ONCOLOGY and RADIOLOGY of KAZAKHSTAN

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STATISTICS
DIAGNOSTICS
TREATMENT
REVIEWS
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The national integrated model of cancer care in Kazakhstan

As we all know, one of the main indicators in cancer care is cancer morbidity. In 2016, it was established about 37 thousand of the new cases of cancer. For further improvement of the quality of cancer care in Kazakhstan, the national integrated model of cancer care was developed. Our integrated model is divided to three levels according to its functionality in each level of cancer care. Additionally, further improvement of Highly Specialized Centers for Radiation Oncology was also determined. Moreover, one of strategic goals of KazIOR is coordination of evolving of cancer care in the regions.

Keywords: national integrated model of cancer care, Highly Specialized Centers for Radiation Oncology, strategic goals of KazIOR

Kazakhstan Cancer Incidence and Mortality Data 1999-2016. As we all know, one of the main indicators in cancer care is cancer incidence. In 2016, 37 thousand new cases have been diagnosed and the total number of cancer patients according to Cancer Registry was over 163 thousand people [1]. This trend is increasing steadily in the country. Nevertheless, the incidence rate is lower compared to other OECD countries. Additionally, the mortality rate is decreasing gradually, nearly two times between 1999-2016 (135.5 and 84.9 respectively). For further improvement of the quality of our registry data, we are modifying the methodology of data entrance according to IARC recommendations [2]. It should be noted that breast cancer is the most common cancer in Kazakhstan, but the main cause of cancer deaths are attributed to lung cancer.

In the context of age-specific cancer mortality - 70% of cancer patients were people of employment age and 43% of this group die the same year, it equals to nearly 7.000 people.

The Integrated Model of Cancer Care in Kazakhstan. According to our integrated model of cancer care, cancer care is divided into three levels, where the first level is represented by examination rooms and oncology cabinets in each primary care facility across the country (1,287 rooms). On the second level, we have 18 oncology centers in each region of Kazakhstan; these centers provide specialized cancer care and follow-up. KazIOR – the
Kazakh Institute of Oncology, as well as five high-tech diagnostic and radiology centers together with three pathology centers are providers of tertiary cancer care. The total number of primary care oncologists and examination rooms are 368, and 1287 accordingly, the total number of exam rooms for men 380, for women 907.

The key performance indicators for the quality assessment of cancer care has been modified and developed for each level of cancer care in Kazakhstan. In detail, the key performance indicators are following: for the 1st level settings the percentage of patients with cancer of visual sites, with stages III-IV (target - 17.1%) and with stage I (target - 23.7%); for the second level settings, mortality (target - 93.5 per 100 thousand) and 5 years overall survival (target is 48.1%). Finally, for the tertiary level settings are – coverage with specialized cancer treatment (target is 87.6%) [3].

The structure of cancer care settings, which are being monitored and administered from Almaty (KazIOR) is presented in the picture-2.

Highly Specialized Centers for Radiation Oncology. Highly Specialized Centers for Radiation Oncology are created five major cities in Almaty, Astana, Karaganda, Semey, Aktobe. Moreover, as these centers are not enough to cover the demand in high-tech radiotherapy, the new centers will be launched in upcoming years [1].

**Strategic and operational goals of KazIOR.** As the KazIOR responsible for all cancer care delivered in Kazakhstan, it has the following Strategic and operational goals to improve cancer state in the country:
- The organization, coordination, monitoring, and evaluation of cancer care in the region.
- The development and implementing of high-tech methods of cancer diagnosis and treatment.
- The science development programs.
- Strengthening and development of human resources.
- Development of palliative and rehabilitation care.

**Science Development Programs in KazIOR.** As any major institution in the world, one of main KazIOR’s goals is to develop scientific programs and increase the overall competence of our physicians. For that purpose, we expand the involvement of young oncologists in multicenter trials and encourage publications in international journals. In detail, between 2016-2017 we have been enrolled in several international clinical trials which are listed below:
- ROCHE - BO25114 Jacob – Clinical study of the effica-
Improvement of Prevention and Early Diagnosis.

There are available several diagnostic and treatment methods for all Kazakhstan citizens. For instance, cancer patients have access to palliative care and psycho-social support in all oncology centers. Currently, government funds six cancer screening programs to all citizens (breast, colorectal, prostate, cervical, gastric, esophagus cancers). Additionally, one of the important topics is personalized medicine – which helps to avoid unnecessary high-cost treatment and gives the possibility to deliver highly effective treatment to the exact patient [4].

Palliative care in Kazakhstan is being developed in collaboration with the Kazakhstan association for Palliative Care and Ministry of Health. Currently, we are working on the Strategic plan of Palliative Care. In detail, we possess total palliative beds – about 1,500 and trained specialists – around 6,700.

It is obvious that we cannot change the situation in cancer care without the support of our society. It is a great challenge to increase the involvement of all population of Kazakhstan, science, schools, institutes, cultural, economic and business partners and others. We must admit that changing mindset of the general community to increase cancer awareness, early detection, and prevention – is the key mainstream in the future development of cancer care in Kazakhstan.

References
Introduction. American Association of Thoracic Surgeons and American Cancer Association recommend an annual screening using low-dose computed tomography (LDCT) for current and former smokers aged 55-80, with a history of smoking 30 packs a year during the previous 15 years. Patients aged 55-79 with a history of smoking of 20 packs a year are also subject to annual screening in the presence of additional concomitant risk factors. Annual screening is also recommended for patients aged 55-79 with a long-standing diagnosis of lung cancer (LC) [1].

Method of chest LDCT is recommended as a top-priority method in the diagnosis of LC in several clinical guidelines and underpins the National Lung Screening Trial (NLST) in the United States. Inclusion criteria: age between 55 and 74; a history of smoking ≥30 packs a year; cessation of smoking less than 15 years ago for former smokers [1-5].

The results of a comparison of LDCT and chest X-ray published by NLST in 2016 show an advantage of LDCT against chest X-ray in early detection of adenocarcinomas and squamous cell lung carcinomas. Small-cell LC which is the most aggressive form of LC is rarely detected at early stages by both of the methods mentioned above [6]. NLST-based screening was found to miss a significant share of LC cases – up to 39%. The combination of NLST inclusion criteria and emphysema symptoms revealed by computed tomography (CT) allows increasing the LC detectability up to 95% and reducing the number of missed LC cases [7].

Numerous studies on early detection of LC confirm the cost-effectiveness of LDCT screening method with a repeated annual examination of patients at high-risk aged 50 to 64. The proposed anti-smoking measures in the framework of the screening program increase LC screening cost-effectiveness from 20% to 45% [8].

Thus, LDCT is the most effective method of LC diagnostics among target population.

International early lung cancer action program I-ELCAP

I-ELCAP experts recommend making a preliminary evidence assessment [9].

Low-dose computed tomography in lung cancer diagnostics

Introduction of low-dose chest computed tomography for early lung cancer diagnostics in target population will increase early lung cancer detection and the cancer survival rate.

Keywords: lung cancer, morbidity, risk factors.

I-ELCAP and NLST USA protocols are based on LDCT method. The detectability of Stage I LC was 82% according to I-ELCAP vs. 67% according to NLST (p<0.0001); the incidence of surgical resection of tumour was 86% and 76%, respectively (p<0.0001); the detection of small tumours that resulted in a significantly higher 5-year survival was 83% and 62%, respectively (p<0.0001). Such differences strongly support the significance of LDCT method for LC screening [10].

The transition from NLST screening (1993-2005) to I-ELCAP screening (2006-2011) in the US has minimized the frequency and extent of surgical interventions for non-malignant diseases. High speed of recovery was reached for LC patients who underwent surgical resection by video-assisted thoracoscopic and sub-lobar resection – from 10% to 34% (P<0.0001) and from 22% to 34% (P=0.01) respectively [9,10].

In 2003-2005, 1000 smokers aged 55+, at high risk of LC, with a history of smoking of 10 years and smoking frequency of 1 pack per day, were examined under I-ELCAP in Canada. LC detectability among at-risk population by basic LDCT was 2.2%; of them, 15 (78%) patients had small-sized early-stage resectable cancerous nodes in lungs [21]. According to another I-ELCAP study, early LC in women (n=25) was growing slower: average doubling time was 313 days vs. 137 days in men (n=11). Most of LC cases (n=62, 73%) detected by screening were surgically resectable [11,12].

I-ELCAP experts believe that LC detected by annual re-screening could often be found during previous CT-testing. Cancer was evident in previous CT-images in 56 (54%) participants of the screening. In 10 patients (18%), cancer has advanced to Stage I by the time of re-screening due to a high rate of LC growth in 54% (p = 0.01) [12, 13].

I-ELCAP experts recommend making a preliminary analysis of the benefits of screening of at-risk patients in relation to their survivability depending on the age, the history of smoking and other additional factors. Such analysis should be made on a personal level for each round of screening [14].

Biopsy of pulmonary nodes in the framework of I-ELCAP screening is recommended depending on the size and percentage of its growth to detect and differentiate the suspicious pulmonary nodes and to reduce the incidence of interventions on benign tumours by 16% [15].

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Correct CT-image interpretation can minimize unnecessary tests and interventions. The adherence to I-ELCAP protocol and constant training of medical staff reduce the number of false-positive results [16].

**Conclusion.** Introduction of I-ELCAP protocol allows reducing the share of false-positive results, avoiding the unnecessary surgical interventions on benign tumours, and also decreasing the share of false-negative findings to reduce the number of missed cases of cancer.

**References**
The International Early Lung Cancer Action Program (I-ELCAP) has developed and implemented the protocol of early lung cancer detection that was approved by the Office of Health Promotion Research, USA. The protocol was developed by one of the I-ELCAP founders, Professor Claudia Henske [1, 2, 3]. The geography of the I-ELCAP program is very broad, and today this protocol underlies the national screening programs around the world.

The scientific teams – participants of I-ELCAP program, should strictly follow the I-ELCAP protocol, which includes primary or baseline screening and frequency of rescreening, which depends on the nature of pulmonary node detected during the primary baseline screening. The pulmonary node growth is assessed in dynamics in percent. The main requirement is to perform a primary LDCT chest scanning and at least one repeated screening [4,5]. The participation of scientists from Kazakhstan in the program and implementation of the protocol should be agreed with the Program administrators.

In addition, the I-ELCAP policy is aimed at continued monitoring of all node-positive patients with confirmed diagnosis of “lung cancer” for at least 10 consecutive years. For higher confidence, the I-ELCAP compiles the database for each participating organization, in which the results of baseline and all subsequent screenings are fully documented. It is also very important to identify and document all cases of temporary diagnosis of lung cancer in all screened patients, indicating the reason for terminating the screening [4].

The ELCAP is improving the protocol for over ten years [5, 6]. The protocol was revised in the framework of the International Conferences organized by the EL Cap group 2 times a year. The I-ELCAP research program is governed by a common protocol [7] and is aimed at a long-term perspective of ongoing screening. The latest updated version of protocol was developed based on in-depth understanding of all aspects of the disease [7, 8].

The structure of the I-ELCAP protocol provides an opportunity for performance of interrelated supportive examinations: various non-CT studies (e.g., saliva, blood, urine), which could be carried out in parallel with LDCT. It ensures the study of respective merits and estimation of the screening cost: cost of CT scan separately and in combination with additional examination methods [1-6].

The early lung cancer protocol for Kazakhstan KZ-ELCAP was approved by I-ELCAP and the Office of Health Promotion Research (USA) experts for its introduction and implementation in the Republic of Kazakhstan. Besides, the ELCAP protocol was approved by the Local scientific ethics committee of the “National Research Cardiac Surgery Center” JSC.

