne und die Beziehung dieser Pathologie mit der Lebensqualität des Pa-

tienten zu untersuchen. Akne beeinträchtigt den psychologischen und emotionalen Zustand der Patienten [8].

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## ПРОБЛЕМЫ ЗДОРОВЬЯ У ДЕТЕЙ И ПОДРОСТКОВ С АКНЕ

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***Аннотация.** Настоящая работа посвящена актуальной проблематике, а именно комплексному характеру заболеваний у подростков с акне. Авторы рассматривают процесс распространенности акне у детей и подростков в разных странах и на территории Российской Федерации с целью установления универсальных и специфичных черт, характерных для данной патологии. В результате представлены и обобщены проблемы со здоровьем, связанные с акне у детей и подростков, выявлена корреляция между акне и психологическим состоянием детей и подростков.*

***Ключевые слова:** акне, психологическое состояние, дети и подростки, возраст, глобальное здоровье.*

## ZUSAMMENHANG DES SERUMSPIEGELS VON GEWEBE-INHIBITOR DER MATRIX-METALLOPROTEINASE-1 UND DES MYOKARDUMBAUS BEI DER PROGRESSION VON CHRONISCHER HERZINSUFFIZIENZ MIT EINER MODERAT REDUZIERTEN EJEKTFRAKTION BEI DIABETES MELLITUS

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**Zusammenfassung.** *Es ist relevant, den Zusammenhang zwischen dem Serumgehalt von Biomarkern und Umbauprozessen im Myokard zu untersuchen, um das Fortschreiten einer chronischen Herzinsuffizienz mit einer mäßig reduzierten Ejektionsfraktion (HFmrEF) bei Patienten mit Diabetes mellitus (DM) zu diagnostizieren. Mit dem Fortschreiten von HFmrEF bei Patienten mit DM kommt es zu einer Zunahme der Fibroseprozesse im Myokard, einem Anstieg des Serumspiegels des Gewebeinhibitors von Matrix-Metalloproteinasen-1 (TIMP-1). Die Umgestaltung des linksventrikulären Myokards bei solchen Patienten wird von einer Zunahme der Volumen- und Indexparameter des linken Herzens begleitet. Der Zusammenhang zwischen der Dynamik des TIMP-1-Serumspiegels und der myokardialen Umbauprozessen bei Patienten mit DM und HFmrEF kann verwendet werden, um die CHI-Progression zu diagnostizieren.*

**Schlüsselwörter:** *chronische Herzinsuffizienz, Diabetes mellitus, Biomarker, Gewebeinhibitor der Matrix-Metalloproteinasen-1, Myokardumbau.*

**Einführung.** Die Kombination von CHI und DM ist eine komplexe komorbide Pathologie mit einem hohen kardiovaskulären Risiko [1]. Sowohl CHI als auch DM haben einen negativen Einfluss auf die Myokardfunktion, was letztendlich zum Myokardumbau und Progression von CHI führt [2].

Profibrotische Prozesse im Myokard führen zur Erhöhung des TIMP-1-Serumgehalts, zur erhöhten Kollagenbildung und zum Myokardumbau [3].

Der Myokardumbau ist durch die ECHO-KG zu bestimmen. Der Zusammenhang zwischen dem Serumgehalt von TIMP-1 und dem myokardialen Umbau kann für Diagnostik von CHI-Progression bei DM verwendet werden. Von Interesse sind die Patienten mit DM und CHI mit einer mäßig reduzierten Ejektionsfraktion (HFmrEF) des linken Ventrikels, da es wenige Literaturdaten zu diesem Thema gibt.

**Ziel der Studie:** Untersuchung der Wirkung vom TIMP-1-Serumspiegel auf die Prozesse des myokardialen Umbaus während der Progression der HFmrEF bei DM.

