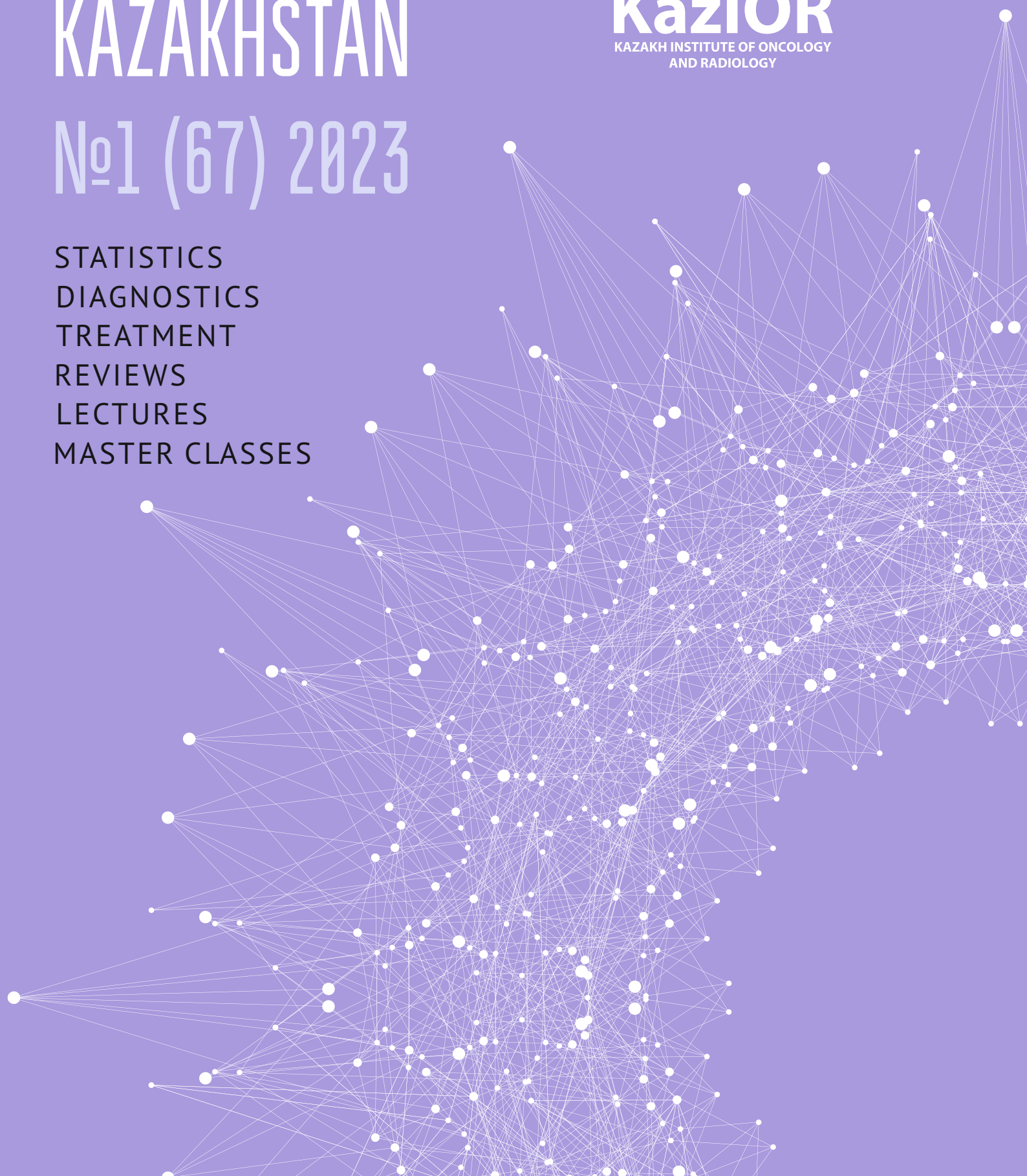


ONCOLOGY and RADIOLOGY of KAZAKHSTAN

№1 (67) 2023



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ONCOLOGY AND RADIOLOGY OF KAZAKHSTAN

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Dear readers!

Welcome to the first issue of the "Oncology and Radiology of Kazakhstan" journal in 2023!

The year starts with a high activity of our authors. We enjoy your interest in publishing exciting research results and practical cases in our journal. However, we would like to remind the authors of our requirements and the necessity to abide strictly by the guidelines for authors.

We offer you 4 articles in English containing serious research results, data analysis, thoughtful methodology, and constructive discussion, which is a profound reflection of the level of the author himself and his knowledge of the international status of approach to scientific research.

The report about a rare case of Kikuchi-Fujimoto's disease in Kazakhstan is noteworthy. It has caused a discussion among editorial board members and reviewers. We are sure that our readers will also be interested in this material, and it will inspire them to search for unique and exciting information!

The coverage of topics for publication is extensive: from using software in ultrasound diagnostics to raising awareness of risk factors for cervical cancer. The latter will interest obstetricians and gynecologists, school doctors, and readers who are not directly related to medicine but have daughters, sisters, and young female friends. We use this opportunity to inform you about the International Summit on Gynecological and Urological Cancer to be held on April 26-28, 2023. The summit will involve politicians in the health field, representatives of international organizations, the leadership of the ministries of health and education, and practitioners. We invite you to participate in this high-level scientific event to receive up-to-date information and obtain new ideas for scientific discoveries, which you can later report in our journal!

I am sure that the proposed articles on immunophenotyping, the results of using adjuvant perfusion thermochemotherapy, endoscopic removal of a rare large occlusive tracheal tumor performed by young specialists, and others will find their readers!

I wish you all health and new creative ideas!

Respectfully Yours,
Dilyara Kaidarova,

Editor-in-Chief of the "Oncology and Radiology of Kazakhstan" journal

ANALYSIS OF THE ACTIVITIES OF THE DEPARTMENT OF ANESTHESIOLOGY AND INTENSIVE CARE of KazIOR FOR 2021-2022

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ABSTRACT

Relevance: The Department of Anesthesiology and Intensive Care of Kazakh Institute of Oncology and Radiology, JSC (KazIOR) is an organized system for providing care to oncological patients, which consists of anesthetic support for all types of oncosurgical operations, postoperative intensive therapy, intensive care for patients in cases of life-threatening conditions during radiation and chemotherapy. High-quality care is possible only with an appropriate level of professional training of medical and nursing staff and a sufficient provision of life-support and monitoring technologies, medicines, and medical products.

The study aimed to analyze the work of the Department of Anesthesiology and Intensive Care in 2021-2022 to further improve the quality of specialized anesthetic and resuscitation care to oncological patients at KazIOR.

Methods: The reporting documentation on clinical activities of the Department of Anesthesiology and Intensive Care for 2021 and 2022 were analyzed.

Results: In 2021-2022, 5517 anesthetics were performed. While the number of anesthetics in 2022 increased by 9.2%, the structure of the types of anesthesia performed remains unchanged. Anesthetic complications were 0.27%, with no anesthetic mortality. The number of patients admitted for postoperative intensive care in 2022 decreased by 6%. The share of patients re-admitted to the Department of Anesthesiology and Intensive Care was 2.1% in 2021 and 2.7% in 2022. The proportion of elderly and senile patients accounted for more than 40% of the intensive care department patients. In 40% of cases, patients suffered from chronic diseases of the cardiovascular system. In the reporting period, the mortality at the Department of Anesthesiology and Intensive Care amounted to 42 cases, including 22 postoperative cases. The postoperative mortality remained approximately the same, while in-hospital and general mortality slightly increased.

Conclusion: The reporting documentation analysis for 2021-2022 showed that the number of anesthesia performed and the total number of patients treated in the Department of Anesthesiology and Intensive Care increases annually, which requires further improvement and modernization of the anesthesiology and intensive care service in oncology.

Keywords: Department of Anesthesiology and Intensive Care, intensive care, anesthetic management, anesthetic complications, anesthetic mortality.

Introduction: Though the first public demonstration of anesthesia dates back to October 16, 1846, anesthesiology as a medical specialty emerged in the second half of the previous century. Further development and allocation of resuscitation and intensive care as a separate specialty were associated with the polio epidemic. In 1952, prof. B.A. Ibsen was the first to create separate intensive care units in Denmark [1, 2].

High-quality anesthesia and resuscitation care require an appropriate level of professional training of medical and nursing personnel and sufficient provision of life support and monitoring technologies, medicines, and medical products.

According to W.L. Lanier, anesthetic mortality in the world by 2000 was 1-2 cases per 200-300 thousand anesthetics [3], while in the 1960-the 1970s, it amounted to 1 case per 28 thousand anesthetics [4]. The development of anesthesiology and resuscitation as a specialty, the creation and improvement of technologies, and the finding of new safe medicines have reduced anesthetic mortality by almost ten times over the past few decades.

The Department of Anesthesiology and Intensive Care (ICU department) of "Kazakh Research Institute of Oncology and Radiology" JSC was established in 1961 as a laboratory of anesthesiology and resuscitation. Today, it is an organized system for providing resuscitation and anesthetic care to cancer patients. It includes anesthetic support for all kinds of oncosurgical operations, postoperative intensive care, and intensive care for life-threatening conditions in oncological patients of a radiological and chemotherapeutic profile.

The Department is fitted with medical equipment in accordance with the "Standard for Organizing the Provision of Anesthetic and Resuscitation Care in the Republic of Kazakhstan" and the order № KR DSM-167/2020 of October 29, 2020 "On approval of Minimum Standards for Equipping Healthcare Organizations with Medical Devices" [5, 6].

Main activities of the ICU department:

- anesthetic management of oncosurgical operations and perioperative management of oncosurgical patients;
- intensive care for cancer patients;

– advisory assistance to other departments, including at the outpatient level.

The study aimed to analyze the work of the Department of Anesthesiology and Intensive Care in 2021–2022 to further improve the quality of specialized anesthetic and resuscitation care to oncological patients in KazIOR.

Materials and Methods: The quarterly, semi-annual, and annual reports on the clinical activities of the ICU department for 2021 and 2022 were analyzed.

Results:

Anesthetic and perioperative management

Perioperative management of patients includes anesthesiological consultation of patients (including at the outpatient level), anesthesiological support for surgical

interventions on the abdominal organs and organs of the retroperitoneal space, small pelvis, organs of the chest, brain and spinal cord, tumors of the head and neck, skin and soft tissues and postoperative management of patients, including observation and treatment in the awakening ward, postoperative intensive care in intensive care and intensive care, as well as counseling of postoperative patients in specialized departments.

In 2021–2022, 5517 anesthetics were performed. While the number of anesthetics in 2022 increased by 9.2%, the structure of the types of anesthesia performed remains unchanged. Anesthesia was provided to patients aged 3 months to 94 years.

Data on the structure and number of anesthetics are presented in Figure 1.

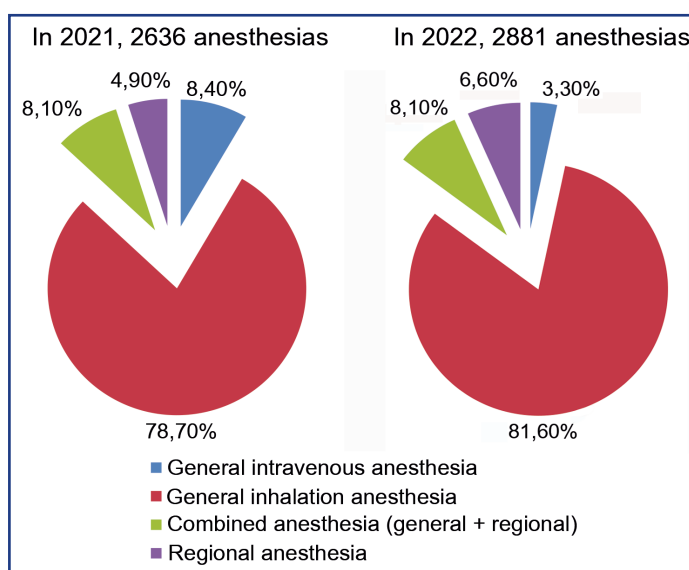


Figure 1 – The structure and number of anesthetics provided at the ICU department of KazIOR, JSC in 2021–2022

In most cases, we performed inhalation anesthesia. According to current data, it is associated with fewer postoperative complications and infections [7]. The pharmacological effects of generation three halogen-containing inhalation anesthetics make them optimal for general anesthesia and agents of choice in modern clinical anesthesiology [8].

Operations on the lower extremities and pelvic organs were performed under regional anesthesia with the preservation of spontaneous breathing.

Total intravenous anesthesia was least frequent and performed in cases where inhalation anesthesia was contraindicated (brain surgery, hemodynamically unstable patients).

Anesthetic complications occurred in 0.27% of cases, which does not exceed global values [9]. See Table 1 for details. Anesthetic mortality was 0% of the total number of anesthetics.

Table 1 – Anesthetic complications at the ICU department of KazIOR, JSC in 2021–2022

Complication	Quantity	
	Abs.	% of all patients
Post-puncture pneumothorax	5	0.090%
Difficult intubation	4	0.072%
Dura puncture	3	0.054%
Desaturation in the postoperative period	1	0.018%
Heart arrhythmia	2	0.036%

Table 2 – Number of patients treated in the post-anesthesia care unit of the ICU department of KazIOR, JSC, in 2021–2022

Patients/years	2021	2022
Absolute numbers	2232	2564
% of all anesthetics	84.6%	88.9%

In 2022, the number of patients treated in the post-anesthesia care unit increased by 4.3% of all anesthetics performed (Table 2).

Intensive therapy in the ICU department

Patients received postoperative intensive care after major surgery, in developing disorders of vital functions during surgery and anesthesia, and in case of severe comorbidity. This category comprised most of the patients

admitted for intensive therapy. The number of patients admitted for intensive postoperative care in 2022 decreased by 6% of the total number of anesthetics, mainly due to an active introduction of Fast-track and ERAS (Enhanced recovery after surgery) concepts (Figure 2) [10, 11].

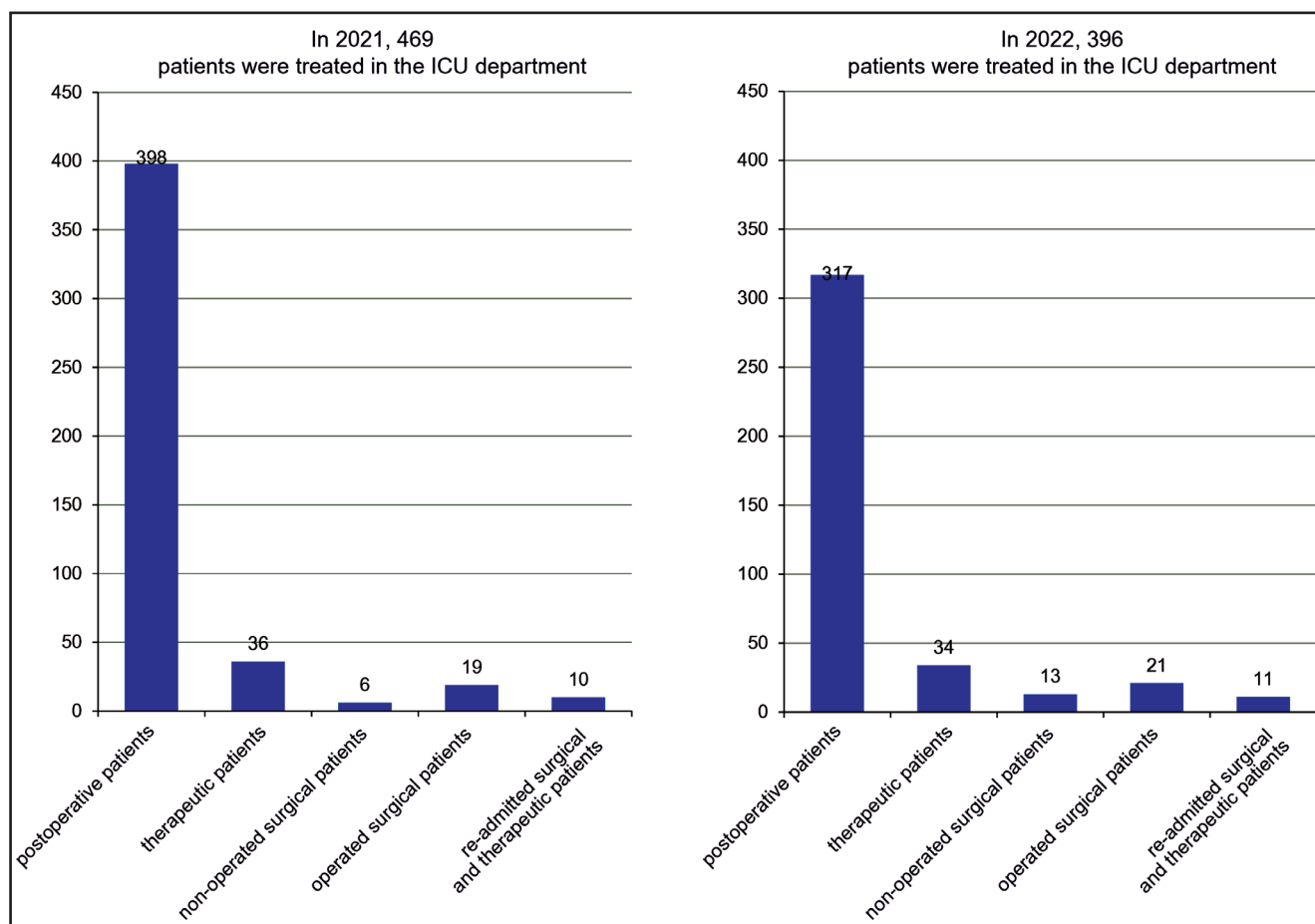


Figure 2 - The structure of patients who received intensive care in the ICU department of KazIOR, JSC in 2021-2022

Therapeutic patients receiving radiological or chemotherapeutic treatment were admitted for intensive care due to the development of complications of specialized treatment or acute emergency conditions that arose during treatment. Their number remained nearly unchanged during the study period.

The main reason for the admittance of non-operated surgical patients was a severe course of the underlying disease requiring intensive care in the ICU department. Their number increased in 2022 owing to cases of planned preoperative preparation.

Operated surgical patients mean those who received surgical treatment according to the volume of surgical intervention and general condition and were treated in the post-anesthesia care unit due to acute postoperative conditions associated with surgery and/or comorbidities. Their number also remained nearly unchanged in 2022.

Patients re-admitted to the ICU department had received intensive care before and were re-admitted to

the ICU department during current hospitalization. The number of re-admitted patients amounted to 2.1% in 2021 and 2.7% in 2022. The main reason for the readmission of operated patients was the complication of surgical treatment (bleeding, failure of anastomoses, etc.). In therapeutic patients, a return for intensive care was often due to a progression of the underlying disease against the background of specialized treatment. Notably, readmission to the ICU department was associated with poorer outcomes, longer hospital stays, and higher treatment costs, which is also a global problem. According to Ponzoni et al. [12], Gudanis and Lebedinsky [13], the average number of patients re-admitted to the ICU department accounts for about 10% of the total number of patients treated in the ICU department.

Table 3 shows the age structure of patients in the ICU department of KazIOR, JSC. Elderly and senile patients account for more than 40% of all ICU patients. The number of patients of these ages increased in 2022.

Table 3 – Age groups of patients of the ICU department of KazIOR, JSC in 2021-2022

Years	Age (abs.,%)				
	Children	Below 40 years	40 to 60 years	60 to 70 years	>70 years
2021	15 (0.65)	404 (15.3%)	1135 (43%)	772 (29%)	310 (11.8%)
2022	3 (0.1%)	467 (16.2%)	1179 (40.9%)	839 (29.1%)	393 (13.6%)

The most common comorbidity were cardiovascular diseases (40% of cases). This trend is observed throughout the world. It can lead to increased mortality, longer stay in a UCU department, and often requires consult-

ing on anesthesia not only at all stages of the perioperative period but also at the outpatient level [14, 15]. Table 4 provides the structure of comorbidities in oncosurgical patients.

Table 4 – The structure of comorbidities in patients of the ICU department of KazIOR, JSC in 2021-2022

Years	Pathology (abs., %)						
	IHD	Stage 1-2 hypertension	Stage 3-4 hypertension	Heart arrhythmia	Diabetes mellitus	Respirator diseases	Other
2021	196 (7.4%)	590 (22.3%)	252 (9.5%)	17 (0.6%)	156 (5.9%)	103 (3.9%)	343 (13.0%)
2022	238 (8.2%)	556 (19.2%)	270 (9.3%)	29 (1.0%)	174 (6.0%)	134 (4.6%)	546 (18.9%)

In 2021-2022, the mortality in the ICU department amounted to 42 cases, including 22 cases of postoperative mortality. The latter remained nearly at the same level, while hospital and total mortality slightly in-

creased over time. In 2021, some fatal cases were due to the coronavirus infection. Increased mortality in 2022 was due to complications associated with the underlying pathology (Table 5).

Table 5 – All types of mortality in the ICU department of KazIOR, JSC in 2021-2022

Mortality	2021		2022	
Postoperative	10 (0.38%)		12 (0.41%)	
	5 – admitted to the ICU after surgery	5 – admitted to the ICU from a specialized department	4 – admitted to the ICU after surgery	8 – admitted to the ICU from a specialized department
Hospital	18 (3.8%)		24 (6.0%)	
Total*	18 (0.67%)		24 (0.81%)	

Note: the percentage was calculated from the total number of patients in the post-anesthesia care unit (2232 in 2021 and 2564 in 2022) and the ICU department (469 in 2021 and 396 in 2022)

Discussion: Anesthesiology, resuscitation, and intensive care are among the most complex and key areas of healthcare. Despite the latest advancements in treating malignancies, cancer patients remain vulnerable and are at high risk of developing conditions that require intensive care. Globally, cancer patients make up to 20% of all ICU patients [16]. Timely diagnosis and hospitalization in the ICU help treat and prevent life-threatening conditions or complications. At that, the number of patients admitted to ICU is growing worldwide. Thus, more than 200,000 adults and children in the UK are admitted to ICU departments every year [17]. The cost of treatment is also growing: i.e., in the US, the cost of treatment increased by 92% from 2000 to 2010 [18]. The increased burden on cancer ICU departments in the world and in Kazakhstan is due to a general increase in the number of cancer patients and a growing share of patients with severe comorbidities and senile age [19]. Besides, the development of anesthesiology has expanded the functional boundaries of operability (today, we can offer safe anesthesia to patients who, 20 years ago, were denied anes-

thesia for surgery), as well as the volume and traumatism of surgical interventions in oncology. All this requires modern and expensive technical and medicinal support, but also a high level of professional training of medical personnel. In recent years, the professional skills of ICU doctors have been expanding in the world: transesophageal echocardiography, ultrasound diagnostics, and endoscopic procedures have become a standard in the training of anesthesiologists-resuscitators [20]. The same trend is observed in Kazakhstan. Training in modern skills is included in the "Roadmap for Improving the Anesthetic and Resuscitation Service in the Republic of Kazakhstan in 2022-2023" [21].

Conclusion: The ICU department activity is a complex multi-level treatment process implemented by highly qualified medical personnel and requires advanced technologies and knowledge. The effectiveness of treatment and safety of patients at all stages of the treatment process is impossible without clear coordination of the ICU department activities and periodic analysis of work with subsequent planning of relevant measures to provide

even better specialized care for cancer patients. The reporting documentation analysis for 2021-2022 showed that the number of anesthesia performed and the total number of patients treated in the ICU department increases annually. This factor increases the burden on the ICU department and requires further improvement and modernization of the anesthesiology and intensive care service in oncology.

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АНДАТПА

«ҚазОРФЗИ» АҚ АНЕСТЕЗИОЛОГИЯ, РЕАНИМАЦИЯ ЖӘНЕ ҚАРҚЫНДЫ ТЕРАПИЯ БӨЛІМШЕСІНІҢ 2021-2022 жылдарға арналған қызметін талдау

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Өзектілігі: «Қазақ онкология және радиология ғылыми-зерттеу институты» акционерлік қоғамының («ҚазОРФЗИ» АҚ) Анестезиология, реанимация және қарқынды терапия бөлімшесі (АРҚТБ) – онкологиялық науқастарға көмек көрсетудің ұйымдастырылған жүйесі, онкохирургиялық операциялардың барлық түрлерін анестезиологиялық қамтамасыз етуден, операциядан кейінгі қарқынды терапиядан, онкологиялық аурулардың, рентгенологиялық және химиотерапиялық бейіндегі пациенттердің өміріне қауіп төндіретін жай-күйлерді дамыту кезіндегі қарқынды терапиядан тұрады. Сапалы көмек дәрігерлік және мейірбикелік кадрларды кәсіби даярлаудың тиісті деңгейінде, тіршілікті қамтамасыз ету және мониторинг технологияларымен, дәрі-дәрмектік заттармен және медициналық мақсаттағы бұйымдармен жеткілікті қамтамасыз етілгенде ғана мүмкін болады.

Зерттеудің мақсаты – «ҚазОРФЗИ» АҚ онкологиялық пациенттеріне мамандандырылған анестезиологиялық және реанимациялық көмек көрсету сапасын одан әрі жақсарту мақсатында 2021-2022 жылдарға арналған АРҚТБ қызметіне талдау жасау.

Әдістері: 2021 және 2022 жылдардағы АРҚТБ клиникалық қызметінің есептік құжаттамасын талдау.

Нәтижелері: 2021-2022 жылдар кезеңінде 5517 анестезия жасалды, бұл ретте 2022 жылы анестезия саны 9,2%-ға ұлғайды, жүргізілген анестезия түрлерінің құрылымы өзгеріссіз қалады. Анестезиологиялық асқынулар 0,27% құрады, ал анестезиологиялық өлім-жітім болған жоқ. Операциядан кейінгі қарқынды терапияға түскен пациенттердің саны 2022 жылы 6%-ға төмендеді. АРҚТБ-не қайта қабылданған пациенттердің саны 2021 жылы 2,1% және 2022 жылы 2,7% құрады. Егде жастағы және кәрілік жастағы пациенттер-

дің үлес салмағы АРҚТБ пациенттерінің жалпы санының 40%-дан астамын құрады. 40% жағдайда пациенттер жүрек-қан тамырлары жүйесінің созылмалы ауруларынан зардап шегеді. Талдау жасалған кезеңде АРҚТБ-дегі өлім-жітім 42 жағдайды құрады, олардың ішінде операциядан кейінгі – 25 жағдай, операциядан кейінгі өлім-жітім шамамен бірдей деңгейде қалды, ал ауруханалық және жалпы өлім-жітім динамикасында аздап өсім байқалды.

Қорытынды: 2021-2022 жылдарға арналған есепті құжаттаманы талдаған кезде, жүргізілген анестезиялардың саны және АРҚТБ-де емделген пациенттердің жалпы саны жыл сайын артып келе жатқаны айқын, бұл онкологиядағы анестезиология және қарқынды терапия қызметін одан әрі жетілдіруді және жаңғыртуды талап етеді.

Түйінді сөздер: АРҚТБ, қарқынды терапия, анестезиологиялық қамтамасыз ету, анестезиологиялық асқынулар, анестезиологиялық өлім-жітім.

АННОТАЦИЯ

АНАЛИЗ ДЕЯТЕЛЬНОСТИ ОТДЕЛЕНИЯ АНЕСТЕЗИОЛОГИИ, РЕАНИМАЦИИ И ИНТЕНСИВНОЙ ТЕРАПИИ АО «КазНИИОнР» за 2021-2022 гг.

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Актуальность: Отделение анестезиологии, реанимации и интенсивной терапии (ОАРИТ) Акционерного Общества «Казахский научно-исследовательский институт онкологии и радиологии» (АО «КазНИИОнР») – это организованная система оказания помощи онкологическим пациентам, заключающаяся в анестезиологическом обеспечении всех видов онкохирургических операций, послеоперационной интенсивной терапии, интенсивной терапии при развитии жизнеугрожающих состояний у онкологических пациентов радиологического и химиотерапевтического профиля. Качественное оказание помощи возможно лишь при соответствующем уровне профессиональной подготовки врачебных и сестринских кадров, достаточном обеспечении технологиями жизнеобеспечения и мониторинга, лекарственными средствами и изделиями медицинского назначения.

Цель исследования – анализ деятельности ОАРИТ за 2021-2022 гг. для дальнейшего улучшения качества оказания специализированной анестезиологической и реанимационной помощи онкологическим пациентам АО «КазНИИОнР».

Методы: Был проведен анализ отчетной документации по клинической деятельности ОАРИТ АО «КазНИИОнР» за 2021 и 2022 гг.

Результаты: За период 2021-2022 гг. выполнено 5517 анестезий, при этом количество анестезий в 2022 г. увеличилось на 9,2%, структура проведенных видов анестезий остается без изменений. Анестезиологические осложнения составили 0,27%, при этом анестезиологической летальности не было. Количество пациентов, поступивших на послеоперационную интенсивную терапию в 2022 г., снизилось на 6%. Количество повторно поступивших пациентов в ОАРИТ составило 2,1% в 2021 г. и 2,7% в 2022 г. Удельный вес пациентов пожилого и старческого возраста составил более 40% от общего числа пациентов ОАРИТ. В 40% случаях пациенты страдали хроническими заболеваниями сердечно-сосудистой системы. Летальность в ОАРИТ за анализируемый период составила 42 случая, их них послеоперационная – 25 случаев, при этом послеоперационная летальность остается примерно на одном уровне, а госпитальная и общая летальность в динамике немного увеличились.

Заключение: При анализе отчетной документации за 2021-2022 гг. становится очевидным, что количество проведенных анестезий и общего количества пролеченных пациентов в ОАРИТ ежегодно увеличивается, что требует дальнейшего совершенствования и модернизации службы анестезиологии и интенсивной терапии в онкологии.

Ключевые слова: Отделение анестезиологии, реанимации и интенсивной терапии (ОАРИТ), интенсивная терапия, анестезиологическое обеспечение, анестезиологические осложнения, анестезиологическая летальность.

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ACCELERATED HIGH-TECH RADIOTHERAPY DURING THE COVID-19

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ABSTRACT

Relevance: COVID-19 impacts the course of cancer depending on the status and volume of cancer patient vaccination against COVID-19.

The study aimed to assess the impact of accelerated high-tech radiation therapy on the course of the oncological process, depending on the status and volume of COVID-19 vaccinations.

Methods: This quantitative and qualitative prospective randomized controlled scientific study was conducted as part of the implementation of the scientific project, "Innovative approach to managing patients with cancer in the context of the COVID pandemic-19," Reg. No. AP13068657. The study involved 221 cancer patients.

Results: COVID-19 was diagnosed in 54/221 (24.4%) of the study participants, 24 (22.4%) in the standard radiotherapy group, and 30 (26.3%) in the experimental radiotherapy group. 49/221 (22.2%) of the participants were vaccinated. COVID-19 was detected in one breast cancer patient in the experimental group (1.5%) two months after vaccination and two patients with prostate cancer (2.4%) four months after vaccination. Relapse-free survival was registered in 59 (85.5%) breast cancer patients in the standard group and 58 (85.3%) in the experimental group. The overall survival of breast cancer patients was 69 (100.0%) in the standard group and 68 (97.0%) in the experimental group. Relapse-free survival was registered in 32 (84.2%) prostate cancer patients in the standard group and 41 (89.1%) patients in the experimental group. The overall survival among prostate cancer patients was 34 (89.5%) in the standard group and 45 (97.8%) in the experimental group. The deaths were not related to COVID-19. The average treatment duration for breast cancer was less by 12.9 days, with prostate cancer – by 18.2 days.

Conclusion: In Kazakhstan, 4.8% of cancer patients with COVID-19 died in 2020-2021. The use of accelerated high-tech radiotherapy is justified in the context of the COVID-19 pandemic. Vaccination can prevent COVID-19 development in cancer patients.

Keywords: radiotherapy, pandemic, COVID-19, oncology, vaccination.

Introduction: At the end of 2019, China informed the World Health Organization (WHO) of a severe respiratory disease caused by SARS CoV-2 severe acute respiratory syndrome coronavirus 2 (COVID-19) [1]. This highly contagious infection with aerosol-droplet and household contact transmission mechanisms with damage to the lung tissue is induced by a new virus strain from the SARS-CoV-2 coronavirus genus [2].

In early March 2020, WHO declared a pandemic due to the rapid global spread of this infection [3]. COVID-19 pandemic restrictions have resulted in a dramatic time shift in cancer care, with hospitals reducing patient visits and implementing remote consultations and telemedicine, postponing elective surgeries, systemic chemotherapy and radiotherapy (RT), elective dispensary supervision, and internal consultations [4]. Unfortunately, epidemiological indicators suggest this pandemic will continue for years [5].

According to global studies, cancer patients are at higher risk of contracting COVID-19 [6]. In addition, the guidelines of the professional oncology communities generally recommend changes in the practice of specific anticancer therapy to minimize immune compromise effects that may predispose to serious complica-

tions during a pandemic [7]. According to a nationwide study in China, receiving chemotherapy or surgery during COVID-19 infection was associated with a higher risk of symptomatic and severe COVID-19 in cancer patients compared with patients who did not receive chemotherapy or surgery (75% versus 43%, $p=0.0026$) [8]. However, a delay in specialized treatment usually results in the deterioration of the patient's condition and the disease progression. At delayed chemotherapy and surgery, RT may play an even more important role in treating most cancers, as RT is one of the few specific treatments that can be safely used with little impact on the immune system [9, 10].