The KZ-ELCAP protocol was successfully implemented in Kazakhstan within the grant research “Early lung cancer diagnostics”, jointly by the scientific team of “National Research Cardiac Surgery Center” JSC and Oncology Center of Astana city, Republican State Enterprise on the Right of Economic Activity (RSE REA).

The research findings were published in Kazakhstani and international peer-reviewed publications, and presented at the Annual I-ELCAP Conference “33rd International Lung Cancer Screening Conference and the 1st International Conference on Early Lung Cancer Treatment”, held on December 4-5 at the Mount Sinai Clinic of Jahan Medical School, New York, USA.

This article presents the analysis of main issues of the last version of protocol, adapted for implementation in clinics of Kazakhstan. The informative and detailed protocol contains the description of work of all participants within the research.

**Main topics of I-ELCAP protocol.** Computed tomography (CT)-images obtained at all stages of baseline and/or repeated screening are compared to the initial low-dose computed tomography (LDCT) images to identify all visible non-calcific nodes.

The central non-transparent node of non-linear character can be “solid”, “partially solid” or “non-solid” (the latter two have the “diffusing glass” transparency), and is located in the parenchyma or endobronchial region.

A node is classified as “non-calcific” if it does comply with the common criteria of a calcifying benign node. The node less than 5 mm in diameter is considered as non-calcific if its density is less than the rib density.

The node of 5-20 mm in diameter is non-calcific if its major part was not calcific and/or calcifying, but did not comply with the classical pattern of a calcifying benign formation, and/or had “spicular” edges.

The node of over 20 mm in diameter is non-calcific if any of its part is not calcific (according to the above specified criteria) [6-8].
The mean size of the length and width is considered the node diameter. The length is measured on one CT-image, where the node maximum length is determined; the width is defined as the longest perpendicular to the node length, measured on the same CT-image.

The changes in other thoracic organs, including mediastinum, heart, soft tissues and bones, are also documented. The mediastinal mass are tumours originating from the mediastinum, including the thymus, heart and esophagus, as well as the thyroid gland tumours extended into the mediastinum. The mediastinal mass and soft tissues tumours are registered in reference to their location and size. The radiologist also documents the visualization of the upper abdomen part with respect to the location and size.

Each coronary artery is identified: main (principal), left anterior descending, circumflex and right arteries. The confirmed calcification in each artery is registered as “no calcification”, or “minimal”, “moderate”, or “marked”. The calcification is graded on the scale from 0 to 3. The “minimal” grade is determined - if less than 1/3 of the entire artery length was calcified, “moderate” - if 1/3 – 2/3 of the entire artery length was calcified, and “marked” - if over 2/3 of the entire artery length is calcified.

The protocol includes the identification of the emphysema degree, which can be defined as “no emphysema”, “minimal”, “moderate”, or “marked”. Each degree is graded from 0 to 3 [4, 6, 7].

**The screening frequency** is determined by the result of baseline CT screening: if the CT screening did not reveal a cancer process, the second CT screening should be repeated after 1 year.

If lung cancer (LC) was diagnosed at stages I, II or IIIA, the patient should participate in screening according to the set schedule, after the interventional procedures.

The researchers are called upon to follow the annual screening protocol. It is not recommended to introduce any changes into the specified interval, since the single screening frequency is required for generalization of the multicentre study results [4, 7, 8, 9].

**Baseline (initial) screening:** The CT-study is considered as “positive” if at least one “solid”, “partially solid” or “endobronchial” node of 5.0 mm or more in diameter is found.

If non-calcific nodes are detected, but all of them are too small to suspect the positive findings, including a non-solid node of any size, the result is regarded as the semi-positive, and the patient has to undergo the LDCT study 12 months after the initial screening.

If no nodes were found and the test was negative, the patient is subject to a repeated CT after 12 months.

In case of detection of “solid” and “partially solid” node of 5 to 15 mm size, the patient should undergo the repeated LDCT after 3 months.

If the node showed the malignant growth (according to the growth assessment scale), the biopsy examination is prescribed.

If there is no growth, or the node is partially or completely resolved, the study is discontinued.

For “solid” and “partially solid” nodes of 15 mm or more in diameter, with suspected cancerous nature, the biopsy examination of the node is prescribed.

In case of suspected latent infection, the course of antibiotic therapy with anaerobic effect is prescribed followed by LDCT examination after 1 month.

If repeated LDCT did not show the node's resolution or the level of malignancy is maintained, the node biopsy is prescribed.

If the biopsy examination did not reveal the lung cancer, the repeated CT-screening is performed in 12 months after the first baseline CT examination [7, 9].

**Repeated (annual) screening** includes compulsory review of the original CT-image that should identify all non-calcific nodes regardless of the size, with special focus on the node(s).

The focus is directed to those nodes that show growth starting from previous screening, of the whole size or the size of solid component detected earlier, or the detection of the solid component in previously non-solid node.

Within repeated screening, the results of LDCT are considered as positive if at least one non-calcific solid or partially solid node with the size of 3 mm or endo-bronchial node with the size of 5.0 mm in diameter of temporary growth was identified. If the new solid or partially solid node was found of the size less than 3 mm or the non-solid node component of any size, the result should be considered as the semi-positive, with prescribed CT screening in 12 months. If the test was negative, the second CT screening should be carried out in 12 months.

In case of detection of non-calcific nodes, and all of them are too small to suspect the positive result, including the non-solid node of any size, the result is regarded as the semi-positive with assigned LDCT in 12 months after the baseline screening.

If the node was not identified, the test should be regarded as the negative with prescribed repeated CT scanning in 12 months.

In case of detection of solid and partially solid node of 5 to 15 mm size, the repeated LDCT is prescribed in 3 months. If the node showed malignant growth (according to the growth assessment scale), the biopsy examination is prescribed. If there is no growth or the node is partially or completely resolved, the study is discontinued.

In case of multiple nodes and suspect to latent infection or inflammation, the course of broad-spectrum antibiotics with anaerobic effect is prescribed, followed by the LDCT scanning in 3 months.

For “solid” and “partially solid” nodes of 15 mm in diameter, the biopsy examination of the node is prescribed.

In case of suspected latent infection, the course of antibiotic therapy with anaerobic effect is prescribed, followed by LDCT examination in 1 month.

If repeated LDCT did not show the node's resolution or the level of malignancy is maintained, the node biopsy is prescribed.

If the biopsy examination did not reveal the lung cancer, the repeated CT-screening is performed in 12 months after the first baseline CT examination.

For all patients of the study with discontinued diagnostic algorithm or with no lung cancer according to the biopsy findings, the second CT screening is performed 12 months after the initial baseline examination [4, 7, 9, 10].
LITERATURE REVIEW

The node growth assessment: a) The growth of the node is determined by increasing or expansion of the node size and/or the "solid" component, "partially solid" node, and/or developing of the "solid" component in non-solid node at subsequent CT scan after the baseline repeated annual CT examination; b) The volume doubling rate assessment, based on measuring of the node size in two specific views. The time between these two views should be adequate for generation of significant detectable changes in the node volume.

The criteria for significant changes (in percentage) of the node diameter or the "solid" component growth in the "partially solid" node: a) for the node <5 mm in diameter – for at least 50%; b) for the node 5-9 mm in diameter – for at least 30%; c) for the node > 10 mm in diameter – for at least 20% [4, 6, 8, 10].

The trans-thoracic fine needle biopsy (TTFNB) is performed in patients with nodes > 8 mm. The TTFNB procedure is carried out under the CT control in outpatient settings with provision of local anaesthesia by one needle puncture.

Samples obtained by TTFNB undergo cytological testing to confirm LC diagnosis by histomorphologic identification of the form of cancer. The images from cytological examination of samples are computerized for further description and classification [7, 10, 11].

Biopsy samples are described and classified according to the standard diagnostic categories.

If the CT-biopsy is not feasible, biopsy with ultrasound guidance, or bronchoscopic biopsy is recommended for patients.

The diagnosis of "lung cancer" is considered to be based on screening diagnostics in case of positive results of baseline CT, regardless of when the diagnosis was really established. The diagnosis is classified as the "lung cancer" in case if the baseline screening revealed the "semi-positive" result, and repeated CT in 12 months detected at least one non-calcific node. If the result of initial CT screening was negative, but the diagnostic examinations showed suspicious findings before the planned annual baseline screening, the diagnosis should be classified as the "temporary LC diagnosis"[12, 13].

Conclusion. Multi-year studies of the I-ELCAP international team have demonstrated the applicability of the I-ELCAP protocol in broad clinical practice.

References


Desmoplastic small round cell tumour: practical cases

Desmoplastic small-cell tumour (DMC) is a rare and highly aggressive malignant tumour of the abdominal cavity. The prognosis for such a tumour is especially unfavorable; the survival range is 17 to 25 months. The article presents a clinical observation of two men aged 28-29 years with a lesion of small pelvis, bronchus and lung. We have studied in detail the morphological pathology, histology and immunohistochemistry of the tumour. Currently, there are no generally accepted DMC treatment protocols. During the treatment, the pathological process progressed in both cases, with one fatal outcome.

**Keywords:** Desmoplastic small-cell tumour (DMC), EWSR1 & WT1 gene expression disorder, presence of t translocation (11:22) (p13, q12), rare pathology.

**Introduction.** Desmoplastic small-cell tumour (DMC) is a rare and highly aggressive malignant tumour with an unfavourable prognosis and polyphenotypic differentiation. The tumour often occurs in children and young men with a specific localization in the abdominal cavity, more rarely in the thoracic cavity, pelvic cavity or scrotum [1]. The DMC diagnosis is based on the histological examination of material and assessment of the immunohistochemical markers expression. The tumour cells can simultaneously express epithelial (cytokeratin, epithelial membrane antigen), neuron-specific (neuron-specific enolase), and myogenic (desmin) markers. In a microscopic study, the cluster of small round blue cells with hyperchromic nuclei is determined in tumour samples between the fragments of collagen fibres. In immunohistochemistry (IHC) tests, the tumour cells express a CD99 antigen in 23% of cases, which is also distinctive feature of Ewing sarcoma. The DMC differential diagnosis should be carried out with the alveolar rhabdomyosarcoma, Ewing sarcoma, neuroblastoma, and malignant lymphoma. The DMC is associated with the presence of t translocation (11:22) (p13, q12), led to EWSR1 and WT1 gene expression disorder [2]. The prognosis for such a tumour is especially unfavourable; the survival range is 17 to 25 months. A 5-year survival rate within the aggressive multimodal chemotherapy regimens (CTR) is registered in no more than 20% of patients due to late detection of the disease [3]. Currently, there are no generally accepted criteria for staging the disease and treatment standards due to rarity of that pathology and difficulty of the tumour diagnostics. The study aimed at demonstration of DMC specific features.

Two DMC cases were observed during 6 months of 2016. In case #1, the DMC diagnosis of the thoracic cavity was established for a man of 29 years old on autopsy. In case #2, the tumour was located in the small pelvis region of a man of 28 years old. The own observations of that pathology and difficulty of the tumour diagnostics. The study aimed at demonstration of DMC specific features.

**Information about the patient № 1:**

Patient B.D., born in 1987, was admitted to the Thoracic Center, KazIOR on 05/10/16 in a moderate condition. Complaints: hyperthermia up to 38°C, cough with hard-to-separate sputum and blood streaks, left chest pain. Anamnesis: the patient felt sick from 29/04/2016 and visited the general practitioner of the city outpatient clinic No.3 with complaints of dry cough and pain in the chest left side. The patient received the nonspecific anti-inflammatory therapy in connection with the community acquired lower lobe pneumonia of the left side. The above mentioned complaints became apparent at the end of July 2016. Chest X-ray of 30/07/2016 revealed the left side multi-segment pneumonia, complicated by exudative pleuritis. The patient was urgently admitted to Astana regional hospital (ARH), where he received treatment from 30/07/2016 to 11/08/2016.