**Materialien und Methoden.** Die Studie umfasste 58 Patienten, 30 Männer (51,7 %) und 28 Frauen (48,3 %), bei denen CHI und DM diagnostiziert wurden, im Alter von 46 bis 73 Jahren. Laut der NYHA-Klassifikation mit einem 6-Minuten-Gegtest wurde CHI - I Funktionsklass (FK) bei 16 Patienten (27,6%), II FK - bei 23 Patienten (39,6%), III FK - bei 19 Patienten (32,8%) diagnostiziert. Alle in die Studie eingeschlossenen Patienten hatten kompensierten Typ-2-DM. Die Kontrollgruppe bestand aus 16 gesunden Personen. Alle Patienten gaben nach Aufklärung ihr Einverständnis zur Studie. Die Einschlusskriterien: Alter über 18 Jahre, Diagnose CHI - I, II oder III FK und Typ-2-DM, mäßig reduzierte Ejektionsfraktion (EF) des linken Ventrikels (LV) laut ECHO-KG (LV EF = 41-49 %) sowie eine Vorgeschichte von Herzinfarkt (HI) mehr als 6 Monate. Die Ausschlusskriterien: akuter Koronarsyndrom, Myokardinfarkt weniger als 6 Monate alt, CHI-IV FK, erhaltene LV EF (50 % und mehr) und reduzierte LV EF (40 % und weniger) laut ECHO-KG, akute Infektionskrankheiten, Alkoholismus, psychische Erkrankungen.

gen. Alle Patienten hatten eine allgemeine klinische Untersuchung, ECHO-KG, biochemische Bluttests (Bestimmung von Kohlenhydrat- und Fettstoffwechsel) gemacht. Die Bestimmung der TIMP-1-Serumspiegels wurde durch ELISA unter Verwendung des Testsystems "Cloud-Clone Corp." durchgeführt (China). Referenzwerte für TIMP-1: 720-830 ng/ml. Echo-KG wurde auf einem MyLab 70-Scanner (Esaote, Italien) gemäß einem Standardprotokoll durchgeführt.

Die statistische Auswertung erfolgte mit dem Programm Statistica 10.0. Quantitative Merkmale wurden bei Normalverteilung als Median und Interquartilsabstände (Me [Q25; Q75]) beschrieben. Für die Analyse der quantitativen Daten wurden die Methoden der pa-

rametrischen (Student's t-Test) und der nicht-parametrischen (Mann-Whitney-Test) Statistik verwendet, Unterschiede wurden bei  $p < 0,05$  als statistisch signifikant gewertet.

Ergebnisse. Um strukturelle und funktionelle Veränderungen im Herzen bei Patienten mit DM und HFmrEF mit der Entwicklung von den kardiovaskulären Ereignissen wie HI zu identifizieren, wurden alle Patienten in 2 Gruppen eingeteilt: Gruppe 1 – Patienten mit CHI und DM, die HI hatten – 27 Personen (46,6 %), Gruppe 2 – Patienten mit CHI und DM ohne HI, 31 Personen (53,4 %). Die Parameter von ECHO-KG bei Patienten dieser Gruppen wurden untersucht. Die Ergebnisse sind in Tabelle 1 dargestellt.

Tabelle 1. Echokardiographische Parameter von Patienten mit HFmrEF und DM, die einen HI hatten, und Patienten mit HFmrEF und DM ohne HI

Indikator	1Gr. CHI+DM+HI n=27 (46,6%)	2Gr. CHI+DM n=31 (53,4%)	Kontrollgruppe n=16
EF LV (Simpson), %	44 (41; 47)	47 (43; 49)	62 (58; 64)
LV EDV, ml	146 (104; 206)**	138 (102; 184)*	114 (92; 127)
LV ESV, ml	82 (61; 114)**	74 (58; 103)*	45 (38; 57)
LVMI, g/m <sup>2</sup>	147 (112; 195)**	126 (105; 162)*	85 (65; 108)
LAVI, ml/m <sup>2</sup>	46,5 (39,0; 58,0)**	41,5 (36,0; 45,0)*	23,6 (19,8; 27,4)