Patients receiving RT usually require a multi-fractional course of treatment. RT cannot be delayed like other treatments without the risk of adverse clinical consequences [11]. During the COVID-19 pandemic, modern methods of radiation therapy continue to be used in the treatment process: intensively modulated radiation therapy (IMRT), volumetric-modulated arc therapy (VMAT), and image-guided radiation therapy (IGRT) [12]. In the context of limited resources during the COVID-19 pandemic, it is necessary to minimize the number of patient visits to a medical facility while

maintaining an identical biologically effective dose, which allows for expanding the possibilities of RT [13].

COVID-19 impacts the course of cancer depending on the status and volume of vaccination of cancer patients against COVID-19. However, the authors could find no published results of RT in cancer patients during the COVID-19 pandemic in the Republic of Kazakhstan.

The study aimed to assess the impact of accelerated high-tech radiation therapy on the course of the oncological process, depending on the status and volume of COVID-19 vaccinations.

Materials and Methods: This quantitative and qualitative prospective randomized controlled scientific study was conducted as part of the implementation of the scientific project of the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan under the calendar plan for 2022 of the scientific project, "Innovative approach to managing patients with cancer in the context of the COVID pandemic-19," Reg. No. AP13068657.

The study involved 114 cancer patients who were administered an RT course by multidisciplinary group decision and a control group of 107 cancer patients. All the patients have signed an informed consent to participate in the study. Patients were randomized by an envelope method in a ratio of 1 to 1 in the experimental and standard radiotherapy groups. Tools for summarizing and grouping materials, compiling and analyzing databases for statistical processing, and visualizing the data obtained were used Microsoft Excel programs and the IBM SPSS Statistics 21 package (trial version). According to the information systems of the Electronic Register of Cancer patients (EROB), the Electronic Register of Inpatients (ERSB), and the medical information system "DamuMed" in cancer patients under dynamic observation, an assessment was made of the status of vaccination against COVID-19, the type of vaccine, its dosage, vaccination period relative to the start or interruption of specialized treatment, relapse-free, and overall survival and the course of the oncological process. Identification of determinants and risk factors of radiation therapy: age, concomitant diseases of the heart and lung system, diabetes mellitus, hormonal therapy, chemotherapy, and body mass index. The determinants for successful RT depended on the RT method.

Results: Despite a certain improvement in COVID-19 epidemiological situation in Kazakhstan, in 2021, 18,502 cancer patients contracted COVID, accounting for 9.5% of cancer patients under dynamic observation (194,510 people). Of them, 898 died from COVID-19, amounting to 0.5% of patients under dynamic observation and 4.5% of those with COVID-19. In 2020, only 4,518 patients contracted COVID-19 (2.4% of those under observation); 199 died from COVID-19 (0.1% of those under observation and 4.4% of those with COVID-19). In 2020-2021, 23,020 cancer patients fell ill with COVID-19, and 1,097 cancer patients died (4.8% of those with COVID-19).

In compliance with the ethical principles reflected in the Helsinki Declaration of Patient Safety ("Ethical

principles for medical research involving a human as a subject," as amended by the 64th WMA General Assembly. – Fortaleza, Brazil, 2013), and in accordance with the law Republic of Kazakhstan, 221 patients were recruited: 137 of them were diagnosed with breast cancer and 84 patients with prostate cancer. Of them, 114 patients received experimental high-tech radiation therapy (68 patients with breast cancer and 46 patients with prostate cancer), a control group of 107 patients (69 patients with breast cancer and 38 patients with prostate cancer) who received high-tech radiotherapy techniques in the standard mode. In both groups, treatment was carried out on a linear electron accelerator from Varian, USA, "TrueBeam," 5 fractions per week under daily control of imaging systems (IGRT) with a comparison of soft tissues and bone structures. The data obtained during the study are subject to the law of normal distribution of data, parametric tests for statistical analysis are used, and a probability of 95% is determined to eliminate the systematic error of the study.

In total, COVID-19 was detected in 54/221 (24.4%) patients included in the study, 24 patients (22.4%) in the standard radiotherapy group, and 30 patients (26.3%) in the experimental radiotherapy group. 49/221 (22.2%) patients in the study group were vaccinated. At the same time, COVID-19 was detected only in 1 breast cancer patient in the experimental radiotherapy group (1.5%) 2 months after she was vaccinated. And COVID-19 was detected in two prostate cancer patients (2.4%) four months after vaccination on average: in one (2.6%) prostate cancer patient one month after vaccination in the standard radiotherapy group, and one (2.2%) prostate cancer patient six months after vaccination in the experimental radiotherapy group.

When analyzed by location, COVID-19 was detected in 32 breast cancer patients (23.4%). Of these, 14 patients (20.3%) were in the standard radiotherapy group, and 18 patients (26.4%) were in the experimental radiotherapy group. COVID-19 was detected in 22 patients with prostate cancer (26.2%), ten patients (26.3%) in the standard radiotherapy group, and 12 patients (26.1%) in the experimental radiotherapy group.

Comparison of relapse-free and overall survival rates and the course of the oncological process: when analyzed by location, relapse-free survival was observed in 59 (85.5%) breast cancer patients in the standard radiotherapy group and 58 (85.3%) breast cancer patients in the experimental radiotherapy group. Overall survival was observed in 69 (100.0%) breast cancer patients in the standard radiotherapy group and 68 (97.0%) breast cancer patients in the experimental radiotherapy group. The deaths were not related to COVID-19.

Disease-free survival was observed in 32 (84.2%) prostate cancer patients in the standard radiotherapy group and 41 (89.1%) prostate cancer patients in the experimental radiotherapy group. Overall survival was observed in 34 (89.5%) prostate cancer patients in the standard radiotherapy group and 45 (97.8%) patients in the experimental radiotherapy group. The deaths were not related to COVID-19.

Discussion: Patient follow-up will continue, but a clear advantage in the experimental RT group is that the average duration of treatment for breast cancer is less by 12.9 days, and for prostate cancer, it is less by 18.2 days. Reducing the number of radiation therapy sessions in the context of the COVID-19 pandemic and saving human and technical resources also reduces waiting times and increases the coverage of radiation therapy for cancer patients. The scientific and socio-economic impact of this scientific study gives impetus to the study of the problem of treating cancer patients in a pandemic and evaluates the results of experimental radiotherapy. The study's results will scientifically substantiate the redistribution of financial resources to increase efficiency in the budgetary financing of radiotherapy services from the state budget by reducing sessions per patient.

Conclusion: In 2020-2021, 23,020 cancer patients fell ill with COVID-19 in Kazakhstan, of which 1,097 cancer patients died from COVID-19, which accounted for 4.8% of those with COVID-19. The use of accelerated high-tech radiotherapy is justified to save human and technical resources, which reduces the queue and waiting time for radiotherapy for cancer patients in the context of the COVID-19 pandemic. Vaccination does not impair outcomes but rather prevents the development of COVID-19 in cancer patients.

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АНДАТПА

COVID-19 ПАНДЕМИЯ ЖАҒДАЙЫНДАҒЫ ЖЕДЕЛДЕТІЛГЕН ЖОҒАРЫТЕХНОЛОГИЯЛЫҚ СӘУЛЕЛІК ТЕРАПИЯ

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Өзектілігі: Қазіргі уақытта вакцинация мәртебесі мен көлеміне және онкологиялық науқастарды COVID-19-ға қарсы вакцинациямен қамтуға байланысты COVID-19-дың онкологиялық аурудың ағымына әсері туралы деректер пайда болды.

Зерттеудің мақсаты – COVID-19-ға қарсы егілген екпенің мәртебесі мен көлеміне байланысты онкологиялық процестің ағымына жеделдетілген жоғары технологиялық сәулелік терапияның әсер етуін бағалау.

Әдістері: Бұл сандық және сапалық перспективті рандомизацияланған бақыланатын ғылыми зерттеу «COVID-19 пандемиясы жағдайында онкологиялық науқастарды басқаруға инновациялық көзқарас» ғылыми жобасын іске асыру шеңберінде жүзеге асырылды, тіркеу нөмірі AP13068657.

Зерттеуге мультидисциплинарлық топтың шешімімен РТ курсы тағайындалған 114 онкологиялық науқастар және 107 онкологиялық науқастардың бақылау тобы қатысты.

Нәтижелері: жалпы зерттеуге қатысқан 221 пациенттің 54-де (24,4%), яғни стандартты сәулелік терапия тобындағы 24 пациентте (22,4%) және эксперименттік сәулелік терапия тобындағы 30 пациентте (26,3%) ғана COVID-19 анықталды. Зерттеуге қатысқан 221 пациенттің 49-на (22,2%) ғана екпе егілді. Бұл ретте COVID-19 сырқаты екпе егілгеннен кейін 2 ай өткен соң эксперименттік терапия (1,5%) тобындағы сүт безі қатерлі ісігімен ауыратын тек 1 пациентте ғана анықталды. Және қуық асты безінің қатерлі ісігімен ауыратын 2 пациентте екпе егілгеннен кейін шамамен 4 айдан кейін COVID-19 анықталды. Сүт безі қатерлі ісігімен ауыратын стандартты терапия тобындағы пациенттердің рецидивсіз өмір сүруі 59 (85,5%) болса, эксперименттік терапия тобындағы пациенттерде рецидивсіз өмір сүру 58 (85,3%)-ды құрады. Сүт безі обыры пациенттерінің жалпы өмір сүру деңгейі стандартты терапия тобында 69 (100,0%) және эксперименттік терапия тобында 68 (97,0%). Қуық асты безі қатерлі ісігі пациенттерінің рецидивсіз өмір сүруі стандартты терапия тобында 32-де (84,2%) және эксперименттік терапия тобында 41-де (89,1%) пациентте байқалды. Қуық асты безінің қатерлі ісігі науқастарының жалпы өмір сүру деңгейі стандартты терапия тобында 34 (89,5%) және эксперименттік терапия тобында 45 (97,8%) құрайды. Өлім-жітім жағдайлары COVID-19-бен байланысты емес. Жеделдетілген жоғары технологиялық сәулелік терапиямен Сүт безі қатерлі ісігін емдеудің орташа ұзақтығы 12,9 күн, ал қуық асты безінің қатерлі ісігін емдеудің ұзақтығы 18,2 күнге аз болады.

Қорытынды: Қазақстанда COVID-19-бен 23020 онкологиялық науқас ауырды, оның ішінде 2020-2021 жылдары 1097 (4,8%) пациент қайтыс болды. Жеделдетілген жоғары технологиялық сәулелік терапияны қолдану COVID-19 пандемиясы жағдайында негізделген. Екпе егу онкологиялық науқастарда COVID-19 дамуын болдырмауға мүмкіндік береді.

Түйінді сөздер: сәулелік терапия, пандемия, COVID-19, онкология, вакцинация.

АННОТАЦИЯ

УСКОРЕННАЯ ВЫСОКОТЕХНОЛОГИЧНАЯ ЛУЧЕВАЯ ТЕРАПИЯ В УСЛОВИЯХ ПАНДЕМИИ COVID-19

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Актуальность: В настоящее время появились данные по влиянию COVID-19 на течение онкологического заболевания в зависимости от статуса и объема вакцинирования и охват онкологических больных вакцинацией против COVID-19.

Цель исследования – оценить влияние ускоренной высокотехнологичной лучевой терапии на течение онкологического процесса в зависимости от статуса и объема вакцинирования против COVID-19.

Методы: Данное количественное и качественное проспективное рандомизированное контролируемое научное исследование проведено в рамках реализации научного проекта «Инновационный подход к ведению онкобольных в условиях пандемии COVID-19», рег. номер AP13068657.

В исследовании приняли участие 114 онкологических больных, которым по решению мультидисциплинарной группы был назначен курс ЛТ, и контрольной группы из 107 онкологических больных.

Результаты: Всего COVID-19 был выявлен у 54 (24,4%) из 221 пациента, вошедших в исследование, в том числе у 24 пациентов (22,4%) в группе стандартной лучевой терапии и 30 пациентов (26,3%) в группе экспериментальной лучевой терапии. Всего 49 (22,2%) из 221 участника исследования были вакцинированы. При этом COVID-19 был выявлен только у 1 пациентки РМЖ в группе экспериментальной терапии (1,5%) через 2 месяца после вакцинации. И COVID-19 был выявлен у 2 пациентов РПЖ (2,4%) в среднем через 4 месяца после того, как они были вакцинированы. Безрецидивная выживаемость пациентов РМЖ у 59 (85,5%) в группе стандартной терапии и у 58 (85,3%) в группе экспериментальной терапии. Общая выживаемость пациентов РМЖ 69 (100,0%) в группе стандартной терапии и 68 (97,0%) в группе экспериментальной терапии. Безрецидивная выживаемость пациентов с РПЖ наблюдалась у 32 (84,2%) в группе стандартной терапии и у 41 (89,1%) в группе экспериментальной терапии. Общая выживаемость пациентов РПЖ составила 34 (89,5%) в группе стандартной терапии и 45 (97,8%) в группе экспериментальной терапии. Случаи смерти не были связаны с COVID-19. Средняя продолжительность курса лечения при РМЖ была меньше на 12,9 дней, при РПЖ – меньше на 18,2 дня.

Заключение: В Казахстане за 2020-2021 гг. умерли 4,8% онкологических больных, заболевших COVID-19. Использование ускоренной высокотехнологичной лучевой терапии обосновано в условиях пандемии COVID-19. Вакцинация позволяет предотвратить развитие COVID-19 у онкологических больных.

Ключевые слова: лучевая терапия, пандемия, COVID-19, онкология, вакцина.

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ASSESSMENT OF AWARENESS AND RISK FACTORS FOR CERVICAL CANCER AMONG YOUNG WOMEN IN ALMATY

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ABSTRACT

Relevance: Currently, in the world, including Kazakhstan, the increasing number of new cervical cancer cases among women of reproductive age is a socio-demographic problem. The increase in cervical cancer incidence among young women, the high prevalence of human papillomavirus (HPV) infection among young sexually active women, the lack of screening programs for the early detection of cervical cancer in young women, the need to take urgent measures to increase awareness of young women about risk factors for cervical cancer and methods of prevention and determined the relevance of this study.

The study aimed to estimate the awareness, identify risk factors for cervical cancer; and assess the state of reproductive health of young women of Almaty by questioning.

Methods: This article presents the results of a survey of young women aged 18 to 32 living in Almaty. Participants received full information on the upcoming survey. The questionnaire collected information on socio-demographic data, awareness of cervical cancer prevention, and women's gynecological history. The questionnaire contained 30 questions in total and took 10 minutes to complete.

Results: Among young women in Almaty, low awareness of primary and secondary prevention of cervical cancer was revealed in all age groups. The most common risk factors for cervical cancer among young women in Almaty were an early onset of sexual activity, smoking, and hormonal contraceptive uptake.

Conclusion: The survey showed the problem of low awareness of girls about cervical cancer and the risk factors for developing cervical cancer. Based on these data, we can state the need for educational work on these issues among young people.

Keywords: cervical cancer; young women; risk factors.

Introduction: About 1800 new cases of cervical cancer and 600 deaths from this disease are registered in the Republic of Kazakhstan each year [1]. In recent years, the number of new cases of cervical cancer among young women has doubled.

About 85% of deaths from cervical cancer worldwide occur in underdeveloped or developing countries. The death rate from cervical cancer in low- and middle-income countries is 18 times higher than in richer countries [2].

Besides, in recent years, the number of new cervical cancer cases among women of reproductive age has increased. Awareness among young women about the factors of cervical cancer development and high awareness of the methods of its prevention will help eliminate this disease.

Sexual behavior. Male and female sexual behavior is the main risk factor for developing cervical cancer. The survey among female prisoners in 1960 first discovered the connection between cervical cancer development and prostitution. Cervical cancer prevalence in those women was 4-6 times higher than in the general population; 9% of prosti-

tuting female prisoners had a cytologically revealed carcinoma in situ. Later, the association of cervical cancer with the number of sexual partners and early onset of sexual activity was established [3].

Sexual activity potentially exposes a woman's body to HPV infection. Women who have had no sexual contacts rarely develop cervical cancer. In contrast, the early onset of sexual life increases the risk of developing cervical cancer because a young woman's cervical epithelium is especially vulnerable to infectious agents and, as a result, is more prone to squamous metaplasia [4].

At that, a woman can contract HIV even from a single sexual partner.

Women are also at higher risk of developing cervical cancer if their male partners have many sexual partners or if they have had female partners with cervical cancer [5].

Male sexual behavior is another important risk factor. Many studies emphasized the value of the "male factor" in developing cervical cancer. I.e., Franceschi & Vaccarella noted high mortality from cervical cancer in women whose partners had a job involving long trips [6]. Buck-

ley et al. studied women who had sexual intercourse only with their husbands and discovered that the risk of cervical neoplasia increases with the number of other sexual partners in their husbands [7].

Smoking. Smoking is a well-known risk factor for developing cancer. In a meta-analysis covering 11 studies published before 2012, Zeng et al. reported that passive smoking significantly increases the risk of developing cervical cancer [8]. A systematic review and meta-analysis by B. Su et al. included 14 studies with 384,995 participants conducted after March 2018 showed an association between smoking with an increased risk of cervical cancer [9].

Smoking women were also found to be at increased risk of developing squamous cell cervical cancer compared to never smoking. The risk of developing squamous cell cervical cancer increased with the number of cigarettes smoked per day but not with the duration of smoking [10].

Several mechanisms are thought to play an important role in cancer development. First, constant smoking can weaken immune function and thereby increase the risk of contracting HPV, which is a significant reason for cervical cancer [11]. Second, nicotine has been proven to promote tumor development [12].

Hormonal contraceptives. Taking oral contraceptives for a long time may increase the risk of cervical cancer. Taking combined oral contraceptives (COCs) can presumably promote carcinogenesis in the cervix and accelerate this process. Taking contraceptives for five years or more is associated with a higher risk of cervical cancer [13].

Gierisch et al. showed an increase in the risk of developing cervical cancer by 10% when taking COCs for less than five years, by 60% when taking COCs for 5-9 years, and a doubled risk when taking COCs for ten and more years [14]. However, the risk of cervical cancer decreased over time when women stopped taking oral contraceptives [15].

Sexually-transmitted infections. Chlamydia trachomatis is a sexually transmitted bacterium. Women with HPV and chlamydial infection have a higher risk of developing cervical cancer. Prolonged inflammation caused by chlamydia makes HPV infection difficult to clear, especially in recurrent chlamydial infections [16].

Herpes simplex virus type 2 (HSV-2) also correlates with a higher-than-usual incidence of cervical cancer [17].

The study aimed to estimate the awareness, identify risk factors for cervical cancer, and assess the state of reproductive health of young women of Almaty by questioning.

Materials and Methods: This article analyzes the intermediate results of a survey of young women living in Almaty. The study included women aged 18 to 31 who were sexually active and able to understand and complete the questionnaire. The girls had to answer each question together with the doctor or on their own.

The questionnaire was developed in three stages: 1) development of questions, 2) building a questionnaire, and 3) translation of the questionnaire into Kazakh and Russian. Before the survey, the content panel was asked to evaluate the validity of the questionnaire content in a two-stage evaluation. The questionnaire was approved by the Local Ethics Commission of "Kazakh Institute of Oncology and Radiology" JSC (KazIOR). The questionnaire was provided with an informed consent form and a cover letter explaining the study's purpose and confirming the respondents' anonymity and voluntary participation.

Stage 1. Before compiling the questionnaire, a literature search was conducted on studies on cervical cancer and its prevention. After a thorough review of the literature, the following three main areas of expertise were selected: 1) risk factors for cervical cancer, 2) knowledge about primary prevention, and 3) knowledge about secondary prevention. Demographics and information about the reproductive health of the interviewees were also included.

Stage 2. The final questionnaire contained 30 questions covering demographic data (1 question), lifestyle (4 questions), gynecological status (12 questions), general knowledge about cervical cancer (3 questions), knowledge of risk factors associated with cervical cancer (3 questions), knowledge about primary prevention of cervical cancer (5 questions), and knowledge about secondary prevention of cervical cancer (3 questions).

Stage 3. The questionnaires were translated into Russian and Kazakh to attract respondents of different ethnicities. The questioning was conducted from August to November 2021 at KazIOR and State Polyclinics No. 17 of Almaty. The respondents' data was coded and entered into a computer.

Results: A total of 228 women took part in the survey. The average age was 24.5 years. The socio-demographic characteristics of the participants are shown in Table 1.

Table 1 – Socio-demographic characteristics of the study participants (n=228)

Question	Answer	Frequency	%
Age	18-23	66	28.9
	24-28	102	44.7
	29-31	60	26.3
Marital status	Married	126	55.2
	Not married	102	44.7
Having children	Yes	103	45.1
	No	125	54.8

This survey touched upon the important topic of the gynecological status of women. Thus, 28.5% of women had a history of pelvic inflammatory disease, 53.9% had

painful menstruation, and 17.5% had irregular menstruation ($p < 0.05$). See Table 2 for their gynecological anamnesis.

Table 2 – Gynecological history of study participants (n=228)

Question	Answer	Q-ty	%
The nature of menstruation	Irregular	40	17.5
	Regular	188	82.4
	Painful	123	53.9
	Non-painful	105	46.05
Presence of a pelvic inflammatory disease	Yes	65	28.5
	No	163	71.4
Presence of a non-inflammatory pelvic disease	Yes	46	20.1
	No	182	79.8

The assessment of risk factors for cervical cancer showed that only 24 (10.5%) respondents had bad habits in the form of smoking, and 12 (5.2%) took COCs.

Knowledge about available preventive services. 44.2% (101) of participants knew about the National Screening Program for Cervical Cancer. The awareness was much higher among women aged 24 to 31.

Regarding the HPV vaccination program, 40.7% (93) of the participants were aware of the vaccination, but only 33.3% (76) of the women would like to be vaccinated against HPV.

Screening visit for cervical cancer. The questionnaire also included questions to young women about their screening experience. 35.9% (82) of respondents were screened at least once. Those who never paid screening visits most often mentioned such barriers as embarrassment, fear of the test and the result, and lack of awareness about screening.

Discussion: This survey revealed limited general knowledge about the prevention of cervical cancer and also made it possible to assess the frequency of risk factors for cervical cancer in young women of Almaty. The most frequently mentioned risk factors for cervical cancer were early onset of sexual activity, smoking, and taking hormonal contraceptives. These responses correspond to published data evidence that sexual behavior is the most common risk factor for cervical cancer [18].

Despite the national screening program for cervical cancer, the study revealed very low awareness about primary and secondary prevention of cervical cancer and limited knowledge about this disease. This could indicate a lack of effective promotion of the program and insufficient public awareness about the role of screening in the prevention of cervical cancer, as well as the need for more frequent coverage of cervical cancer problems in the country.

The assessment revealed a very low awareness of the cervical cancer preventive services available in the country compared to European countries [19]. Those who knew about the program had many misconceptions about who was invited for screening and at what frequency.

The questioning established age as the most significant variable. At that, older women (24-31 years), i.e., those currently targeted by the screening program, were better informed.

Therefore, in expanding the national screening program to other age groups while preserving the recommended 4-year examination interval, the public shall be informed of the advantages of screening and the harms of frequent screening, such as overtreatment and increased psychological anxiety about screening. Clarification should also be given to healthcare professionals who tend to recommend frequent screening for women with normal risk levels.

Conclusion: This survey provides a better understanding that young women are vulnerable groups regarding knowledge about cervical cancer and attendance at screening events. The results showed the need to increase health literacy in young women and conduct a health promotion campaign to improve knowledge about cervical cancer risk factors and attendance at screening events.

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АНДАТПА

АЛМАТЫ ҚАЛАСЫНДАҒЫ ЖАС ӘЙЕЛДЕР АРАСЫНДА ЖАТЫР МОЙНЫ ОБЫРЫНЫҢ ҚАУІП ФАКТОРЛАРЫ МЕН ХАБАРДАРЛЫҒЫН БАҒАЛАУ

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Өзектілігі: Қазіргі уақытта әлемде, оның ішінде Қазақстанда әлеуметтік-демографиялық проблема болып табылатын репродуктивті жастағы әйелдер арасында жаңа жағдайлардың көбеюі байқалады. Жас әйелдер арасында жатыр мойны обырының аурушаңдығының артуы, жас жыныстық белсенді әйелдер арасында HPV инфекциясының жоғары таралуы, жас әйелдерде жатыр мойны обырын ерте анықтау бойынша скринингтік бағдарламалардың болмауы, ақпараттандыруды арттыру үшін шұғыл шаралар қабылдау қажеттілігі, жас әйелдер жатыр мойны обырының қауіп факторлары және алдын алу әдістері туралы және осы зерттеудің өзектілігін анықтады

Зерттеудің мақсаты – Алматы қаласындағы жас әйелдер арасында жатыр мойны обырының қауіп факторларын анықтау және хабардарлықты бағалау

Әдістері: Мақалада Алматы қаласындағы 18 бен 32 жас аралығындағы жас әйелдер арасында жүргізілген сауалнаманың аралық нәтижелерінің аналитикалық зерттеуі берілген. Қатысушылар алдағы сауалнама бойынша толық ақпарат алды. Сауалнама әлеуметтік-демографиялық деректер, жатыр мойны обырының алдын алу туралы хабардар болу және әйелдердің гинекологиялық тарихы туралы ақпарат жинады. Сауалнама барлығы 30 сұрақтан тұрды және толтыруға 10 минут уақыт берілді.

Нәтижелері: Алматы қаласындағы жас әйелдер арасында жатыр мойны обырының бастапқы және қайталама профилактикасы бойынша барлық жас топтарында хабардарлықтың төмендігі анықталды. Алматы қаласындағы жас әйелдер арасында жатыр мойны обырының қауіп факторларын бағалау кезінде жыныстық белсенділіктің ерте басталуы, темекі шегу және гормоналды контрацептивтерді қабылдау жиі кездеседі.

Қорытынды: Сауалнама қыздардың жатыр мойны обыры және жатыр мойны обырының даму қауіп факторлары туралы хабардарлығының төмендігі проблемасын көрсетті. Осы деректерге сүйене отырып, жастар арасында осы мәселелер бойынша тәрбие жұмысын жүргізу қажеттілігі туралы қорытынды жасауға болады.

Түйінді сөздер: жатыр мойны обыры, жас әйелдер, қауіп факторлары.

АННОТАЦИЯ

ОЦЕНКА ИНФОРМИРОВАННОСТИ И ФАКТОРОВ РИСКА РШМ СРЕДИ МОЛОДЫХ ЖЕНЩИН г. АЛМАТЫ

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Актуальность: В настоящее время в мире, в том числе в Казахстане, отмечается увеличение числа новых случаев рака шейки матки (РШМ) среди женщин репродуктивного возраста, что является социально-демографической проблемой. Рост заболеваемости РШМ среди молодых женщин, высокая распространенность вируса папилломы человека (ВПЧ) среди молодых сексуально активных женщин, отсутствие скрининговых программ по раннему выявлению РШМ у молодых женщин, необходимость принятия неотложных мер по повышению информированности молодых женщин о факторах риска РШМ и методах профилактики и определили актуальность настоящего исследования.

Цель исследования – оценить информированность и выявить факторы риска РШМ, также оценить состояние репродуктивного здоровья молодых женщин г. Алматы методом анкетирования.

Методы: В статье представлено аналитическое исследование промежуточных результатов опроса молодых женщин г. Алматы в возрасте от 18 до 32 лет. Участницы получили полную информацию по предстоящему анкетированию. Анкета включала вопросы о социально-демографических показателях, осведомленности о профилактике РШМ и гинекологическом анамнезе женщин. Всего анкета содержала 30 вопросов, на её заполнение требовалось 10 мин.

Результаты: Выявлена низкая информированность о первичной и вторичной профилактике РШМ во всех возрастных группах молодых женщин г. Алматы. При оценке факторов риска РШМ среди молодых женщин г. Алматы методом анкетирования наиболее часто упоминались раннее начало половой жизни, курение и прием гормональных контрацептивов.

Заключение: Анкетирование показало низкую информированность девушек о РШМ и факторах риска развития РШМ. На основании этих данных можно сделать выводы о необходимости просветительской работы среди молодежи по данным вопросам.

Ключевые слова: рак шейки матки (РШМ), молодые женщины, факторы риска.

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S-DETECT SOFTWARE AS A TOOL FOR ULTRASOUND DIAGNOSIS OF THYROID LESIONS

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ABSTRACT

Relevance: Thyroid cancer (TC) is the most common oncological pathology of the endocrine organs. According to the International Agency for Research on Cancer (IARC), 567,233 new cases of thyroid cancer were registered worldwide in 2018. According to IARC, in 2018, 486 new cases were detected in Kazakhstan, which accounted for 1.4% of all cases in Asian countries. TC ranks 10th in the overall structure of cancer incidence globally; TC accounts for 3.1% of all cases of primary malignant tumors. Despite the relatively low incidence, the problems of pathogenesis have been extremely relevant in recent decades due to the increasing prevalence of thyroid cancer. Samsung Medison introduced AI-based S-Detect to improve sensitivity, specificity, and accuracy in the differential diagnosis of thyroid masses.

The study aimed to explore the S-Detect program capacities in differential diagnostics of thyroid masses.

Methods: 75 patients with focal lesions in the thyroid gland were examined using the Samsung Medison RS85 ultrasound machine equipped with the S-Detect program; additionally, Doppler and non-Doppler methods were used.

Results: The S-Detect program made it possible to make a correct diagnosis in 97% of patients (73 of 75), which was confirmed by the results of morphological verification (histology, cytology). The sonoelastography method showed correct results in 91% of patients (68 of 75).

Conclusion: The use of the S-Detect program for thyroid examination positively affects the diagnostic value of ultrasound in the differential diagnosis of thyroid masses, increasing the sensitivity, specificity, and accuracy of diagnosis, as well as avoiding redundant biopsies.

Keywords: ultrasound diagnostics, S-Detect, TI-RADS, sonoelastography, thyroid formations.

Introduction: According to the International Agency for Research on Cancer (IARC), 567,233 new cases of thyroid cancer were registered worldwide in 2018. According to IARC, in 2018, 486 new cases were detected in Kazakhstan, which accounted for 1.4% of all cases in Asian countries [1].

Given the large number of patients with various focal masses in the thyroid gland, the diagnostic problem of masses requiring biopsy becomes evident. Malignant masses are detected in 50% of cases on cytological examination [1, 2].

In late November 2018, Samsung Medison introduced S-Detect, an artificial intelligence-based program. The S-Detect system analyzes thyroid masses in B-mode ultrasound, helps to standardize reports, and classifies nodular masses according to the TI-RADS (Thyroid Imaging Reporting and Diagnostic System) [3].

The TI-RADS system is a classification of sure signs detected during ultrasound examination of the thyroid gland according to the risk of malignancy. The scale makes it possible to significantly improve the interpretation of detected thyroid pathology and standardize the treatment and diagnostic algorithm [4].

TI-RADS classification

TI-RADS 1 – normal thyroid gland;

TI-RADS 2 – benign thyroid changes;

TI-RADS 3 – probably benign thyroid changes;

TI-RADS 4 – suspected malignant thyroid changes;

TI-RADS 5 – probably malignant thyroid changes (more than 80% chance of malignancy);

TI-RADS 6 – malignant process (morphologically confirmed).

One of the additional methods for differential diagnosis of a thyroid mass is ultrasound sonoelastography. Elastography is a special ultrasound examination mode that examines tissue stiffness and elasticity. The method allows up to 80-85% of cases to diagnose nodules, nodal formations, and other pathological processes. Healthy tissues have high elasticity, but the presence of pathological changes increases their rigidity tenfold. A specialist who performs elastography evaluates tissue elasticity through quantitative and qualitative analysis of color elastograms. The multiplicity of increase in pathological changes in relation to healthy tissue is also assessed [5].

The study aimed to explore the S-Detect program capacities in differential diagnostics of thyroid masses.

Materials and methods: The study was performed at “Kazakh Institute of Oncology and Radiology” JSC

(KazIOR) on a Samsung Medison RS85 ultrasound machine by L3-12A and LA2-9A linear probe.

The study group included 75 patients with focal lesions in the thyroid gland.

The S-Detect function was used in addition to Doppler and non-Doppler methods to analyze thyroid masses in B-mode. The essence of the technique is as follows: when using the S-detect function, the program offers automatic contouring with the choice of several image template options, the most similar to the selected nidus; contouring can also be performed manually. Based on the selected template, the system offers the operator a classification and probable scoring of the thyroid mass using the standard TI-RADS lexicon. S-Detect Thyroid technology uses a “deep learning” algorithm that uses an array of data (Big Data) derived from accumulating information from thyroid ultrasound scans. The neoplasms classified

as categories 4-6 are considered malignant, and those classified as categories 1-3 are considered benign [6].

Ultrasonic sonoelastography can also be used for differential diagnosis of thyroid masses. E-Thyroid software automatically calculates the Elasticity Contrast Index (ECI) of a selected thyroid gland area [7]. The linear probe is used for thyroid gland analysis. Elastography results are classified according to the Rago ball scale. Green-colored masses 1-3 or 1-2 are presumed benign and blue-colored masses 4-5 or 3-4 are presumed malignant [8]. E-Thyroid analysis results in tissues with greater stiffness being colored blue in the image and tissues with less stiffness being colored red [9].