The thoracic surgeon has recommended a left side diagnostic video-assisted thoracoscopic surgery (LDVATS) with biopsy of pleural specimen. The LDVATS, thoracotomy, pneumolysis, decortications and biopsy were performed on 29/08/16. Histological examination N18473-75 of 08/09/2016 showed exudative pleuritis with nonspecific inflammation and focuses of bleeding. On September 15, 2016, the patient had a progression of heart failure and the elevated hyperthermia. The patient was again urgently hospitalized to the therapeutic department of ARH. After the left side pleural puncture on 21/09/2016, the patient was diagnosed with Left side blocked pleuritis. Tuberculosis?

The patient was on hospital treatment in AN Syzganov National Scientific Center of Surgery on October 3-5, 2016 where the cover-glass preparations and glass blocks were re-reviewed. Histological examination N14254-265 of 05/10/2016 showed a diffuse malignant mesothelioma (epithelioid type ICD - O code 9052/3). The patient was sent to KazIOR for further treatment.

**The diagnostic and clinical data of patient №1:**


Status after thoracoscopy. At admission to the Thoracic Center: the general status - moderately severe due to the underlying illness. The patient was in critical condition during 5 days in the hospital. On 10/10/2016 at 06:35 a.m., biological death of the patient was registered by the critical care physician on duty during examination continued with resuscitation.

**Summary from the autopsy report:** In the autopsy of the left pleural cavity, the tumour infiltrated into the intercostal muscles, pericardium, heart epicardium, with cuff wrapping of aorta and pulmonary trunk was revealed. The tumour invaded into the left lung and left bronchus tissue, with complete obturation of its lumen, as well as into the diaphragm on the left side, with involvement of the left
adrenal gland in the tumor process.

The heart failure progression, caused by fibropericarditis and myocardium atrophic changes, led to formation of mixed-type blood clot in the lumen of right ventricle, pulmonary trunk and its branches with sharp narrowing of their lumen; development of the respiratory failure manifested in the left-side total pneumonia with formation of multiple hemorrhagic pulmonary infarction. The formed thromboembolism obtruated the pulmonary artery trunk and has caused death. Histological findings are presented in the Figure 1.

**Figure 1** – Hystological preparation of the bronchus wall tissue with small-cell tumour consisting of desmoplastic stroma with round cells nests and trabecula, with major foci of necrosis

**Immunohistochemical (IHC) examination data:** Results of immunohistochemistry are shown in the Figure 2: Cytokeratin AE1/AE3 was positive on tumour cells. CD99 (Figure 2a), CD45 (Figure 2b), CalretininTTF1, WT1, Desmin (Figure 2c) - were negative. Ki67 - 35% (“on hot spot”) (Figure 2d).

The morphological picture and immune phenotype correspond to the desmoplastic small-cell tumour of pleura with peribronchial growth (ISD-O Code 8806/3). Post-mortem diagnosis based on histological and immunological tests was different from the established clinical diagnosis: Small-cell tumour of pleura with invasion to pericardium, epicardium, basic left bronchus, lung tissue, cupula of diaphragm left side (autopsy material N9/16, immunohistochemical examination No337/16). Complications: chronic heart failure, dystrophic myocardium changes, thrombosis of the central liver veins with central lobular necrosis of hepatocytes. Fibropericarditis. Progressing pulmonary insufficiency: left-sided total bronchopneumonia, left lung multiple haemorrhagic infarction.

The discrepancy between the clinical and post-mortem diagnosis of the underlying disease was stated by the category I due to the patient's critical condition, challenges in that disease diagnostics, the inpatient stay in the hospital for 5 days, as well as a polyphenotypic features in the form of epithelial and mesenchymal markers co-expression.

**Information about the patient № 2:**

Patient E.B., born in 1988, was hospitalized to the Abdominal Oncology Center, KazIOR on 16/08/2016. Complaints: feeling of weight and discomfort in hypogastrium. The patient was examined by M.O. Kuzikeev, MD, the Head of the Center who has offered a specialized treatment. Anamnesis: the patient felt sick and experienced the a.m. symptoms since June 2016. He visited the A.N. Syzganov National Scientific Center of Surgery where he underwent the following examination: 1) Abdominal ultrasound on 04/08/16: formations in the liver parenchyma – metastases. Gallbladder wall polyps. Space-occupying mass in the abdominal cavity and small pelvis. Fluid traces in the abdominal cavity. 2) Abdominal CT on 05/08/2016: The mesenchymal abdominal tumour of unknown genesis (germ-cell sarcoma) with liver metastases. Ascites. Cytological examination N10123-10135 as of 09/08/2016:
Liver formation. Small pelvis retroperitoneal formation. Conclusion: Neuroblastoma, sympathoblastoma. Based on the aforesaid, he was clinically diagnosed with abdominal cancer St (T4NXM1) with liver metastasis.

**Diagnostic and clinical data of the patient N 2:** At admission to KazIOR, the first stage of recommended treatment included surgical removal of the main focus with further PCT courses. The surgery was conducted on 26/08/2016: laparotomy, revision of the abdominal cavity organs, partial removal of the abdominal cavity tumour with referral of postoperative material for histological examination (Figure 3), superimposition of bypass ileotransverse anastomosis, colostomy and abdominal drainage.

![Figure 3](image3.png)

**Figure 3** – Postoperative retroperitoneum material

The postoperative period was relatively satisfactory, without complications. The patient was discharged on 07/09/2016 for corresponding outpatient antitumour treatment.

**Histological examination:** Microscopy N49834-38 of 2016: Multiple trabecular structures are defined among multiple fibrotic stroma, from small rounded and oval cells with moderately polymorphous rounded and oval cells with rosette-like structures; there are foci of myxomatosis (Figure 4). Conclusion: Morphological picture is typical for desmoplastic small-cell tumour (DMC).

**IHC examination:** IHC study N3268-70 of 2016: PanCK, Desmin were diffuse-positive on tumour cells (Figure 5A, B). WT1 - negative on tumour cells (Figure 5C).

**Conclusion:** Immune phenotype corresponds to a desmoplastic small round cell tumour.

Post-mortem diagnosis based on histological and immunohistochemical tests: DMC.

**Discussion and summary:** The observed cases have great practical importance, since they are registered extremely rare in pathoanatomical practice. The diagnostics of that type of tumours was rather challenging for clinicians due to the difficult-to-recognize symptomatology [3]. The multidisciplinary approach and individual therapy play the leading role in treatment of patients with that pathology. It is necessary to define precisely the localization of that tumour, prove morphologically its belonging to that type of tumours, determine the role of surgical treatment and chemoradiotherapy, and advantages of the new methods of treatment (intensive modulation radiotherapy and hyperthermic intraperitoneal chemotherapy). With respect to the study of genetic changes associated with the development of that tumour type, in the future it can provide an opportunity for establishing of pathogenesis and discovering of the new therapeutic targets in DMC treatment.

**References**


Evaluation of the capacity of cytological method in lung tumour diagnostics using liquid biopsy. Use of immunocytochemistry in lung tumour diagnostics allows expanding the capacity of modern cytomorphological methods, to diagnose primary-multiple neoplasms and the extent of pathological process and verify the diagnosis at the preoperative stage.

**Keywords:** cytological diagnostics, lung tumours, immunocytochemical method.

Lung cancer (LC) is one of the most common malignancies. In Russia and Kazakhstan, 59,111 new cases of LC were registered in 2012. During the last 5 years, the absolute number of cases has decreased by 4.4% in men, and increased by 3.8% in women. The share LC in total cancer morbidity ranged from 10.5% to 17.26% in men, and from 2.5% to 5.2% in women [4].

Cytological method is one of the most popular among other complex methods of preoperative diagnostics of LC, with quite a high sensitivity of 89.4% to 97.3%, and the specificity of 79-98%. The diagnosis of carcinoma is confirmed in 83%: in 62% of patients with the tumour the root area, in 79% of patients with the tumour in the middle area, and in 88% of patients with mantle tumours. The method efficiency is about 70% for neoplasm less than 3 cm (T1) in diameter, 85-90% for neoplasm over 3 cm (T2-T3) in diameter. Cytological examination of material obtained by fine needle aspiration biopsy allows determining the histological form in 65% of cases and establishing the degree of tumour differentiation in 40% of cases [1, 6, 7, 12]. Such complications, as haemothorax, hydrothorax and implantation metastases, are extremely rare [5].

The distribution of patients depending on the form of lung disease (including benign and infectious types) is the following: epithelial malignant tumours – 27.9%, metastatic tumours – 0.9%, sarcomas – 0.5% [8]. According to the clinical picture the lung cancer is classified as a non-small cell lung cancer (NSCLC) and small cell lung cancer (SmCLC) [14]. Of all lung malignant neoplasms the carcinoma compose 95%. At this, a squamous cell lung carcinoma (SqCLC) is more common in men – 44% of all cases vs. 25% in women. On the contrary, adenocarcinoma is more common in women – 42% of all cases vs. 28% in men. Small cell and large cell carcinomas are detected in 20% of cases, and carcinoma simplex – in 9% of cases [14]. The implementation of morphological criteria with account of classification of lung neoplasms provides an opportunity for cytologists-histologists to make an accurate diagnostics for further treatment of patients according to the relevant protocol.

Given the fact that cytological method is the initial morphological diagnostic test, its results largely define future therapeutic tactics. However, there are challenges in diagnostics of low differentiated carcinoma, anaplastic and dysmorphic cancer, metastatic neoplasms. It justifies the need for additional more specific methods such as the immunocytochemistry (ICC) test [2]. In this regard, ICC is one of the tools which permits to:

- differentiate these types of cancer,
- clarify the histogenesis in the preoperative stage,
- diagnose the primary-multiple lesions,
- determine the degree of expansion, and
- assess some of prognostic indicators and the tumour sensitivity to chemo-hormone therapy [1]. The significant markers for primary lung tumour diagnostics include: CK7, CK20, thyroid transcription factor TTF-1, chromogranin A, synaptophysin, CD56; surfactant proteins; p63 and CK5/6 [10, 17, 18, 19]. According to the literature, the expression of TTF1 in pulmonary adenocarcinoma (PAC) ranges from 73% to 92% [9, 11, 13, 15, 17]. This antigen is not an immediate goal for targeted therapy but it could serve as a relevant prediction factor – the sensitivity marker in selection of therapy with pemetrexed. In their research on a small-volume material, Maoxin Wu and Beverly Wang et al. (2003) have studied and demonstrated the relevance of using the ICC-markers p63 and TTF-1 for differential diagnostics of low differentiated SqCLCs and SmCLCs. The authors highlighted that staining of nuclear TTF-1 was positive and more evidence in 20 (87%) of 23 cases of SmCLC (14/17 histologic sections, 6/6 cytoblocks). These authors confirmed that the TTF-1 was the factor which defined the differentiation of lung and thyroid cells. Its expression was revealed in 81-100% cases of SmCLC, and only rare SqCLCs showed a positive staining of TTF-1 antigen – 7-9% [16]. In addition to TTF-1 expression, SmCLC was confirmed by positive reaction to synaptophysin (strong, diffuse), chromogranin A (focally), and NSE (focally, weak).

p63 protein plays an important role in keeping of integrity and differentiation of squamous epithelium, supporting the balance between basaloid and undifferentiated stem cells. The research findings have shown that the sensitivity and specificity of IHC identification of p63 protein as a marker of the squamous cell carcinoma detection was 100%. The positive and negative prognostic value and overall accuracy of the method (correct classification) were also equal to 100%. TTF-1 and p63 as nuclear proteins allow avoiding the problems associated with the detection of cytoplasmic antigens in tumour cells with sparse cytoplasm. The use of CK7 and CK20 ensures the possibility to establish whether the lung tumour is a primary adenocarcinoma (AC) (CK7- and CK20-), a mucus-producing AC (CK7 + and CK20 +) or a metastasis of gastrointestinal cancer (CK7- and CK20+) [16, 17, 19].