Hinweis: \* -  $p < 0,05$  im Vergleich zur Kontrollgruppe

\*\* -  $p < 0,05$  verglichen mit Gruppe 2 (HFmrEF und DM)

Als Ergebnis der ECHO-KG-Studie wurde eine signifikante Erhöhung der volumetrischen Parameter des linken Ventrikels (LV) und des linken Vorhofs (LA) bei Patienten beider Gruppen im Vergleich zur Kontrollgruppe sowie eine signifikante Erhöhung dieser Parameter bei Patienten der 1. Gruppe im Vergleich zur 2. Gruppe: LV EDV - um 15,2%, LV ESV - um 12,9%, die Werte LVMI - um 21,4%, LAVI - um 19,3%. Linksventrikulärer Myokardumbau wurde aufgedeckt: konzentrische Hypertrophie in

der 1. Gruppe - 14,8%, in der 2. Gruppe - 54,8%; konzentrischer Umbau des LV-Myokards in der 1. Gruppe - 37,1%, in der 2. Gruppe - 38,7%; exzentrische Hypertrophie in der 1. Gruppe - 48,1%, in der 2. Gruppe - 6,5%. Um die Dynamik des TIMP-1-Serumspiegels während der CHI-Progression zu bestimmen, wurde der Inhalt dieses Biomarkers bei Patienten mit CHI und DM mit HI, sowie bei Patienten mit CHI und DM ohne HI untersucht. Die Ergebnisse sind in Tabelle 2 dargestellt.

Tabelle 2. TIMP-1-Serumspiegel bei Patienten mit CHI und DM mit HI, und Patienten mit CHI und DM ohne HI

Indikator	1Gr. CHI+DM+HI n=27 (46,6%)	2Gr. CHI+DM n=31 (53,4%)	Kontrollgruppe n=16
TIMP-1, ng/ml	2428,3 (1762,3-2429,5)**	1291,5 (941,8-1828,3)*	738,8 (641,6-863,4)

Hinweis: \* -  $p < 0,05$  im Vergleich zur Kontrollgruppe,

\*\* -  $p < 0,05$  verglichen mit der 2. Gruppe (HFmrEF und DM)

Der TIMP-1-Spiegel bei Patienten mit CHI und DM war 1,7-mal höher als in der Kontrollgruppe. Ein signifikanter Anstieg des TIMP-1-Serumspiegels bei Patienten der 1.

Gruppe im Vergleich zur 2. Gruppe um 1,9-mal wurde festgestellt.

**Diskussion.** Eine wichtige Rolle beim myokardialen Umbau spielt ein chronischer Entzündungsprozess, der von einer zunehmenden

TNF- $\alpha$ -Produktion begleitet wird. Erhöhte Produktion von TNF- $\alpha$  trägt zur übermäßigen Bildung und Aktivierung von Matrix-Metalloproteinasen bei [4]. Erhöhte TIMP-1-Produktion entwickelt sich als Reaktion auf eine erhöhte MMP-Produktion. TIMP-1 verstärkt die Kollagensynthese, gefolgt von der Myokardfibrose und dem Myokardumbau [5].

Die Verstärkung profibrotischer Prozesse während der Myokardfibrose nach einem Herzinfarkt wird vom signifikanten Anstieg des TIMP-1-Serumspiegels begleitet [6]. Hyperglykämie, Hyperinsulinämie und Insulinresistenz bei DM potenzieren Fibroseprozesse in der extrazellulären Matrix [7]. Die Dynamik von TIMP-1 in unserer Studie ist auf die Zunahme von Fibroseprozessen und myokardialen Umbau bei Patienten mit CHI und DM mit Progression von CHI und kardiovaskulären Ereignissen zurückzuführen.