Results: According to the results obtained by morphological verification, S-Detect Thyroid ultrasound program, and sonoelastography, the following conclusions were drawn (Table 1):

Table 1 – Distribution of pathologies by nosological forms

Pathology	Type of examination		
	Morphological verification	S-Detect Thyroid ultrasound function	Sonoelastography method
Thyroid cancer	10 (13.3%)	12 (16%)	15 (20%)
Adenoma	14 (18.6%)	14 (18.6%)	16 (21.3%)
Cyst	15 (20%)	15 (20%)	15 (20%)
Pseudoknot (in the hypertrophic form of auto-immune thyroiditis)	17 (22.6%)	15 (20%)	10 (13.3%)
Colloid goiter	19 (25.3%)	19 (25.3%)	19 (25.3%)

Assessment of masses by S-Detect coincided with morphological verification in 73 of 75 cases (97%); S-Detect interpreted all high-risk lesions by TI-RADS

as probably malignant. The sonoelastography score matched the morphological verification in 68 of 75 cases (91%).

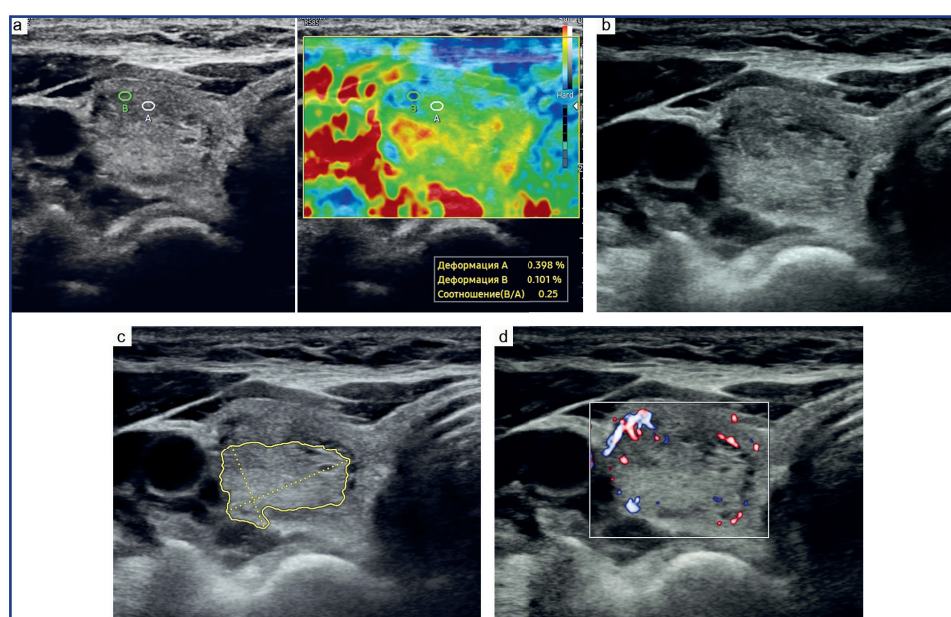


Figure 1 – Colloidal goiter (cross-sectional view):
a – elastography, b – B-mode, c – S-detect, d – CDI mode

Figure 1a shows an image of a colloidal thyroid goiter obtained by elastography. Figures 1b (B-mode) and 1c (S-detect method) visualize the parenchyma of the thyroid gland with a coarse-grained, heterogeneous structure. Figure 1d (CDI mode) shows increased vascularization. Zones of

the hypoechogenic structure are visible along the entire surface.

Conclusion: Elastography (a) showed Rago type 2 – a benign process. S-detect – TI-RADS 2 (benign changes of the thyroid gland). Morphological verification has confirmed a colloidal goiter.

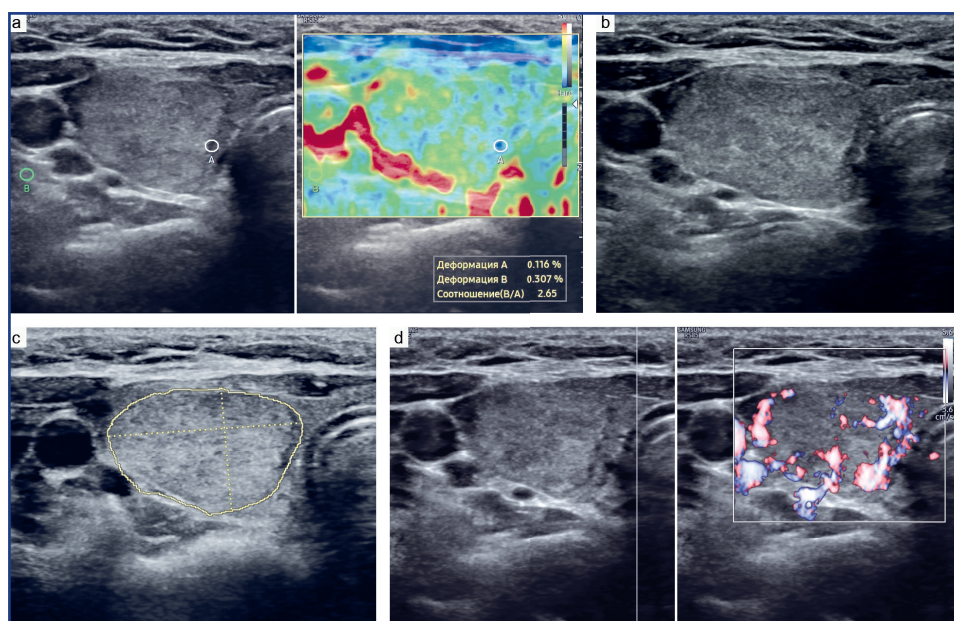


Figure 2 – Adenoma (in transverse section):
a – elastography, b – B-mode, c – S-detect, d – CDI mode

Figure 2a shows an image of medium-density (stiffness) thyroid parenchyma obtained by elastography. Figures 2b (B-mode) and 2c (S-detect method) visualize an echogenic circular mass with a homogeneous structure, an anechoic rim, and even precise contours. Fig-

ure 2d (CDI mode) shows perinodular blood flow.

Conclusion: Elastography (a) – Rago type 2 – delicate process. S-detect – TI-RADS 2 (benign changes of the thyroid gland), CDI mode (d) – perinodular blood flow; Morphological verification - thyroid adenoma.

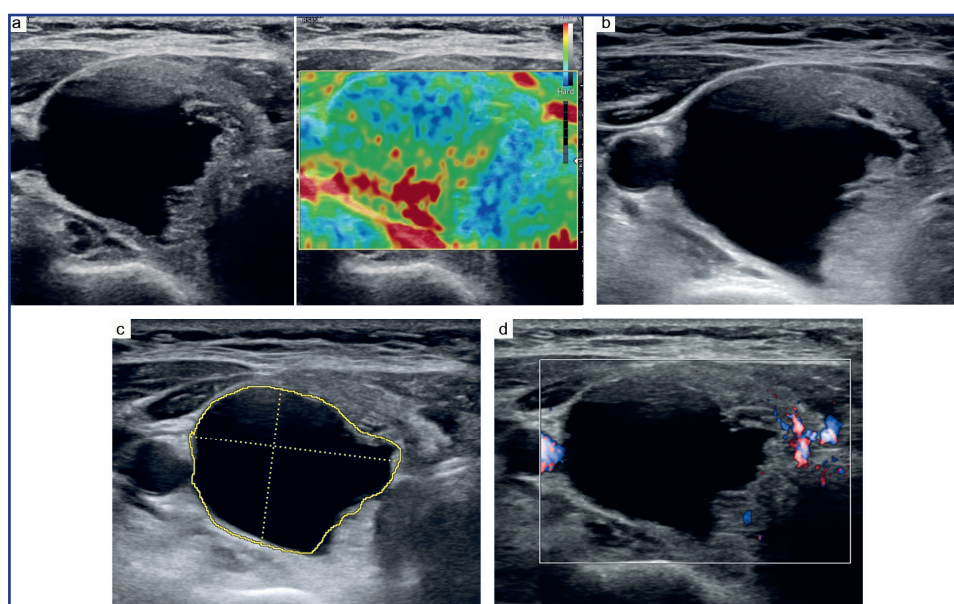


Figure 3 – Thyroid cyst (in cross-section):
a – elastography, b – B-mode, c – S-detect, d – CDI mode

Figure 3a shows an image of a thyroid cyst obtained by elastography. Figures 3b (B-mode) and 3c (S-detect method) show an anechoic circular mass, homogeneous structure with even, precise contours. Figure 3d (CDI mode) shows an avascular mass.

Conclusion: Elastography (a) – type 1 on Rago scale – a delicate process, S-detect – TI-RADS 2 (benign thyroid gland changes). Morphological verification – a thyroid cyst.

Figure 4a shows an image of thyroid cancer obtained by elastography. Figures 4b (B-mode) and 4c (S-detect method) visualize a mass of reduced echogenicity with indistinct uneven contours and multiple calcinates. Figure 4d (CDI mode) shows perinodular vascularization.

Conclusion: Elastography – Rago type 5 – a malignant mass. S-detect – TI-RADS 5 (probably malignant changes of the thyroid gland). Morphological verification – thyroid cancer.

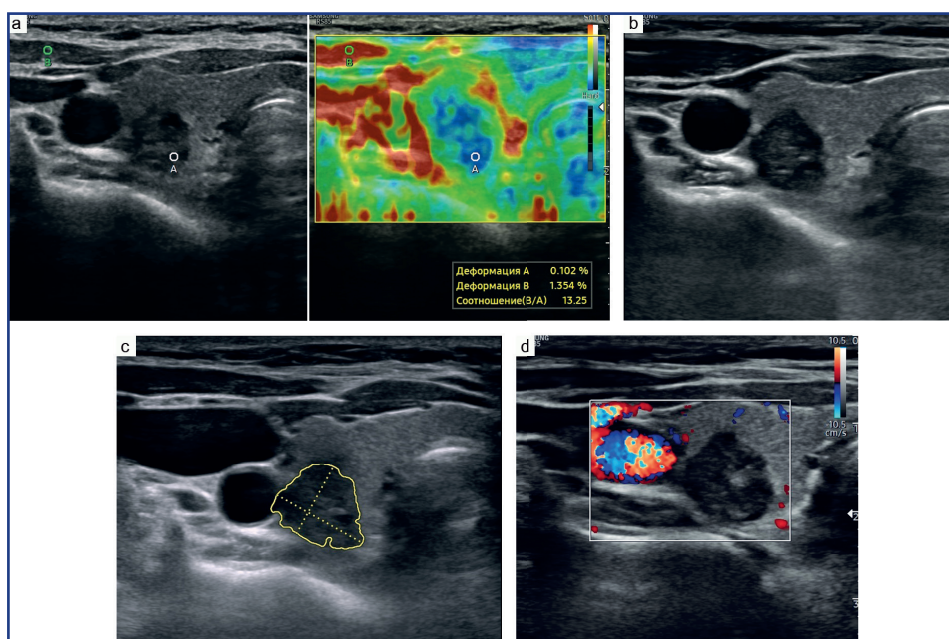


Figure 4 – Thyroid cancer (cross-sectional view):
a – elastography, b – B-mode, B – S-detect, d – CDI mode

Discussion: Our study of using artificial intelligence-based S-Detect ultrasound function in diagnosing thyroid masses showed concordance with the results of morphological verification in 73 of 75 cases (97%). The S-Detect function interpreted all lesions of high risk according to TI-RADS as probably malignant. Discrepancies between S-Detect conclusions and morphological verification results were observed in two cases (2.67%, 2/75). The S-Detect function demonstrated exemplary performance in comparing thyroid masses with B-mode, Doppler, and non-Doppler studies and sonoelastography. Using the S-Detect ultrasound function increased the diagnostic value of ultrasonography for thyroid masses due to a specificity of 97.3% and sensitivity of 98%. In the presence of a thyroid mass, the S-Detect ultrasound function detected the mass, highlighted its borders, and displayed a characteristic of the mass.

The sonoelastography assessment coincided with morphological verification in 68 of 75 cases (91%). The final comparative results of the study show the poten-

tial efficacy of S-Detect (97%) versus sonoelastography (91%).

A well-known study by the School of Medical Ultrasound at AECC University College (UK) compared the S-Detect program and standard thyroid ultrasound in recognizing neoplasms according to the British Thyroid Association (BTA) classification. Researchers used S-Detect to classify a nodule in the thyroid gland, and the result was compared with the sonologist's classification on the same image. The study aimed to assess the potential clinical relevance of the S-Detect program to clinical practice in the United Kingdom. A total of 51 National Healthcare Service patients with thyroid nodules were examined using an ultrasound machine RS80 (Samsung Medison, Co. Ltd., Korea) equipped with the S-Detect program, according to BTA guidelines. The following results were obtained: 2 of 51 cases were classified as positive using the S-Detect program, and the sonologist, i.e., were true positives. The S-Detect program did not classify as unfortunate any cases that

would have been classified as positive by the sonologist, i.e., no false negatives were recorded. S-Detect and the sonologist classified 41 cases as unfavorable, i.e., 41 negative cases were identified. Eight cases classified as positive by S-Detect were unfavorable by the sonologist, giving a false-positive rate of 16.3% (8/51). The sensitivity of the S-Detect program was 100%, reflecting its ability to detect disease, if any. The specificity of the S-Detect program was 83.7%, reflecting its ability to correctly classify the absence of disease [10].

S-Detect ultrasound function was also used in KazIOR to diagnose breast neoplasms on a Samsung Medison RS85 ultrasound machine. In addition to B-mode, CDI and Power Doppler Imaging (PDI), S-Detect, and sonoelastography method were used to analyze neoplasms. In case of discrepancy in the conclusions, the final diagnosis was established based on morphological verification. The ultrasound findings of breast neoplasms in 50 women were included in the study. The S-Detect program diagnosed the neoplasm correctly and gave results similar to morphological verification (histology, cytology) in 87-93% of cases (46 of 50 neoplasms) [11].

The S-Detect ultrasound function to assess thyroid lesions is a new technological addition designed to improve the accuracy of radiologists performing ultrasound examinations. Chang et al. reported that the use of the S-Detect thyroid ultrasound function to differentiate malignant from benign neoplasms showed accuracy similar to that obtained by visual examination by radiologists. Choi *et al.* evaluated 102 thyroid nodules in 89 patients (including 43 malignant and 59 benign masses) and found that the S-Detect ultrasound function showed similar sensitivity as the experienced radiologist (90.7% versus 88.4%, $P > 0.99$) [12].

Data from a meta-analysis aimed to determine the accuracy of S-Detect ultrasound function in the differential diagnosis of thyroid nodules. The meta-analysis was performed using STATA software ver. 14.0 and Meta-Disc ver. 1.4. Summary statistics were calculated for sensitivity (Sen), specificity (Spe), positive and negative likelihood ratios (LR+/LR-), diagnostic odds ratio (DOR), and receiver operating characteristic (SROC) curves. The Cochrane Q-statistic and I² criteria were used to assess potential heterogeneity between studies. In addition, sensitivity analyses were performed to assess the effect of individual studies on the overall estimate, and meta-regression analyses were performed to examine potential sources of heterogeneity. The data obtained from a study of 1,595 benign and 1,118 malignant nodes showed that the composite Sen value was 0.87, the Spe value was 0.74, and the DOR

value was 18.83. The above results show that S-Detect is highly accurate in clinical diagnostics of thyroid nodules, so it is an excellent diagnostic tool. According to the results of this meta-analysis, S-Detect can accurately distinguish malignant thyroid nodules from benign ones [13].

The above results show that S-Detect does not tend to under-classify foci. The method is radiologically safe, fast, and has no contraindications. Therefore, examination with S-Detect enables the doctor, without puncture, to determine the presence and stage of the fibrotic process in tissues and to follow the dynamics of pathological changes.

Of course, along with the significant advantages of the S-Detect function, there are also limitations. For example, after classifying a mass with S-Detect, the doctor sometimes has to manually use some functions, such as "associated symptoms" and "special cases," to get a broader picture when diagnosing. In our study, we also noticed that additional manual contouring of the borders of some large formations provided more reliable results of using the ultrasonic S-Detect function than automatic contouring. The reason was that automatic mode does not always cover the entire mass area or capture an excessive area.

Nevertheless, the advantages of S-Detect are undeniable. Another advantage of this program is that S-Detect is based on a deep learning algorithm. This automated diagnostic system is integrated into ultrasound equipment, representing artificial intelligence technology, allowing radiologists to recognize and classify benign and malignant masses, reducing the burden on the physician and improving the diagnostic process based on lesion signatures.

S-Detect can be used in both top-tier hospitals and smaller local hospitals. This tool can help small hospitals improve the quality of diagnostics of malignant thyroid tumors.

Conclusion: Thus, the S-Detect ultrasound function has a high potential for use in modern clinical practice as an additional method of thyroid examination.

For example, compression sonoelastography is an operator-dependent technique and largely depends on the qualification and experience of the physician.

The S-Detect ultrasound function automatically highlights the border, and adjustments can be made to the area of interest manually if necessary, and the result is displayed on the screen.

The S-Detect ultrasound function is a simple and very effective method of differentiating focal changes in the thyroid gland.

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АНДАТПА

S-DETECT БАҒДАРЛАМАЛЫҚ ҚҰРАЛЫ ҚАЛҚАНША БЕЗІНІҢ ЗАҚЫМДАНУЫН УЛЬТРАДЫБЫСТЫҚ ДИАГНОСТИКАЛАУ ҚҰРАЛЫ РЕТІНДЕ

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Өзектілігі: Қалқанша безі (ҚБ) онкология саласында жиі кездесетін эндокринологиялық мүше.

Халықаралық онкологиялық зерттеулер агенттігінің (IARC) мәліметі бойынша, 2018 жылы дүние жүзінде қалқанша безінің қатерлі ісігінің 567 233 жаңа жағдайы тіркелген. IARC мәліметтері бойынша, 2018 жылы Қазақстанда 486 жаңа жағдай анықталды, бұл Азия елдеріндегі барлық жағдайлардың 1,4%-ын құрады.

Қалқанша безінің қатерлі ісігі әлемде онкологиялық аурулардың жалпы құрылымында 10-шы орынды алады, қалқанша безінің қатерлі ісігі біріншілік қатерлі ісіктердің барлық жағдайларының 3,1% құрайды. Аурудың салыстырмалы түрде төмен болуына қарамастан, патогенез проблемалары соңғы онжылдықтарда қалқанша безінің қатерлі ісігінің таралуының артуына байланысты өте өзекті болып табылады.

Samsung Medison қалқанша безінің массаларының дифференциалды диагностикасында сезімталдықты, ерекшелікті және дәлдікті жақсарту үшін жасанды интеллект негізіндегі S-Detect енгізді.

Зерттеудің мақсаты – Қалқанша безінің массасын дифференциалды диагностикалауда S-Detect бағдарламасының мүмкіндіктерін зерттеу.

Әдістері: Қалқанша безінде ошақты зақымдануы бар 75 науқас S-Detect бағдарламасымен жабдықталған Samsung Medison RS85 ультрадыбыстық аппаратының көмегімен қаралды; қосымша, доплерлік және доплерлік емес әдістер қолданылды.

Нәтижелері: S-Detect бағдарламасы 97% жағдайда (75 адамның 73-інде) дұрыс диагноз қоюға мүмкіндік берді, бұл морфологиялық тексеру (гистология, цитология) нәтижелерімен расталды. Соноэластография әдісі 91% жағдайда (75 адамның 68-і) дұрыс нәтиже көрсетті.

Қорытынды: Қалқанша безді зерттеу үшін S-Detect бағдарламасын пайдалану қалқанша безінің массаларының дифференциалды диагностикасында ультрадыбыстың диагностикалық мәніне оң әсер етеді, диагностиканың сезімталдығын, ерекшелігін және дәлдігін арттырады, сонымен қатар артық биопсияларды болдырмайды.

Түйінді сөздер: ультрадыбыстық диагностика, S-Detect, TI-RADS, соноэластография, қалқанша түзіліс.

АННОТАЦИЯ

ПРОГРАММНОЕ ОБЕСПЕЧЕНИЕ S-DETECT КАК ИНСТРУМЕНТ УЛЬТРАЗВУКОВОЙ ДИАГНОСТИКИ ОБРАЗОВАНИЙ ЩИТОВИДНОЙ ЖЕЛЕЗЫ

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Актуальность: Рак щитовидной железы (РЩЖ) – наиболее часто встречающаяся онкологическая патология эндокринных органов. Согласно данным Международного агентства по исследованию рака (МАИР) во всем мире в 2018 г. зарегистрировано 567 233 новых случаев РЩЖ. По данным МАИР в 2018 г. в Казахстане было выявлено 486 новых случаев, что составило 1,4% от всех случаев в странах Азии.

РЩЖ занимает 10-е место в общей структуре онкозаболеваемости в мире, на долю РЩЖ приходится 3,1% всех случаев первичных злокачественных образований. Несмотря на относительно низкую заболеваемость, проблемы патогенеза чрезвычайно актуальны в последние десятилетия в связи с ростом распространенности РЩЖ.

Компания Samsung Medison представила программу S-Detect на основе искусственного интеллекта для повышения чувствительности, специфичности и точности в дифференциальной диагностике образований щитовидной железы.

Цель исследования – изучить возможности программы S-Detect в дифференциальной диагностике образований щитовидной железы.

Методы: 75 пациентов с очаговыми образованиями в щитовидной железе были обследованы с использованием ультразвукового аппарата Samsung Medison RS85, оснащенного программой S-Detect; дополнительно применялись доплеровские и не доплеровские методы.

Результаты: Программа S-Detect позволила верно поставить диагноз в 97% (73 из 75 человек) случаев, что было подтверждено результатами морфологической верификации (гистология, цитология). Метод соноэластографии показал верные результаты в 91% (68 из 75 человек) случаев.

Заключение: Применение программы S-Detect для обследования щитовидной железы положительно влияет на диагностическую ценность ультразвукового исследования в дифференциальной диагностике образований щитовидной железы, повышая чувствительность, специфичность и точность диагностики, а также позволяя избежать избыточных биопсий.

Ключевые слова: ультразвуковая диагностика, S-Detect, TI-RADS, соноэластография, образования щитовидной железы.

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ENDOSCOPIC REMOVAL OF A RARE LARGE OCCLUSIVE TRACHEAL TUMOR WITH LIMITED TECHNICAL CAPABILITIES

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ABSTRACT

Relevance: Tracheal tumors often do not cause symptoms until they grow to a size that causes significant airway obstruction, which is the reason for the delay in diagnosis. Diagnosis may also be delayed due to non-specific symptoms, such as cough, wheezing, and shortness of breath, which can occur in other conditions such as asthma and chronic obstructive pulmonary disease. The symptoms that appear may vary depending on the type and location of the tumor. The literature does not sufficiently cover the experience of treating large occlusive tracheal tumors using segmental tracheal resection, endoscopic treatment, or radiation therapy. In scientific literature, the number of published studies with long-term results of endoscopic treatment or radiation therapy of such occlusive tracheal tumors is limited, and this problem requires further study. This article describes the first recorded case of endoscopic removal of a large occlusive tracheal tumor.

The study aimed to show the possibility and effectiveness of endoscopic treatment using a minimum set of endoscopic equipment.

Methods: This article presents a case of successful minimally invasive endoscopic treatment of a large occlusive tracheal tumor.

Results: A large obstructing tumor of the trachea that almost completely blocked the trachea lumen was removed in one block by endoscopic loop resection.

Conclusion: The presented clinical case describes the experience of successful endoscopic removal of a rare occlusive tumor of the trachea, which caused shortness of breath at rest and during exercise. For the first time in Kazakhstan, based on the National Scientific Cancer Center, we performed a unique minimally invasive operation to remove a tracheal tumor, while other clinics offered thoracotomic surgical resection methods.

Keywords: tracheal tumor; tracheal obstruction; endoscopic treatment; occlusive tumor; schwannoma.

Introduction: The trachea connects the larynx to the two main bronchi that supply air to the lungs. Tumors of the trachea can either arise from itself, known as primary tracheal tumors or occur due to direct invasion from nearby structures. Primary tracheal tumors can either be malignant or benign. Malignant primary tracheal tumors, including squamous cell carcinomas and adenoid cystic carcinomas, are more common. Benign primary tracheal tumors include endobronchial hamartomas and squamous cell papillomas [1, 2].

Tracheal tumors often do not produce symptoms until they have grown to a size to cause significant airway obstruction. Therefore, there is a common delay in clinical presentation and diagnosis. Diagnosis may also be delayed due to the presentation of non-specific symptoms such as cough, wheeze, and shortness of breath that can occur in other conditions, such as asthma and chronic obstructive pulmonary disease [3]. When symptoms do appear, they may vary depending on the tumor type and anatomical location. Primary tracheal tumors other than adenoid cystic or squamous cell carcinoma are uncommon and have a heterogeneous histologic appearance. The experience regarding their treatment and long-term outcome is limited, and alternatives to segmental tracheal resection, including endoscopic treatment or radiation, continue to be explored [4].

Overall survival in rare respiratory tract tumors depends on many factors, including the malignant potential of the tumor, concomitant diseases of the patient, localization, and risks associated with the treatment method. Benign tumors are usually localized and can be reduced without or with minimal risk of recurrence. Surgical resection is usually associated with a very low recurrence of benign tumors. Endoscopic removal is associated with varying degrees of recurrence, but

repeated removal is usually possible. Success in endoscopic removal of tracheal neoplasms depends on the tumor size, the patient's condition, and the quality of surgical procedure and anesthetic management.

Unfortunately, endoscopic removal of large benign tumors of the trachea in Kazakhstan is not performed due to insufficient experience of endoscopists and a lack of necessary endoscopic consumables. For that reason, thoracic surgeons often remove such neoplasms via open access. New endoscopic instruments allow for the safe removal of such large formations. However, not all such instruments are available in our country. This article describes the first successful endoscopic removal of a large occlusive tracheal tumor using a minimal selection of endoscopic instruments.

The study aimed to show the possibility and effectiveness of endoscopic treatment even with minimal equipment.

Materials and Methods: The article describes a successful minimally invasive endoscopic treatment of a large occlusive tracheal tumor.

Information about the patient: The patient, a 34-year-old man, was hospitalized in early August 2020 at the National Cancer Research Center for examination and surgical treatment of a tumor in the upper third of the trachea. According to the patient, he had been ill for a month when he first experienced a lack of air.

Clinical data: The patient's condition at admission was relatively satisfactory. Clinical manifestations of decompensation of the functions of vital organs and systems were not noted.

Diagnostics: Laboratory parameters are within acceptable values. Electrocardiography without acute coronary pathology, conduction, and rhythm disorders.

At the outpatient stage (August 2020), a bronchoscopy revealed a tumor of the upper third of the trachea, completely obstructing the tracheal lumen, causing the patient to have shortness of breath both during physical exertion and at rest.

The chest CT (August 2020) conducted in the National Research Oncology Center (Astana, Kazakhstan) revealed a tumor 2.4x2.3 cm in size, with a leg of 13 mm and a density of

up to 40 U (Figure 1). Next, the patient underwent a video bronchoscopy under additional oxygenation through a nasal catheter. Bronchoscopy revealed a volumetric tumor of the upper third of the trachea, almost completely obstructing its lumen, dense consistency, and pink surface.

Based on clinical data, anamnesis, and tumor localization, the patient was diagnosed with a benign tracheal tumor.



Figure 1 – CT image of the tracheal tumor

Treatment: Endoscopic loop resection with subsequent morphological verification was administered due to increased shortness of breath at rest. The first stage included endoscopic intubation with an 8.0 tube. Bronchoscopy of the upper third of the trachea revealed an oval tumor with exophytic growth, 3.5x2.5 cm in size, occupying almost the entire lumen of the trachea, pink in color, dense in palpation, on a thick leg. Next, the tumor was removed using a diathermic loop in the ForceCoag-2 90 Wt mode. The bed was well-main-

tained after coagulation, without signs of wall damage. The patient was extubated with simultaneous tumor extraction from the tracheal lumen. Then the patient was re-intubated under endoscopic control using a bronchoscope and transferred to the recovery room, where he was extubated after 15 minutes and transferred to the clinical department. The patient's anesthetic benefit consisted of deep sedation with propofol 600 mg, short-term muscle relaxation, and oxygen support (Figure 2).



Figure 2 – Images of the tracheal tumor

Results: In the first hours after the operation, the patient did not complain of shortness of breath; breathing did not suffer; his quality of life improved. Morphologically, the removed tumor was a tracheal schwannoma (Figure 3). The patient was discharged in satisfactory condition on Day 3 after endoscopic resection.

The presented case is the first successful experience of endoscopic removal of a large occlusive primary tumor recorded in Kazakhstan. Endoscopic neoplasm removal improved the quality of life immediately after surgery, and the postoperative period was short.

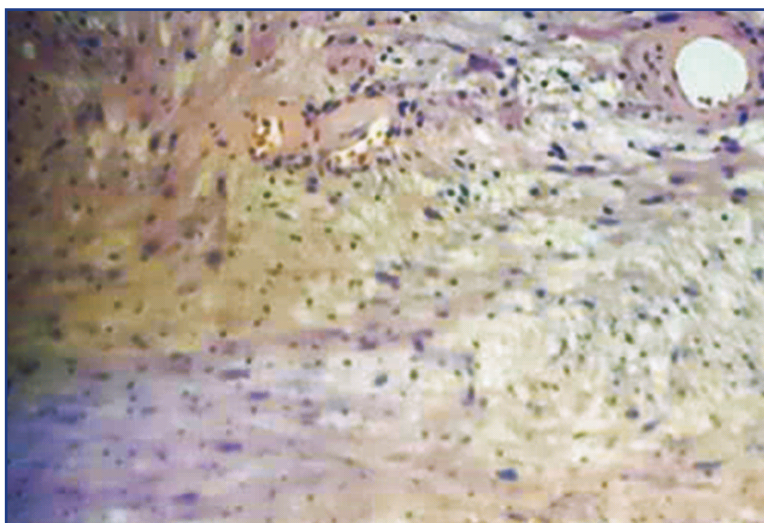


Figure 3 – Photo of the tracheal tumor micro preparation

Timeline:

The timeline of this clinical case is presented in table 1.

Table 1 – Timeline of a clinical case of endoscopic treatment of a benign tracheal tumor

First visit to a doctor	July 2020
Tumor detection	August 7, 2020
Tumor growth over time	August 12, 2020
Admission to the hospital	August 13, 2020
Endoscopic treatment	August 14, 2020
Discharge from the hospital	August 16, 2020

Discussion: Endoscopic methods develop rapidly and gradually replace traditional thoracic and abdominal surgery methods. Endoscopic treatment can be radical in removing benign and borderline tumors; in malignant tumors, it can be palliative for recanalizing the lumen of hollow organs, stenting, and prosthetics. A wider introduction of endoscopic methods requires a retrospective study of long-term endoscopic treatment outcomes, assessing treatment radicality and effectiveness and the presence and tactics for complications. Successful endoscopic resection of such large tracheal tumors requires an experienced team of an endoscopist and an anesthesiologist. This surgery requires a rigid bronchoscope and an argon plasma coagulator. Since this was our first experience removing such a tumor and we did not possess a rigid bronchoscope, we decided to perform a loop resection of the tumor and its subsequent extraction from the trachea with simultaneous patient extubation.

Conclusion: Given the insidious progression of benign tracheal tumors, their diagnostics remain an intricate task. Despite low differentiation of cases of airway obstruction, they may turn out to be dangerous due to

almost complete tracheal obstruction, as in the case described. The tumors can involve several important paratracheal structures, making resection and reconstruction more challenging. Extensive damages also complicate operational planning. The choice between endobronchial removal or surgical resection still depends on the patient and tumor characteristics and the experience of the endoscopist and anesthetic team [5]. Small, fully endoluminal tumors with a limited spread in the tracheobronchial tree and a low risk of recurrence, as well as poor candidates for surgery, can benefit from endobronchial removal and avoid the pain of surgical removal and reconstruction.

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АНДАТПА

ТЕХНИКАЛЫҚ МҮМКІНДІКТЕРІ ШЕКТЕУЛІ ТРАХЕЯНЫҢ СИРЕК КЕЗДЕСЕТІН ІРІ ОККЛЮЗИЯЛЫҚ ІСІГІН ЭНДОСКОПИЯЛЫҚ АЛЫП ТАСТАУ

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Өзектілігі: трахея ісіктері көбінесе тыныс алу жолдарының айтарлықтай кедергісін тудыратын мәлишерге дейін симптомдар тудырмайды, бұл диагноздың кешігуіне себеп болады. Демікпе және созылмалы обструктивті өкпе ауруы сияқты басқа жағдайларда пайда болуы мүмкін жөтел, ысқырық және ентігу сияқты спецификалық емес белгілердің көрінуіне байланысты диагнозды кейінге қалдыруға болады. Пайда болған белгілер ісіктің түріне және орналасуына байланысты өзгеруі мүмкін. Трахеяның сегменттік резекциясын, эндоскопиялық лечение немесе сәулелік терапияны қоса алғанда, үлкен окклюзивті трахея ісігін емдеу тәжірибесі әдебиетте жеткілікті түрде қамтылмаған. Әлемдік ғылыми әдебиеттерде мұндай окклюзиялық трахея ісіктерін эндоскопиялық емдеудің немесе сәулелік терапияның ұзақ мерзімді нәтижелері бар жарияланған зерттеулердің саны шектеулі және бұл мәселе қосымша зерттеуді қажет етеді. Бұл мақалада трахеяның үлкен окклюзиялық ісігін эндоскопиялық алып тастаудың алғашқы тіркелген жағдайы сипатталған.

Зерттеудің мақсаты – эндоскопиялық жабдықтың минималды жиынтығын пайдалану кезінде эндоскопиялық емдеудің мүмкіндігі мен тиімділігін көрсету.

Әдістері: Бұл мақалада трахеяның үлкен окклюзиялық ісігін сәтті минималды инвазивті эндоскопиялық емдеу жағдайы келтірілген.