**Aim of the study.** Assessment of the potential of immunocytochemical method in cytological diagnostics of primary and metastatic lung tumours using Cytospin liquid technology.
Materials and methods. In 2014-2015, the laboratory of clinical cytology of NN Blokhin Russian Medical Research Center of Oncology, RAMS has conducted 955 immunocytochemical (ICC) tests on the material of 291 patients with various types of cancer. Of them, 118 patients (77 men and 41 women) underwent 440 ICC to clarify if their lung tumours were primary or metastatic. The majority of patients had the clinical diagnosis of "lung cancer", in one third of cases the doctor did not exclude the secondary affection of lung by metastasis of another tumour.

The cytological material was obtained by application of the trans-thoracic needle biopsy in 105 patients (89%), bronchoscopic examination in 7 patients (5.9%), bronchial aspiration in 4 patients (3.4%). In one study the sputum ICC test (0.85%) was performed, and in another study the imprint of the main bronchus piece has been examined (0.85%).

ICC tests were made using Ventana immunohisto-stainer (BenchMark ULTRA), and the Dako monoclonal antibodies (MCAB) was used for total cytokeratins (clone MNF116, dilution 1:50-1:100), cytokeratin 20 (clone K520.8, dilution 1:25-1:50), cytokeratin 5/6 (clone DS/16 B4, dilution 1:50), TTF-1 (clone BG7G3/1, dilution 1:200), chromogranin A (clone DAK-A3, dilution 1:100-1:200), synaptophysin (clone SY38, dilution 1:10-1:20), Cdx2 (clone DAK Cdx2, 1:50), RCC (clone SPM3/4, dilution 1:50), Melan A (clone A103, diluted 1:25), HMB 45 (clone HMB45, dilution 1:50), ER α (clone 1D5, dilution 1:60), PR (clone RgR 636, dilution 1:50), tiroglobulin (clone DAK-Tg6, dilution 1:100), CA125 (clone M11, dilution 1:20), CD45 (clone 2B11 + PP7/26), S100 protein (anti-S100 polyclonal rabbit antibody, dilution 1:400), Vimentin (clone V9, dilution 1:100); monoclonal rabbit antibody Cell Marque: to CD56 (MRQ-42, dilution 1: 250), cytokeratin 7 (OV-TL 12/30, dilution 1:400). The cytological preparations were stained with Mayer’s haematoxilin and placed under a cover-glass with use of the Canadian balsam. The tests were performed on the cytological monolayer smears obtained by accumulation of punctuate on the special nutrient medium with followed centrifugation on the Cytospin-3 system at 1000 g/min during 5 minutes (Cytospin-technology).

Taking into account the cytological conclusion statements, the material was divided into several groups:

Primary pulmonary adenocarcinoma (PAC) established with confidence,

Provisional diagnosis of PAC,

Low differentiated cancer, likely a non-small cell type,

Differential diagnosis of primary PAC and metastasis,

Malignant tumour of non-epithelial nature (Table 1).

Of 118 patients, the PAC cytological diagnosis established with confidence in 55 cases, with ICC confirmation by CK7 and TTF1 positive expression in 94.5% of cases (Figures 1, 2, 3). The marked expression of CK20 has been observed in 50% of primary PAC tests, which was typical for mucinous carcinomas (Figures 1, 2, 3).

In that group of conclusion statements, in one case the adenocarcinoma (AC) showed the TTF-1 negative phenotype, and the metastasis of intestine AC has been detected in another case, with recorded Cdx2 and CK20 expression (with CK7-/TTF-1) in the immunocytochemical tests (Figures 4, 5; Table 1).

In 6 out of 118 cases, the PAC provisional diagnosis has been made. After ICC tests, the PAC diagnosis (TTF1+/CK7+) has been confirmed in 2 cases, the TTF1 expression was not detected in 4 cases (Table 1).

<table>
<thead>
<tr>
<th>Types of cytological statements</th>
<th>Number of observations</th>
<th>Number of samples referred to ICC – ICC statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC (established with confidence)</td>
<td>55 (46,6 %)</td>
<td>52 – PAC (established with confidence)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 – PAC (provisional)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 – Metastasis of intestine AC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 – ICC is non-informative</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – PAC (provisional)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 – PAC (established with confidence)</td>
</tr>
<tr>
<td>AC (provisional)</td>
<td>6 (5,08%)</td>
<td>15 – PAC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – SmC carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 – SqC carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 – ICC is non-informative</td>
</tr>
<tr>
<td>Low differentiated carcinoma!</td>
<td>22 (18,6%)</td>
<td>13 – PAC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – Metastasis of intestine AC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – Metastasis of renal cell carcinoma (RCC)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – Metastasis of urothelial cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 – Metastasis of breast cancer (BC)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – ICC is non-informative</td>
</tr>
<tr>
<td>Primary PAC or metastasis of another tumour</td>
<td>31 (26,3%)</td>
<td>4 – Metastasis of kidney cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 – Metastasis of breast cancer (BC)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – ICC is non-informative</td>
</tr>
<tr>
<td>Malignant tumour of non-epithelial nature</td>
<td>4 (3,4%)</td>
<td>2 – Malignant tumour of non-epithelial nature/ detalization was not required</td>
</tr>
<tr>
<td>Non-informative tests</td>
<td>–</td>
<td>7 (5.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>118 (100%)</td>
<td></td>
</tr>
</tbody>
</table>
In 31 cases, the metastasis of another tumor was the subject for exclusion. After ICC examination, the primary PAC (TTF1+/SC7+) was verified in 13 cases (Table 2). The metastasis of intestine AC (Cdx2+/CK20+/TTF1-/CK7-) was detected in 4 cases, the metastasis of RCC (RCC+/CK20-/TTF1-/CK7-) - in 4 cases, the metastasis of urothelial carcinoma (CK20+/TTF1-/CK7+) - in 4 cases, and the metastatic BC (RE+/CK20-/TTF1-/CK7+) - in 2 cases (Figures 6, 7, 8, 9, 10, 11).

**Table 2** – Comparison of cytograms with ICC examination findings

<table>
<thead>
<tr>
<th>Types of cytological statements</th>
<th>Cases, n</th>
<th>No. of samples referred to ICC – ICC opinions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary PAC?</td>
<td>31 (26.32%)</td>
<td>13- PAC: (1- MFMC-RCC) (1 – MFMC-endometrial cancer)</td>
</tr>
<tr>
<td>Metastases in the lung?</td>
<td></td>
<td>4 – Intestinal AC metastasis</td>
</tr>
<tr>
<td>Primary-multiple tumour?</td>
<td></td>
<td>4 – RCC metastasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – Urothelial cancer metastasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 – BC metastasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – ICC is non-informative</td>
</tr>
</tbody>
</table>

Note: MFMC - Multifocal metachronous cancer
**Figure 6** - Cytogram of metastatic papillary RCC in the lung, X200

**Figure 7** – Positive cytoplasmic ICC-reaction of RCC in cells of papillary RCC, X200

**Figure 8** – Negative cytoplasmic ICC-reaction of TTF1 in cells of papillary RCC, X200

**Figure 9** – Cytogram of metastatic BC in the lung, X200

**Figure 10** – Positive nuclear ICC-reaction of endometrial cancer (EC) in cells of BC metastasis, X200

**Figure 11** – Negative nuclear ICC-reaction of TTF1 in BC cells, X200
One fifth of the studied cases belonged to the low differentiated carcinomas – the most difficult for cytomorphological verification tumours (Table 3). ICC examination has proven primary PAC in 15 out of 22 (18.6%) cases (TTF1+/CK7+). Expression of neuroendocrinological markers of synaptophysin, chromogranin A, CD56 and TTF1+ in the absence of reaction from MCAB to SK7-/SK20-, allowed confirming the SmCLC diagnosis in 4 cases, and SqCLC – in 1 case (CK5/6+/TTF1-/CK7-/CK20-) (Figures 12,13,14,15,16).

Table 3 – ICC data for low differentiated carcinomas

<table>
<thead>
<tr>
<th>Types of cytological statements</th>
<th>Number of observations</th>
<th>Number of samples referred to ICC – ICC statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low differentiated cancer! NSCLC?</td>
<td>31 (26.32%)</td>
<td>15 – PAC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 – Small cell cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 – RCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 – ICC is non-informative/evident inflammatory component, few tumours cells</td>
</tr>
</tbody>
</table>

Figure 12 – Cytogram of small cell lung cancer (SmCLC), X1000

Figure 13 – Positive ICC reaction of chromogranin A in SmCLC cells, X200

Figure 14 – Positive ICC reaction of synaptophysin in SmCLC cells, X200

Figure 15 – Positive ICC reaction of CD56 in SmCLC cells, X200

Figure 16 – Positive ICC reaction of TTF1 SmCLC cells, X200
The group of malignant tumours of non-epithelial nature was the smallest one, with only 4 observations, of which in 2 cases the melanoma metastases have been confirmed by the ICC reactions with markers to melanosome antigens of HMB45, Melan A, and S100 protein. In 2 cases, the presence of recurrent lung tumour of a non-epithelial nature (EMA-/common cytokeratins-/vimentin+) has to be confirmed or excluded without further clarification.

The non-informative material composed in total 5.9%, and was due to evident dystrophic and degenerative changes of cells obtained from necrosis foci, cystic changes, and limited amount of material.

**Conclusion.** The demonstrated sensitivity of 955 ICC tests conducted on the material of 291 patients with various cancer types within the scope of determination of primary lung carcinoma, histological type of cancer, and metastatic tumours, organ belonging was 95.6%.

1. During the ICC examination of PAC, the TTF-1 expression was observed in 90.6%. The detection of this marker in 24% of cases led to establishing of diagnosis of the primary PAC with confidence.

2. The application of ICC tests in low differentiated carcinomas and undifferentiated neoplasms permitted to verify the primary PAC in 53% of cases, and detect the metastasis and its organ belonging in 27% of cases.

3. In ICC tests of low differentiated carcinomas, 20% of them were classified as a small cell lung cancer (SmCLC), and 80% as a non-small cell lung cancer (NSCLC).

4. The use of ICC tests in case of primary-multiple cancer is considered essential.

Thus, the use of immunocytochemistry in lung cancer diagnostics allows expanding the potential of modern cytomorphological methods, clarifying the histogenesis of the neoplasm at the preparative stage, diagnosing the primary-multiple neoplasms and determining the degree of pathological process.

**References**


Prospects of nuclear medicine in diagnostics and treatment of breast cancer bone metastases

Nuclear Medicine (NM) is widely used in breast cancer diagnostics and treatment. This article analyzes the statistical data of the Republic’s oncological service for 2015 in terms of determining the number of breast cancer patients requiring the radionuclide diagnostics (RND) and radionuclide therapy (RNT).

**Keywords:** breast cancer, nuclear medicine, radionuclide diagnosis, radionuclide therapy, scintigraphy, positron emission tomography.