Ein Anstieg des TIMP-1-Serumspiegels während der CHI-Progression steht in engem Zusammenhang mit starken Stoffwechselstörungen, mit myokardialer Struktur und Funktion sowie dem Myokardumbau. Aktuelle Studien zufolge haben Patienten mit HFmrEF erhöhte Werte von LV-Volumenparametern und LV-IMM [8]. Als Ergebnis unserer Studie wurde bei allen Patienten ein LV-Umbau mit einem signifikanten Anstieg von LV EDV, LV ESV, LV IMM, LAVI im Vergleich zur Kontrollgruppe sowie einem signifikanten Anstieg dieser Parameter in der 1. Gruppe festgestellt im Vergleich zur 2. Grup-

pe. Der Umbau des Myokards und der Koronargefäße trägt zur Beeinträchtigung der LV-diastolischen Funktion bei [9]. Der Zusammenhang zwischen strukturellen und funktionellen myokardialen Störungen und Umbau mit TIMP-1 -Serumspiegel kann verwendet werden, um die Progression von CHI bei DM zu diagnostizieren.

**Schlussfolgerungen.** 1. Progression von CHI führt zur Myokardfibrose und zum Anstieg des TIMP-1 -Serumspiegels und als Folge zum Myokardumbau bei Patienten mit DM und CHI.

2. Bei Patienten mit DM und CHI wird der Myokardumbau von einer Zunahme des Volumens und der Indexparameter des linken Herzens, der Entwicklung einer konzentrischen Hypertrophie und einem konzentrischen Umbau des linken Ventrikels begleitet. Patienten mit DM und CHI mit HI haben höhere Werte von Volumen- und Indexparametern des linken Herzens im Vergleich zu Patienten mit DM und CHI, es wird bei Entwicklung der exzentrischen Hypertrophie und des konzentrischen Umbaus des linken Ventrikels begleitet.

3. TIMP-1 -Serumspiegel bei Patienten mit DM und CHI mit HI übersteigen die bei Patienten mit DM und CHI ohne HI signifikant, sodass die Dynamik dieses Biomarkers verwendet werden kann, um die CHI-Progression bei Patienten mit DM zu diagnostizieren.

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### **ВЗАИМОСВЯЗЬ СЫВОРОТОЧНОГО УРОВНЯ ТКАНЕВОГО ИНГИБИТОРА МАТРИКСНОЙ МЕТАЛЛОПРОТЕИНАЗЫ-1 И ВОССТАНОВЛЕНИЯ МИОКАРДА ПРИ ПРОГРЕССИРОВАНИИ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ С УМЕРЕННЫМ СНИЖЕНИЕМ ФРАКЦИИ ВЫБРОСА ПРИ САХАРНОМ ДИАБЕТЕ**

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***Аннотация.** Изучение связи сывороточных уровней биомаркеров с процессами ремоделирования миокарда актуально для диагностики прогрессирования хронической сердечной недостаточности (ХСН) с умеренно сниженной фракцией выброса (HFmrEF) у больных сахарным диабетом (СД). При прогрессировании СНмрФВ у больных СД отмечается нарастание фиброзных процессов в миокарде, повышение сывороточного уровня тканевого ингибитора матриксных металлопротеиназ-1 (ТИМП-1). Ремоделирование миокарда левого желудочка у таких больных сопровождается увеличением объемных и индексных параметров левого сердца. Изучение взаимосвязи между динамикой уровня ТИМП-1 в сыровотке крови и процессами ремоделирования миокарда у больных СД с HFmrEF может быть использовано для диагностики прогрессирования ХСН.*

***Ключевые слова:** хроническая сердечная недостаточность, сахарный диабет, биомаркеры, тканевой ингибитор матриксной металлопротеиназы-1, ремоделирование миокарда.*

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**Résumé.** *Cet article est consacré au sujet de la nutrition de la population. L'article révèle les aspects de la formation des prix et leur dépendance à l'égard de la qualité des aliments, qui constituent la base du panier de consommation. Les principaux objectifs de la politique alimentaire ont été mis en évidence. La liste de principales caractéristiques des produits qui affectent l'état de santé a également été établie.*

**Mots clés:** *nutrition de la population, produits, qualité, prix.*

**Introduction.** Garantir la sécurité alimentaire est l'une des priorités de la politique de l'État dans le domaine de la nutrition saine de la population de la Fédération de Russie. De plus, le problème de la sécurité alimentaire et de leur consommation responsable est d'actualité dans le monde entier.