Нәтижелері: эндоскопиялық клдік резекция нәтижесінде трахеяның люменін толығымен жабатын трахеяның үлкен обтура-торлық ісігі бір блоппен жойылды.

Қорытынды: ұсынылған клиникалық жағдай тыныштықта және жаттығу кезінде ентігуді тудырған сирек кездесетін окклюзиялық трахея ісігін сәтті эндоскопиялық алып тастау тәжірибесін сипаттайды. Қазақстанда алғаш рет Ұлттық ғылыми онкологиялық орталық базасында біз трахея ісігін жою бойынша бірегей миниинвазивті операция жасадық, ал басқа клиникаларда резекцияның торакотомиялық хирургиялық әдістері ұсынылды.

Түйінді сөздер: трахея ісігі, трахеяның бітелуі, эндоскопиялық емдеу, окклюзиялық ісік, шваннома.

АННОТАЦИЯ

ЭНДОСКОПИЧЕСКОЕ УДАЛЕНИЕ РЕДКОЙ КРУПНОЙ ОККЛЮЗИОННОЙ ОПУХОЛИ ТРАХЕИ С ОГРАНИЧЕННЫМИ ТЕХНИЧЕСКИМИ ВОЗМОЖНОСТЯМИ

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Актуальность: Опухоли трахеи часто не вызывают симптомов до тех пор, пока они не вырастут до размеров, вызывающих значительную обструкцию дыхательных путей, что является причиной задержки в постановке диагноза. Диагностика также может быть отсрочена из-за проявления неспецифических симптомов, таких как кашель, свистящее дыхание и одышка, которые могут возникать при таких состояниях, как астма и хроническая обструктивная болезнь легких. Появляющиеся симптомы могут варьировать в зависимости от типа и локализации опухоли. Опыт в отношении лечения крупной окклюзионной опухоли трахеи, включая сегментарную резекцию трахеи, эндоскопическое лечение или лучевую терапию, недостаточно освещен в литературе. В мировой научной литературе количество опубликованных исследований с отдаленными результатами эндоскопического лечения или лучевой терапии таких окклюзионных опухолей трахеи ограничено, и эта проблема требует дальнейшего изучения. В этой статье описывается первый зарегистрированный случай эндоскопического удаления большой окклюзионной опухоли трахеи.

Цель исследования – показать возможность и эффективность эндоскопического лечения при использовании минимального набора эндоскопического оборудования.

Методы: В данной статье представлен случай успешного малоинвазивного эндоскопического лечения крупной окклюзионной опухоли трахеи.

Результаты: В результате эндоскопической петлевой резекции одним блоком удалена крупная обтурирующая опухоль трахеи, практически полностью перекрывавшая просвет трахеи.

Заключение: Представленный клинический случай описывает опыт успешного эндоскопического удаления редкой окклюзионной опухоли трахеи, которая вызывала одышку в покое и при физической нагрузке. Впервые в Казахстане на базе Национального научного онкологического центра нами была проведена уникальная малоинвазивная операция по удалению опухоли трахеи, в то время как в других клиниках предлагались торакотомические хирургические методы резекции.

Ключевые слова: опухоль трахеи, обструкция трахеи, эндоскопическое лечение, окклюзионная опухоль, шваннома.

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RESULTS OF USING ADJUVANT PERFUSION CHEMOTHERAPY IN RADICAL TREATMENT OF INFILTRATIVE GASTRIC CANCER

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ABSTRACT

Relevance: Given the high biological aggressiveness of infiltrative gastric cancer warranting a need for a multimodal approach to its radical treatment employing adjuvant perfusion thermochemotherapy (HIPEC) and systemic adjuvant polychemotherapy, the goal of the present study was to assess the efficacy and expediency of such an approach.

The study aimed to evaluate the effectiveness of a combination of HIPEC and systemic adjuvant polychemotherapy in patients radically operated on for infiltrative forms of gastric cancer pT4a-bN0-3M0.

Methods: The study examined the long-term results of radical treatment for gastric cancer in 141 patients (pT4a-bN0-3M0, Borrmann type III-IV).

Of them, 18 patients underwent a multimodal treatment, including radical surgery in combination with HIPEC and systemic adjuvant polychemotherapy (ACT) (oxaliplatin 100 mg/m² (on day 1 of the cycle), capecitabine 1.000 mg/m² or tegafur 10-15 mg/kg (2 times per day, on days 1-14 of the cycle, with a 7-day break between cycles, 8 cycles) – HIPEC/ACT group. For comparison purposes, we used the data on 55 radically operated patients (surgery control) and 68 other patients who underwent radical surgery in combination with HIPEC (cisplatin 50 mg/m² + doxorubicin 50 mg/m², 42°C, one hour). The long-term treatment results were evaluated using competing risks analysis, the Kaplan-Meier multiplier method, and multivariate analysis (Cox and Fine-Gray models).

Results: The multimodal treatment group showed a decrease in unfavorable outcomes associated with tumor progression ($\beta = -2.14$, RR 0.12, 95% CI 0.04-0.38, $p < 0.001$), a decrease in the risk of carcinomatosis ($\beta = -1.99$, RR 0.14, 95% CI 0.04-0.44, $p < 0.001$), and better five-year survival rates compared to the control groups. The adjusted survival was $81.9 \pm 9.5\%$ ($p = 0.003$), the progression-free survival was $82.2 \pm 9.3\%$ ($p < 0.001$), and the dissemination-free survival was $81.9 \pm 9.5\%$ ($p < 0.001$).

Conclusion: It is advisable to supplement the standard approach for infiltrative gastric cancer (radical surgery and systemic polychemotherapy) with perfusion HIPEC to prolong the remission of the tumor process.

Keywords: gastric cancer, adjuvant hyperthermic intraperitoneal chemotherapy (AHIPEC), adjuvant systemic polychemotherapy (ACT).

Introduction: High invasive and metastatic potential of infiltrative forms of gastric cancer (GC) causes early progression of the tumor process even in radically operated patients [1]. The latter determines the necessity of complex treatment to prevent the development of various variants of cancer progression, both implantation metastases and systemic progression in the form of lymphohematogenous metastasis. The current strategy of radical treatment of locally advanced cancer involves the use of perioperative or adjuvant polychemotherapy (APChT) [2, 3], which cannot prevent the development of metachronous peritoneal dissemination (MPD) due to insufficient effective penetration of chemotherapy from the systemic blood flow into the peritoneal tissue due to the presence of hemato-peritoneal barrier. Several recent publications emphasize the excellent use of adjuvant perfusion thermochemotherapy (APTChT) for this purpose [4]. It is also noted the necessity of its com-

bination with APChT to prevent the systemic progression of GC [5-7].

The study aimed to evaluate the effectiveness of a combination of HIPEC and systemic adjuvant polychemotherapy in patients radically operated on for infiltrative forms of gastric cancer pT4a-bN0-3M0.

Materials and methods: The study was conducted at the Republican Scientific and Practical Center of Oncology and Medical Radiology, named after N.N. Alexandrov, in 2008-2021. Data on the treatment results of 141 patients radically operated for GC stage IIB-IIIC (type III-IV according to Borrmann, 1926) were used to prepare this article. In 18 patients, a previously developed comprehensive approach to treatment [5-7], which included, in addition to radical surgery, a combination of APTChT (cisplatin, doxorubicin, 42°C, 1 hour) in combination with 7-8 courses of APChT (oxaliplatin, capecitabine or tegafur) – APTChT+APChT group – was

used. We used data from patients included in a previously conducted prospective randomized trial [8] for a comparative evaluation of the effect of this comprehensive approach on the progression pattern and survival rates, in which two groups were formed: 1) the APTChT group (68 people, including 42 men, 26 women; mean age, 56 ± 8 years) – APTChT was used in treatment in ad-

dition to radical surgery in the mode presented above; 2) the surgical control (SC) group (55 people, including 34 men, 21 women; mean age, 56 ± 9 years) (Table 1). Adjuvant therapy in the comparison groups was not performed according to the standards of GC treatment valid in the Republic of Belarus at the time of the prospective randomized study.

Table 1 - Characteristics of the study patients

Sign	SC group, n=55 (%)	APTChT group, n=68 (%)	APTChT + APChT group, n=18 (%)	p
Age (years), mean \pm SD	56.0 \pm 10.0	56.0 \pm 8.0	56.0 \pm 8.0	0.951
Gender				0.725
Male	34 (61.8)	42 (61.8)	13 (72.2)	
Female	21 (38.2)	26 (38.2)	5 (27.8)	
pT				0.626
pT4a	48 (87.3)	55 (80.9)	15 (83.3)	
pT4b	7 (12.7)	13 (19.1)	3 (16.7)	
pN				0.576
pN0	14 (25.5)	23 (33.8)	7 (38.9)	
pN1	6 (10.8)	8 (11.8)	3 (16.6)	
pN2	14 (25.5)	15 (22.1)	1 (5.6)	
pN3	21 (38.2)	22 (32.3)	7 (38.9)	
G				0.139
GI	4 (7.3)	6 (8.8)	1 (5.6)	
GII	9 (16.4)	17 (25)	4 (22.2)	
GIII	29 (52.7)	39 (57.4)	13 (72.2)	
GIV	13 (23.6)	6 (8.8)	0	

Note: SD – standard deviation

We assessed the following to evaluate the long-term results of treatment: adjusted survival (the event of death from the cause related to GC); progression-free survival (the event of registration of GC progression and death from the cause related to GC); dissemination-free survival (the event of registration of tumor dissemination through peritoneum and death from the cause related to GC were taken as the event of calculation).

The Kaplan-Meier multiplier method with the calculation of the standard error (SE) using the Greenwood formula was used to estimate survival rates. Surveillance was coded as "complete" if event data were available, and if no event information was available, as "censored." Competing risk analysis was used to analyze the pattern of progression, assessing the cumulative incidence (CI) of GC progression with the development of a) MPD; b) distant lymphohematogenous metastases (DLHM). Cumulative incidence was understood as an intensive index, reflecting the accumulation of the events considered over a specific time interval in the observation dynamics. The following events were considered when assessing the CI of GC progression variants: for MPD - the occurrence of progression with the development of carcinomatosis regardless of other progression variants if they were established simultaneously; for DLHM - cases of any progression in the absence of signs of carcinomatosis.

Comparing CIs of progression variants for two groups was performed using the Grey criterion [9]. The Fine-Gray model was used to determine unfavorable prognosis factors of metachronous peritoneal dissemination [10]. A nonparametric Cox proportional hazards model [11] was used to assess the effect of the used treatment option and tumor process characteristics on survival rate. The Bonferroni multiple-comparison correction was taken into account in paired comparisons.

Statistical analysis of the data was performed using the RV statistical package. 3.1.1 (GPL license) using *survival* [12] and *cmprsk* [13] packages.

Results: The median follow-up in the APTChT+APChT group was 84 months, and 104 months in the comparison groups.

The tendency to the improvement of long-term results of treatment in the most prognostically unfavorable cohort of patients noted during the interim evaluation of the results of this study [5, 6, 7] remained despite the increase of several patients in APTChT + APChT group and increase of follow-up period. In particular, the integrated treatment approach used reduced both the total number of cases of cancer progression and the incidence of MPD, which in the APTChT + APChT, APTChT, and SC groups were: the rate of progression – 16.7%; 55.9%, 87.3% ($p < 0.001$); 2) the rate

of MPD – 0%; 23.5%; 78.2% ($p < 0.001$), respectively. In addition, there were no cases of MPD and metachronous metastases in the liver in the APTChT+APChT group, the most frequent progression variants in the two comparison groups during the follow-up period.

The above demonstrated a change in the GC progression structure against the background of APTChT and

APChT, manifested by a significant reduction in MPD frequency. These changes led, in turn, to changes in the cumulative incidence of the considered variants of cancer progression: there were no MPD cases (KI of this variant of progression – 0), and cumulative incidence of DLHM was comparable with the GC group and statistically significantly lower in comparison with the APTChT group (Table 2).

Table 2 – Five-year cumulative incidence of gastric cancer progression variants

Cumulative incidence (CI)	Patient group/Value of cumulative incidence (%±SE)			p_{Gray}
	APTChT + APChT	APTChT	SC	
CI of peritoneal dissemination*	0	23.6±5.2	75.1±6.1	<0.001
CI of DLHM**	17.1 ±9.3	28.0±5.5	5.5±3.1	0.007

Notes:

* - the onset of progression with the development of MPD independent of the other progression variant, if they were established at the same time, was considered as an event;

** - any progression in the absence of MPD signs was considered an event.

Reduced incidence and CI of GC progression, including the development of MPD, when using APTChT+APChT combination in radically operated patients resulted in increased 5-year survival rate: In the APTChT+APChT, APTChT, and SC groups: 1) adjusted survival – 81.9±9.5%; 45.1±6.4%; 30.5±6.4%, respectively ($p=0.003$); 2) progression-free survival – 82.2±9.3%; 43.7±6.3%; 18.2±5.2%, respectively ($p < 0.001$); 3) dissemination-free survival – 81.9±9.5%; 45.2±6.3%; 21.3±5.6%, respectively ($p < 0.001$).

A multivariate analysis using the following prognostic models was performed to determine the com-

bined effect of many factors determining both the local spread of the tumor process (pN) and the amount of antitumor treatment performed on the clinical course of GC in the long term after undergoing radical treatment:

Cox model - to assess risk factors for the onset of an adverse outcome due to GC progression (Table 3);

Fine & Gray model – to determine the risk factors of MPD as the most frequent and prognostically unfavorable variant of infiltrative GC progression (in comparison with DLHM) (Table 4).

Table 3 – Estimation of the relative risk of an adverse outcome associated with GC progression (Cox model)

Factors associated with adverse outcome	Results of regression analysis		
	β	RR (95% CI)*	p
pN1-2 versus pN0	0.84	2.3 (1.3-4.3)	0.007
pN3 versus pN0	1.58	4.8 (2.6-9)	<0.001
Type of surgery: Standard or combined gastrectomy versus Subtotal gastric resection	0.57	1.8 (1.1-2.8)	0.018
Surgical treatment + APTChT versus Surgical treatment	-0.76	0.47 (0.3-0.72)	<0.001
Surgical treatment + APTChT + APChT versus Surgical treatment	-2.14	0.12 (0.04-0.38)	<0.001

Notes: RR - relative risk; CI - confidence interval

Table 4 - Assessment of relative risk of progression with development of metachronous peritoneal dissemination (Fine & Gray model)

Factors associated with the development of metachronous peritoneal dissemination	Results of regression analysis		
	β	RR (95% CI)*	p
pN1-2 versus pN0	0.84	2.3 (1.2-4.4)	0.009
pN3 versus pN0	1.48	4.4 (2.3-8.2)	<0.001
Type of surgery: Standard or combined gastrectomy versus Subtotal gastric resection	0.51	1.7 (1.03-2.7)	0.039
Surgical treatment + APTChT versus Surgical treatment	-0.65	0.52 (0.34- 0.81)	0.004
Surgical treatment + APTChT + APChT versus Surgical treatment	-1.99	0.14 (0.04-0.44)	<0.001

Notes: RR - relative risk; CI - confidence interval

Several well-known predictors of the adverse clinical course of GC, used in this study as inclusion criteria, were not included in the model: a) macroscopic growth form – Borrmann type III-IV; b) tumor invasion of serous gastric membrane or tumor transition to adjacent structures – pT4a-b.

It was found that the risk factors of adverse outcomes due to GC progression (Cox's model, Table 3) and the development of metachronous peritoneal dissemination (Fine & Gray model, Table 4) were:

1. Metastatic involvement of regional lymph nodes - an increase in the risk of adverse outcomes associated with GC progression and the risk of MPD development was noted in parallel with an increase in the degree of metastatic involvement of regional lymph nodes. It was previously noted when evaluating the interim results of this study [5, 6, 7] and is consistent with the literature [14].

2. Necessity of gastrectomy in standard or combined variant due to more extended tumorous process (compared to subtotal gastric resection).

The use of APTChT in an isolated variant and combined with systemic APChT reduced the risk of adverse outcomes associated with GC progression and the risk of MPD, which had been previously noted in the previous stages of the study [7]. However, it is noteworthy that the achieved effect was maintained despite an increase in the follow-up median.

The latter emphasizes the importance of APTChT (or intraperitoneal chemotherapy in any known variants) in the complex treatment of patients radically operated on for infiltrative GC. This helps prevent the most prognostically unfavorable variant of GC progression, such as metachronous peritoneal dissemination.

Discussion: The presented results of our studies demonstrate the necessity and appropriateness of APTChT as a compulsory component of the complex treatment of infiltrative forms of GC, which does not contradict modern standards of radical treatment of this pathology, involving in addition to surgical treatment of the use of one of the options of systemic chemotherapy, perioperative or adjuvant.

It was previously noted that the undoubted advantage of combining intraperitoneal and systemic chemotherapy in radically operated for infiltrative forms of GC is the simultaneous prevention of various options of GC progression: a) metachronous peritoneal dissemination due to elimination of free tumor cells from the peritoneal cavity by APTChT; b) systemic progression of GC by APChT [1, 5, 15, 16]. The results demonstrated above emphasize the adequacy of such an approach to improve

the long-term results of treatment of this category of patients, as well as demonstrate long-term remission of tumor process in patients of the prognostically unfavorable category (infiltrative cancer, metastatic lesion of regional lymph collection, invasion of serous lining of the stomach).

A differentiated approach to the definition of anti-tumor treatment based on individual assessment of the probability of metachronous peritoneal dissemination using prognostic models is a promising way to improve the results of locally disseminated GC treatment. The latter will allow supplementing the standard volume of treatment measures with perfusion thermochemotherapy exactly in patients with an objectively established high risk of MPD development, thus preventing excessive treatment in patients with low (or standard risk) of the considered variant of progression and avoiding undesirable complications associated with the unreasonable performance of APTChT and APChT [1, 4, 15, 16].

Conclusion: Using a combination of systemic APChT and APTChT is reasonable to increase the remission period of the tumor process in the radical treatment of infiltrative forms of pT4a-bN0-3M0 GC.

Complementing radical surgical treatment with perfusion thermochemotherapy (cisplatin, doxorubicin, at 42°C, 1 hour) and 7-8 courses of adjuvant polychemotherapy (oxaliplatin combined with capecitabine or tegafur) reduces the risk of metachronous peritoneal dissemination ($\beta = -0.65$, RR 0.52, 95% CI 0.34-0.81, $p = 0.004$) and the risk of gastric cancer progression in either variant ($\beta = -0.76$, RR 0.47, 95% CI 0.3-0.72, $p < 0.001$). This improves the survival of prognostically unfavorable patients.

The development of prognostic models allows estimating the risk of metachronous peritoneal dissemination for an individual approach to determining the volume of radical treatment of locally advanced gastric cancer, including its infiltrative forms, which seems actual.

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АНДАТПА

АСҚАЗАН ОБЫРЫНЫҢ ИНФИЛЬТРАТИВТІ ТҮРЛЕРІН ТҮБЕГЕЙЛІ ЕМДЕУДЕ АДЬЮВАНТТЫ ПЕРФУЗИЯЛЫҚ ТЕРМОХИМИОТЕРАПИЯНЫ ҚОЛДАНУ НӘТИЖЕЛЕРІ

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Өзектілігі: асқазан қатерлі ісігінің инфилтративті түрлерінің жоғары биологиялық агрессивтілігі адыювантты перфузиялық термoxимioтepaпия мен жүйелік адыювантты полиxимioтepaпияны қолдана отырып, оларды түбегейлі емдеуде кешенді тәсіл ретінде қажет етіледі.

Зерттеудің мақсаты – pT4a-bN0-3M0 асқазан қатерлі ісігінің инфилтративті түрлеріне түбегейлі операция жасалған емделушілерде адыювантты полиxимioтepaпия мен жүйелік адыювантты перфузиялық термoxимioтepaпия комбинациясының тиімділігін бағалау.

Әдістері: Асқазан қатерлі ісігіне байланысты түбегейлі операция жасалған 141 пациенттің (pT4a-bN0-3M0, R. Bormann бойынша III-IV тип) емдеу нәтижелеріне талдау жүргізілді, олардың 18-не адыювантты перфузиялық термoxимioтepaпиямен және жүйелік адыювантты перфузиялық термoxимioтepaпиямен түбегейлі операцияның комбинациясын қамтитын кешенді емдеу жүргізілді (оксалиплатин 100 мг/м² (1 күн курс), капецитабин 1000 мг/м² немесе тегафур 10-15 мг/кг (тәулігіне 2 рет, курстың 1-14 күні), үзіліс 7 күн, 8 курс) – адыювантты перфузиялық термoxимioтepaпия+ адыювантты перфузиялық термoxимioтepaпия тобы. Салыстыру топтары ретінде 55 түбегейлі хирургиялық пациенттің (хирургиялық бақылау) деректері, сондай-ақ түбегейлі операция адыювантты перфузиялық термoxимioтepaпиямен толықтырылған 68 пациенттің деректері пайдаланылды (цисплатин 50 мг/м² + доксорубин 50 мг/м², 42°C, 1 сағат) – адыювантты перфузиялық термoxимioтepaпия тобы. Ұзақ мерзімді емдеу нәтижелерін бағалау үшін бәсекелес тәуекелдерді талдау, Каплан-Мейерді көбейту әдісі, көп факторлы талдау (Кокс моделі, Файн-Грей моделі) қолданылды.

Нәтижелері: кешенді емдеу тобында ісік процесінің өрісуіне байланысты қолайсыз нәтиженің туындау қаупінің төмендеуі байқалды – $\beta = -2,14$; ор 0,12 (95% с.і 0,04–0,38), $p < 0,001$, сондай – ақ канцероматоздың даму қаупі – $\beta = -1,99$; ОР 0,14 (95% с.і 0,04–0,44), $p < 0,001$; 5 жылдық өмір сүру деңгейінің жоғарылауы (бақылау топтарымен салыстырғанда): түзетілген – $81,9 \pm 9,5\%$ ($p = 0,003$); прогрессиясыз өмір сүру – $82,2 \pm 9,3\%$ ($p < 0,001$); таралудан бос өмір сүру – $81,9 \pm 9,5\%$ ($p < 0,001$).

Қорытынды: асқазан қатерлі ісігінің инфилтративті түрлерін түбегейлі хирургиялық емдеуден кейін ісік процесінің ремиссия мерзімін ұзарту үшін перфузиялық интраоперациялық интраперитонеальді термoxимioтepaпия жүргізу арқылы стандартты тәсілді (жүйелік полиxимioтepaпиямен біріктірілген операция) толықтыру орынды.

Түйінді сөздер: асқазан қатерлі ісігі, адыювантты перфузиялық термoxимioтepaпия (АПТХТ), адыювантты жүйелік полиxимioтepaпия (АЖПХТ).

АННОТАЦИЯ

РЕЗУЛЬТАТЫ ПРИМЕНЕНИЯ АДЬЮВАНТНОЙ ПЕРФУЗИОННОЙ ТЕРМОХИМИОТЕРАПИИ ПРИ РАДИКАЛЬНОМ ЛЕЧЕНИИ ИНФИЛЬТРАТИВНЫХ ФОРМ РАКА ЖЕЛУДКА

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Актуальность: Высокая биологическая агрессивность инфильтративных форм рака желудка диктует необходимость комплексного подхода к их радикальному лечению с применением адьювантной перфузионной термoxимииотерапии (АПТХТ) и системной адьювантной полихимиотерапии (АПХТ).

Цель исследования – оценить эффективность комбинации АПТХТ и системной АПХТ у пациентов, радикально оперированных по поводу инфильтративных форм рака желудка pT4a-bN0-3M0.

Методы: Проведен анализ результатов лечения 141 радикально оперированного по поводу РЖ (pT4a-bN0-3M0, III-IV тип по R.Borrmann) пациента, у 18 из которых было проведено комплексное лечение, включающее комбинацию радикальной операции с АПТХТ и системной АПХТ (оксалиплатин 100 мг/м² (1 день курса), капецитабин 1000 мг/м² или тегафур 10-15 мг/кг (2 раза/сутки, 1-14 день курса), перерыв 7 дней, 8 курсов) – группа АПТХТ+АПХТ. В качестве групп сравнения использовали данные 55 радикально оперированных пациентов (хирургический контроль), а также 68 пациентов, у которых радикальная операция была дополнена АПТХТ (цисплатин 50 мг/м² + доксорубин 50 мг/м², 42°C, 1 час) – группа АПТХТ. Для оценки отдаленных результатов лечения использованы анализ конкурирующих рисков, метод множительных оценок Каплана-Мейера, многофакторный анализ (модель Кокса, модель Файна-Грея).

Результаты: В группе комплексного лечения отмечено снижение риска наступления неблагоприятного исхода, связанного с прогрессированием опухолевого процесса – $\beta = -2,14$; ОР 0,12 (95% ДИ 0,04-0,38), $p < 0,001$, а также риска развития канцероматоза – $\beta = -1,99$; ОР 0,14 (95% ДИ 0,04-0,44), $p < 0,001$; увеличение показателей 5-летней выживаемости (в сравнении с группами контроля): скорректированной – $81,9 \pm 9,5\%$ ($p = 0,003$); выживаемости, свободной от прогрессирования – $82,2 \pm 9,3\%$ ($p < 0,001$); выживаемости, свободной от диссеминации – $81,9 \pm 9,5\%$ ($p < 0,001$).

Заключение: Для увеличения сроков ремиссии опухолевого процесса после радикального хирургического лечения инфильтративных форм рака желудка целесообразно дополнение стандартного подхода (операция в сочетании с системной полихимиотерапией) проведением перфузионной интраоперационной интраперитонеальной термoxимииотерапии.

Ключевые слова: рак желудка, адьювантная перфузионная термoxимииотерапия (АПТХТ), адьювантная системная полихимиотерапия (АПХТ).

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UPGRADING OF LAPAROSCOPIC INTERVENTION OF THE PROSTATE GLAND TUMORS

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ABSTRACT

Relevance: Laparoscopic surgery supplies many benefits due to lower postoperative sequelae. Laparoscopic radical prostatectomy has become a first-line treatment for patients with localized prostate cancer worldwide.

The study aimed to compare outcomes after traditional laparoscopic extraperitoneal radical prostatectomy with modified laparoscopic extraperitoneal radical prostatectomy (MLERPE).

Methods: All information about patient treatment for this historical cohort study was obtained from the "Electronic In-patient Registry" of the Republic of Kazakhstan. The study included case records of 94 patients who underwent laparoscopic extraperitoneal radical prostatectomy from 2017 to 2021. Of them, 45 underwent a modified laparoscopic prostatectomy, and 49 – a traditional laparoscopic prostatectomy. Data are presented as the means \pm standard deviation or as frequencies and percentages. Pearson's Chi-square was used for qualitative data. T-test and Mann-Whitney U test were used to compare the means of the two groups. The statistical significance level was 0.05.

Results: We revealed significant differences between the laboratory parameters of both groups after surgery. The mean difference in hemoglobin level between the two groups was 14.04, the mean difference in erythrocyte level was 0.69, the mean difference in leukocyte level was 1.26, and the mean difference in ESR level was 2.01. All differences were statistically significant ($p=0.000$). We found a statistical difference in the duration of operation and hospital stay between the two groups ($p=0.000$).

Conclusion: The modified laparoscopic technique avoids adverse worse outcomes such as bleeding, pneumoperitoneum, and decreasing oxygen saturation. This technique is also beneficial in the early postoperative period for excluding peritonitis, and the late postoperative period avoids adhesive processes.

Keywords: Prostate gland tumors, prostate cancer, laparoscopic surgery, extraperitoneal prostatectomy, clinical outcome, Kazakhstan.

Introduction: Laparoscopy is a method of examining the peritoneal cavity and its contents by opening the abdominal cavity and obtaining its image using a lighted telescope. Laparoscopic surgery lowers postoperative sequelae and is a more suitable surgical procedure than traditional prostatectomy. In addition, better visualization of the operative site improves the quality of surgery due to optical enlargement and the maneuverability of the laparoscope, which provides a previously unobtainable anatomical view.

Laparoscopic radical prostatectomy was first executed in 1991 by Schuessler et al. [1]. Then an initial series with nine cases was published in 1997 [2]. However, the authors concluded that 'laparoscopic is not an efficacious surgical alternative to open prostatectomy for malignancy.' Since then, laparoscopy has undergone many modifications. Guillonnet and Vallancien described an LPR Montsouris technique that allowed surgery in less than three hours [3]. The new decision was implemented to avoid complications associated with the transperitoneal route [4, 5]. Preperitoneal access proposed by Raboy and colleagues [6] was used and justified in a series of 42 cases by Bollens and co-workers in 2001 [7].

Comparing laparoscopic techniques and open procedures supplied more benefits for laparoscopic procedures due to diminishing postoperative hospital stay, quick return to physical activity, and through advanced optical systems, better vision of the operative field [8]. For patients

with localized prostate cancer, laparoscopic radical prostatectomy is the best treatment method [9]. Laparoscopic radical prostatectomy has become a first-line treatment for patients with localized prostate cancer worldwide.

The study aimed to compare outcomes after traditional laparoscopic extraperitoneal radical prostatectomy with modified laparoscopic extraperitoneal radical prostatectomy (MLERPE).

Materials and Methods: This historical cohort study involved case reports of 94 patients with prostate cancer who underwent laparoscopic extraperitoneal radical prostatectomy surgery at the East Kazakhstan region multi-profile Center of Oncology and Surgery in Oskemen, the Center of Nuclear Medicine and Oncology in Semey, and the Kazakh Institute of Oncology and Radiology in Almaty between 2017 and 2021. Of them, 45 underwent MLERPE, and 49 patients with traditional laparoscopic extraperitoneal radical prostatectomy (TLERPE). We compared clinical outcomes such as blood count, duration of operation, and hospital stay after TLERPE and MLERPE.

All information about patient treatment was obtained from the electronic patient registry – an information system entitled "Electronic In-patient Registry" (EIPR) that comprises health records of all patients hospitalized at healthcare facilities in Kazakhstan. Approval from the Ethical Committee of Semey Medical University (Semey, Kazakhstan) was obtained (Protocol №2, October 18, 2019).

The MLERPE technique received patent protection in the RK on December 31, 2021, under patent no. 35437, "Method for preparing the operating place for extraperitoneal endoscopic treatment tumors of the prostate gland."

The choice of statistical criteria for data analysis depended on the type of analyzed variables. We used descriptive statistics to analyze the data. Pearson's Chi-square was used for qualitative data. Data are presented as the means \pm standard deviation or as frequencies and percentages. If the test statistic followed a normal distribution, we used Student's T-Test to compare the means of two independent groups.

If the test statistic did not follow a normal distribution, we used the Mann-Whitney U test to compare the means of the two groups. The statistical significance was 0.05. Analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (SSMU Semey city).

By nationality, 40,4% of patients were Kazakh, 50,0% were Russians, and other nationalities composed 9,6%. The average age of patients was 68.7 (± 3.93) years, and most patients had the IIIB stage disease. The two groups had no statistical difference in age or disease stage. The main characteristics of patients are presented in Table 1.

Table 1 – Patient characteristics

Characteristics	MLERPE	TLERPE	All
Age (yr.), mean (SD)	68.6 (3.97)	68.7 (3.94)	68.7 (3.94)
Nationality, n (%)			
Kazakh	17 (37.8%)	21 (42.9%)	38 (40.4%)
Russian	23 (51.1%)	24 (49.0%)	47 (50.0%)
Other	5 (11.1%)	4 (8.2%)	9 (9.6%)
Disease stage, n (%)			
IA	1 (2.2%)	1 (2.0%)	2 (2.1%)
IB	1 (2.2%)	1 (2.0%)	2 (2.1%)
IIA	6 (13.3%)	6 (12.2%)	12 (12.8%)
IIB	10 (22.2%)	10 (20.4%)	20 (21.3%)
IIIA	12 (26.7%)	15 (30.6%)	27 (28.7%)
IIIB	15 (33.3%)	16 (32.7%)	31 (33.0%)

Results:

A comparison of mean clinical parameters in two groups before and after surgery is presented in Table 2.

Table 2 – Comparison of mean clinical parameters in two groups before and after surgery

Characteristics	MLERPE	TLERPE	p-value
Duration of operation (minutes), Me (Q1; Q3)	90.0 (90.0; 107.5)	110.0 (110.0; 120)	U=272.2, Z=-6.61, p=0.000
Duration of hospital stay (day), Me (Q1; Q3)	9.0 (9.0; 10.0)	11.9 (11.0; 12.0)	U=55.5, Z=-8.12, p=0.000
Before surgery, the mean (SD)			
Hemoglobin (g/L)	137.5 (11.9)	137.7 (11.3)	t=-0.067, df=92, p=0.947
Erythrocytes ($10^{12}/L$)	4.98 (0.40)	4.94 (0.52)	t=0.407, df=92, p=0.685
Leukocytes ($10^9/L$)	6.11 (1.11)	6.16 (1.07)	t=-0.232, df=92, p=0.817
ESR (mm/H)	12.4 (3.09)	13.10 (3.11)	t=0.993, df=92, p=0.323
After surgery, the mean (SD)			
Hemoglobin (g/L)	136.3 (10.6)	123.6 (9.6)	t=6.10, df=92, p=0.000
Erythrocytes ($10^{12}/L$)	4.91 (0.42)	4.24 (0.52)	t=6.80, df=92, p=0.000
Leukocytes ($10^9/L$)	6.16 (1.09)	7.43 (1.28)	t=-5.19, df=92, p=0.000
ESR (mm/H)	14.2 (3.02)	17.6 (3.16)	t=-5.24, df=92, p=0.000

We found a statistical difference between the two groups in the duration of operation ($p=0.000$) and length of hospital stay ($p=0.000$).