**Relevance.** Nuclear medicine (NM) plays an important role in diagnostics and treatment of breast cancer (BC). Of the radionuclide diagnostic methods (RND), the one-photon emission computer tomography (OPECT/CT) and positron emission tomography combined with computed tomography (PET/CT) with use of osteotropic and tumour-tropic γ-emitting and positron (β+)-emitting radionuclides or compounds labelled by them are widely implemented in practice. In defining of BC prevalence, the broad application belongs to the glucose labelled with a positron-emitting radionuclide $^{18}$F. The osteotropic radionuclides emitting β-particles-electron or their labelled osteotropic compounds are used for the radionuclide therapy (RNT) of bone metastases.

The whole body scintigraphy (OPECT/CT) with introduction of the $^{99m}$Tc-labelled phosphate complex is commonly used as the basic NM method. In application of the whole-body scintigraphy the bone metastases are detected 3-6 months earlier in 30-50% of patients than after use of X-ray examination [1-3]. The implementation of PET/CT with fluorodeoxyglucose ($^{18}$F-FDG) in diagnostics of the malignant process prevalence depends on availability of the method [4, 5].

The radionuclide diagnostics is also important in detection of sentinel lymph nodes (SLE). A radionuclide search of sentinel lymph nodes is carried out by pre-introduction of a colloid solution with a particle size of 50-80 nm, labelled with $^{99m}$Tc into the tumour tissue, primarily on the tumour periphery and in several points [2]. Within the OPECT/CT procedure, in 20 minutes and 2 hours after the introduction of radioactive drug (RAD), the sentinel lymph nodes are found. The intraoperative detection is performed with use of a radiation meter – the gamma probe. An “Intraoperative navigation system” declipse® SPECT (Germany) is more expensive, complex and reliable method for SLE surgery. In case of detection of tumour cells in SLE based on findings of express-biopsy, the volume of surgical operation is expanded, in case of absence of tumour cells - the standard volume of surgery is performed. The detection of SLE by implementation of the radionuclide method with express-biopsy provides an opportunity for objective determination of the surgical intervention volume.

The radionuclide therapy (RNT) with radiant β-particles – radionuclide electrons, or their labelled osteotropic compounds – is widely used to treat bone metastases [6-10]. The RAD introduced intravenously is distributed by blood flow throughout the body and accumulated in the affected area in a greater degree. The RNT is also called the systemic radiation therapy. Currently, within RNT the $^{153}$Sm-EDTMP is broadly used, with its ability to relieve the pain syndrome, improve the quality of life in the majority of patients with bone metastases. The accumulation of osteotropic EDTMR labelled with β-emitting $^{153}$Sm in bone metastases leads to the bone metabolism imbalance due to “internal radiation exposure”, thereby obtaining the reduction of tumour infiltration.

**Aim of the study.** Determine the need for development of the nuclear medicine for diagnostics and treatment of breast cancer bone metastases.


**Findings and discussion.** The analysis of statistical data of cancer service of the Republic of Kazakhstan for 2015 showed the overall increase of the number of patients with breast cancer and decrease of the number of patients with advanced stages of the disease. Thus, in 2015, the number of patients with BC in Kazakhstan made in total 31 352 (registered and newly diagnosed), of them 2 280 patients had the III-IV stages of breast cancer. In patients with BC at stages III-IV the probability of having the bone metastases is significantly higher than in the initial stage of disease. The radionuclide examination of patients with breast cancer of I-II stages has detected the bone metastases in 5% of cases. That indicator could have a higher value, however the nuclear medicine in Kazakhstan is not commonly used due unavailability of these diagnostic methods.

The breast cancer statistical indicators analysis demonstrated the need for a wide introduction of the radionuclide method in detection of the sentinel lymph nodes, led to determination of adequate volume of the surgical intervention.

Taking into account the large proportion of patients with advanced stages of breast cancer, the broad introduc-
tion of the radionuclide therapy in treatment of the breast
cancer bone metastases is required.

**Conclusion.** Nuclear medicine (NM) plays an important role in diagnostics and treatment of breast cancer bone metastases. It is necessary to develop and commonly introduce the radionuclide methods of diagnostics and treatment in practice of cancer facilities of the Republic of Kazakhstan, which will improve the quality of life and increase the life expectancy of patients with breast cancer.

**References**


Comparative analysis of the results of screening and routine inspection on early detection of cervical cancer in West Kazakhstan region in 2015-2016. Proposals on further improvement of routine inspection

The organization of oncogynecological service is aimed at timely detection and treatment of precancerous pathology and tumours of female genital system. The existing system of medical institutions includes medical outpatient clinics, observation rooms by polyclinics, women’s consultations, and centralized cytological laboratories of the regional oncological dispensary. Hence, today it is practically impossible to trace the continuity between the mentioned organizations due to the absence of a common database for the registration of conducted surveys, there are no opportunities for a detailed statistical analysis of the newly detected and treated cases. This problem can be solved by introducing a single information system that will allow real-time tracking of detection and treatment of cancer cases and precancerous pathologies. This problem becomes especially acute due to the ongoing screening activities and annual preventive examinations. Whereas oncological dispensaries act as most important coordinators of efficient organization of oncogynecological service, the existence of a common automated system will increase the level of tracking, detection and treatment at the local level, and will reduce the risk of new advanced cases, in particular, for cervical cancer.

Keywords: cancer, cervix, incidence, mortality, screening, malignant neoplasms of cervix.

Introduction. Cervical cancer (CC) is a pressing problem of modern oncology all over the world. The cervical cancer is a frequent malignant tumour in the structure of oncogynecological pathology of Kazakhstan, and according to the incidence rate, occupies the 3rd place in the female cancer structure. Notwithstanding of existing reliable and non-complex screening test – the cytology of smears from cervix uteri and cervical canal – the advanced malignancy of cervical cancer remains high in Kazakhstan, and in West-Kazakhstan oblast (WK) composed 12.9% at the end of 2015.

The CC cytological screening was integrated into the system of annual mass routine inspection of Kazakhstan in 2008. The Order No.607 of October 15, 2007 “On improvement of routine inspection of certain adult population groups” aimed at examination of target groups including women aged 35, 40, 45, 50, 55 and 60 years old. The Order No.145 of 16 March, 2011 “On amendments to the Order No.685 of acting minister of health RK as of November 10, 2009 “On approval of rules of routine medical inspections of target population groups” also included women of 30 years old into the target group for examination.

The screening for CC in Kazakhstan covered 392.507 women in 2015. As a result of performed screening 211 cases of cervical cancer have been detected - 0.05% (euro standard = 0.01- 0.02%).

In 2015 the incidence rate of cervical cancer in WK exceeded the average national level by 6.7%, and ranked 3rd in the incidence structure of female population and 6th in the cancer structure of entire population RK.

Since 2015 in the WK regional cancer centre 460 women with CC diagnosis were on a dispensary medical check-up. The analysis of main indicators over the last 5 years (2011-2015) reflecting the dynamics of incidence of cervical cancer among women of West-Kazakhstan region, Uralsk city has been carried out.

The analysis showed the decline of CC incidence from 12.0 to 11.1 per 100 thousand population in the studied period (Figure 1).

CC as a visually accessible organ pathology is characterized by such an important indicator as advanced development which means the detection of disease at stages III-IV.

As a result of the study, the timely detection of CC at stages I-III has improved up to 77.3-81.4% of patients in the last 3 years. Adequately organized detection of CC on a systemic basis provides a potential for significant reduction of CC incidence in 10-15 years (Figure 3).
Late diagnostics of CC defines further prognosis for the disease course, making challenging the woman recovery and reproductive function retention, and sometimes it becomes an impossible task. Besides, it leads to decrease of the therapy efficiency several times in comparison with CC detection at early stages.

The screening aimed at detection of the pre-cancer pathologies and early (non-invasive) forms of CC.

Figure 2 shows the dynamics of advanced development of CC staring from 2011.

The diagram shows the proportion of patients with cervical cancer detected at III-IV stage of the disease. Thus, in 2007 the advanced development was recorded in 17.9%, in other words, 0.02% of screened women had advanced cancer. Following the introduction of mass cytological screening and well-organized work of PHC examination cabinets, an overall positive dynamics was recorded in 2015: the advanced forms of cervical cancer has declined from 21.9% (2011) to 12.9% (2015).

In the system of oncogynecological service, the interaction and feedback from each level of care play an extremely important role. Within the framework of current Order of the Ministry of health RK No.540 as of 12.08.2011, the supervision and organization function belongs to the city and district oncologists. The doctors-oncologists control the performance of patient examination rooms and interaction between staff of patient examination room and female clinic, supervise the quality of medical screening of women with background and pre-malignant pathology, also analyse the cytological examination of women, including the screening activities aimed at early detection of cancer diseases.

The examination rooms are the first level of care and an important element of the oncogynecological service at local level. In 2016, within the framework of implementation of the Roadmap for Integrated Management Model of Oncological Diseases for 2016-2019, the monitoring of availability of sufficient equipment, tools and qualified personnel has been conducted throughout the whole year. All midwives of the patient examination rooms underwent a specialized training on the basis of regional dispensary. Besides, the midwifery staff is regularly trained in the workshops conducted by oncologists of oblast cancer dispensaries twice a year on issues of diagnostics of cancer with visual localization. Currently, 95 patient examination rooms operate on the basis of all city and district polyclinics of the region, of them only in 6 districts the patient examination rooms provide the service for less than full-time shift.

The obtained results are presented in Tables 1 and 2.

### Table 1 – Routine inspection, 2014-2016

<table>
<thead>
<tr>
<th>Year</th>
<th>Women examined, total</th>
<th>Cancer detected</th>
<th>Pre-cancer detected</th>
<th>Samples of improper quality</th>
<th>Non-informative samples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Abs.</td>
<td>%</td>
<td>Abs.</td>
<td>%</td>
</tr>
<tr>
<td>2014</td>
<td>22752</td>
<td>7</td>
<td>0,03</td>
<td>131</td>
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<tr>
<td>2015</td>
<td>45405</td>
<td>30</td>
<td>0,06</td>
<td>479</td>
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<tr>
<td>2016</td>
<td>51095</td>
<td>24</td>
<td>0,04</td>
<td>358</td>
<td>0,7</td>
</tr>
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</table>

### Table 2 – Screening for cervical cancer (CC), 2014-2016

<table>
<thead>
<tr>
<th>Year</th>
<th>Women examined, total</th>
<th>Cancer detected</th>
<th>Pre-cancer detected</th>
<th>Samples of improper quality</th>
<th>Non-informative samples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Abs.</td>
<td>%</td>
<td>Abs.</td>
<td>%</td>
</tr>
<tr>
<td>2014</td>
<td>19755</td>
<td>13</td>
<td>0,07</td>
<td>347</td>
<td>1,7</td>
</tr>
<tr>
<td>2015</td>
<td>15487</td>
<td>13</td>
<td>0,08</td>
<td>528</td>
<td>3,4</td>
</tr>
<tr>
<td>2016</td>
<td>15468</td>
<td>17</td>
<td>0,1</td>
<td>347</td>
<td>2,2</td>
</tr>
</tbody>
</table>
As a result, the allotment of material referred to cytological examination after gynaecological check-up of women in the examination rooms has been increased – from 42,507 in 2014 to 66,563 in 2016.

The results of screening for CC in 2014-2016 have shown a growth in number of detected cancer cases, a decrease in the share of non-informative samples and samples of improper quality. All the findings were uploaded into an automated information system (AIS).

According to the results of routine inspection, the coverage rate has increased 2-fold, the cancer detection has grown 3-fold; however, there is a growth of non-informative samples and samples of improper quality by more than 12%.