En même temps, dans le contexte d'une pandémie d'une nouvelle infection à coronavirus, comme d'une charge anthropique élevée, la valeur hygiénique la plus importante pour la santé publique est le niveau de réception de matières premières et de denrées alimentaires de qualité appropriée sur le marché alimentaire, comme leur consommation rationnelle.

Dans la région de Voronej, sur le plan régional, des études ont été menées pour analyser la structure nutritionnelle de la population de la région, pour évaluer le niveau de maladies d'origine alimentaire de la population. De plus, une alimentation déséquilibrée a été classée comme facteur de risque régional prioritaire d'affaiblissement de la défense antioxydante de l'organisme sous l'influence de facteurs environnementaux défavorables dans une ville industrielle.

Des études similaires réalisées dans des pays européens ont montré que la garantie d'une alimentation de haute qualité est l'objectif stratégique le plus important de ces régions.

La France, en tant que première puissance agricole du Conseil européen, dispose d'une législation forte dans le domaine de la qualité

alimentaire régie par les ministères de l'agriculture, de la santé et du commerce, et la région dispose d'un corps législatif qui prescrit les actions du législateur en matière de qualité alimentaire [1-5].

L'objectif de l'étude était d'analyser les données régionales dans le cadre du projet national «Démographie» sur la répartition des prix et de la qualité des produits alimentaires.

**Méthodes de recherche.** Les données de stock du suivi régional de la qualité et de la sécurité sanitaire des aliments pour 2017-2020, qui est réalisé à base de données du FBUZ "Centre d'hygiène et d'épidémiologie dans la région de Voronej", ainsi que le matériel du module de programme du projet national "Démographie", dans le cadre duquel 755 objets commerciaux ont été surveillés (conformément à la liste approuvée par le Centre fédéral d'hygiène et d'épidémiologie de Rospotrebnadzor), 627 questionnaires ont été préparés et soumis, y compris les branches.

À la suite de l'échantillonnage de produits alimentaires sur les sites commerciaux, 614 échantillons de divers produits ont été examinés. Le choix des produits est formé sur à la base de leur valeur nutritionnelle et de leur capacité à répondre aux besoins du corps humain en nutriments essentiels. Pour l'étude, 60 échantillons de viande et de produits à base de viande ont été prélevés comme principales sources de protéines; échantillons de lait et de produits laitiers à hauteur de 150 échantillons; ainsi que des échantillons de



produits de la pêche au nombre de 38 échantillons. Entant que principales sources de matières grasses, des échantillons de viande et de produits carnés comme ceux de lait et de produits laitiers ont été étudiés. En tant que source de fibres alimentaires, de gluten, d'oligo-éléments et de vitamines hydrosolubles - pain en quantité de 102 unités.

Des recherches en laboratoire ont été réalisées conformément à la MR 2.3.7.0168-20 « Evaluation de la qualité des produits alimentaires et évaluation de l'accès de la population aux produits alimentaires domestiques permettant d'éliminer les carences en macro- et micronutriments. Directives» et comprenait l'évaluation des indicateurs de qualité et de sécurité des produits alimentaires selon la norme d'Etat GOST.

Nous avons analysé les indicateurs d'évaluation des chances et du risque relatif d'acheter un produit de mauvaise qualité à bas prix par rapport à l'achat d'un produit de qualité à un prix élevé.

**Résultats.** Pour le groupe de la viande et des produits carnés, on a constaté que les indicateurs de qualité et de sécurité des produits ne dépendent pas de la catégorie de prix à laquelle ils appartiennent. Les parts d'échantillons de produits ne répondant pas aux exigences en matière de qualité et de sécurité dans les gammes de prix bas et haut sont respectivement environ égales à 42,9 et 45,5%.