There is no statistical difference in mean clinical parameters in both groups before surgery (Table 2). However, we noted significant differences between clinical parameters in the two groups after surgery.

Discussion: Laparoscopic procedures in the East Kazakhstan region multi-profile "Center of Oncology and Surgery" were launched to meet the global trend in urology, the interests and expectations of patients from laparoscopy, and the increasing importance of laparoscopy in Kazakhstan [10].

We carried out many laparoscopic operations on patients with prostate cancer and tried to improve this technique. A method of upgrading this procedure was proposed by Umurzakov in his Ph.D. thesis [10]. This surgery could be rec-

ommended for prostate gland tumors. In the known method of laparoscopic extraperitoneal radical prostatectomy, they create a cavity between the muscles of the anterior abdominal side and the peritoneum before surgery. In the extraperitoneal technique, a 2 cm incision is made along the midline 1 cm below the navel. After opening the anterior leaflet of aponeurosis and pulling the rectus abdominal muscle backward, a finger dissection is performed to access the Retzius space. Then, a dissector balloon is pasted toward the bosom, and up to 800 ml of gas is insufflated under visual control. After creating the working area, the balloon dissector is removed, and an optical trocar is installed. Four working trocars are installed in the extraperitoneal space under the optics control. Trocars 1 and 2 are installed along the pararectal line in the space of the iliac spines, 5 mm to the right and 10 mm to the left [10]. Then, a standard prostatectomy is performed following an established technique [1, 6, 11].

However, this surgery has some restrictions. Trocars installed at 40–60% injure the peritoneum, and gas is inflated into the abdominal space. This has adverse outcomes, such as pressure on the diaphragm. The bladder is pressed into the area of surgical intervention, and there is a high probability of damage to the lower abdominal and iliac vessels. Our invention solves the problem of injuring the peritoneum, pumping gas into the abdominal space, and injuring the pelvis's vessels. This technique helps avoid adverse outcomes such as bleeding, pneumoperitoneum, and decreased oxygen saturation [10].

The main difference between TLERPE and MLERPE is the placing of working trocars. Traditionally, the balloon dissector is withdrawn after creating the working area, an optical trocar is installed, and four working trocars are placed extraperitoneal under the optics control. In our technique, the balloon dissector is withdrawn after creating the work area, and four working trocars placement is controlled by the index finger, which palpates the lower epigastric vessels from the inside [10].

We compare hospital outcomes of both techniques. As is seen in tables 2 and 3, the initial data of patients in both groups was equal. Our technique allows for avoiding bleeding, which is indirectly evidenced by clinical results. Our method keeps lower epigastric vessels under control from the inside. The comparison showed a significant difference between the blood parameters of both groups.

We revealed significant differences between the laboratory parameters of both groups after surgery. The hemoglobin level in the TLERPE group visibly decreased compared to the MLERPE group. The mean difference in hemoglobin level between the two groups was 14.04, which was significant ($p=0.000$). The erythrocyte level in the TLERPE group decreased compared to the MLERPE group. The mean difference in erythrocyte level between the two groups was 0.69, with a significant difference ($p=0.000$). The leukocyte level in the TLERPE group visibly increased compared to the MLERPE group. The mean difference in leukocyte level between the two groups was 1.26, which is significant ($p=0.000$). ESR level in the TLERPE group visibly increased compared to the MLERPE group. The mean difference in ESR level between the two groups was 2.01. It is a significant difference ($p=0.000$).

The TLERPE operation took longer ($Me=110.0$ min) compared to MLERPE ($Me=90.0$ min), with $U=272.2$, $Z=-6.61$, $p=0.000$. The hospital stay in the TLERPE group was longer ($Me=11.9$ min) than MLERPE ($Me=9.0$ min), with $U=55.5$, $Z=-8.12$, $p=0.000$.

Conclusion: The placement of trocars is the main difference between traditional laparoscopic and our techniques.

The traditional laparoscopic procedure suggests four working trocars placed extraperitoneal under the optics control. We recommend installing the four working trocars under the control of the index finger, which palpates the lower epigastric vessels from the inside. Our technique avoids adverse worse outcomes such as bleeding, pneumoperitoneum, and decreasing oxygen saturation. Our technique is also beneficial in the early postoperative period for excluding peritonitis, and the late postoperative period avoids adhesive processes.

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АНДАТПА

ҚУЫҚ АСТЫ БЕЗІНІҢ ІСІКТЕРІНЕ ЛАПАРОСКОПИЯЛЫҚ АРАЛАСУДЫ ЖЕТІЛДІРҮ

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Өзектілігі: Лапароскопиялық хирургия көптеген пайда әкелді. Лапароскопиялық хирургияның мақсаты-операциядан кейінгі асқынуларды азайту. Лапароскопиялық радикалды простатэктомия әлемнің көптеген елдерінде локализацияланған простата обыры бар науқастарды емдеудің бірінші әдісі болды.

Зерттеудің мақсаты – дәстүрлі лапароскопиялық экстраперитонеальді радикалды простатэктомиядан өткен науқастардағы операциядан кейінгі нәтижелерді жетілдірілген лапароскопиялық экстраперитонеальді радикалды простатэктомиямен салыстыру болды.

Әдістері: Бұл тарихи когорттық зерттеуге науқастардың емдеу туралы барлық ақпарат "Стационарлық науқастардың электрондық тіркелімінен" алынды. Зерттеуге 2017-2021 жылдар аралығында лапароскопиялық перитонеальді радикалды простатэктомиядан өткен 94 пациенттің медициналық ауру тарихы енгізілді. Оның ішінде 45 пациент модификацияланған лапароскопиялық простатэктомиямен емделді, 49 пациент дәстүрлі лапароскопиялық простатэктомиямен емделді. Деректер орташа мәндер, стандартты ауытқу немесе жиіліктер мен пайыздар түрінде ұсынылған. Сапалы деректер үшін Пирсонның Хи-квадраты қолданылды. Екі топ арасын салыстыру үшін студенттің *t* критерийі, Манн-Уитнидің *U* критерийі қолданылды. Маңыздылықтың статистикалық деңгейі 0,05 болды.

Нәтижелері: Операциядан кейінгі екі топтағы зертханалық көрсеткіштердің орташа мәндері статистикалық маңызды айырмашылыққа ие болды. Екі топ арасындағы гемоглобиннің орташа айырмашылығы 14,04 болды, эритроциттердің орташа айырмашылығы 0,69 болды, ақ қан клеткаларының орташа айырмашылығы 1,26 болды, ЭТЖ орташа айырмашылығы 2,01 болды, Барлық айырмашылықтар статистикалық маңызды болды ($p=0,000$). Екі топ арасында операция ұзақтығының және ауруханада болудың статистикалық маңызды айырмашылығы анықталды ($p=0,000$).

Қорытынды: Экстраперитонеальді лапароскопияның өзгертілген әдісі қан кету, пневмоперитонеум және оттегінің азаюы сияқты жағымсыз асқынуларды болдырмауға көмектеседі. Біздің техникамыз сонымен қатар перитонит сияқты операциядан кейінгі ерте асқынуларды болдырмайды және операциядан кейінгі кезеңде адгезияны болдырмайды.

Түйінді сөздер: Қуық асты безінің ісіктері, қуық асты безінің қатерлі ісігі, лапароскопиялық хирургия, перитонеальді емес простатэктомиа, клиникалық нәтижелер, Қазақстан.

АННОТАЦИЯ

СОВЕРШЕНСТВОВАНИЕ ЛАПАРОСКОПИЧЕСКОГО ВМЕШАТЕЛЬСТВА ПРИ ОПУХОЛЯХ ПРЕДСТАТЕЛЬНОЙ ЖЕЛЕЗЫ

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Актуальность: Лапароскопическая хирургия принесла много пользы. Целью лапароскопической хирургии является снижение послеоперационных осложнений. Лапароскопическая радикальная простатэктомия стала методом первой линии лечения пациентов с локализованным раком предстательной железы во многих странах мира.

Цель исследования – сравнение послеоперационных исходов у пациентов перенесших традиционную лапароскопическую экстраперитонеальную радикальную простатэктомию с усовершенствованной лапароскопической экстраперитонеальной радикальной простатэктомией.

Методы: Вся информация о лечении пациентов для данного исторического когортного исследования была извлечена из «Электронного регистра стационарных больных». В исследование были включены истории болезни 94 пациентов, перенесших лапароскопическую внебрюшинную радикальную простатэктомию за 2017-2021 гг. Из них 45 были пролечены модифицированной лапароскопической простатэктомией, 49 – традиционной лапароскопической простатэктомией. Данные представлены в виде средних значений, стандартного отклонения, или частот и процентов. Для качественных данных использовался Хи-квадрат Пирсона. Для сравнения средних двух групп использовались *t*-критерий Стьюдента, *U*-критерий Манна-Уитни. Статистический уровень значимости был равен 0,05.

Результаты: Мы выявили достоверные различия между лабораторными показателями обеих групп после операции. Средняя разница показателя гемоглобина между двумя группами составила 14,04, средняя разница показателя эритроцитов – 0,69, средняя разница показателей лейкоцитов – 1,26, средняя разница СОЭ – 2,01. Все различия были статистически значимыми ($p=0,000$). Была выявлена статистически значимая разница длительности операции и пребывания в больнице между двумя группами ($p=0,000$).

Заключение: Модифицированный метод экстраперитонеальной лапароскопии помогает избежать неблагоприятных осложнений, таких как кровотечение, пневмоперитонеум и снижение насыщения кислородом. Наша методика также позволяет избежать ранних послеоперационных осложнений, таких как перитонит, а в позднем послеоперационном периоде позволяет избежать спаечных процессов.

Ключевые слова: Опухоли предстательной железы, рак предстательной железы, лапароскопическая хирургия, внебрюшинная простатэктомия, клинические исходы, Казахстан.

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THE VALUE OF METHODS FOR DIAGNOSING ALVEOLAR RHABDOMYOSARCOMA: A CLINICAL CASE

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ABSTRACT

Relevance: Rhabdomyosarcoma is extremely rare in practice. Clinical manifestations of rhabdomyosarcoma are diverse, which complicates the timely diagnosis of diseases of this group. The use of modern diagnostic methods in the complex will allow for accurate diagnosing and choosing proper treatment tactics.

The study aimed to evaluate the informativeness of various research methods in diagnosing alveolar rhabdomyosarcoma.

Methods: The article describes a clinical case of a male patient with the diagnosis: "Alveolar rhabdomyosarcoma with metastasis of the lungs, pleura, peripheral, subclavian, inguinal lymph nodes, pelvis, bone marrow" presented as a lymphoproliferative disease, diagnosed at the medical center of Marat Ospanov State Medical University (Aktobe, Kazakhstan).

Results: The immunohistochemistry results "The histological structure of the tumor and its immunophenotype correspond to alveolar rhabdomyosarcoma. The immunophenotype of the bone marrow sample: **CD45neg-CD56+CD7+CD2+CD3+CD38+CD34-** did not exclude a solid tumor.

Conclusion: This clinical case aroused great interest in our medical institution due to its rarity, thereby revealing difficulties in diagnosing a patient with multiple life-threatening tumor lesions. The clinical case again proves that alveolar rhabdomyosarcoma is characterized by an extremely aggressive course and an unfavorable prognosis. A long and accurate examination, including IHC, flow cytometry, and morphological studies, was required to verify the diagnosis. These results should be considered in the differential diagnosis of neuroblastoma and rhabdomyosarcoma.

Keywords: clinical case, rhabdomyosarcoma, flow cytometry, immunohistochemistry.

Introduction: Early cancer diagnostics is the key to adequate management of patients and improvement and outcome of the disease. Soft tissue sarcoma accounts for about 7% of cancers in children and 1% in adults [1]. Advances in molecular biology and genetics have also made it possible to better understand the pathogenesis of rhabdomyosarcoma. These approaches continue to provide a platform to improve diagnostics, disease classification, patient risk stratification, and management strategies. Although rare, rhabdomyosarcoma is a relatively common form of childhood cancer and is the most common soft tissue sarcoma in children. The overall incidence of rhabdomyosarcoma is approximately 4.5 patients per million people <20 years of age. In the United States, rhabdomyosarcoma is approximately 350 new cases per year. Based on data from the Surveillance, Epidemiology, and End Results (SEER) program, rhabdomyosarcoma's incidence varies by age and histology [2]. This article describes the immunophenotyping of the bone marrow by flow cytometry with the verification of the rhabdomyosarcoma diagnosis by immunohistochemistry (IHC).

Despite the advances in understanding this disease's biology, few clinical studies are specific to rhabdomyosarcoma. Therefore, several important questions remain unanswered regarding how and what

diagnostic method to use to verify the rhabdomyosarcoma diagnosis.

This study aimed to evaluate the informativeness of various research methods in diagnosing alveolar rhabdomyosarcoma.

Materials and methods: The article presents a description of a clinical case of alveolar rhabdomyosarcoma with metastasis of the lungs, pleura, peripheral, subclavian, inguinal lymph nodes, small pelvis, bone marrow, presented as a lymphoproliferative disease, diagnosed at the Medical Center of West Kazakhstan Marat Ospanov Medical University (Aktobe, Kazakhstan).

Clinical case:

Patient information: Patient O., born in 2003, was admitted to the Department of Hematology of the Medical Center of West Kazakhstan Marat Ospanov Medical University with the suspected lymphoproliferative disease, acute leukemia.

Clinical data: Based on the anamnesis vitae, it is known that the debut of the disease took place in August 2022, after hypothermia of contact with cold water. The patient addressed a physician at the place of residence and was administered treatment but could not name the drugs or provide an extract from medical records. After treatment, there was no improvement, and myalgia increased, as well

as weakness in the upper limbs joined. Then a rheumatologist examined the patient, and a preliminary diagnosis was made: "Paraneoplastic inflammatory myopathy with a high degree of activity, damage to the reticuloendothelial system (lymphadenopathy of the para-aortic and external inguinal and cervical lymph nodes), retroperitoneal lymphoma, hepatosplenomegaly. Exclude blood disease (lymphoproliferative disease, leukemia)."

Anamnesis vitae: The patient grew and developed according to age and gender.

Objective data: The general condition of moderate severity due to the activity of the autoimmune process. Peripheral lymph nodes: an enlarged anterior cervical lymph node on the left, 3.5x3.0 cm in size, painless. Palpation: Pain in the inguinal region, enlarged lymph nodes on both sides. Body temperature: 36.8-37.0°C. There is no visible pathology from the side of the osteoarticular system, but the patient moves with difficulty due to severe myalgia. There are no swollen joints. Movement in the peripheral joints in complete, moderate pain in the knee joints. Pal-

pation: pain in the lower and upper extremities' muscles on both sides.

Diagnostics:

Complete blood count, September 2022: leukocytes – $12.6 \times 10^9/L$, hemoglobin – 65 g/L, platelets – $31 \times 10^9/L$,

Biochemical blood test, September 2022: creatinine – 401 $\mu\text{mol/L}$, urea – 18.2 mmol/L, ALT – 9.4 U/L, AST – 38.4 U/L, total bilirubin – 6.8 $\mu\text{mol/L}$, total protein – 48 g/L.

Myelography, bone marrow immunophenotyping (IPT), and lymph node IHC were performed to exclude hemoblastosis, given the preliminary diagnosis of lymphoproliferative disease and acute leukemia.

Myelogram, September (2022). Bone marrow is cellular, predominantly represented by cells of the lymphoid lineage. The remaining hematopoietic lineage is depressed. Megakaryocytes were not found. Blast cells in the blood (bone marrow) – 60.5%. Conclusion: Acute lymphoblastic leukemia (ALL) (Figure 1).

The rhabdomyosarcoma cells were mistaken for blast cells, and ALL was diagnosed accordingly.

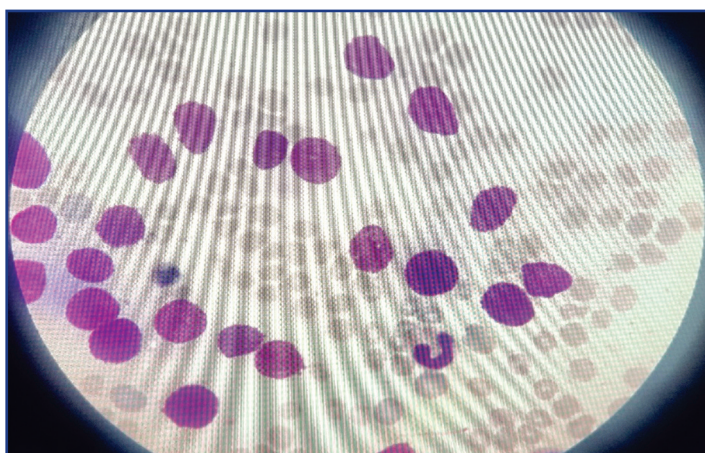


Figure 1 – Myelogram. Picture of acute lymphoblastic leukemia in patient O., 20 years old
(Olympus microscope, Olympus Corporation, Japan)

To identify the immunophenotype, we used the following:

Screening (verification) panel: CD45 KrO/ CD3 PB/ CD2 FITC /CD56 PE /CD19 ECD/ CD5 PC5.5/ CD34 PC7/ CD8 APC/ CD38 APC-A700.

All monoclonal antibodies available at the laboratory were added to the panel to clarify the immunophenotype of the CD45 neg CD56+ population and exclude neoplasia from mature lymphocytes.

IPT of bone marrow cells, September 2022: CD45neg CD56+, the resulting immunophenotype CD45neg-CD56+CD7+CD2+CD3+CD38+CD34- did not exclude a solid tumor (Figure 2).

The bone marrow trepanobiopsy histopathological preparations were sent for review at the UNIM reference laboratory (Moscow, RF). The conclusion was, "The morphological picture in the bone marrow and the

identified immunophenotype characterize the metastasis of alveolar rhabdomyosarcoma (cranial-nasopharyngeal localization?). Data in favor of a tumor of a hematolymphoid nature, including acute leukemia, were not found".

The histological preparations were revised at the UNIM reference laboratory. The material from the lymph node from the inguinal region underwent an IHC study at the pathoanatomical laboratory of the Medical Center of West Kazakhstan Marat Ospanov Medical University. The conclusion was, "The histological structure of the tumor and its immunophenotype are consistent with alveolar rhabdomyosarcoma. ICD-10:C80.0 ICD-O: 8920/3; Alveolar rhabdomyosarcoma; ALVEOLAR RHABDOMYOSARCOMA; C809; UNKNOWN; considering the above data, a malignant process of a hematopoietic nature was excluded" (Figures 3, 4).

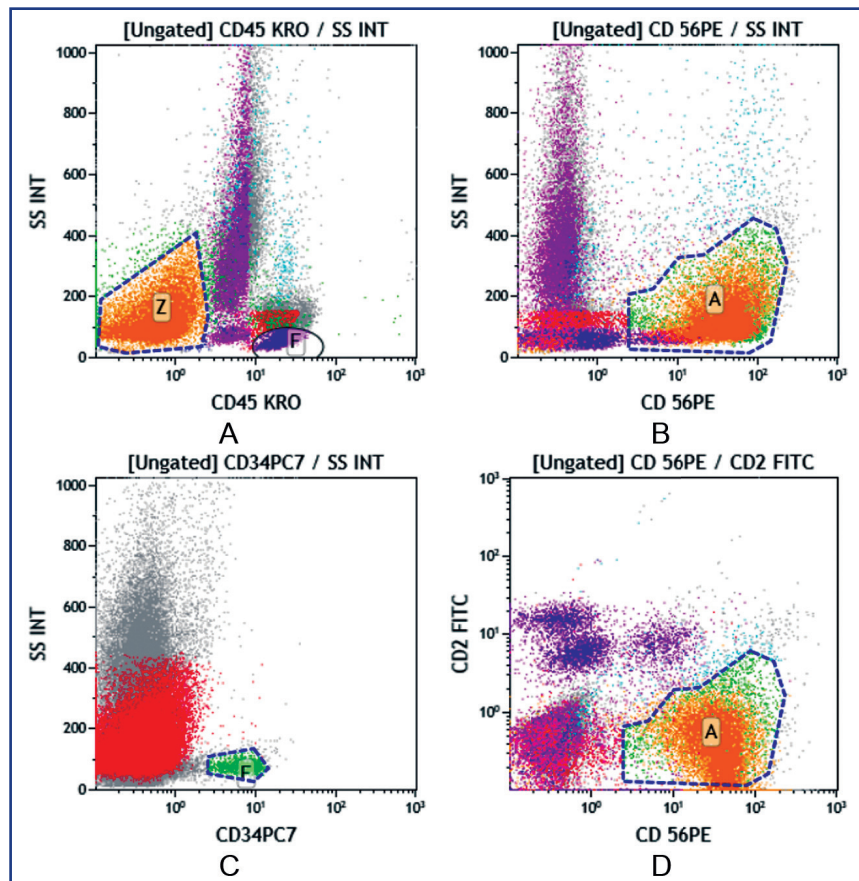


Figure 2 - Histogram of patient O., 20 years old, with a diagnosis of alveolar rhabdomyosarcoma:
 A – CD45neg-, B – CD56+, C – CD34-, D – CD56+CD2+ (performed on Navios 10/3 flow cytometer, Beckman Coulter, USA)

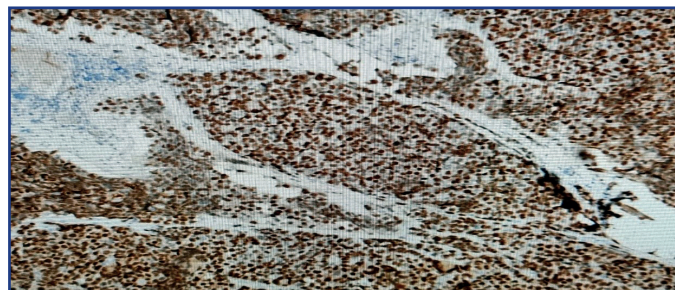


Figure 3 – Alveolar structures of the lymph node in alveolar rhabdomyosarcoma (analysis was performed on a digital slice scanner MAGSCANER KF-PRO-120, China)

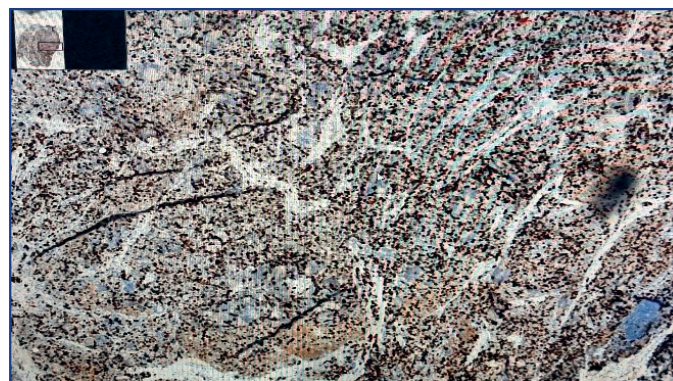


Figure 4 – CD56 (dot-like staining in part of the cells of the lymph node) in alveolar rhabdomyosarcoma (analysis was performed on a digital slice scanner MAGSCANER KF-PRO-120, China)

Treatment: The treatment was symptomatic and included blood transfusion therapy, sodium chloride, to-rasemide, metronidazole, levofloxacin, Mycosan, fluconazole orally, analgesic mixture, ketoprofen, tramadol, ursodeoxycholic acid, aminocaproic acid, etamsylate, tranexamic acid, metoclopramide, and furosemide.

Against the background of symptomatic treatment, the effect was minimal. It was due to the severity of the patient's condition upon admission and generalized damage by tumor cells to all vital tissues, organs, and systems which led to death.

Figure 5 shows the timeline of this clinical case.

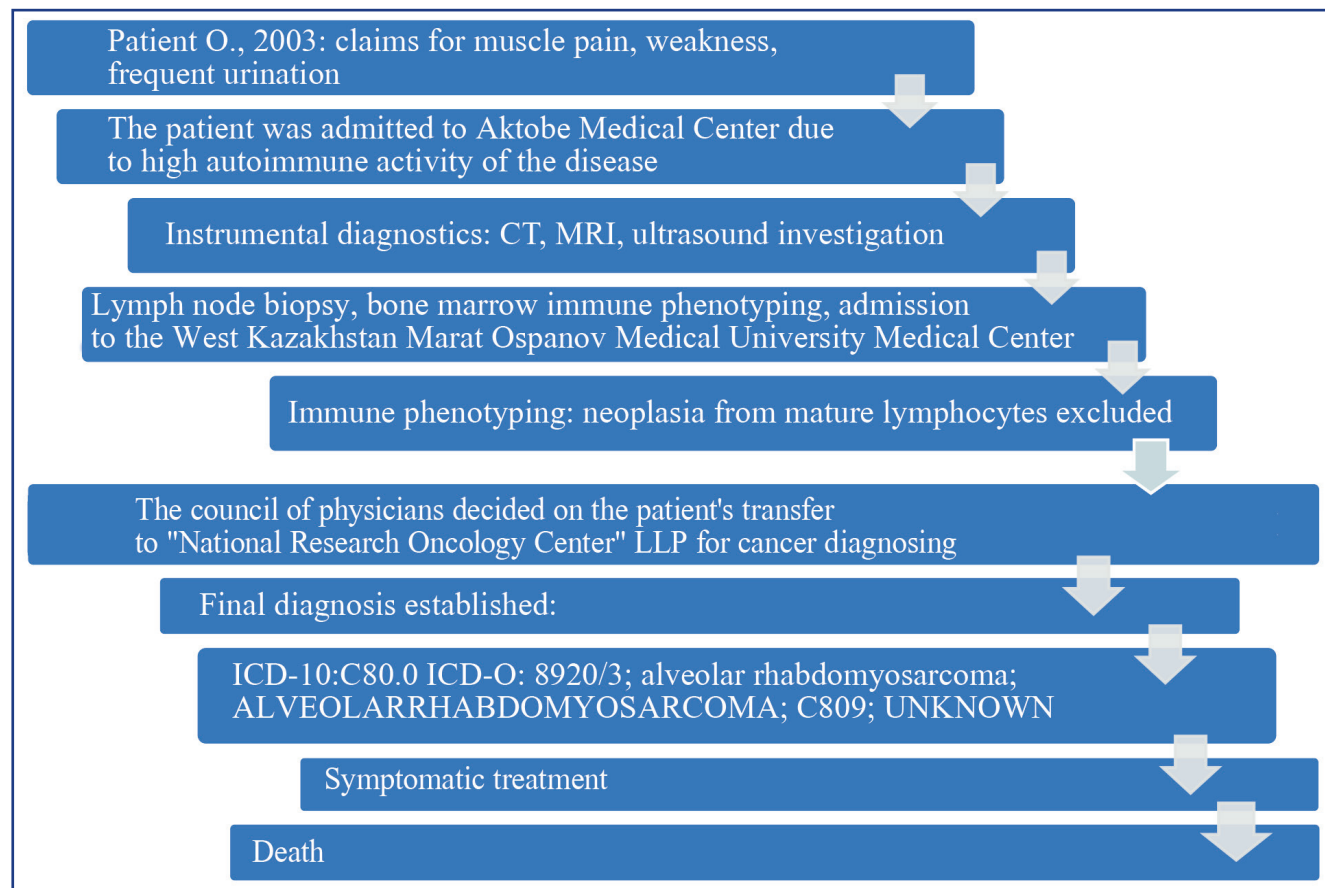


Figure 5 – Timeline of the clinical case of alveolar rhabdomyosarcoma in patient O., 20 years

Discussion: Patients with rhabdomyosarcoma have a poor prognosis. Detecting rhabdomyosarcoma tumor cells in the bone marrow is essential for clinical staging and risk assessment. In the presented clinical case, the histological and IHC opinion was made after comparing with the conclusion of the reference laboratory in Moscow. However, according to the conclusion of the myelogram, ALL was diagnosed, which made differential diagnosis extremely difficult. Simultaneous manifestation of a solid tumor was also not excluded.

Currently, leukemia/lymphoma and other hematopoietic malignancies' diagnosing relies mainly on immunophenotyping results [1, 2], in addition to cytomorphological/histopathological and molecular data [3, 4]. In contrast, the definitive diagnosis of non-hematopoietic (solid) tumors is based on histopathological examination of tissue samples followed by IHC staining for relatively broad panels of markers and further molecular studies in specific diagnostic tumor subtypes [5]. This approach, used for diagnostic screening of solid tumors

in general, is time-consuming, resulting in a delay in the final diagnosis in a significant proportion of patients [1-4].

Multiparametric flow cytometry (MFC) is a key method for the immunophenotypic diagnosis of acute leukemia and chronic lymphoproliferative diseases. MFC can simultaneously assess several tumor cells [6]. Nevertheless, MFC is not part of routine diagnostics of solid tumors [4-6]. It is mainly due to the need to obtain (fresh) suspensions of individual cells and that, unlike IHC, MFC does not provide information on the structure and location of tumor cells in tissues [7]. Therefore, early studies on the use of MFC in solid tumors mainly focused on detecting disseminated disease in the bone marrow [8, 9]. Those studies revealed different antigen expression profiles among metastatic non-hematopoietic bone marrow tumor cells. Some profiles are closely associated (or even specific) with some diagnostic subtypes of solid tumors [10]. For example, the expression of CD90⁺, CD56⁺, and CD57^{-/+} in the absence of CD45 is most often observed in rhabdomyosarcoma tumor cells [11].

A single combination of antibodies has been developed and validated for rapid and accurate diagnostic screening, targeting, and classification of solid tumors in children and adolescents. In addition, monoclonal antibodies can be used as an additional tool to conventional histopathology for diagnosing and classifying childhood cancer [12].

Further multicentre validation of the Solid Tumor Orientation Tube (STOT) classification of solid tumors is ongoing in the EuroFlow consortium, with particular attention to the detection of blast cells and other rare non-hematopoietic tumor types [9]. This clinical case demonstrates the difficulties in diagnosing patients with multiple life-threatening tumor lesions. The need to develop molecular genetic studies and expand the range of diagnostic capabilities of flow cytometry is an integral part of treating oncohematological diseases [13, 14].

Conclusion: This clinical case aroused great interest among the specialists of our medical institution due to its rarity. It revealed difficulties in diagnosing an early-age patient with multiple life-threatening tumor lesions. An extremely aggressive course and an unfavorable prognosis of alveolar rhabdomyosarcoma have been proven again. Verifying this diagnosis required a long and comprehensive examination, including IHC, flow cytometry, and morphological studies. The results should be considered in the differential diagnostics of neuroblastoma and rhabdomyosarcoma.

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АНДАТПА

АЛЬВЕОЛЯРЛЫ РАБДОМИОСАРКОМАНЫ ДИАГНОСТИКАЛАУ ӘДІСТЕРІНІҢ МАҢЫЗЫ: КЛИНИКАЛЫҚ ЖАҒДАЙ

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Өзектілігі: Рабдомиосаркома іс жүзінде өте сирек кездеседі. Рабдомиосаркоманың клиникалық көріністері әртүрлі, бұл осы топтың ауруларын уақтылы диагностикалауды қиындатады. Кешенде диагностиканың заманауи әдістерін қолдану дәл диагнозға және одан әрі емдеу тактикасына қол жеткізуге мүмкіндік береді.

Зерттеудің мақсаты – альвеолярлы рабдомиосаркоманы диагностикалаудағы әртүрлі зерттеу әдістерінің ақпараттылығын бағалау.

Әдістері: мақалада Марат Оспанов атындағы БҚМУ медициналық орталығында (Ақтөбе, Қазақстан) диагноз қойылған лимфопролиферативті ауру ретінде ұсынылатын "өкпе, плевра, перифериялық, субклавиялық, шан лимфа түйіндері, кіші жамбас, сүйек кемігінің метастазы бар альвеолярлы рабдомиосаркома" диагнозы қойылған Ер пациенттің клиникалық жағдайы сипатталған.

Нәтижелері: Иммуногистохимияға сәйкес: "ісіктің гистологиялық құрылымы және оның иммунофенотипі альвеолярлы рабдомиосаркомаға сәйкес келеді.

Сүйек кемігі үлгісінің иммунофенотипі: **CD45neg-CD56+CD7+CD2+CD3+CD38+CD34**-қатты ісікті жоққа шығармады.

Қорытынды: Бұл клиникалық жағдай біздің медициналық мекемеде сирек кездесетіндігіне байланысты үлкен қызығушылық тудырды және осылайша көптеген өмірге қауіп төндіретін ісік зақымдануы бар науқасты диагностикалаудағы қиындықтарды анықтады. Клиникалық жағдай альвеолярлы рабдомиосаркоманың өте агрессивті ағыммен және қолайсыз болжаммен сипатталатынын тағы бір рет дәлелдейді. Диагнозды тексеру үшін IGH, ағынды цитофлуориметрия және морфологиялық зерттеулерді қоса, ұзақ және дәл тексеру қажет болды. Алынған нәтижелер нейробластома мен рабдомиосаркоманың дифференциалды диагностикасында ескерілуі керек.

Түйінді сөздер: клиникалық жағдай, рабдомиосаркома, ағынды цитофлуориметрия, иммуногистохимия.