**Findings and conclusions.** The current situation analysis shows that the findings of cytological material within the screening mode are more informative and comprehensive than it is found within the routine inspection. In this regard, the detection rate of cancer and pre-cancer pathology by screening is significantly higher than within the routine inspection. Thus, in 2016 the detection rate of cervical cancer during the screening versus the routine inspection was 0.04% and 0.1%, and pre-cancer pathology - 2.2% and 0.7%, respectively.

The low performance of routine inspection is due to both the use of different staining methods (in screening – Pap test, during routine inspection – Romanovsky test), and lack of adequate control of the results obtained. In comparison, the efficiency of screening activities is not in doubt; at the same time it is necessary to focus special attention to the effectiveness of routine inspection due to its high annual coverage of over 50,000 women. Especially this pressing problem is manifested during the retrospective analysis of neglected cervical cancer cases in women outside of the screening age, who had a long-term background disease in the anamnesis, and moreover, the annual routine inspection with a cytological smear-sampling was either absent or was not informative.

Over the last three years, the number of women covered by routine inspection has increased from 22,752 to 51,095. At the same time, the dynamics of detection of the cervix uteri malignant pathologies has not changed and its high annual coverage of over 50,000 women. Especially this pressing problem is manifested during the retrospective analysis of neglected cervical cancer cases in women outside of the screening age, who had a long-term background disease in the anamnesis, and moreover, the annual routine inspection with a cytological smear-sampling was either absent or was not informative.

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Over the last three years, the number of women covered by routine inspection has increased from 22,752 to 51,095. At the same time, the dynamics of detection of the cervix uteri malignant pathologies has not changed and the problem of neglected cases is still relevant. This situation indicates the need for revision of approaches to monitoring of the routine inspection mode.

One of the reasons of low effectiveness of the routine inspection is lack of control over the smears quality, lack of timely delivery of information of women about the findings of examination, no single register for previously obtained examinations and treatment interventions [2]. In order to exclude the above-mentioned shortcomings and provision of uninterrupted registration of all examinations including all data from diagnostics to recovery, it is necessary to develop and introduce the single information system for annual routine inspection, since, unfortunately as of today, there is no analogue of that system within previously mentioned parameters.

The introduction of updated system will increase the efficiency of laboratories owing to the timely provision of the tests conclusion, opportunity for search based on request, and dynamic comparative analysis of the earlier obtained findings. Through this process the doctors will receive a convenient and reliable tool for data storage and analysis with relevant possibility for comprehensive analysis of information and collating of required reporting documents [3].

The whole set of tools will serve as an indispensable instrument for monitoring of the coverage, control of the smear-sampling quality and timely delivery of all results of examination directly to women (by SMS notification).

Thus, oncogynecological service should be a well-established system that includes not only detection of cancer pathologies, but should be also responsible for implementation of relevant complex of automated procedures for the timely data transfer, registration of performed examinations and provision of recovery interventions [4].

**References**


Main difficulties of counseling cancer patients at the stage of acceptance of diagnosis

The diagnosis of cancer is the strongest stress for the patient and his family, because in the mind of any person, the term “cancer” is synonymous with doom, death. With this patient there are a number of problems related to social adaptation has a strong influence on the quality of life and a good attitude to treatment. Often, the awareness of the unfavorable outlook leads a person to severe depression, thereby complicating the reaction on the disease and its treatment. The purpose of this article is a review of the main difficulties faced by the psychologist working with cancer patients, recently learned about his diagnosis and the main method of psychological assistance at the stage of making diagnosis performs psychological counseling. On the basis of theoretical analysis of clinical cases on the subject stands out a conclusion on the importance of psychological work with cancer patients at the stage of making diagnosis.

Keywords: diagnosis, depression, rehabilitation, psychocorrection, psychotherapy.

“There are three of us: the patient, the doctor and the disease. The side the patient chose will get a win” Hippocrates

Various diseases currently subject the patient’s psyche to easy or severe changes only due to their clinical manifestations. These changes are clearly manifested in patients with malignant tumours. The diagnoses of “malignant tumour” leads to a very severe psycho-emotional crisis resulting in the following negative mental states: panic, depression, hypochondria, apathy, and etc. These conditions significantly complicate the course of the disease. According to the observations of the American psychologist Elizabeth Kubler-Ross, in the context of the diagnosed malignant tumour the patients’ reaction is passing through the following stages:

1. Denial. The patient does not believe in what happened to him/her.

2. Anger. Dissatisfaction with the physician’s work; hatred of healthy people.

3. Bargaining. An attempt to conclude a contract with fate. The patient’s belief that if a coin falls on the tail side, he/she will recover.

4. Depression. Loss of will to live, panic and resentment.

5. Adoption. “I have got through meaningful and interesting life. Now I can die” [1].

According to the Prof. A.V. Gnezdilov, “Changes in patients’ and their relatives’ psyche go through several periods:

1. The period of crisis, negative information on the disease and its predictions are like a thunderbolt from a clear sky for the patient.

2. The period of denial; the rejection of information.

3. The period of aggression.

4. The period of depression.

5. The period of adoption – acceptance of one’s fate” [2].

If we briefly review some of the findings of many specialists that were evidenced in practice, not only the successful treatment outcome but also psychological and social rehabilitation, return to a full life in the family and the society, as well as the patient’s attitude towards the disease aimed at combating are manifested as the patient’s proactive approach to life.

Many factors in the acceptance of an oncolgy diagnosis depend on further psychological adaptation of the patient. In our context, the concept of “acceptance of diagnosis” is not the person’s acceptance of this truth with the possibility of living a certain time or a long life, but his/her readiness towards the disease aimed at combating are manifested as the patient’s proactive approach to life.

The most important factor in the acceptance of diagnosis is a state of uncertainty. This condition is closely related to the period of diagnosis, as well as with the initial therapy course. At the same time, this basic factor leads to the excitation of such conditions as fear, anxiety and panic. The primary task of correction in this direction, i.e. counselling, is aimed at helping the patient to deeply understand the situation and adapt to the further perspective of laying the groundwork of understanding.

In the basic approach to counselling, the factor of a state of uncertainty leads to a full disclosure of what is happening in the most important period. The stage-by-stage action plan, covering the social life and day-to-day routine and other aspects, shall correlate to the patient’s disease. Another method of counselling is the work towards understanding of fears related to this period of uncertainty. Such methods depends on the choice of a consulting psychologist and includes various forms of psychodiagnostics, art therapy, elements of psychodrama, psycho-corrective techniques aimed at establishing a close contact with the patient’s emotional state.
It should be specially noted that during such psychological work the consulting psychologist may face an explicit manifestation of alexithymia. However, many experts dealing with onco patients consider this symptom as a main form of psychological defence. Such a state of the patient emotionally complicates the consulting work but is an important warning sign. At that, the inability to work with one’s own emotions can act as an important mechanism and can become the only effective tool.

During the period of diagnosis, the relationship between the patient and his/her relatives is often difficult. People surrounding the patient do not understand how to behave in this situation and are not ready for the obstacles in mutual communication. It affects the psychological state of the patient who needs understanding and love from relatives but cannot accept help. This circumstance causes normal communicative deprivation in the patient and complicates the further rehabilitation process. It is in this period that a psychologist can become a mediator between the patient and his/her loved ones. On the other hand, good terms between the patient and his/her consultant can become an interpretation of a family communication. Thus, the psychologist standing on the position of an expert gives the patient complete information on certain circumstances; an impossibility to obtain a clear idea can harm the patient. At the same time, the consultant provides the loved ones with information about the patient’s psychological state.

At the time of accepting the diagnosis, psychological work with patients involves a number of fundamental problems. Overcoming them will help the patient to adapt to the diagnosis and will facilitate the treatment process.

Such a personality-psychic manifestation as a state of uncertainty, a fear of uncertainty or a fatal probability is characteristic not only for the period of accepting the diagnosis but it is very important to study such manifestations in this period to support the future psycho-correcting or psychotherapeutic practice that can become another powerful resources in the patient’s rehabilitation.

References
Treatment outcomes in patients with recurrent thoracic esophageal cancer after surgery

The article focuses on treatment outcomes of patients with recurrent cancer in the esophageal-gastric anastomosis after surgery. The results of radiotherapy and combination therapy of these patients with modern chemotherapeutic agents are presented.

Keywords: recurrent esophageal cancer, radiotherapy, combination therapy, chemotherapy.

Relevance. Despite the emphatic successes gained in diagnostics and treatment of patients with esophageal cancer, the main cohort of patients (up to 80%) admitted to specialized esophageal clinics – is represented by the individuals with a widespread tumor process of III-IV stages of the disease [1-3].

The low tumour sensitivity to modern chemotherapeutic agents, the palliative and short-term effect of radiotherapy make the surgical intervention - the method of choice - in treatment of patients with that type of disease. The radical resection of esophagus with extensive removal of lymph nodes contributes to the long-term survival of patients even at the advanced stage of esophageal cancer [4].

The issue of selection of optimal tactics in treatment of recurrent esophageal cancer with marked stenosis of the esophagus lumen remains to be debatable. Many authors report about encouraging outcomes obtained after implementation of methods outside the traditional radiation treatment, such as, concomitant radiotherapy, combined radiotherapy with hyperthermia, chemotherapy, laser destruction of tumours [5-7].

The relevance of the study is justified by the following: the diversity of approaches in treatment and significant risk of surgery in patients with esophageal cancer; advanced age of patients with concomitant diseases; high recurrence rate; low sensitivity of esophagus tumour to modern chemotherapeutic agents and radiotherapy.

Aim of the study: Improve the outcomes and treatment tactics of patients with esophageal cancer as a result of implementation of modern methods of combined treatment.

Materials and methods: The study included 63 patients with cancer recurrence in the area of esophageal-gastric anastomosis. The cohort of patients was divided into 2 groups. Group 1 included 32 patients with cancer recurrence in the area of esophageal-gastric anastomosis; these patients were treated by the radiation therapy on the background of introduction of chemotherapeutic agents. The chemotherapeutics of various options was carried out simultaneously in each stage of the split course of radiotherapy. The total boost dose (TBD) ranged from 50 to 70 Gy.

Group 2was a control group of 31 patients with cancer recurrence in the area of esophageal-gastric anastomosis; these patients received only radiation therapy: tele-gamma-therapy in the single boost dose (SBD) mode of 2 Gy. During two stages of tele-irradiation the total boost dose (TBD) was 50-55 Gy. The second stage of radiation treatment started after 2-3 weeks of the first stage completion. The esophageal stenting in the area of tumour-induced stenosis has been performed in patients with the first degree dysphagia.

The cohort of patients included to the study was maximum homogeneous across the main predictive features, permitting to conduct a correct comparative analysis of specified above options of conservative therapy of recurrent esophagus cancer.

A comprehensive assessment of efficiency of chemoradiation treatment included the use of X-Ray, endoscopic, morphological and other methods of examination. The patients with disseminated tumour process and multiple distant metastases were not included to the study.

Findings and discussion

The analysis of findings of application of tele-radiation therapy in esophageal cancer at a single mode, and in combination with various options of drug treatment, revealed a higher efficiency of radiotherapy in combination with chemotherapy.

The immediate complete clinical effect after the chemo-radiotherapy was achieved in 13 of 32 patients (41%).

The three-year survival after the chemo-radiotherapy was observed in 12 patients (40%), after the radiotherapy - in 4 of 31 patients (12%).