Pour le groupe poisson et produits de la pêche, il est établi que la qualité et la sécurité des produits ne dépendent pas de la catégorie de prix à laquelle ils appartiennent. Les parts d'échantillons de produits ne sont pas satisfaits aux obligations en matière de qualité et de sécurité dans la gamme de prix bas et dans la gamme de prix haut sont respectivement environ égales à 37,5 - 40,0%.

Pour le groupe des pains et produits de boulangerie, on a révélé l'impossibilité d'indiquer de manière fiable la dépendance des indicateurs caractérisant leur qualité et leur sécurité vis-à-vis de la catégorie de prix à laquelle ils appartiennent.

En même temps, le risque relatif d'acheter un produit de mauvaise qualité à bas prix par rapport à l'achat d'un produit similaire à un prix élevé est assez important. Les parts d'échantillons de produits ne répondant pas aux

exigences en termes de qualité et de sécurité dans les gammes de prix bas et haut diffèrent: les produits de boulangerie à un coût bas plus souvent que ceux à prix élevé ne répondent pas aux normes de qualité et de sécurité en vigueur 66,7 et 45,8% respectivement.

Pour le groupe du lait et des produits laitiers, il est établi qu'il n'est pas non plus possible d'indiquer de manière fiable la dépendance des indicateurs caractérisant leur qualité et leur sécurité par rapport à la catégorie de prix à laquelle ils appartiennent.

Pour ce groupe de produits, l'attention est attirée sur le fait que les produits laitiers à prix élevé plus souvent que ceux à bas prix ne répondent pas aux normes de qualité et de sécurité actuelles: 56,5 et 32,0% respectivement. Par conséquent, on peut affirmer qu'il existe un risque d'acheter un produit de mauvaise qualité à un coût élevé, et qu'il est plus élevé que le risque d'acheter un produit de mauvaise qualité à bas prix.

**Conclusions.** En général, les conclusions suivantes peuvent être tirées des résultats de l'analyse:

1) La gamme de prix des produits individuels varie considérablement.

2) Le nombre d'études de produits alimentaires, comme les résultats d'évaluation de leur conformité et de leur non-conformité aux normes en vigueur, ne permettent pas de confirmer ou d'infirmer l'hypothèse sur la dépendance des indicateurs caractérisant leur qualité et leur sécurité à l'égard du prix, car dans aucun des cas la significativité des différences n'a été obtenue selon le critère X<sup>2</sup>.

3) Parmi les quatre groupes de produits (viande et produits carnés, poisson et produits à base de poisson, pain et produits de boulangerie, lait et produits laitiers), uniquement pour les produits de boulangerie, le risque relatif d'acheter un produit de mauvaise qualité à bas prix, par rapport à l'achat d'un produit similaire à un prix élevé, est assez important. La proportion d'échantillons de produits panifiés qui ne sont pas satisfaits aux obligations en termes de qualité et de sécurité dans les gammes de prix bas et haut peut sensiblement varier: les produits panifiés à bas prix plus souvent que ceux à prix élevé ne répondent pas aux exigences de qualité et aux normes de sécurité.

4) Il est nécessaire d'augmenter le nombre de recherches des produits alimentaires socialement significatifs et biologiquement précieux pour l'alimentation quotidienne en matière de leur conformité aux indicateurs de qualité et de sécurité dans le cadre de la mise

en œuvre de la composante régionale du programme fédéral «Démographie » dont le but est d'assurer la sécurité hygiénique de la population et tester l'hypothèse sur la dépendance des indicateurs étudiés de la tarification.

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*Аннотация.* Данная статья посвящена теме питания населения. В статье раскрыты аспекты формирования цен и их зависимость от качества продуктов питания, составляющих основу потребительской корзины. Выделены главные цели в продовольственной политике. Также составлен перечень основных характеристик продуктов, влияющих на состояние здоровья.

*Ключевые слова:* питание населения, продукты, качество, цена.

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