АННОТАЦИЯ

ЦЕННОСТЬ МЕТОДОВ ДИАГНОСТИКИ АЛЬВЕОЛЯРНОЙ РАБДОМИОСАРКОМЫ: КЛИНИЧЕСКИЙ СЛУЧАЙ

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Актуальность: Рабдомиосаркома на практике встречается крайне редко. Клинические проявления рабдомиосаркомы многообразны, что затрудняет своевременную диагностику заболеваний данной группы. Использование современных методов диагностики в комплексе позволяет добиться постановки точного диагноза и выбора корректной тактики лечения.

Цель исследования – оценить информативность различных методов исследования в диагностике альвеолярной рабдомиосаркомы.

Методы: В статье описан клинический случай пациента мужского пола с альвеолярной рабдомиосаркомой с метастазом легких, плевры, периферических, подпочечных, паховых лимфоузлов, малого таза, костного мозга, презентировавшейся как лимфопролиферативное заболевание и диагностированной в медицинском центре ЗКМУ имени Марата Оспанова (Актобе, Казахстан).

Результаты: По данным иммуногистохимии: «Гистологическая структура опухоли и ее иммунофенотип соответствуют альвеолярной рабдомиосаркоме.

Иммунофенотип образца костного мозга: **CD45neg-CD56+CD7+CD2+CD3+CD38+CD34**- не исключал солидную опухоль.

Заключение: Данный клинический случай вызвал в нашем медицинском учреждении огромный интерес в связи со своей редкостью и тем самым выявил трудности в диагностике пациента с множественным жизнеугрожающим опухолевым поражением. Клинический случай еще раз доказывает, что альвеолярная рабдомиосаркома характеризуется крайне агрессивным течением и неблагоприятным прогнозом. Для верификации диагноза требовалось длительное и точное обследование, включая ИГХ, проточную цитофлуориметрию и морфологические исследования. Полученные результаты необходимо учитывать при дифференциальной диагностике нейробластомы и рабдомиосаркомы в подростковом возрасте.

Ключевые слова: клинический случай, рабдомиосаркома, проточная цитофлуориметрия, иммуногистохимия (ИГХ).

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EVALUATION OF KIDNEY FUNCTION IN AN ELDERLY PATIENT WITH ACUTE MYELOBLASTIC LEUKEMIA AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION: A CASE REPORT

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ABSTRACT

Relevance: Kidney functions in treating acute myeloblastic leukemia (AML) undergo serious effects, especially in elderly patients. Chemotherapeutic drugs used to prepare for hematopoietic stem cell transplantation (HSCT) inevitably affect elderly patients' kidney function. Moreover, involutive changes in the kidneys can physiologically decrease kidney function.

The study aimed to evaluate kidney function in an elderly patient with AML after HSCT.

Methods: The article describes a clinical case of AML in an elderly patient who underwent allogeneic HSCT.

Results: We analyzed the dynamics of the functional state from the moment of registration of AML to +100 days after HSCT. During the entire follow-up period, we did not detect any renal dysfunction in the elderly patient. Despite the HSCT and the effects of nephrotoxic drugs in an elderly patient + 100 days after HSCT, kidney function was preserved.

Conclusion: The described case highlights the importance of maintaining renal function in elderly patients after HSCT and long-term renal monitoring.

Keywords: hematopoietic stem cell transplantation (HSCT), bone marrow transplantation, acute myeloblastic leukemia (AML), renal failure, case report, glomerular filtration rate, complications, elderly patients.

Introduction: Currently, the treatment of elderly patients with acute myeloblastic leukemia (AML) is decided individually depending on the risk-benefit ratio, and the choice of treatment varies from hematopoietic stem cell transplantation (HSCT) to palliative therapy [1, 2]. At the same time, preserving kidney function in elderly patients treated for AML is crucial [3, 4]. Chemotherapeutic drugs used to prepare for hematopoietic stem cell transplantation (HSCT) inevitably affect elderly patients' kidney function [5-7]. Meanwhile, involutive changes in the kidneys and changes in hemodynamics in elderly patients could physiologically decrease renal function [8-10]. Particular attention among the elderly with AML is required by patients with concomitant chronic diseases, which in many cases determine the treatment tactics of an elderly patient. According to worldwide data, there is scant information about the state of the kidneys in elderly patients with AML in HSCT conditions.

The study aimed to evaluate kidney function in an elderly patient with AML after HSCT.

Materials and Methods: The article describes a clinical case of AML in an elderly patient who underwent allogeneic HSCT (Allo HSCT).

Patient Information: Patient N, 60 years old, applied to the National Scientific Center of Oncology (Astana, Kazakh-

stan) complaining of breath shortness and decreased exercise tolerance. She was diagnosed with AML (M4, high-risk group) after cytological examination of blood and bone marrow, cytochemical examination of blast cells, immunophenotyping on a flow cytofluorimeter, standard cytogenetic examination, molecular genetic examination by FISH and the cerebrospinal fluid analysis (Table 1).

Table 1 – Characteristics of the patient with AML

Parameter	Value
Gender	Female
Age	60 years
Nationality	Slavic
AML FAB-classification:	M4, a high-risk group
Myelogram	Blast cells 56%
Immunophenotyping	CD45dim40,0%, CD45moderate
Cytogenetic study	No mutation identified
Molecular genetic research by FISH method	No t(9;22)(q34;q11) translocation detected

Clinical parameters: The patient was registered for chronic viral hepatitis B and chronic cholecystitis. The outpatient medical card reported normal blood pressure levels. The patient's general condition was of moderate severity due to the underlying disease. Clinical symptoms from the vital organs

were not observed. Organs of urination: The kidney area was not visually altered. Urination was independent; the urine was yellow. The diuresis was adequate, 1.8-2.2 liters per day.

Diagnostics: The patient underwent cytological studies of blood and bone marrow, cytochemical examination of blast cells, immunophenotyping on a flow cytofluorimeter, standard cytogenetic examination, and molecular genetic examination by the FISH method.

In order to assess the renal functions of the patient, general clinical laboratory and instrumental methods of examination were carried out.

Treatment: The patient's treatment included induction courses of chemotherapy according to the 7+3 DNR 60mg/m² scheme. Bone marrow remission was not achieved in the first course of treatment. However, it was achieved after 21 days of the second course with 1.5% blast cells in the control myelogram. Subsequently, the patient underwent consolidating chemotherapy courses: 7+3 IdA12 mg/m², three courses with Azacitidine, two courses of IDAC, and the supporting course of 5+CF. During the treatment, the myelogram showed 1.5 to 2.4% of blast cells in the blood.

Further, in May 2022, the patient underwent Allo HSCT from a 100% compatible relative donor (sister). The conditioning regimen included Busulfan 232 mg per os from -5D to -3D and Fludarabine IV 45 mg/day from -7D to -2D. After the conditioning, the patient received 380 ml of suspended hematopoietic stem cells, amounting to 5.5 million CD34/kg. The initial preventive treatment of graft-versus-host disease (GvHD) was carried out using cyclophosphane at 50 mg/kg from +3D to +5D and tacrolimus at 1.7 mg/day. Complications after Allo HSCT included febrile neutropenia and invasive pulmonary aspergillosis. These complications required additional antiviral, antibacterial, and antifungal therapy. On Day 16 after Allo HSCT, the patient developed neutrophilic engraftment; the leukocyte level was above 1x10⁹/L. After Day 13, her platelet count exceeded 20x10⁹/L. According to the examination +100 days after HSCT, the bone marrow remission (myelogram-blasts of 2% per 500 cells) and complete donor chimerism (100%) were preserved.

The patient examinations +100 days after Allo HSCT revealed no pronounced changes in kidney function (Table 2).

Table 2 – Timeline of laboratory parameters of an elderly patient before and after HSCT

Parameter / Timing	Before HSCT	10 days after HSCT	18 days after HSCT	30 days after HSCT	90 days after HSCT	100 days after HSCT
Total protein, g/L	56.7	63.8	53.1	57.5	63.4	72.6
Albumin, g/L	30.1	36.7	29.3	34.3	31.2	42.1
Uric acid, μmol/L	280	242	150	386	423	607
Alkaline phosphatase, units/L	66	92	48	61	73	111
Urea, mmol/L	2.4	2.9	1.5	5.0	5.9	7.5
Creatinine, mkmol/L	72.4	73.3	78.6	74.5	95.7	94.6
GFR, ml/min/1.73 m ²	78	77	71	75	56	57

During the observation period, the excretory function of the kidneys in the studied patient was preserved. During the examination, no pathological changes were detected in the urinary sediment, and the daily diuresis was within 2200 ml.

Ultrasound diagnostics revealed no significant changes in kidney size or parenchymal thickness before and after HSCT. Kidney computed tomography also revealed no changes in kidney size before or after HSCT (Figures 1).

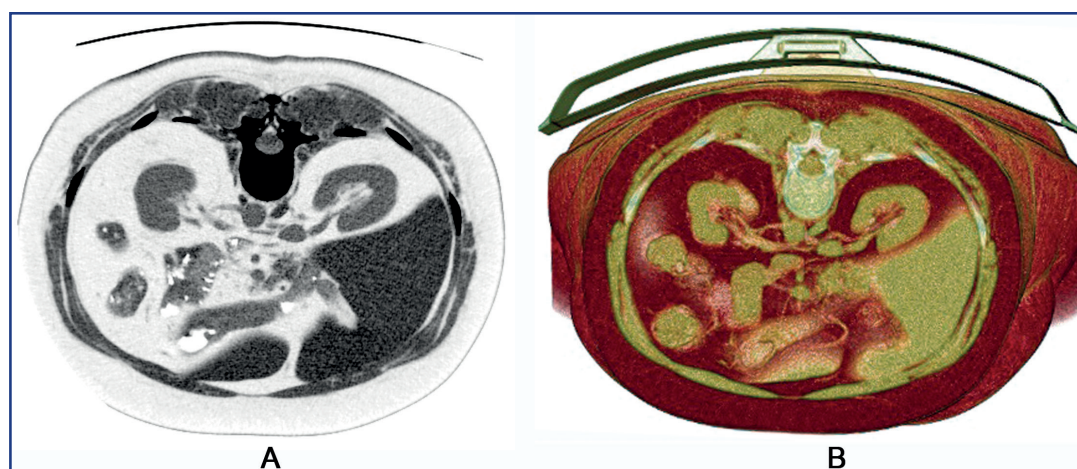


Figure 1 – CT of kidney and kidney vessels in a patient with AML before (A) and after (B) Allo HSCT

An ultrasonic Doppler examination showed no decrease in blood flow of the renal vessels. Considering the duration of immunosuppressive therapy (+100 days) and

no signs of GvHD, Prograf was continued at a reduced dose of 0.5 mg per day for one month and canceled afterward.

Discussion: According to the results of the conducted studies, the survival rate in elderly patients with acute leukemia has an unfavorable prognosis [11]. Meanwhile, the authors believe that the outcome of treatment in elderly patients depends not only on the disease but also on medical care, including active and supportive therapy.

In addition, it is now known that there is a high mortality rate of patients with acute leukemia worldwide, especially the elderly, who are increasingly less likely to undergo HSCT. At the same time, according to recent studies, it is known that a decrease in kidney function is associated with mortality in HSCT recipients.

In the presented study, we regularly monitored the patient's kidney function from the moment of registration to +100 days after HSCT. The studied patient did not have a period of exacerbation of concomitant diseases, and the patient did not have serious complications after HSCT, such as GVHD, which could also affect kidney function.

We believe preserved kidney function is key for long-term remission and survival of elderly patients after HSCT. Hopefully, our clinical case could help practitioners treat elderly patients with acute leukemia, especially in Kazakhstan, and expand the indications for HSCT. At the same time, we believe that more extensive studies are needed to obtain a more detailed report on the functional state of the kidneys in elderly recipients of HSCT. Based on this case, we want to emphasize the importance of monitoring kidney function and management tactics of elderly HSCT recipients, which in turn may affect the survival of elderly patients.

Conclusion: In our study, we presented the case of an elderly patient with AML who underwent HSCT. Despite long nephrotoxic chemotherapy, antifungal and antiviral therapy, kidney function in an elderly patient was preserved for +100 days after HSCT. The results of our clinical case reflect the importance of assessing the functional

state of the kidneys in elderly patients with AML before and after HSCT to determine early renal dysfunction and long-term monitoring.

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АНДАТПА

ГЕМОПОЭТИКАЛЫҚ ДІҢ ЖАСУШАЛАРЫН ТРАНСПЛАНТАЦИЯЛАУДАН КЕЙІН ЖЕДЕЛ МИЕЛОБЛАСТИКАЛЫҚ ЛЕЙКЕМИЯМЕН АУЫРАТЫН ЕГДЕ ЖАСТАҒЫ НАУҚАСТЫҢ БҮЙРЕК ҚЫЗМЕТІН БАҒАЛАУ: КЛИНИКАЛЫҚ ЖАҒДАЙ

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Өзектілігі: жедел миелобластикалық лейкозды емдеудегі бүйрек қызметі, әсіресе егде жастағы науқастарда ауыр әсерге ұшырайды. Егде жастағы пациенттерді бірқатар химиотерапиялық препараттарды қолдана отырып, ГДЖТ-ге дайындау сөзсіз бүйрек функциясына улы әсер етеді, сонымен қатар бүйректегі инволюциялық өзгерістер бүйрек қызметін физиологиялық тұрғыдан төмендетуі мүмкін.

Зерттеудің мақсаты – ГДЖТ-тен кейінгі жедел миелобластикалық лейкозиямен ауыратын егде жастағы науқастың бүйрек қызметін бағалау болды.

Әдістері: біз аллогенді ГДЖТ жүргізілген жедел миелобластикалық лейкозиямен ауыратын егде жастағы науқастың клиникалық жағдайын ұсындық.

Нәтижелері: біз егде жастағы науқастың жедел миелобластикалық лейкозия тіркелген сәттен бастап ГДЖТ-ден кейін +100 күнге дейінгі функционалдық жағдайының динамикасын талдадық. Бақылау кезеңінде біз егде жастағы науқаста бүйрек ауруларын анықтаған жоқпыз. Егде жастағы науқаста ГДЖТ және нефротоксикалық препараттардың әсеріне қарамастан, ГДЖТ кейін +100 күн, бүйрек қызметі сақталды.

Қорытынды: бұл жағдай егде жастағы емделушілерде ГДЖТ-дан кейін бүйрек қызметін сақтаудың және бүйрек қызметін ұзақ уақыт бақылаудың маңыздылығын көрсетеді.

Түйінді сөздер: гемопоэтикалық дің жасушаларын трансплантациялау, сүйек кемігін трансплантациялау, жедел миелобластикалық лейкозия, бүйрек жеткіліксіздігі, клиникалық жағдай, шумақтық сүзілу жылдамдығы, асқынулар, егде жастағы науқастар.

АННОТАЦИЯ

ОЦЕНКА ФУНКЦИЙ ПОЧЕК У ПОЖИЛОГО ПАЦИЕНТА С ОСТРЫМ МИЕЛОБЛАСТНЫМ ЛЕЙКОЗОМ ПОСЛЕ ТРАНСПЛАНТАЦИИ ГЕМОПОЭТИЧЕСКИХ СТВОЛОВЫХ КЛЕТОК: КЛИНИЧЕСКИЙ СЛУЧАЙ

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Актуальность: Функции почек при лечении острого миелобластного лейкоза подвергаются серьезным воздействиям, особенно у пожилых пациентов. Подготовка пожилых пациентов к ТГСК с использованием ряда химиотерапевтических препаратов неизбежно оказывает токсическое действие на функцию почек, к тому же инволютивные изменения в почках могут физиологически снижать функцию почек.

Цель исследования – оценить функцию почек у пожилого пациента с острым миелобластным лейкозом после ТГСК.

Методы: В статье представлен клинический случай острого миелобластного лейкоза у пожилого пациента, которому была проведена аллогенная ТГСК.

Результаты: Мы проанализировали динамику функционального состояния у пожилого больного с момента регистрации острого миелобластного лейкоза до +100 дней после трансплантации гемопоэтических стволовых клеток (ТГСК). В течение всего периода наблюдения мы не выявили почечных нарушений у пожилого пациента. Несмотря на ТГСК и воздействие нефротоксических препаратов у пожилого пациента на + 100 дней после ТГСК, функция почек была сохранена.

Заключение: Описанный случай подчеркивает важность поддержания функции почек у пожилых пациентов после ТГСК и длительного мониторинга функции почек.

Ключевые слова: трансплантация гемопоэтических стволовых клеток, трансплантация костного мозга, острый миелобластный лейкоз, почечная недостаточность, клинический случай, скорость клубочковой фильтрации, осложнения, пожилые пациенты.

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KIKUCHI-FUJIMOTO DISEASE: THE FIRST CLINICAL OBSERVATION OF A RARE CASE IN KAZAKHSTAN

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ABSTRACT

Relevance: Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare underlying cause of benign lymphadenopathy, typically accompanied by fever and fatigue. Diagnosing this rare condition causes difficulties. Even though more than half a century has passed since the first described case, KFD is still hard to diagnose. Therefore it is of utmost importance to perform all the necessary diagnostic tests to avoid misdiagnosing and prescribing the wrong and often too-aggressive treatment. This paper describes the first clinical case of KFD in the Republic of Kazakhstan.

The study aimed to share the clinical course and the specifics of a diagnostic search involving histological and immunohistochemical tests in KFD.

Methods: The paper describes a clinical case of KFD.

Results: We reported a case of KFD in a 35-year-old man who applied for cervical lymphadenopathy and fever. The diagnosis was made on histological and immunohistochemical analysis of a lymph node. Rapid regression of lymphadenopathy marked the evolution of the disease.

Conclusion: This clinical observation describes a rare case of KFD; its cases have not been previously described in Kazakhstan. KFD is prone to benign course and spontaneous regression. However, difficulties remain in KFD diagnosis since symptoms such as lymphadenopathy and fever more often resemble lymphoma or tuberculosis. Non-tumor lymphadenopathy can also produce high metabolic activity manifested by an intensive accumulation of radiopharmaceuticals, according to PET-CT. Clinicians should be highly suspicious of KFD in young patients with cervical lymphadenopathy and fever to avoid misdiagnosis.

Keywords: Kikuchi-Fujimoto disease (KFD), histiocytic necrotizing lymphadenitis, lymphoma, lymphadenopathy.

Introduction: Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare underlying cause of benign lymphadenopathy, typically accompanied by fever and fatigue. The first case of KFD was reported in Japan in 1972. Since then, the disease has been reported worldwide, with most cases in Asia [1, 2]. In addition to lymphadenopathy, most commonly cervical, other symptoms such as nausea, weight loss, night sweats, and fatigue may be present in the clinic of KFD. Because of its rare occurrence and non-specific clinical picture, in 40% of cases, KFD is mistaken for other diseases accompanied by lymphadenopathy (e.g., lymphoma, tuberculous lymphadenitis, autoimmune diseases, and non-specific inflammation) [3]. Even though more than half a century has passed since the first described case, KFD is still hard to diagnose this disease in clinical practice. Therefore it is of utmost importance to perform all the necessary diagnostic tests to avoid misdiagnosing and prescribing the wrong and often too-aggressive treatment [4].

The study aimed to share the clinical course and the specifics of a diagnostic search involving histological and immunohistochemical tests in KFD.

Materials and methods: This paper describes a clinical case of KFD in a 35-year-old man. The patient was examined at Hematology Center LLP in Karaganda.

Histological examination of the lymph node was performed at the Department of Pathological Anatomy of the Pavlov First Saint Petersburg State Medical University of the Ministry of Health of the Russian Federation under the supervision of Professor V.V. Baikov, holder of a habilitation degree in Medicine.

Patient information: A young man of 35 years sought medical care due to increasing fever and painful cervical lymphadenopathy.

Clinical Data: Since January 2022, the patient has been bothered by sub-febrile fever up to 37.5°C. At the end of January 2022, the patient discovered a mass gradually increasing on the right side of his neck. Since then, periodic episodes of febrile fever up to 39.8–40.0°C have also occurred. Since early February 2022, the mass on the neck became painful on contact. The patient noted profuse night sweating and no weight loss. Asymmetry of the neck was notable during the objective examination. A volumetric mass up to 2 cm in diameter was palpable on the right side. It was dense and slightly painful on palpation, and displacement was preserved.

Diagnostics: Laboratory indices were within the acceptable values. PCR results for viral hepatitis B and C and HIV were negative. *Peripheral blood immunophenotyping* was performed due to suspected lymphoproliferative dis-

ease: no CD23/CD43/ FMC7/ CD20/ CD19 immunophenotype aberrations were found. No immunophenotypic evidence in peripheral blood for pathological lymphoproliferation (T or B linear) was obtained. *Whole-body PET-CT in February 2022*: showed high metabolic activity in enlarged lymph nodes of the jugular, supraclavicular, superficial and deep cervical groups on both sides, intrathoracic paratracheal on the right, bifurcation, subcarinal and axillary on two sides, which was consistent with lesions in lymphoma.

Histological examination of the lymph node (February 2022): The histological preparation had extensive fields/foci of macrophages/histiocytes and giant cells with plasmacytoid dendritic cell morphology. There were foci of necrosis without cellular reaction. Figure 1 shows pronounced cellular decay without cellular involvement, and the preparation contains extensive fields/foci of macrophages/histiocytes and giant cells with plasmacytoid dendritic cell morphology.

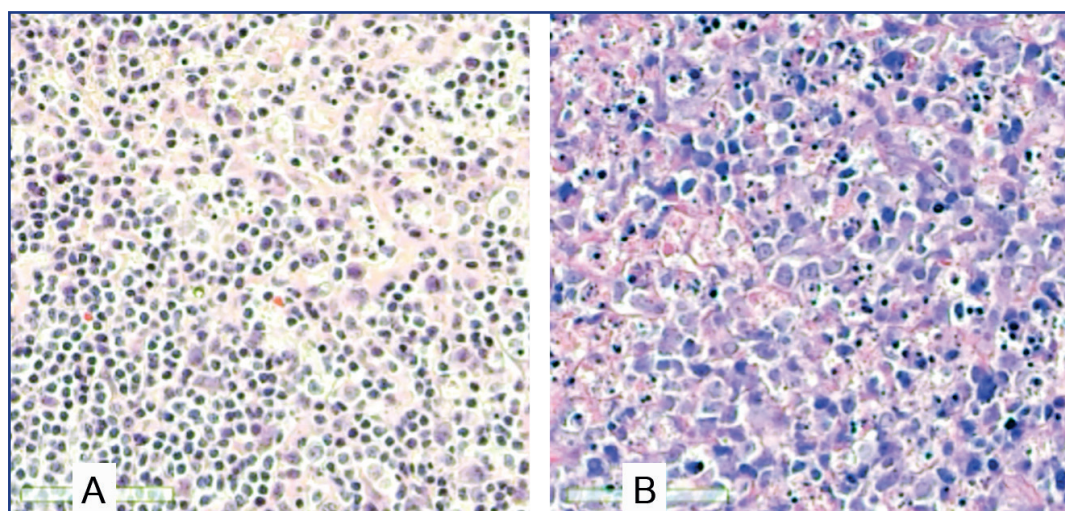


Figure 1 – Histological examination of a lymph node in a 35-year-old man with Kikuchi-Fujimoto disease: A – Hematoxylin-eosin staining, B – Azur-eosin staining. Magn. x400

Immunohistochemical study of the lymph node (February 2022): Most of the cells in the node express CD45(LCA). B-cell clusters (CD20+, Pax-5+) are not large, partly friable, and located mainly under the capsule. Part of them has follicular structures. T-cells (CD3+) sharply prevail, and CD8+ cells predominate in subpopulation composition. Some T-cells are moderately large, and nuclei are enlightened or with thinly vesicular chromatin patterns. Large dense

or loose clusters of plasmacytoid dendritic cells (CD123+), macrophages/histiocytes (CD68+), some cells co-express MPO – T-cells and macrophages/histiocytes stained in reaction with antibodies to CD4. CD30+ cells are in moderate numbers, lying predominantly solitary. The proliferation index among infiltrate cells (outside residual follicles, by Ki-67) is about 30%. No expression of EBV (LMP), ALK, or TdI was detected (Figure 2).

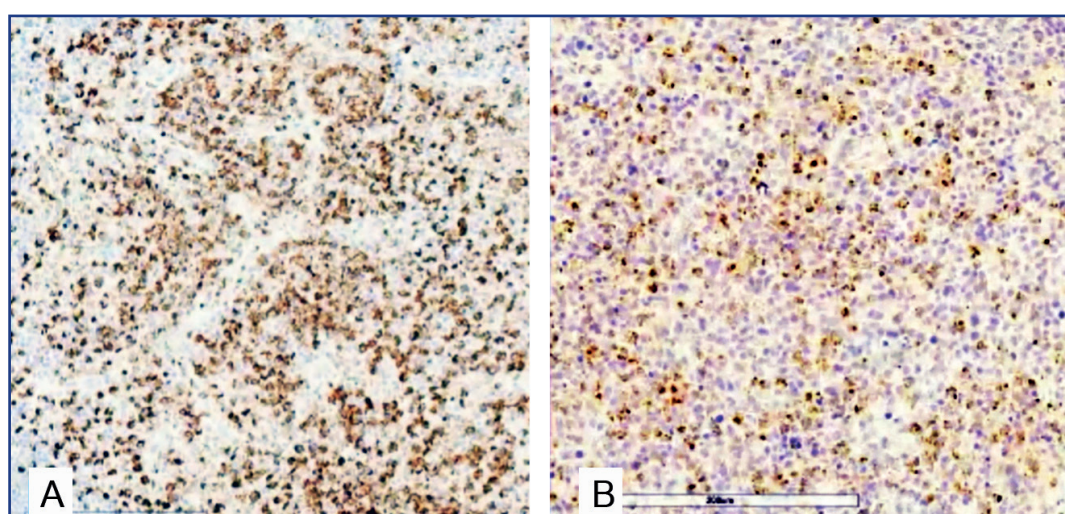


Figure 2 – Immunohistochemical examination of a lymph node in a 35-year-old man with Kikuchi-Fujimoto disease: A – cells expressing CD68, B – myeloperoxidase expression. Magn. x400

The immunohistochemical pattern was generally consistent with that observed in the histiocytic necrotizing lymphadenitis – necrotic stage of KFD. Considering that similar histological changes may correspond to autoimmune diseases, we screened for connective tissue diseases: antibodies to double-stranded DNA, antinuclear autoantibodies, and rheumatoid factor were examined. Screening results (March 2022) – negative. Based on the tests, the patient was diagnosed with KFD, necrotic stage.

Treatment: The patient received symptomatic treatment: nonsteroidal anti-inflammatory drugs for febrile spiral. No specific therapy was given.

Results: Since March 2022, the patient has had decreased clinical manifestations of the disease, normalized body temperature, and decreased size of peripheral lymph nodes. Since the middle of March 2022, the patient did not seek medical help, and his further fate is unknown.

Timeline: Figure 3 shows the dynamics of clinical manifestations of KFD in this patient with gradual regression of symptoms.

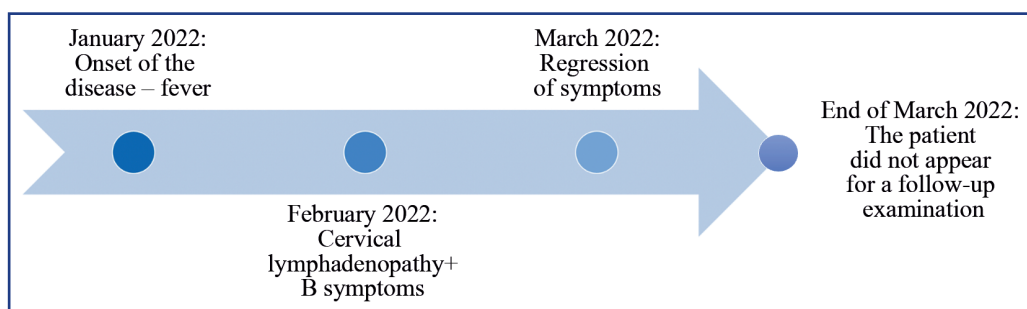


Figure 3 – Timeline of a clinical case in a 35-year-old man with Kikuchi-Fujimoto disease

Discussion: No possibility of determining the further course of the disease because the patient did not appear for the follow-up examination, did not seek medical attention after the regression of symptoms of the disease, and further fate is unknown.

KFD is a disease with a favorable prognosis and a tendency to regress independently. KFD primarily includes lymphadenopathy (most often cervical localization) and a fever of 38 to 40°C for 4-6 weeks, corresponding to the patient's clinic described above. A maculopapular rash with pronounced pruritus and mild hepatosplenomegaly up to +2 cm from under the costal margin may also occur. The difficulty of diagnosis is related to possible histological mimicry of KFD in other diseases, such as lymphomas. In a study by L.P. Menasce et al., among 27 patients with revision-assessed KFD, 88.8% of patients (n=24) were initially misdiagnosed with non-Hodgkin's lymphoma [5].

There is no standard treatment plan for KFD, as the disease is rare and individualized. The primary treatment for KFD is symptom relief, i.e., symptomatic therapy. Antibiotics are ineffective, but their use may be appropriate in immunocompromised patients to prevent the development of potential bacterial infections [6]. In addition, using glucocorticosteroids may alleviate symptoms and shorten the course of the disease. In addition, prednisolone has been used in treating pregnant women with KFD and effectively reduces disease manifestations.

Conclusion: KFD is a rare disease prone to benign course and spontaneous regression. However, there re-

main difficulties in diagnosing this disease. For example, differential diagnostics should be performed with malignant hematological neoplasms, infectious lymphadenopathy (of specific and non-specific etiology), and autoimmune diseases. The described clinical case is interesting because non-tumor lymphadenopathy can resemble a lesion in lymphoma and even produce high metabolic activity manifested by an intensive accumulation of radiopharmaceuticals, according to PET-CT data.

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АНДАТПА

КИКУЧИ-ФУДЖИМОТО СЫРҚАТЫ: ҚАЗАҚСТАНДА СІРЕК КЕЗДЕСЕТІН ЖАҒДАЙДЫҢ АЛҒАШҚЫ КЛИНИКАЛЫҚ БАҚЫЛАУЫ

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Өзектілігі: Кикучи-Фуджимото сырқаты, сондай-ақ гистиоцитарлық некротикалық лимфаденит деп те аталады, субфебрильді температурамен және жалпы әлсіздікпен бірге жүретін сирек қатерсіз лимфаденопатияның бірі болып табылады. Сырқат сирек кездесетіндіктен, диагностикада көптеген қиындықтар бар. Кикучи-Фуджимото сырқатының алғашқы жағдайын сипаттағаннан кейін жарты ғасырдан астам уақыт өтті, бірақ клиникалық тәжірибеде бұл сырқатты диагностикалауда әлі де қиындықтар бар, сондықтан қате диагноз қоюды және одан туындайтын дұрыс емес және жасі агрессивті емдеу тактикасын болдырмау үшін қажетті диагностикалық процедураларды жүргізу өте маңызды. Бұл мақала-Қазақстан Республикасындағы Кикучи-Фуджимото сырқатының клиникалық жағдайының ең алғашқы сипаттамасы.

Зерттеудің мақсаты – Кикучи-Фуджимото сырқатының гистологиялық және иммуногистохимиялық ерекшеліктерін ескере отырып, клиникалық ағымын және диагностикалық іздеу барысын сипаттау.

Әдістері: Кикучи-Фуджимото сырқатының клиникалық жағдайын сипаттау.

Нәтижелері: біз жастыр мойны лимфаденопатиясы мен безгегі туралы хабарлаған 35 жастағы ер адамда Кикучи-Фуджимото сырқатының жағдайы туралы хабарладық. Диагноз лимфа түйінінің биоптатын гистологиялық және иммуногистохимиялық талдау негізінде жасалды. Аурудың эволюциясы лимфаденопатияның жылдам регрессиясымен ерекшеленді.

Қорытынды: бұл клиникалық байқау Кикучи-Фуджимото сырқатының сирек жағдайын сипаттайды; авторлар Қазақстанда бұрын сипатталған ауру жағдайларын таппаған. Кикучи-Фуджимото сырқатының қатерсіз ағымға және өздігінен регрессияға бейімділіктен сипатталады. Алайда, бұл ауруды диагностикалауда қиындықтар қалады, өйткені лимфаденопатия және қызба сияқты белгілер көбінесе лимфомаға немесе туберкулезге ұқсайды; сонымен қатар, ісіксіз лимфаденопатия тіпті жоғары метаболиттік белсенділікті тудыруы мүмкін, бұл ПЭТ - КТ-ға сәйкес радиофармацевтикалық препараттың қарқынды жинақталуымен көрінеді. Қате диагнозды болдырмау үшін дәрігерлер жастыр мойны лимфаденопатиясы және безгегі бар жас пациенттерде Кикучи-Фуджимото ауруына жоғары күдіктен қарауы керек.

Түйінді сөздер: Кикучи-Фуджимото сырқаты, некротикалық гистиоцитарлық лимфаденит, лимфома, лимфаденопатия.

АННОТАЦИЯ

БОЛЕЗНЬ КИКУЧИ-ФУДЖИМОТО: ПЕРВОЕ КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ РЕДКОГО СЛУЧАЯ В РЕСПУБЛИКЕ КАЗАХСТАН

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Актуальность: Болезнь Кикучи-Фуджимото (БКФ), также известная как гистиоцитарный некротизирующий лимфаденит, является редкой причиной доброкачественной лимфаденопатии, которая сопровождается субфебрильной лихорадкой и общей слабостью. Прошло более полувека после описания первого случая БКФ, однако в клинической практике до сих пор существуют трудности в диагностике данного заболевания. Поэтому крайне важно провести необходимые диагностические процедуры во избежание постановки ошибочного диагноза и выбора неверной лечебной, часто агрессивной, тактики. Данная статья – первое описание клинического случая БКФ в Республике Казахстан.