Of studied poly-chemotherapy options, the combination of 5-FU with Capcetabine and cisplatin found to be more advantageous. The immediate complete clinical effect was observed in 49% (16 of 32 patients), the three-year survival was 29% (10 patients). With respect to use of doxorubicin with Oxaliplatin, the immediate complete clinical effect was gained in 41% (13 of 32 patients); the three-year survival was 27% (8 patients).

Conclusion. The rational use of potential of antitumour compounds aimed at enhancement of the radiation effect permits to achieve the relevant improvement of immediate and long-term outcomes of treatment of recurrent esophagus cancer.

References
Demographic and clinical-morphological features of patients with metastatic breast cancer with over-expression of Her-2/neu receptors based on the results of the PH + oeBE study

The demographic and clinical-morphological parameters in patients with metastatic Her-positive breast cancer (BC) were presented based on the retrospective, descriptive, cohort study PH + oeBE. The study included relevant data from medical records of patients with diagnosed and morphologically confirmed HER2-positive metastatic breast cancer.

Keywords: breast cancer (BC), metastases, HER2-positive cancer, demographic parameters, immunohistochemistry, morphology.

Relevance. Breast cancer (BC) is a heterogeneous disease, the prognosis and the course of which depends on the molecular-genetic and clinical patterns of tumour in each individual case. It is known that the over-expression of human epidermal growth factor receptor (HER2) is associated with low survival, high risk of metastasis and low susceptibility to cytostatics [1]. The potential of targeted therapy in oncology, in particular, the trastuzumab monoclonal antibody affecting the HER2 extracellular domain has been demonstrated in studies with trastuzumab in adjuvant mode. These studies showed a nearly two-fold reduction of recurrence risk, which reverse the prognostic value of the HER2 receptors over-expression [2-4].

In Kazakhstan the introduction of targeted therapy with trastuzumab was launched in 2001. Lapatinib is used only since 2011. However, lack of complete data about the treatment regimens for metastatic HER2 + breast cancer in CIS countries, including Kazakhstan, led to initiation of the retrospective observational study of treatment methods used in recent years in clinical practice in patients with HER2-positive locally spread or metastatic breast cancer.

The article presents the analysis of clinical and morphological parameters of metastatic BC with over-expression of Her-2/neu based on the retrospective, descriptive, cohort study PH + oeBE. The study included relevant data from medical records of patients with diagnosed and morphologically confirmed HER2-positive metastatic breast cancer.

Study design. The study PH + oeBE - is the retrospective, descriptive, cohort study of the phase IV. It was performed in 3 CIS countries: Russian Federation, Ukraine and Republic of Kazakhstan. Data on patients with primary-disseminated and metastatic HER2-positive BC were obtained from patient medical records. The study included patients with breast cancer diagnosis established within the timeframe of January 1, 2010 to November 30, 2011. The follow-up period was from January 02, 2010 to November 30, 2013. Thus, the required data for patients were gathered for follow-up period of at least 24 months with one of the following outcomes: patient death, patient loss for follow-up, follow-up care, or completion of follow-up.

Materials and methods. The study included relevant data on women aged from 18 years old and upward with known date of diagnosis of metastatic or progressive breast cancer with morphologically confirmed HER2-positive type. The routine procedure for HER2-testing without re-sampling of tissues was an important pre-requisite for inclusion. The detection of synchronous cancer of other localization was the criteria for withdrawal.

The cohort size of 241 patients was determined on the basis of availability of suitable patients. The statistical methods for reflection of the study outcomes included the variables generalized for all patients within the study and descriptive statistics. The formal statistical comparison of the study outcomes between the treatment groups was not conducted. Missing or incorrect data were not included to the statistical analysis.

Findings. The demographic and clinical-morphological parameters of patients with metastatic Her-positive breast cancer presented in the Table 1.

The median age of patients with primary breast cancer diagnostics was 52.3±11.5 years, and with metastases 53.8±11.2 years. Over 1/3 of patients, 35.7% (86), belonged to a premenopausal age, about half of them - 46.9% (113) had a postmenopausal status, and in 17.4% (42) of cases the menopause status was unknown.

The distribution of patients by disease stages (TNM) of the primary breast cancer diagnosis was as follows: more
than half of patients, 56.0% (135), had a tumour size of 2-5 cm during the primary diagnostics, which corresponded to the stage T2. The tumours less than 2 cm, T0-T1, were observed only in 12.0% of patients. In 11.2% of (27) cases, the tumour was classified as the cancer of stage T3. The tumour with lesion of chest wall or skin has been detected in 1/5 of patients during the primary diagnostics, classified as T4 stage of disease.

The regional lymph node involvement was observed in 192 (83.4%) cases, 9 (3.7%) patients did not have confirmed data (Nx). The remote metastases were detected in 24 (10.0%) patients, in 2 (0.8%) cases no evidence of presence or absence of remote metastases was found within the primary diagnostics (Mx).

Thus, the distribution of patients by clinical stages of disease was the following: stage I was diagnosed in 5.0% (12) patients, stage II - in 47.3% (114), stage III - in 37.8% (91), and stage IV – in 10% (24) of patients.

Assessment of BC morphological subtypes showed that an invasive carcinoma was diagnosed in a majority of patients: flow type - 50.2% (121), lobular - 3.7% (9), mixed - 1.2% (3). The ductal carcinoma was detected in situ in 20.3% (49) of cases. In assessing the degree of tumour differentiation (G), it was found that the routine study of that indicator is not mandatory for all centres, therefore, in large proportion of patients - 105 (43.6%), the data on the tumour malignancy degree were not obtained. In remaining cases, the average (G2) and low (G3) degree of tumour differentiation was recorded with approximately same frequency - 25.7% (62) and 27.0% (65) of patients, respectively. In 1 (0.4%) case the morphological assessment corresponded to the anaplastic carcinoma (G4).

Table 1 - Demographic and clinical-morphological parameters in patients with metastatic Her-positive breast cancer within the primary diagnostics of the disease

<table>
<thead>
<tr>
<th>Profile of patients</th>
<th>241</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at primary diagnostics of BC (CO)</td>
<td>52.3 (11.5)</td>
</tr>
<tr>
<td>Median age (min-max)</td>
<td>52.4 (23.0-88.0)</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>(43.9-60.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Menopausal status (n)</th>
<th>241</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perimenopause</td>
<td>86 (35.7%)</td>
</tr>
<tr>
<td>Postmenopause</td>
<td>113 (46.9%)</td>
</tr>
<tr>
<td>Unknown status</td>
<td>42 (17.4%)</td>
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</table>

<table>
<thead>
<tr>
<th>Distribution by disease stages</th>
<th>241</th>
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</thead>
<tbody>
<tr>
<td>Primary tumour T (n)</td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>0</td>
</tr>
<tr>
<td>T1</td>
<td>28 (11.6%)</td>
</tr>
<tr>
<td>T2</td>
<td>135 (56.0%)</td>
</tr>
<tr>
<td>T3</td>
<td>27 (11.2%)</td>
</tr>
<tr>
<td>T4</td>
<td>50 (20.7%)</td>
</tr>
<tr>
<td>TX</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regional lymph nodes N (n)</th>
<th>241</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>40 (16.6%)</td>
</tr>
<tr>
<td>N1</td>
<td>118 (49.0%)</td>
</tr>
<tr>
<td>N2</td>
<td>61 (25.3%)</td>
</tr>
<tr>
<td>N3</td>
<td>13 (5.4%)</td>
</tr>
<tr>
<td>NX</td>
<td>9 (3.7%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Remote metastases M (n)</th>
<th>241</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>215 (89.2%)</td>
</tr>
<tr>
<td>M1</td>
<td>24 (10.0%)</td>
</tr>
<tr>
<td>MX</td>
<td>2 (0.8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical stage (n)</th>
<th>241</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>12 (5.0%)</td>
</tr>
<tr>
<td>II</td>
<td>114 (47.3%)</td>
</tr>
<tr>
<td>III</td>
<td>91 (37.8%)</td>
</tr>
<tr>
<td>IV</td>
<td>24 (10.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Histological type of tumour</th>
<th>241</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow carcinoma in situ</td>
<td>49 (20.3%)</td>
</tr>
<tr>
<td>Lobular carcinoma in situ</td>
<td>3 (1.2%)</td>
</tr>
<tr>
<td>Invasive lobular carcinoma</td>
<td>9 (3.7%)</td>
</tr>
<tr>
<td>Invasive breast carcinoma</td>
<td>3 (1.2%)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (15.4%)</td>
</tr>
<tr>
<td>No data</td>
<td>20 (8.3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Degree of the tumour differentiation</th>
<th>241</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1: high degree of differentiation (low degree of malignancy)</td>
<td>8 (3.3%)</td>
</tr>
<tr>
<td>G2: average degree of differentiation (intermediate degree of malignancy)</td>
<td>62 (25.7%)</td>
</tr>
<tr>
<td>G3: low degree of differentiation (high degree of malignancy)</td>
<td>65 (27.0%)</td>
</tr>
<tr>
<td>G4: undifferentiated tumour (high degree of malignancy)</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>GX: degree of differentiation is not possible to determine (unknown malignancy)</td>
<td>0</td>
</tr>
<tr>
<td>No data</td>
<td>105 (43.6%)</td>
</tr>
</tbody>
</table>
Table 2 presents the clinical parameters of patients with Her-positive metastatic breast cancer. The diagnostics of metastatic process revealed that the general status of patients in most cases (56.5%) was satisfactory and corresponded to 0-1 score of the ECOG scale. The medium severity condition (2 scores on the ECOG scale) was established in 29 patients (12.0%), and grave condition - only in 7 patients (2.9%), including 1 case (0.4%) classified as extremely critical condition.

Analysis of the metastases rate of various organs and systems showed that the extra-ostial metastases were detected in 237 cases (98.3%), at this the rate of visceral metastases with liver damage and/or lung was observed in 92 patients (38.8%).

Table 2 - Clinical parameters of patients with Her-positive metastatic breast cancer

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Total number of patients (n=241)</th>
<th>Patients with primary-metastatic BC, IV stage (n=24)</th>
<th>Patients with BC progression, I-III stages (n=217)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at remote metastases diagnostics</td>
<td>N=241</td>
<td>N=24</td>
<td>N=217</td>
</tr>
<tr>
<td>Mean age at primary diagnostics of BC (CO)</td>
<td>53.8 (11.2)</td>
<td>56.3 (13.5)</td>
<td>53.5 (10.9)</td>
</tr>
<tr>
<td>Median age (min-max)</td>
<td>53.7 (25.0-88.0)</td>
<td>56.2 (36.0-88.0)</td>
<td>53.6 (25.0-78.0)</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>(45.9-60.9)</td>
<td>(45.5-63.4)</td>
<td>(45.9-60.9)</td>
</tr>
<tr>
<td>Status according to ECOG in diagnostics of remote metastases</td>
<td>N=241</td>
<td>N=24</td>
<td>N=217</td>
</tr>
<tr>
<td>0</td>
<td>24 (10.0%)</td>
<td>2 (8.3%)</td>
<td>22 (10.1%)</td>
</tr>
<tr>
<td>1</td>
<td>112 (46.5%)</td>
<td>6 (25.0%)</td>
<td>106 (48.8%)</td>
</tr>
<tr>
<td>2</td>
<td>29 (12.0%)</td>
<td>3 (12.5%)</td>
<td>26 (12.0%)</td>
</tr>
<tr>
<td>3</td>
<td>6 (2.5%)</td>
<td>0</td>
<td>6 (2.8%)</td>
</tr>
<tr>
<td>4</td>
<td>1 (0.4%)</td>
<td>0</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>No data</td>
<td>69 (28.6%)</td>
<td>13 (54.2%)</td>
<td>56 (25.8%)</td>
</tr>
<tr>
<td>Localization of metastases</td>
<td>N=241</td>
<td>N=24</td>
<td>N=217</td>
</tr>
<tr>
<td>Liver</td>
<td>49 (20.3%)</td>
<td>11 (45.8%)</td>
<td>38 (17.5%)</td>
</tr>
<tr>
<td>Lung</td>
<td>63 (26.1%)</td>
<td>7 (29.2%)</td>
<td>56 (25.8%)</td>
</tr>
<tr>
<td>Bones</td>
<td>88 (36.5%)</td>
<td>15 (62.5%)</td>
<td>73 (33.6%)</td>
</tr>
<tr>
<td>CNS/cerebrum</td>
<td>30 (12.4%)</td>
<td>1 (4.2%)</td>
<td>29 (13.4%)</td>
</tr>
<tr>
<td>Soft tissues</td>
<td>51 (21.2%)</td>
<td>3 (12.5%)</td>
<td>48 (22.1%)</td>
</tr>
<tr>
<td>Other</td>
<td>132 (54.8%)</td>
<td>12 (50.0%)</td>
<td>120 (55.3%)</td>
</tr>
</tbody>
</table>

Note: patients could have one or more foci of metastasis

The bone metastases among patients within the study were detected in 36.5% of cases. Subsequently, the metastatic foci were distributed by the rate of secondary affection of various organs and tissues the following way: in lungs - 26.1%, in soft tissues - 21.2%, in liver - 20.3% of patients.