Цель исследования – описать клиническое течение болезни Кикучи-Фуджимото и ход диагностического поиска с учётом гистологических и иммуногистохимических особенностей.

Методы: В статье приведено описание клинического случая БКФ.

Результаты: У 35-летнего мужчины, который обратился по поводу шейной лимфаденопатии и лихорадки, на основании гистологического и иммуногистохимического анализа биоптата лимфатического узла была диагностирована БКФ. Эволюция заболевания была отмечена быстрой регрессией лимфаденопатии.

Заключение: Данное клиническое наблюдение описывает редкий случай БКФ; ранее описанных случаев заболевания в Казахстане авторы не нашли. БКФ характеризуется склонностью к доброкачественному течению и спонтанному регрессу. Однако остаются трудности в диагностике данного заболевания, так как такие симптомы, как лимфаденопатия и лихорадка чаще напоминают лимфому или туберкулез. Кроме того, неопухольная лимфаденопатия может даже давать высокую метаболитическую активность, которая проявляется интенсивным накоплением радиофармпрепарата по данным ПЭТ-КТ. Клиницистам следует с высокой степенью подозрения относиться к БКФ у молодых пациентов с шейной лимфаденопатией и лихорадкой, чтобы избежать ошибочного диагноза.

Ключевые слова: болезнь Кикучи-Фуджимото (БКФ), некротизирующий гистиоцитарный лимфаденит, лимфома, лимфаденопатия.

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MODERN CONCEPTS OF ARTIFICIAL LUNG VENTILATION DURING GENERAL ANESTHESIA IN CANCER PATIENTS: A LITERATURE REVIEW

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ABSTRACT

Relevance: Among patients who have undergone extensive surgical interventions under general anesthesia with artificial ventilation (ventilator), various postoperative respiratory complications of an obstructive or restrictive nature are often found

The study aimed to generalize current data from systematic reviews, meta-analyses, and scientific publications on the use of preventive and therapeutic strategies for lung ventilation to improve the quality of anesthetic care for cancer patients.

Methods: The PubMed Electronic Database (NCBI) was searched to identify randomized controlled and prospective observational studies, systematic reviews, and meta-analyses, as well as scientific articles published in English between 2016 and 2023 that focused on the results of application and comparison of lung protective ventilation strategies with conventional mechanical ventilation in patients undergoing major and prolonged surgery.

Results: As a result of a comparison of data from a review of large-scale scientific studies and articles, a relationship was established between the use of a protective lung ventilation strategy with a low tidal volume (6–8 mL/kg of ideal body weight), in combination with individualized PEEP, periodic lung recruitment maneuvers and significant improvement in clinical outcomes, respiratory complications, early mortality and length of hospital stay in patients undergoing surgery.

Conclusion: Using protective lung ventilation during anesthesia during major surgical interventions reduces the incidence of postoperative pulmonary complications.

Keywords: modern concepts of mechanical ventilation, postoperative pulmonary complications, low tidal volume, individualized PEEP.

Introduction: More than 230 million surgical interventions are performed annually in the world. Postoperative pulmonary complications are one of the most serious consequences that have a negative effect on treatment outcomes and post-surgical mortality [1].

Postoperative pulmonary complications occur in 11–33% of operated patients [2].

Large tidal volumes were initially recommended to prevent the occurrence of atelectasis and hypoxemia during general anesthesia for major abdominal and thoracic surgery [3].

According to many studies, during IVL, the alveolar epithelium was damaged due to mechanical overstretching and inflammatory cytokines were released, such as tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), IL-8 and 10, which contribute to the activation of macrophages and neutrophils. These cells produce large amounts of collagenase and elastase and release large amounts of active oxygen. All of these substances can directly or indirectly destroy alveolar epithelial cells or even vascular endothelial cells, resulting in damage to lung tissue [4].

In most studies, the primary outcome was the frequency of postoperative pulmonary complications defined as the combination of any respiratory infection, respiratory failure, pleural effusion, atelectasis, or pneumothorax following the European Perioperative Clinical Outcome consensus statement (Table 1) [5]. The length of stay in the hospital and the intensive care unit (ICU) and in-hospital mortality were also assessed [6].

Some large-scale studies utilized p/f index, arterial oxygen tension (PaO₂) and PCO₂ in arterial blood before, during, and after trachea extubation in ICU, etCO₂, dead-space fraction (Vd/Vt), and lung compliance as estimates of the use of protective lung ventilation during surgery [7].

The study aimed to generalize current data from systematic reviews, meta-analyses, and scientific publications on the use of preventive and therapeutic strategies for lung ventilation to improve the quality of anesthetic care for cancer patients.

Materials and Methods: The PubMed (NCBI) database was searched for randomized controlled trials (RCT) and

prospective observational studies, systematic reviews, meta-analyses and scientific articles published in English from 2016 to 2023 and focusing mainly on the outcomes and comparison of lung protective ventilation strategies and conventional mechanical ventilation in patients undergoing extensive and prolonged surgical interventions. RCT and prospective observational studies, systematic reviews,

meta-analyses and scientific articles on the use of a lung protective ventilation strategy during surgery in pregnant women, children and patients with underlying chronic lung diseases were excluded.

This analytical review included 11 systematic reviews and meta-analyses, 11 RCTs, 1 retrospective study, and 1 review of foreign recommendations.

Table 1 – Definition of postoperative respiratory complications according to the European consensus statement on perioperative clinical outcomes [5]

Complication	Definition
Respiratory infection	Patient has received antibiotics for a suspected respiratory infection and met one or more of the following criteria: new or changed sputum, new or changed lung opacities, fever, white blood cell count $>12 \times 10^9/l$.
Respiratory failure	Postoperative $PaO_2 < 8$ kPa (60 mmHg) on room air, a $PaO_2:FiO_2 < 40$ kPa (300 mmHg) or arterial oxyhaemoglobin saturation measured with pulse oximetry $< 90\%$ and requiring oxygen therapy.
Pleural effusion	Chest radiograph demonstrating blunting of the costophrenic angle, loss of sharp silhouette of the ipsilateral hemidiaphragm in upright position, evidence of displacement of adjacent anatomical structures or (in supine position) a hazy opacity in one hemithorax with preserved vascular shadows.
Atelectasis	Lung opacification with a shift of the mediastinum, hilum or hemidiaphragm toward the affected area, and compensatory over-inflation in the adjacent non-atelectatic lung.
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura.

Results: The conducted review of scientific publications, results of RCTs and prospective observational studies, systematic reviews, and meta-analyses that compared lung protective ventilation strategies and conventional mechanical ventilation in various surgical interventions (cardiac surgery, abdominal surgery, laparoscopic surgery, neurosurgery, spinal surgery, and thoracic surgery) showed that lung protective ventilation strategy during anesthesia that includes low tidal volume, optimal positive end-expiratory pressure (PEEP) and periodic lung recruitment maneuvers might improve intraoperative oxygenation of the body and pulmonary mechanics and reduce the incidence of early postoperative atelectasis [7-11].

A meta-analysis conducted by Yang et al. to compare mechanical ventilation with low tidal volume ($n=521$) and conventional lung ventilation ($n=533$) and their impact on the postoperative incidence of atelectasis, lung infection, acute lung injury (acute respiratory distress syndrome), and length of hospital stay, included 16 studies with a total of 1054 patients. The analysis revealed a statistically significant reduction in postoperative lung infection (OR (odds ratio) = 0.21, 95% CI (confidence interval) 0.09-0.50, P-value (significance level) = 0.0003), atelectasis (OR=0.36, 95% CI 0.20-0.64, P-value = 0.006), acute lung injury (OR=0.15, 95% CI 0.04-0.61, P-value = 0.008), and duration of hospital stay (mean difference = -2.08, 95% CI -3.95 to -0.21, P-value = 0.03) when using lung-protective ventilation (LTV, PEEP, recruitment maneuvers) compared with conventional ventilation during general anesthesia [12].

The use of lung-protective ventilation in surgical interventions through laparotomic access, as well as during laparoscopic abdominal and gynecological operations and robot-assisted laparoscopic prostatectomy, significantly reduces the incidence of postoperative pulmonary complications due to improved pulmonary function and intraoperative body oxygenation [13-16].

In an RCT by Liu et al., ventilation with a low tidal volume of 6-8 mL/kg ideal body weight (IBW), moderate PEEP-6, and periodic recruitment maneuvers (every 30 minutes in the study) improve pulmonary mechanics during anesthesia of more than 6 hours and reduce the development of postoperative respiratory complications (Figure 1) [17]. The researchers also reported an increase in static compliance of the lungs (Cstat) (Fig. 2) and a reduction in driving pressure (Figure 3) during lung-protective ventilation compared with conventional laparoscopic lung ventilation. Figures 2 & 3 provide mean \pm standard deviation. The difference between the two groups was significant at $p < 0.05$ [18].

Moreover, an RCT by Park et al. on the study of the parameters of protective ventilation of the lungs during laparoscopic operations in hepatobiliary surgery proved the positive effect of the lung recruitment maneuver on oxygenation. This might be due to optimal alveolar recruitment, improved regional pulmonary ventilation, and normalization of the ventilation-perfusion ratio, as evidenced by a decrease in the alveolar-arterial oxygen gradient ($AaDO_2$). The effect of PEEP was due to the maintenance of adequate alveolar gas exchange. Significance when compared with group R was $P < 0.05$ (Figure 4) [9].

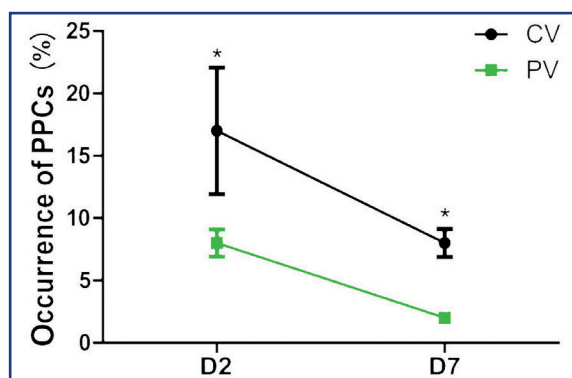
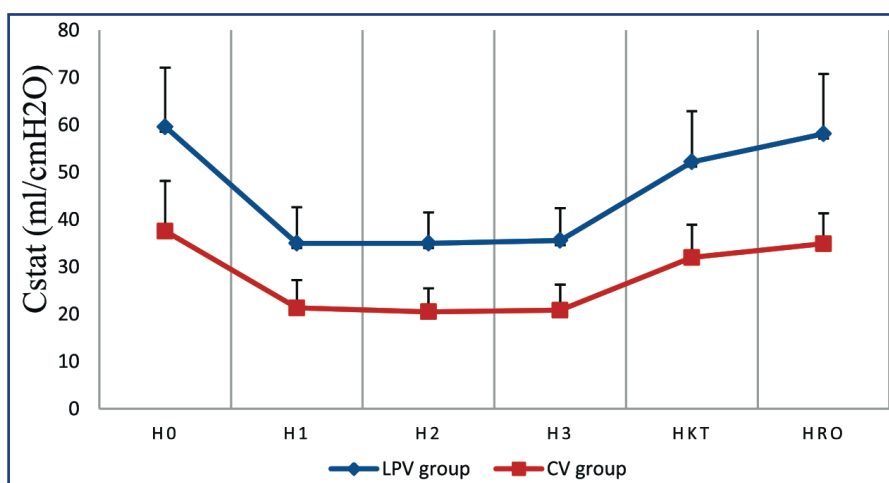
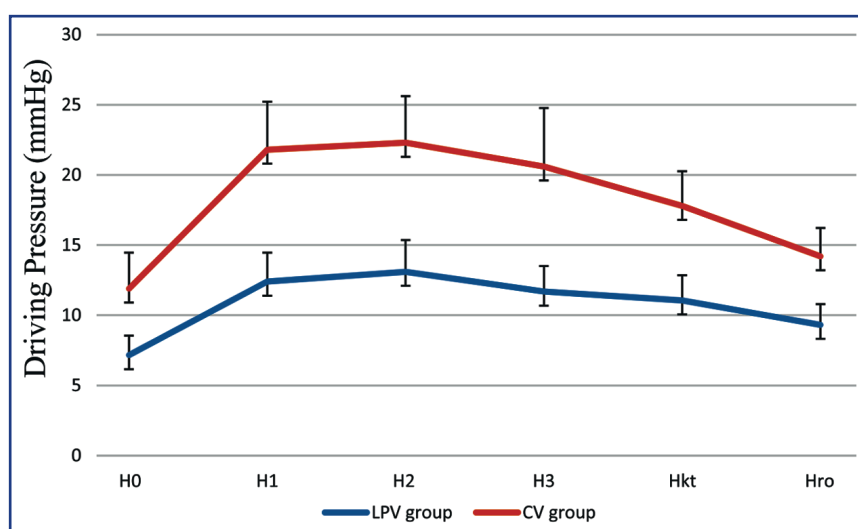


Figure 1 – Occurrence of postoperative pulmonary complications (PPCs) on day 2 (D2) and day 7 (D7) after surgery in patients with ventilation time longer than 6 h treated with protective ventilation (PV) and conventional ventilation (CV) [17]



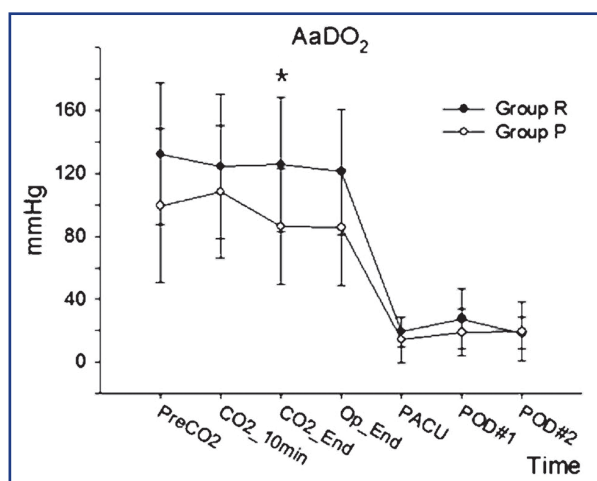
Abbreviations (axis X): H0 (after intubation), H1 (30 min after pneumoperitoneum), H2 (1 h after pneumoperitoneum), H3 (2 h after pneumoperitoneum), Hkt (10 min after pneumoperitoneum stopped), Hro (before extubation)

Figure 2 – Changes in intraoperative pulmonary static compliance (Cstat) in the groups with protective ventilation (LPV) and conventional ventilation (CV) [18]



Abbreviations (axis X): H0 (after intubation), H1 (30 min after pneumoperitoneum), H2 (1 h after pneumoperitoneum), H3 (2 h after pneumoperitoneum), Hkt (10 min after pneumoperitoneum stopped), Hro (before extubation)

Figure 3 – Intraoperative driving pressure in the groups with protective ventilation (LPV) and conventional ventilation (CV) [18]



Legend: Axis Y – Pressure (mm Hg). Axis X – Time: PreCO₂: after the anesthetic induction; CO₂_10 min: 10 min after pneumoperitoneum; CO₂_20 min: 20 min after pneumoperitoneum; CO₂_end: end of pneumoperitoneum; Op_end: operation end; PACU: post-anesthesia care unit; POD#1: postoperative 24 h; POD#2: postoperative 48 h * $P \leq 0.05$ compared with group R

Charts – Group R: Conventional ventilation with alveolar recruitment maneuver (ARM) group; Group P: protective lung ventilation group;

Figure 4 – Oxygenation of the patients with AaDO₂ [9]

Standard AaDO₂ in a healthy person is 10 to 40 mm Hg. It also depends on venous shunting due to hypoxic pulmonary vasoconstriction. At venous blood bypass above 30-35%, an increase in the oxygen fraction in the inhaled mixture does not lead to a noticeable increase in the partial pressure of oxygen in the body and is accompanied by a significant increase in AaDO₂ – above 100-200 mm Hg.

Patients after cardiac surgical interventions involving opening (often bilateral) of the pleural cavities, operations on the heart, switched off from the blood circulation, in conditions of hyperkalemia, using a heart-lung machine, are more prone to postoperative pulmonary atelectasis [19].

In an RCT in patients with hypoxemia after heart surgery in an ICU in Brazil (December 2011-2014) by Costa Leme et al., the use of an intensive lung recruitment strategy was associated with less severe pulmonary complications and improved survival among hospitalized patients compared to moderate lung recruitment strategy (Figures 5 & 6). Figure 5 shows the severity of postoperative pulmonary complications: grade 0 represents no symptoms or signals; grade 1, one of the following: dry cough, abnormal lung findings and temperature 37.5°C or higher with normal chest radiograph, or dyspnea without other documented cause; grade 2 means two of the following: productive cough, bronchospasm, hypoxemia ($\text{SpO}_2 \leq 90\%$) at room air, atelectasis with gross radiological confirmation (concordance of 2 independent experts) plus either temperature higher than 37.5°C, or abnormal lung find-

ings, hypercarbia ($\text{PaCO}_2 > 50$ mm Hg) requiring treatment; grade 3 is one of the following: pleural effusion resulting in thoracentesis, pneumonia, pneumothorax, extended noninvasive ventilation, or reintubation lasting less than 48 hours; grade 4 means reintubation or invasive mechanical ventilation for 48 hours or more; and grade 5 – death before hospital discharge. In the intensive strategy group, the patients underwent three lung recruitment cycles (60 sec each), comprised of PEEP 30 cm H₂O, pressure ventilation, inspiratory pressure 15 cm H₂O, respiratory rate 15 per minute, inspiratory time 1.5 seconds, and FiO₂ 0.40. During the intervals (60 sec) between the recruitment cycles and further the patients were ventilated or pressure-controlled with controlled driving pressure to obtain a VT of 6 mL/kg body weight, an inspiratory time of 1 second, PEEP of 13 cm H₂O, and a minimum respiratory rate to maintain PaCO₂ between 35- and 45-mm Hg. No hemodynamic instability was observed during the recruitment maneuver [20].

In addition to the benefits of applying the lung protective ventilation concept, Wang et al. proved that a low tidal volume in combination with an appropriate can inhibit the release of inflammatory cytokines such as tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), interleukin-10 (IL-10). There are several publications on the impact of various artificial lung ventilation regimens on inflammatory cytokines in elderly patients after gastric and colonic surgery under general anesthesia (Table 2) [4, 21].

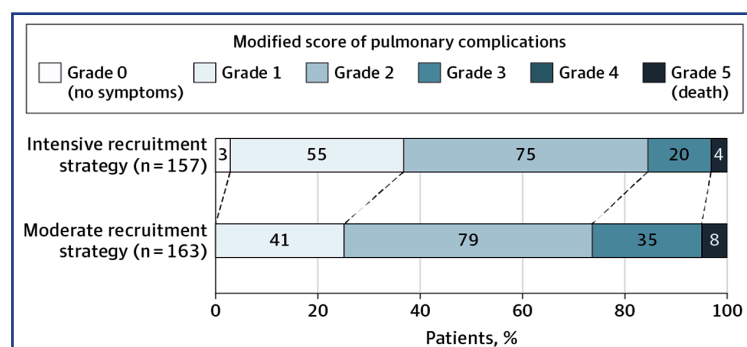


Figure 5 – Modified stratification of early postoperative complications [20]

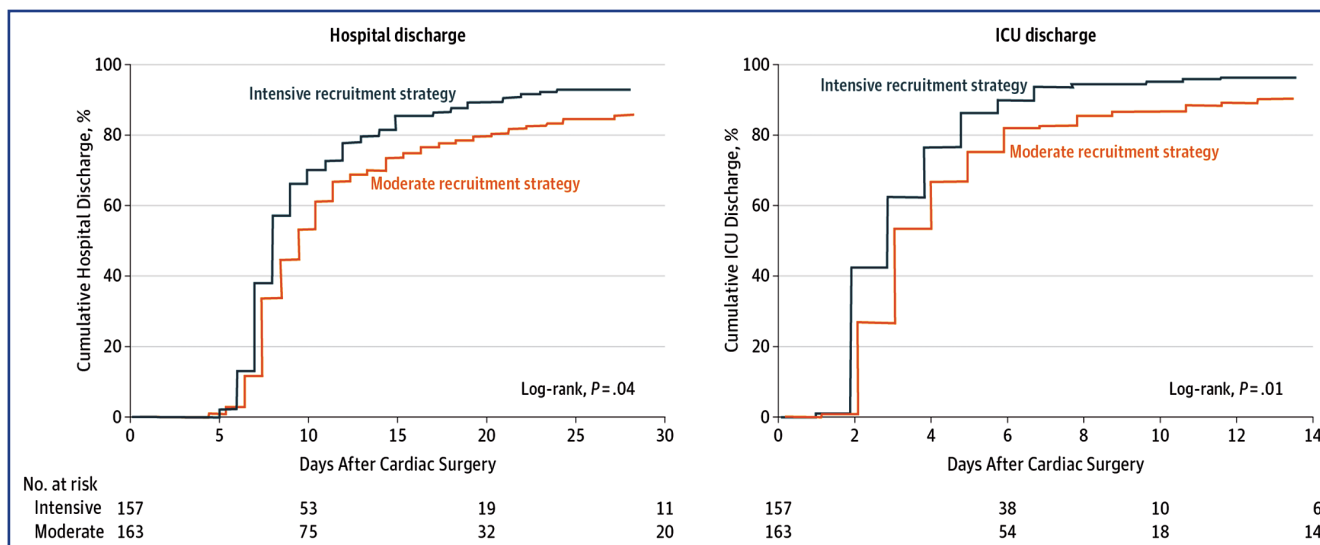


Figure 6 – Kaplan-Meier survival analysis for time to hospital discharge and Intensive Care Unit discharge among patients after cardiac surgery

Table 2 – Comparison of serum inflammatory factor levels before and after operation between the two groups (mean ± SD) [4]

Group	TNF-α (ng/mL)		IL-6 (pg/mL)		IL-10 (pg/mL)	
	Preoperative	4 h after operation	Preoperative	4 h after operation	Preoperative	4 h after operation
Group A (n=60)	43.26±6.80	76.65±8.77	47.14±5.50	56.94±7.30	34.62±5.10	29.51±4.75
Group B (n=60)	45.10±6.55	89.28±12.64	45.03±6.28	69.71±10.38	36.36±6.15	25.83±5.08
value t	-1.510	-6.359	1.958	-7.795	-1.687	4.099
value P	0.134	0.000	0.053	0.000	0.094	0.000

Notes:

TNF-α – tumor necrosis factor-α; IL – interleukin;

Group A – tidal volume 6.0 mL/kg + PEEP 5.0 cm H₂O;Group B – VT 6.0 mL/kg IBW + PEEP (8.0 cmH₂O);

P value – 0.09.

Though the protective role of more physiological tidal volume was established at 6-8 mL/kg IBW, additional protection provided by PEEP remains unclear. The authors suggested that individually titrated PEEP during anesthesia may improve lung function during and after surgery.

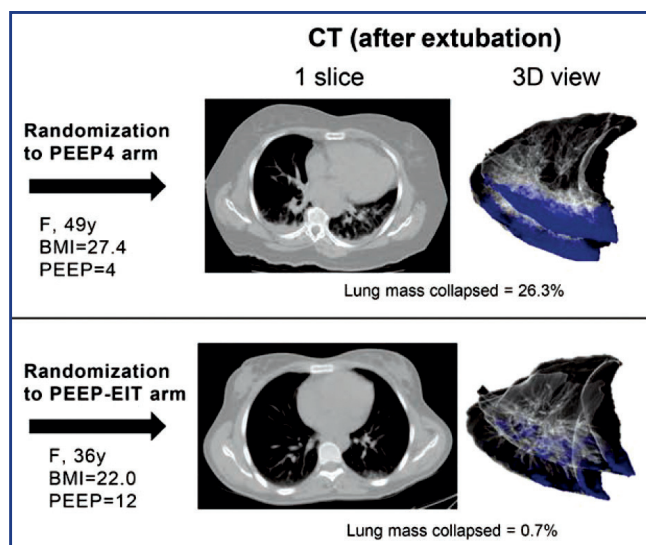
In recent years, it has been proven that a more rational approach to lung ventilation during anesthesia may change the incidence of postoperative pulmonary complications [22]. Thus, Pereira et al. showed

that individualized PEEP measurements could reduce postoperative atelectasis measured by electrical impedance computed tomography (PEEP-EIT) while improving intraoperative oxygenation of the body and reducing the driving pressure level (Figure 7) [23].

Regarding the use of a lung protective ventilation strategy during anesthesia for major thoracic interventions against the background of one-lung ventilation, in 4 large-scale meta-analyses among 16 trials, the authors came to the same conclusion that driving pres-

sure – oriented ventilation with low tidal volume with PEEP and periodic recruitment maneuvers – reduces the Vd/Vt by 5.9%. It also increases arterial oxygen tension (PaO₂) – the lung recruitment maneuver increases

blood PaO₂ by 82 mm Hg and PEEP by 30 mm Hg; improves lung compliance by 4.3 mL/cm H₂O; and reduces the incidence of postoperative pulmonary complications (Figure 9) [7, 24].



Abbreviations: BMI, body mass index; CT, computed tomography

Figure 7 – Examples of EIT images (at PEEP-EIT and PEEP of 4 cm H₂O) and CT images (after extubation) of two patients: top – a patient randomized for PEEP4 arm; bottom – a patient randomized for PEEP-EIT arm. One axial slice of the lung computed tomography and 3D reconstruction of the lungs show the collapsed lung in blue (areas between –200 to +100 UH)

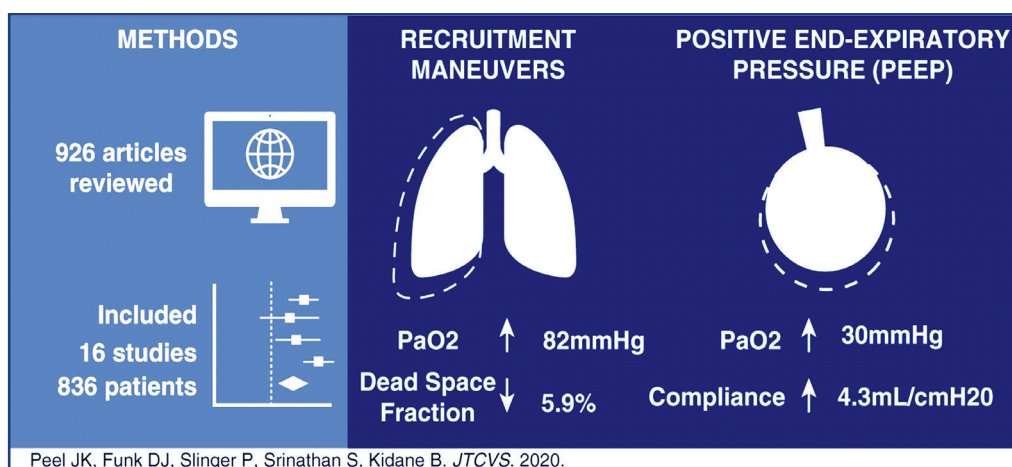


Figure 9 – PEEP and recruitment maneuvers during one-lung ventilation and their positive effect on lung function [7]

Conclusion: Our analysis of the modern strategy for applying lung protective ventilation during anesthesia in long and extensive surgical interventions showed that this approach effectively reduces the incidence of postoperative pulmonary complications. All detected publications evidenced a positive impact of lung protection methods on the course of the surgical and postoperative period. The simplicity of protection principles enables routine use of this methodology in anesthesiologic practice.

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АНДАТПА

ОНКОЛОГИЯЛЫҚ НАУҚАСТАРДА ЖАЛПЫ АНЕСТЕЗИЯ КЕЗІНДЕ ӨКПЕНІҢ ЖАСАНДЫ ЖЕЛДЕНУІНІҢ ЗАМАНАУИ ТҰЖЫРЫМДАМАЛАРЫ: ӘДЕБИЕТКЕ ШОЛУ

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Өзектілігі: Өкпенің жасанды вентилициясы (ЖЖЖ) арқылы жалпы анестезиямен кең көлемді хирургиялық операциядан өткен пациенттер арасында обструктивті немесе рестриктивті сипаттағы әртүрлі операциядан кейінгі тыныс алу жолдарының асқынулары жиі кездеседі.

Зерттеудің мақсаты – онкологиялық науқастарға анестезиялық көмек көрсету сапасын арттыру мақсатында жүйелі шолулар мен мета-талдаулардың ағындағы деректерін, өкпе вентилициясының профилактикалық және емдік стратегияларын қолдану жөніндегі ғылыми деректерді жалпылау.

Әдістері: PubMed электронды дерекқорында (NCBI) рандомизацияланған бақыланатын және перспективалық бақылау зерттеулерін, жүз-йелі шолулар мен мета-талдауларды, сондай-ақ 2016 және 2023 жылдар аралығында ағылшын тілінде жарияланған, өкпенің қорғанысты жасалуды және ауыр және ұзақ хирургиялық операцияға ұшыраған науқастарда әдеттегі механикалық желдету арқылы қорғаныс жасалуды стратегиялары және оның нәтижелеріне салыстыруға бағытталған ғылыми мақалаларды анықтау үшін іздестірілу жүргізілді.

Нәтижелері: Кең көлемді ғылыми зерттеулер мен мақалаларды шолу деректерін салыстыру нәтижесінде өкпенің қорғаныс вентилиациясының стратегиясын қолдану мақсатында тыныс алу көлемі төмен (6-8 мл/кг идеалды дене салмағына), жекелендірілген РЕЕР, өкпені мезгіл-мезгіл жинау маневрі жасалынған жағдайда клиникалық нәтижелердің айтарлықтай жақсаруы, тыныс алу жолдарының асқынулары, ерте өлім-жітім және хирургиялық операция жасалған науқастарда ауруханада болу ұзақтығы азайғаны анықталды.

Қорытынды: Ірі хирургиялық араласулар кезінде анестезия кезінде өкпенің қорғанышты жасалуды тұжырымдамасын қолдану операциядан кейінгі өкпе асқынуларының жиілігін төмендетеді.

Түйінді сөздер: механикалық желдетудің заманауи тұжырымдамалары, операциядан кейінгі өкпелік асқынулар, тыныс алудың төмен көлемі, жекеленген оң экспираторлық қысым.

АННОТАЦИЯ

СОВРЕМЕННЫЕ КОНЦЕПЦИИ ИСКУССТВЕННОЙ ВЕНТИЛЯЦИИ ЛЕГКИХ ВО ВРЕМЯ ОБЩЕЙ АНЕСТЕЗИИ У ОНКОЛОГИЧЕСКИХ ПАЦИЕНТОВ: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: Среди пациентов, перенесших обширные оперативные вмешательства под общей анестезией с искусственной вентилиацией легких, нередко встречаются различные послеоперационные респираторные осложнения обструктивного или рестриктивного характера.

Цель исследования – обобщить актуальные данные систематических обзоров, мета-анализов и научных публикаций о применении профилактических и лечебных стратегий вентилиации легких с целью повышения качества оказания анестезиологической помощи онкологическим пациентам.

Методы: Был проведен поиск в электронной базе данных PubMed (NCBI), для выявления рандомизированных контролируемых и проспективных обсервационных исследований, систематических обзоров и мета-анализов, а также научных статей, опубликованных на английском языке с 2016 по 2023 годы, в которых основное внимание уделялось результатам применения и сравнения стратегий защитной вентилиации легких при традиционной механической вентилиации у пациентов, перенесших обширные и длительные оперативные вмешательства.

Результаты: В результате сопоставления данных проведенного обзора крупномасштабных научных исследований и статей установлена взаимосвязь между использованием стратегии защитной вентилиации легких с низким дыхательным объемом (6-8 мл/кг идеальной массы тела), в сочетании с индивидуализированным показателем положительного давления в конце выдоха, периодическими маневрами рекрутмента легких и значительным улучшением клинических исходов, уменьшением количества осложнений со стороны дыхательной системы, сокращением ранней летальности и продолжительности пребывания в стационаре у пациентов, перенесших хирургические вмешательства.

Заключение: Применение концепции защитной вентилиации легких во время анестезии, при обширных оперативных вмешательствах снижает частоту развития послеоперационных легочных осложнений.

Ключевые слова: современные концепции искусственной вентилиации легких (ИВЛ), послеоперационные легочные осложнения, низкий дыхательный объем (ДО), индивидуализированный показатель положительного давления в конце выдоха (ПДКВ).

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PET/CT DISADVANTAGES IN PATIENTS WITH LYMPHOMA: A LITERATURE REVIEW

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ABSTRACT

Relevance: Positron emission tomography combined with computed tomography (PET/CT) is a young and promising technique for lymphoproliferative diseases' primary detection, staging, and evaluation of the treatment results. However, at this stage of nuclear medicine development, some shortcomings in PET/CT diagnostics of lymphomas using 18Fluorodeoxyglucose (F18-FDG) affect its reliability to a certain extent.

The study aimed to evaluate the physical and technical weaknesses of F18-FDG PET/CT in diagnosing lymphomas and review the analytical methods that affect opinion accuracy.

Methods: The articles on the use of F18-FDG PET/CT in diagnosing lymphomas, its reliability, and methods for optimizing were searched in the PUBMED database for 2012-2022.

Results: One of the main shortcomings of F18-FDG PET/CT in diagnosing lymphomas is the Deauville 5-point scale, which does not fully meet clinical requirements. This scale has some disadvantages, including low inter-reader agreement and an unreliable reference organ for F18-FDG accumulation. Mathematical algorithms for correction to the patient's weight also require optimization.

Conclusion: Some of the existing deficiencies can be improved at the software level and through educating staff about the importance of changing the SUV calculation method. However, other deficiencies, such as classifications that do not meet clinical requirements, require more efforts at the level of international experts and much more in-depth study of this issue to avoid such shortcomings of new staging methods. However, even considering all the shortcomings described, at the moment, PET/CT with F18-FDG is one of the most reliable modalities available, both for the initial detection and for evaluating the therapy effectiveness in patients with lymphomas.

Keywords: Positron emission tomography (PET/CT), lymphoma, Deauville, SUV, 18 Fluorodeoxyglucose (F18-FDG), tumor staging.

Introduction: Positron emission tomography with computed tomography (PET/CT) is a hybrid radioisotope method for diagnosing various diseases based on the difference in radiopharmaceutical absorption. A radiopharmaceutical, or a tracer, is a two-component drug consisting of a radioisotope and a biological molecule. The radioisotope emits photons that a PET/CT detector can capture. The detector can recognize the radiopharmaceutical accumulation sites and determine the accumulation level. The biological molecule delivers the radioisotope directly to the pathological tissue and makes the radioisotope as tropic to the tissue as possible.

As an alternative to previously used mono-PET scanners, most countries now use PET/CT to analyze structural changes together with functional conditions. The most common radiopharmaceutical is F18-FDG, which is analogous to glucose. Most malignant tumors have high proliferative activity, and most of their energy comes from glucose. Because of this, malignant tumors consume significantly more glucose than benign tumors and normal tissue. This allows us-

ing F18-FDG for initial disease detection, staging, and prognosis [1, 2].

After intravenous administration, the drug is distributed throughout the circulatory system. Further, it accumulates most strongly in organs with a physiologically high capture of radiopharmaceuticals and malignant tumors with high proliferative activity. Physiologically, the brain, myocardium, kidneys, and bladder have high levels of F18-FDG accumulation.

F18-FDG accumulation in tissues is measured by Standardized Uptake Value (SUV) calculated as:

$$SUV = \frac{A}{dose} \times bodyweight$$

Where A is the concentration of radioactivity in the area of interest (MBq/mL), dose – the administered dose (MBq), and bodyweight – the patient's body weight.

PET/CT diagnostics includes several stages: 1 – administration of a radiopharmaceutical dose considering the patient's body weight, 2 – scanning, 3 – post-processing, and 4 – analysis and interpretation. While the dose administration and scanning follow certain pre-set algo-

rithms and depend more on the PET/CT scanner performance and manufacturability, post-processing and interpretation of the results are quite variable. Namely, stages 3 and 4 of the examination have some weaknesses and are subject to improvement and modernization.

Considering the complexity and multicomponent nature of PET/CT examination, each stage allows different execution options with varying degrees of correctness. Such variability of execution options can significantly affect the reliability of the results. Many authors, some mentioned in this review, offer solutions to improve the PET/CT correctness and the reliability of the result interpretation.

The study aimed to evaluate the physical and technical weaknesses of F18-FDG PET/CT in diagnosing lymphomas and review the analytical methods that affect opinion accuracy.

Materials and methods: The articles on the use of F18-FDG PET/CT in diagnosing lymphomas, its reliability, and methods for optimizing were searched in the PUBMED, MEDLINE, and Cochrane databases over the last ten years.

A literature review was conducted on the Pubmed database for 2012-2022 for the following keywords: "PET/CT in the diagnosis of lymphomas," "relevance of PET/CT with P18-FDG in the diagnosis of lymphomas," and "sensitivity and specificity of PET/CT with P18-FDG in the diagnosis of lymphomas". This literature review includes 27 references.

Results: Lugano classification is the most common for staging lymphomas. However, it is quite complicated and focuses more on CT sizes than radiopharmaceutical accumulation during PET. This increases the risk of false positive results with a residual fibrous but metabolically inactive tumor [3].

Lugano classification also includes the five-point Deauville scale (5D) reflecting the metabolic status of a lymphoma lesion. This allows tracking of both structural and metabolic changes in patients with lymphoma. The Deauville classification is based on a 5-point scale that compares the tumor uptake with the physiological levels of uptake in the brain, liver, and mediastinum (Fig. 1).

Thus, Score 1 means no pathological FDG uptake; Score 2 means moderate accumulation in the tumor \leq mediastinum; Score 3 means that accumulation in the tumor is higher than in mediastinum but lower than in the liver; Score 4 means that accumulation in the tumor is slightly higher than in the liver; and Score 5 means a much higher accumulation compared to the liver (sometimes close to the accumulation in the brain).

Previously it was believed that the mediastinum (blood pool) and the liver have a relatively stable accumulation level. This made it possible to level out differences related to patients, examination protocols, the PET scanner's characteristics, and the knowledge level of the radiologist interpreting this result.

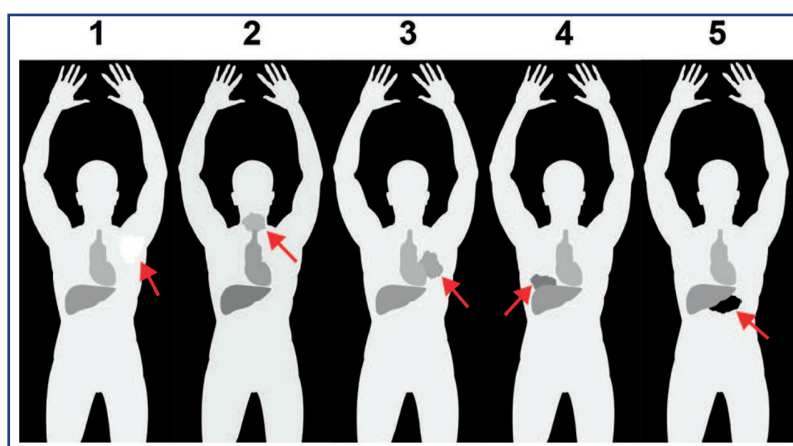


Figure 1 – The five-point Deauville scale [20]

Even if 5D performed better in terms of prognosis than only SUV or the CT part comparison [5-7], this scale has several further problems associated with its clinical use.

Score 5 on the Deauville 5D scale

One disadvantage of the 5D scale is an inefficient ranking of results at high capture rates in two studies compared over time. For example, a patient Scored five at the initial PET/CT. Then, an intermediate PET/CT showed a decrease in the formation volume and maxi-

mum metabolic activity, with clear clinical progress. However, SUVmax remained higher than in the liver, and the report will still give 5 points on the 5D scale (Fig. 2). Thus, the treating oncologist who will compare the primary and intermediate Scores may be misled that there is no effect of therapy. This may lead to an unjustified increase in treatment courses or the dose of chemoradiotherapy, a change in the treatment protocol, and a decrease in treatment efficacy.

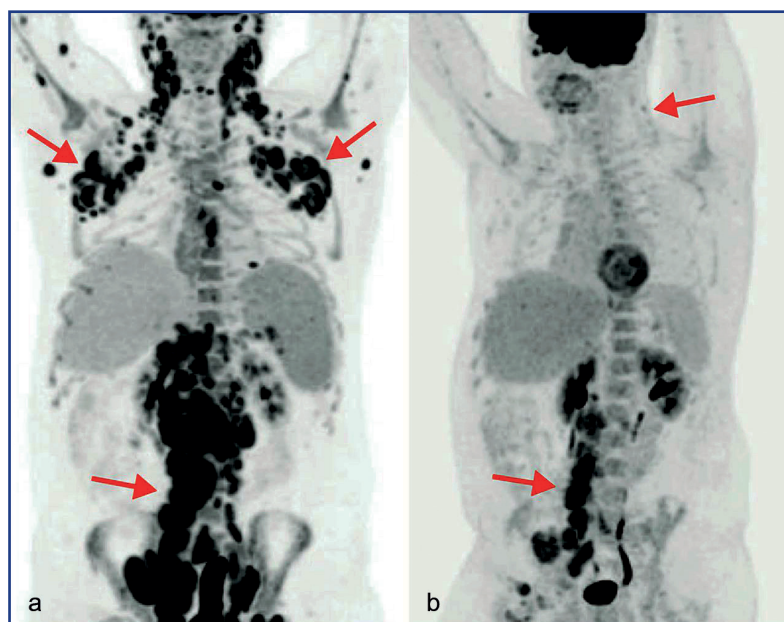


Figure 2 – Score 5 on the 5D scale: a – before treatment, b – intermediate PET/CT. Arrows indicate affected areas [20]

Score 3 on the Deauville 5D scale

Scores 1 & 2 on the Deauville 5D scale are considered a complete or partial metabolic response, that is, a positive effect of treatment, while Scores 4 & 5 are perceived as a lack of response or progress of the disease [8], meaning ineffective therapy. However, Score 3 raises doubts: is there a response to therapy or not? In most cases, Score 3 is perceived as a complete metabolic response, a positive treatment result [9]. Still, some studies on de-escalation of therapy consider Score 3 as a non-adequate response meaning insufficient treatment. [10]. This leads to over-diagnostics and over-treatment to avoid relapse [5].

Congruency among doctors

Using SUV to measure relative accumulation by tissues/organs facilitates comparison between patients and has been proposed as a basis for diagnosis. However, SUV is a semi-quantitative indicator. There are two main reasons why using any threshold to decide on a positive or negative result is wrong. First, primary detection and staging should not depend on the exact SUV level because, for such purposes, it is often sufficient to compare the SUV values in the area of interest and the surrounding tissue. Second, SUV is highly variable due to physical and biological parameters. In particular, studies have shown that using SUV thresholds (like $SUV > 2.5$) to identify a nodule or mass as benign or malignant often gives invalid results. Many benign infectious/inflammatory processes may have a high uptake of F18-FDG with a high SUV value. Conversely, many indolent or slow-growing malignancies may have minimal uptake and low SUV values.

Besides the variability of SUVs, the lack of a unified SUV measurement algorithm produces a high risk of subjective assessment by the describing radiologist. Thus, in several studies, the congruency between the analyzing doctors using 5D was very low [11-13]; that is, different doctors evaluated the same patients differently. Using a binary scoring system increased the congruency between clinicians, allowing them to accept Scores 1, 2 & 3 as negative and Scores 4 & 5 – as positive [11, 14].

The tumor-to-liver SUV ratio (SUVTLR)

As described above, the liver is one of the guides used by nuclear medicine doctors for 5D scoring (Fig. 1). There are several methods for measuring the level of uptake in the liver: a round 2D on one slice [15, 16] and a spherical 3D [17]. 2D measurement considers the isotope capture activity on only one slice, which reduces the reliability of the results. Moreover, the accumulation in the liver does not remain stable. It may be affected by chemotherapy due to reversible changes in the liver parenchyma, such as steatosis and duct obstruction, that CT, MRI, or ultrasound examination can detect. Besides, different chemotherapy protocols can have a different effect on the level of metabolism and, therefore, on the SUV of the liver. For example, the ABVD effect on liver metabolism differs much from the effect of MOPP or BEACOPP schemes. Therefore, the interpretation of the liver SUV at intermediate PET/CT shall consider the duration of chemotherapy and the types of chemotherapy drugs used in the treatment [18].

The patient's body weight

The radiopharmaceutical dose administered to a patient is measured in mega becquerels (MBq) and de-

depends on the patient's body weight. The usual dose is 1.2 MBq of 18F-FDG per 1 kg of body weight. Formula 1 shows that SUV is calculated based on the patient's body weight. However, it has long been known that adipose tissue uptakes much less 18F-FDG than other tissues so SUV can vary greatly depending on the body structure. Therefore, an alternative method for calculating SUV normalized by lean body mass (SUL Lean body mass (LBM) represents the weight of lean connective, muscle, and nervous tissues. The classic formula for calculating LBM considers gender, height, and body weight. Though some studies reported the possibility of obtaining a reliable LBM by scanning a limited part of the body on a CT scanner [19, 20], the most common is the James equation: $LBM = 1,1bw - 123\left(\frac{bw}{h}\right)^2$ for man and $LBM = 1,07bw - 148\left(\frac{bw}{h}\right)$ for women. Modern scanners use the James equation to calculate LBM. SUL is calculated as $SUL = \frac{A}{dose} \times LBM$ [21]. As in a usual SUV equation, it is assumed that F18-FDG is evenly distributed over the body. However, real and calculated SUVs can vary greatly, especially in patients with large body weights [22, 23]. Therefore, SUL is a more stable and reliable value [24]. Studies also support the significant difference between SUV and SUL in the liver [25], which is critical in evaluating treatment outcomes in patients with lymphomas. Unfortunately, in most cases, including PET centers in Kazakhstan, they still use SUVs instead of SUL.

Discussion: Lymphoma classification and staging have evolved from 1950, when the three-component Peters classification was first introduced, to 2011, when the Lugano classification was proposed. In 1976, the World Health Organization introduced the concept of a radiological and quantitative assessment of response to cancer therapy using CT and quantitative tumor measurements [4]. Since then, radiology has been tasked both with the initial diagnosis and evaluating the treatment efficacy. Today, this task is becoming increasingly important in light of the emergence of new therapeutic drugs and the growing popularity of personalized therapy. The ability of PET/CT to determine not only tumor anatomy but also its metabolic status provides more reliable information about the effect of therapy much earlier than traditional computer tomography [26, 27].

Lugano classification, approved in 2011 at the congress of leaders in this field in Lugano, Switzerland, has become the first specific system for evaluating the effectiveness of therapy in malignant lymphoma. The first results of studies evaluating response to treatment using this scale were published as early as 2014 [5, 8, 9]. Lugano classification became the standard to assess the response to treatment. This clas-

sification was based on CT measurements of up to 6 lesions measuring at least 1.5 cm for nodal lesions and at least 1.0 cm for extranodal lesions. Each formation was measured in 2 projections, then these measurements were multiplied, and the sum of multiplications before treatment was compared with the sum of multiplications after treatment to quantify response to therapy [5].

Such a procedure was very laborious and lengthy. Even more significant in comparing the two surveys was that such procedures were difficult to reproduce. Studies showed a large variation in the assessments of the same formations by different radiologists. Besides, in this case, it remained unclear whether the formation was a fibrous tissue remaining after treatment or a viable tumor [3].

Today, we evidence the rapid development of nuclear medicine. More new radiopharmaceuticals become available for clinical use; new calculation and image analysis methods emerge. However, the classical PET/CT with 18F-FDG and SUV calculation remains the most common research method for a wide variety of pathologies, including cancers.

18F-FDG is suitable for lymphoma visualization due to the high proliferative activity of most lymphomas. PET/CT can be used for primary detection, staging, and evaluating the results of lymphoma treatment. Despite the clear advantages of PET/CT over more traditional CT and MRI methods, including the ability to assess both structural changes and – even more important – the metabolic status, this method has its shortcomings, as described above. Now there is a clear trend towards simplifying these methods due to too complex and difficult to replicate the analysis methods, including algorithms for evaluating PET/CT results [8].

Conclusion: Since nuclear medicine is one of the youngest fields of medicine and due to the general trend of describing only the positive aspects of various methods of diagnosis and treatment, only a few publications reveal the weaknesses of a particular method. However, this review summarizes the most obvious shortcomings of PET/CT in diagnosing lymphomas. Some of the existing deficiencies, such as PET/CT adjustment for LBM, can be improved at the software level and through educating staff about the importance of changing the SUV calculation method. However, other deficiencies, such as classifications that do not meet clinical requirements, require more efforts at the level of international experts and much more in-depth study of this issue to avoid such shortcomings of new staging methods. Therefore, even being the most high-tech and expensive radiological procedure, PET/CT with F18-FDG has shortcomings that should be known to both nuclear medicine physicians and oncologists involved in diagnosing and treating lymphomas.

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АНДАТПА

ЛИМФОПРОЛИФЕРАТИВТІ АУРУЛАРДЫ ДИАГНОСТИКАЛАУДАҒЫ ПЭТ/КТ ЗЕРТТЕУЛЕРІНІҢ КЕМШІЛІКТЕРІ: ӘДЕБИЕТТЕРГЕ ШОЛУ

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Өзектілігі: Компьютерлік томографиямен (ПЭТ/КТ) біріктірілген позитронды-эмиссиялық томография лимфопролиферативті ауруларды емдеу нәтижелерін алғашқы анықтау, стадирлеу және бағалау үшін жас және перспективалы әдіс болып табылады. Алайда,

ядролық медицинаның дамуының осы кезеңінде 18 фтор-Дезоксиглюкозбен (F18-FDG) лимфомалардың ПЭТ / КТ диагностикасында оның сенімділігіне белгілі бір дәрежеде немесе басқа да бірқатар кемшіліктер бар.

Зерттеудің мақсаты – F18-FDG мен ПЭТ/КТ-ның әлсіз жақтарын лимфомаларды диагностикалауда физика-техникалық жағынан да, қорытындының дұрыстығына әсер ететін талдау әдістерін де зерттеу.

Әдістері: Мақалада 2012-2022 жылдарға арналған PABMED дерекқорындағы дереккөздерге шолу берілген. лимфомалардың диагностикасында F18-FDG бар PET/CT қолдану, оның сенімділігі және осы зерттеуді оңтайландыру әдістері туралы.

Нәтижелері: Лимфоманы диагностикалаудағы F18-FDG мен ПЭТ/КТ-ның басты кемшіліктерінің бірі-клиникалық талаптарға толық сәйкес келмейтін Deauville емдеу нәтижелерін бағалау шкаласы. Бұл шкала бірқатар әлсіз жақтарға ие, оның ішінде дәрігерлер арасындағы төмен сәйкестік және F18-FDG жинақтаудың сенімді емес органы Олар сондай-ақ пациенттің салмағын түзетудің математикалық алгоритмін оңтайландыруды талап етеді.

Қорытынды: Кейбір кемшіліктерді бағдарламалық жасақтама деңгейінде шешуге болады және қызметкерлерге SUV есептеу әдісін өзгертудің маңыздылығы туралы түсіндіруге болады, бірақ басқа да кемшіліктер, мысалы, әсіктеудің клиникалық талаптарына толық сәйкес келмейтін халықаралық сарапшылар деңгейінде айтарлықтай күш салуды және жаңа кезең әдістерінің осындай кемшіліктерін болдырмау үшін осы мәселені тереңірек зерттеуді қажет етеді. Дегенмен, тіпті сипатталған барлық кемшіліктерді ескере отырып, F18-ФДГ ПЭТ/КТ қазіргі уақытта лимфоманы бастапқы анықтау үшін де, емдеудің тиімділігін бағалау үшін де қол жетімді ең сенімді әдістердің бірі болып табылады.

Түйінді сөздер: позитронды-эмиссиялық томография (ПЭТ/КТ), лимфома, Deauville, SUV, 18-фтор-дезоксиглюкоза (F18-ФДГ), ісік сатысы.

АННОТАЦИЯ

НЕДОСТАТКИ ПЭТ/КТ ИССЛЕДОВАНИЯ ПРИ ДИАГНОСТИКЕ ЛИМФОПРОЛИФЕРАТИВНЫХ ЗАБОЛЕВАНИЙ: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: Позитронно-эмиссионная томография совмещенная с компьютерной томографией (ПЭТ/КТ) является молодой и перспективной методикой для первичного выявления, стадирования и оценки результатов лечения лимфопролиферативных заболеваний. Однако, на данном этапе развития ядерной медицины, в ПЭТ/КТ диагностике лимфом с 18Фтор-Дезоксиглюкозой (F18-FDG) есть ряд недостатков, в той или иной степени оказывающие на ее достоверность.

Цель исследования – изучить слабые стороны ПЭТ/КТ с F18-FDG в диагностике лимфом с физико-технической стороны и методы анализа, влияющие на достоверность заключения.

Методы: В статье представлен обзор источников из базы PUBMED за 2012-2022 гг. по применению ПЭТ/КТ с F18-FDG в диагностике лимфом, его достоверности, и методов оптимизации данного исследования.

Результаты: Одним из главных недостатков ПЭТ/КТ с F18-FDG в диагностике лимфом является не полностью отвечающая клиническим требованиям шкала оценки результатов лечения Deauville. Данная шкала имеет ряд слабых сторон, включая низкую согласованность между врачами и недостоверный орган-ориентир накопления F18-FDG. Также требуют оптимизации математические алгоритмы коррекции к весу пациента.

Заключение: Некоторые из имеющихся недостатков можно решить на уровне программного обеспечения и разъяснения персоналу о важности изменения метода расчета SUV, но другие недостатки, как например не совсем отвечающие клиническим требованиям классификации требуют более значительных усилий на уровне международных экспертов и значительного более глубокого изучения данного вопроса во избежание подобных изъяснов новых методов стадирования. Однако, даже учитывая все описанные недостатки, на данный момент, ПЭТ/КТ с F18-ФДГ является одной из самых достоверных модальностей из имеющихся, как для первичного выявления, так и для оценки эффективности лечения лимфом.

Ключевые слова: Позитронно-эмиссионная томография (ПЭТ/КТ), лимфома, Deauville, SUV, 18Фтор-Дезоксиглюкоза (F18-FDG), стадирование опухолей.

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S.S. SADYKOV – A HISTORIAN, CHRONOGRAPHER, SCIENTIST, RADIOLOGIST, AND EDUCATOR

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ABSTRACT

Candidate of Medical Sciences, professor, radiologist of the highest category, and experienced teacher Sain Sadykovich Sadykov was born on February 6, 1943, in the village of Taskabak (Oymaut), Bayganinsky district of Aktobe region. In 1991 he defended his Ph.D. thesis.

The introduction of his developments into healthcare practice has improved the quality of life of patients with lung, esophageal, uterine, and pharyngeal cancers.

“Teaching is a very responsible and necessary profession from the point of view of educating young doctors,” says Sain Sadykovich. “A teacher should teach but also educate students with special care and diligence.”

Sain Sadykov is the author of more than 230 academic affairs, including six monographs, 11 educational textbooks, three guidelines, and one copyright certificate. He wrote 90% of his textbooks in the native language. His contribution to developing the Kazakh language in medicine, especially in radiation therapy, is huge. S.S. Sadykov was awarded several medals and certificates of honor for many years of conscientious work.

Sain S. Sadykov celebrates his eightieth anniversary surrounded by his wife, son, daughter, grandchildren, and great-grandchildren. We wish our dear veteran a long life filled with satisfaction from a happily lived path next to respected friends and a caring, loving family.



Photo 1 – Sayin Sadykov

Sayin Sadykovich Sadykov – Candidate of Medical Sciences, professor, radiologist of the highest category, and experienced teacher – was born on February 6, 1943, in the village of Taskabak (Oymaut), Bayganinsky district, Aktobe region.

Having graduated from the Medical Faculty of the Aktobe State Medical Institute in 1968, he headed the surgical department in Khromtau, Aktobe region, for two years.

In 1970, he joined the Kazakh Institute of Oncology and Radiology (KazIOR) as a junior researcher. In 1987, he became a Senior Researcher in Clinical Radiology Department. In 1992, he was reappointed as a senior researcher; from 1996 to 1999, he headed that department. In 1991, S. Sadykov defended his candidate's thesis on “Comparative results of disassembly of doses in different ways in treating lung cancer with radiation.” Introducing his findings into healthcare practice has improved the quality of life of patients with lung, esophageal, uterine, and pharyngeal cancers. Since that year, he has been an Assistant Professor and later an Associate Professor at the Kazakh National Medical University (KazNMU). In 1999, he became a Professor at the Department of Oncology, Mammology, and Radiation Therapy, after being awarded the title of associate professor by the Higher Attestation Commission under the Ministry of Education.

The great philosopher Abu Nasir Al-Farabi said, “If a nation does not know its history, if a country loses its history, then its citizens have no way to go.” Our ancestor Balasaguni said, “The future begins with the knowledge of the past.”



Photo 2 – Sayin Sadykov with his family: his mother, his spouse Bagilash, his brother, and his daughter Venera



Photo 3 – Prof. H. Abisatov and prof. S. Sadykov

In April 2008, the Academic Council of Asfendiyarov Kaz-NMU appointed him the title of Academic Professor. During

his job, the doctor has updated all chapters on radiation therapy in several educational and methodological edi-

tions for interns, students, and teachers and supplemented them with Kazakh translations. He prepared case reports and tests in Kazakh for all faculties, residents, and interns.

S. Sadykov participated in scientific research on cancer radiation treatment, focusing on increasing the tumor sensitivity to ionizing radiation.



Photo 4 – S. Sadykov's teacher, Doctor of Medical Sciences, Prof., Academician of the National Academy of Sciences of the RK, S.B. Balmukhanov and Master of Sciences, Prof. Magzhan Sain

Back in 1989, during a one-month medical course in Minsk, Belarus, a professor who lectured in Radiology spoke about his scientific work aimed at treating esophageal and lung diseases with radiation sources and increasing sensitivity to ionizing radiation. Only our domestic scientists noted the unique role of academicians S.B. Balmukhanov, Zh.N. Abdrakhmanov, N.A. Azhigaliyev, S.S. Sadykov, and others in advancing this field.

"Teaching is a very demanding and necessary vocation for training young doctors," says Sain Sadykovich. "A teacher should treat each student with special kindness, as his own kid, and tirelessly engage in education and training."

The great Abai said, "Do not hurry; keep your mind open, and you will succeed in teaching a kid." A teacher is not only a pedagogue but a mentor. No wonder our grandfather Abu-Nasir al-Farabi, a famous thinker of our people, who was called the second Aristotle in the world, said, "Knowledge without education is the worst enemy of humanity."

On this occasion, in connection with the 77th anniversary of Sakeng, we decided to quote a poem dedicated to the teacher by interns (group 644-1.2, the academic year 2019):

Qürmetti Sadyquly Saiyn aǵai,
 Medisina salasynda mälım aǵai.
 50 jyl elı üşın eñbek etse,
 Bolmaidy jaqsylyǵyn baıandamai.
 Halqym dep, talai eñbek atqarypty,
 Birneşe tös belgımen maqtalypty.
 Turalap kelgen nauqas ajaldardan
 Talaidy araşalap ap qalypty.
 Önerdi aqyndyqty joldas qylǵan,
 Ömirin sal seriler jalǵastyrǵan.
 Aǵaiym şeşendıkpen söylegende,
 Sözendı menmın - degen aljastyrǵan.
 Ülgı alyp aǵaiyma jastar erdi,
 Ğylymda köp jańalyq aşqan edı.
 Zerttep qazaǵymnyñ şejiresin,
 Ülesin tarihqada qosqan edı.
 När berdi şäkirtterdiñ sanasyna,
 Eñbekqyp "Onkologia" salasynda.
 Jıyma şaqty kıtaptyñ avtorysyz
 Şyqtyñyz mañdai termen dara şyñǵa.
 Aǵaiym, jasai bersin türyp baǵy,
 Berik bop apaimenen yryqtary.
 Aǵaiym, közımızge jas körined
 Jııttei qylşyldaǵan qyryqtaǵy.

Osyndai aǵailarmen maqtanamyz,
Aǵaidyń ızın basyp baq tabamyz.
Sıñırıp boıǵa bergen tәlimderin,
El üşin bızde qyzmet atqaramyz.

Bız sızdı asqar tauǵa teñeremiz,
Keñeisin әrqaşanda keregeñiz.
Adamzat ұrpaǵymen myñjasaidy,
Köbeisin nemeremen-şöbereñiz.

Aǵaiym жүrsız bızge bilim berip,
Jüreik aǵai жүrgen ızge erip.
Jetpis jeti jasyñyz qūtty bolsyn,
Toi jasañyz taǵyda жүzge kelip.

Sain Sadykov has authored more than 230 academic papers, including six monographs, 11 educational textbooks, three guidelines, and one author's certificate. 90% of the textbooks he wrote in his native language. His contribution to developing the Kazakh language in medicine, especially in radiation therapy, is enormous.

Sayin Sadykov has not lost the generosity of our forefathers. He possesses deep knowledge, speaks softly, and stays calm and cool-head. These are the qualities of a real teacher who can raise people's spirits in any environment and multiply their wealth. He captivates people with his unique personality, open arms, and free speech. A person energized by his warmth does not want to leave him.

We are in respectful relations with Sayin Sadykov. He knows genealogical history well; his stories are full of proverbs and sayings; he tells them without haste, and he is a poet. During any corporate holidays, the first word was to Sayin, who began his dedications in verses. It is not only Saken's pious image that makes him unique on the outside but also his nature, which shows the richness of his inner spiritual world and his honest intention. He cannot stay indifferent to the changes and troubles of life; his morality does not allow him to do so.



Photo 5 – Sain Sadykovich Sadykov with his colleagues

Last February, Sayin Sadykov celebrated his 60th wedding anniversary. His wife Bagilash, to the glory of Sayin, gave life to their daughter Venera and their son Magzhan, who received a moral upbringing. Venera is a qualified economist; she graduated from the famous Institute of National Economy. Her daughter Zhanar graduated from the Institute of International

Relations and is a teacher at this educational institution, and her granddaughter Arailym is a student at that University. His son Magzhan followed in his father's footsteps; he graduated from the Medical University and defended his Ph.D. thesis. Magzhan is a qualified doctor and an Academic Professor. The daughter-in-law Zauresh is a Police Major. Daniyar,

the eldest grandson, is a university student in Turkey. Nurmukhambet, who got his great-uncle's name, is a high school student. Sayin Sadykov and his spouse Bagilash are happy in the company of their grandchildren.

For many years of conscientious work, Sayin Sadykov was awarded several medals (7) and Certificates of Honor (2).

Today, on his 80th anniversary, we wish Sayin Sadykov a long and happy life!

АНДАТПА

САЙЫН САДЫҚҰЛЫНЫҢ ТҰЛА БОЙЫ ТҰНЫП ТҰРҒАН ТАРИХ, ШЕРТІП ҚАЛСАҢ ШЕЖІРЕ, ДӘРІГЕР РАДИОЛОГ, ҒАЛЫМ ЖӘНЕ ҰЛАҒАТТЫ ҰСТАЗ

К. Толғатайұлы¹, У.Қ. Жұмасhev¹, Т.Т. Садыкова¹, С.А. Есенқұлова¹, А.К. Джакпиебаева¹, А. Ақбар¹

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Медицина ғылымдарының кандидаты, профессор, жоғарғы санатты дәрігер радиолог, тәжірибелі педагог Сайын Садықұлы Садықов 1943 жылы 6 ақпанда Ақтөбе облысы, Байғанин ауданының Тасқабақ (Оймауыт) ауылында дүниеге келген. 1991 жылы кандидаттық диссертациясын қорғады.

Денсаулық сақтау тәжірибесіне оның ашқан жаңалықтарын енгізу нәтижесінде өкпе, өңеш, жатыр, жұтқыншақ қатерлі ісіктерімен ауыраған науқастардың өмір сүруі сапасы жақсарды.

– Ұстаздық ұрпақ тәрбиесі тұрғысынан өте жауапты, әрі қажетті мамандық, ұстаз әр балаға ерекше мейріммен өз баласындай көріп, жалықпай білім мен тәрбие беруі керек-дейді Сайын Садықұлы.

Садықов С. – 230-дан астам ғылыми жұмыстардың авторы. Соның ішінде 6 монография, 11-оқулық, 3 тиімді ұсыныстар, 1 авторлық куәлік жазған. Осы жазған еңбектерінің 90% ана тілінде. Оның медицина саласында қазақ тілін дамытуда, әсіресе сәуле көзімен емдеуде қосқан үлесі орасан зор.

Көп жылғы еңбегі үшін С. Садықов бірнеше медальдармен және Құрмет грамоталарымен марапатталды. Бүгінде сексен жасқа толған мерейлі той үстінде Саин Садықұлының қанша жасқа келседе қартаймауына, асқар таудай балаларының әкесі барда ешқашан ортаймауына, той-тойға ұласып, жасқа жас қосылып, ұзаққа бақытты ғұмыр кеуіне тілек білдіреміз!

АННОТАЦИЯ

С.С. САДЫКОВ – ИСТОРИК, ЛЕТОПИСЕЦ, УЧЕНЫЙ, ВРАЧ РАДИОЛОГ И ПЕДАГОГ

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Кандидат медицинских наук, профессор, врач-радиолог высшей категории, опытный педагог Саин Садыкович Садыков родился 6 февраля 1943 года в селе Таскабак (Оймаут) Байганинского района Актыубинской области. В 1991 году защитил кандидатскую диссертацию. Внедрение в практику здравоохранения его разработок улучшило качество жизни больных раком легких, пищевода, матки и глотки.

«Преподавание – очень ответственная и нужная профессия с точки зрения воспитания молодых врачей, – говорит Саин Садыкович. – Учитель должен не только учить, но и воспитывать обучающихся с особым вниманием и усердием».

Садыков С. – автор более 230 научных работ, включая 6 монографий, 11 учебников, 3 методических рекомендации, 1 свидетельство об авторском праве. 90% учебников написаны им на родном языке. Его вклад в развитие казахского языка в области медицины, особенно в лучевой терапии, огромен.

За многолетний труд С.С. Садыков награжден несколькими медалями и почетными грамотами.

Свой восьмидесятый юбилей Саин Садыкович встречает в теплом семейном кругу, в окружении жены, сына, дочери, внуков и правнуков. Желаем нашему ветерану долгих лет жизни, наполненных чувством удовлетворения от счастливо прожитого пути, рядом с уважаемыми друзьями и заботливой, любящей семьей.

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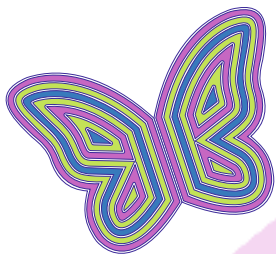
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