The demographic parameters and distribution of metastatic foci in patients with primary metastatic process had some peculiarities. The mean age in metastatic breast cancer diagnostics was 56.3 ± 13.5 years, while the age ranged from 36 to 88 years old. In more than half of studied cases the data on status of patients with primary metastatic process were not provided. In remaining 11 cases (45.8%), the general status was assessed as “satisfactory” or “near satisfactory”. In this category of patients, the visceral metastases with liver and/or lung affection were detected more frequently (62.5%), the bone metastases were found with the same frequency. During initial diagnostics the cerebrum metastasis was detected only in 1 patient (4.2%).

In detection of remote metastases the mean age of patients with stages I-III of disease composed 53.5 ± 10.9 years. Within the course of metastatic disease development, the assessment of general status of patients according to ECOG scale was absent in the medical records in 56 cases (25.8%). The analysis of data of remaining 161 patients evidenced that the disease progression with development of remote metastatic foci had affected the general status of patients toward aggravation only in 7 patients (3.3%). The majority of patients, 154 (70.8%), had a satisfactory status.

The metastatic process was diagnosed within detection of deposits in liver – 17.5% (38) of patients, in lungs – 25.8% (56), in bones – 33.6% (73), in cerebrum – 13.4% (29), in soft tissues – 22.1% (48), accordingly. In 55.3% of patients (120) the metastases were detected in other tissues and organs.

Based on the immunohistochemical tests (IHC) findings, the positive oestrogen receptor (ER+) status was detected in 46.5% of patients (112), and progesterone receptor (PR) status was revealed in 38.2% of patients (92). The study of proliferative activity status by data of research centres was not obligatory. The index Ki6 was determined only in 60 patients (24.9%); in 75.1% of patients the status of index Ki6 was unknown. In 33 cases (55%) the index Ki67 has been rated as high (>15%) (Table 3).

As is evident from Table 3, luminal B-type tumours were found in almost half of the cases of metastatic breast cancer with Her-2/neu hyperexpression (49.8%). The frequency of Her-positive non-luminal breast cancer was 39.0%.
Table 3 - Results of immunohistochemical studies in patients with metastatic HER2-positive breast cancer

<table>
<thead>
<tr>
<th>Results of immunohistochemical studies</th>
<th>N=241</th>
</tr>
</thead>
<tbody>
<tr>
<td>The oestrogen receptors (ER) status</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>112 (46.5%)</td>
</tr>
<tr>
<td>Negative</td>
<td>102 (42.3%)</td>
</tr>
<tr>
<td>No data</td>
<td>27 (11.2%)</td>
</tr>
<tr>
<td>The progesterone receptor (PR) status</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>92 (38.2%)</td>
</tr>
<tr>
<td>Negative</td>
<td>122 (50.6%)</td>
</tr>
<tr>
<td>No data</td>
<td>27 (11.2%)</td>
</tr>
<tr>
<td>Hormonal receptor status</td>
<td></td>
</tr>
<tr>
<td>ER+/PR+</td>
<td>84 (34.9%)</td>
</tr>
<tr>
<td>ER+/PR-</td>
<td>28 (11.6%)</td>
</tr>
<tr>
<td>ER-/PR+</td>
<td>8 (3.3%)</td>
</tr>
<tr>
<td>ER-/PR-</td>
<td>94 (39.0%)</td>
</tr>
<tr>
<td>No data</td>
<td>27 (11.2%)</td>
</tr>
</tbody>
</table>

| Proliferative activity, index Ki67   |       |
| ≤15% (low)                           | 17 (7.1%) |
| 16 - 30% (medium)                    | 10 (4.1%) |
| >30% (high)                          | 33 (13.7%) |
| No data                              | 181 (75.1%) |

Discussion. The article presents the data on demographic, clinical, morphological and molecular-biological parameters of metastatic breast cancer with confirmed high expression of Her-2 receptor. These data were obtained within the retrospective population study aimed at understanding of overall picture in diagnostics and treatment of patients based on examples of 7 cancer centres of the Russian Federation, Ukraine and the Republic of Kazakhstan. Eventually, the study had some limitations due to its retrospective nature and inability to request some missing data from research staff, especially when it was related to the primary staging and assessment of general status of patients. The morphological and IHC examinations in full range according to modern diagnostic protocols were available not in all cancer centres.

However, the findings obtained within the study permit to make the following conclusions:

The patients with metastatic breast cancer in the majority of cases (56.5%) remain the active satisfactory status, which corresponds to 0-1 score on ECOG scale. The share of patients with grave and extremely critical condition composes only 2.9%.

In patients with confirmed hyper-expression of Her-2/neu receptors, the bone metastases were detected in 1/3 of cases - 36.5%, the visceral metastases with liver and lung affection were revealed with approximately same frequency - 20.3% and 26.1%, respectively.

The luminal B type tumour among patients with metastatic Her-positive breast cancer is more common than the Her-positive non-luminal type of cancer (49.8% vs. 39.0%).

References
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«PROGRESS AND CONTROVERSIES IN GYNECOLOGICAL ONCOLOGY & BREAST CANCER»
under the auspices of CGH/IGCS/EURAMA

Almaty,
October 4-6,
2017
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THE RESULTS OF NEOADJUVANT INTRAARTERIAL CHEMOTHERAPY COMBINED WITH MILD HYPERTERMIA IN LOCALLY ADVANCED BREAST CANCER PATIENTS

Immediate results of the treatment of 121 female patients with locally advanced breast cancer (LABC) stages IIb – IIIa are estimated in this research. The main group included 62 LABC patients that have been given 4 courses of the system-selective neoadjuvant chemotherapy (SSNACT) by the CAP scheme with intraarterial injection of carboplatin 300 mg/m² and cyclophosphamide 600 mg/m² and systemic injection of doxorubicin 50 mg/m². Patients underwent mild hyperthermia (MH) on the affected area 30 min after the infusion of chemotherapeutic agents. The procedure lasted 30 min with output power of 50 W. The control group included 59 LABC patients that have been given SSNACT by the same scheme but without MH.

The mammography by means of the efficacy evaluation of treatment according to RECIST was conducted 3 weeks after the last year of SSNACT course. In patients of the main group, complete tumour response was found in 9 (14,52±4,47)% and 5 (8,47±3,63)% - control (p>0.05) groups. The partial tumour response was diagnosed in 30 (48,39±6,35)% patients of the main and 21 (35,59±2,86)% - control (p>0.05) groups. Stabilization process was detected in 19 (30,65±5,85)% patients of the main group and in 24 (40,68±6,40)% of the control group (p>0.05). The tumour progression was found in 4 (6,45±3,12)% of the main and 9 (15,25±4,68)% of the control group (p>0.05).

Surgery was carried out after analyzing the response to neoadjuvant treatment. Breast conserving surgeries were provided in 33 patients (53,23±6,34)% of the main group, of the control group – 24 patients (40,68±6,40)% (p<0.05). The TRAM/LD-flap reconstruction was done in 5 (8,06±3,46)% patients of the main group and in 3 (5,08±2,86)% of the control patients (p>0,05). Skin sparing mastectomy with immediate endoprosthesis was provided in 5 (8,06±3,46)% patients of the main group and in 4 (6,78±3,27)% patients of the control group (p>0,05).

It was determined that the use of MH with SSNACT in the treatment of LABC patients affected by allows to increase the amount of the complete tumour response cases by 6.04% and partial tumour response cases by 12.79%. The supplement of SSNACT with MH sessions allows increasing the use of breast conserving surgery by 12.55% and the use of reconstructive surgery - by 4.26%.

EVALUATION OF CHEMOTHERAPY EFFICIENCY IN PATIENTS WITH PRIMARY INOPERABLE BREAST CANCER

Objective. According to Ukrainian Cancer Registry data the incidence of breast cancer was 67,3 and the mortality rate - 30,2 cases per 100,000 female population in 2015. Despite progress in the early diagnosis nearly 20 % of the new patients with primary breast cancer have locally advanced disease that is often primarily inoperable.

Preoperative therapy increases the frequency of the radical surgery. However, locally advanced breast cancer is often resistant to standard treatment and requires special approaches to therapy.

Despite the increasing usage of preoperative chemotherapy full morphological response, disease-free and overall survival indicators remain poor for patients with locally advanced disease. The combined use of chemotherapy and radiation therapy amplifies cytotoxic effect by summation general and local antitumour effects, especially in resistant forms. Modifiers are used to amplify radiation tumour destruction and lead to overcoming the resistance of malignant cells. One of these modifiers is tegafur, it damages the mechanisms of DNA repair and cell cycle synchronization, increasing radiodestruction of tumour cells.

Purpose – to improve the efficiency of complex treatment in patients with primary inoperable locally
advanced breast cancer overcoming resistance and increasing of the tumor control.

Patients and methods. The study included 107 patients with primary inoperable breast cancer with II-IA-IIIC stage of disease who had no positive effect after neoadjuvant chemotherapy based on anthracyclines (AC, FAC, AT). 52 patients in the control group had a course of traditional external beam radiotherapy (RT), in 55 patients of the study group RT was supplemented by using modifiers (fluoropyrimidines). Tegafur was administrated oral 800 mg in the morning and 400 mg in the evening throughout the RT course, all patients were given the necessary maintenance therapy.

Results. The effect of the cytostatic therapy was better in patients who received RT with tegafur, 36 patients (65,45%) had complete and partial tumour response. Still, total and partial regression was registered only in 22 patients (42,31%) of the control group(p<0.05). Tumors became operable in 92,3% of patients in study group vs 76,6 % in control group. Pathological complete response was observed in 12,55% patients of the study group after surgery.

Conclusion. The use of chemoradiotherapy with fluoropyrimidines enhances the effect of antitumour therapy, overcomes the resistance and increases the incidence of tumour regression, improves locoregional control and is a technique of choice for primarily inoperable breast cancer treatment.

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IMMUNOHISTOCHEMICAL PROFILE OF ENDOMETRIAL ADENOCARCINOMA: P53 OVEREXPRESSION AND BCL-2 PERSISTENCE IN PAPILLARY SEROUS AND ENDOMETRIOID SUBTYPES OF ENDOMETRIAL CARCINOMA

Endometrial adenocarcinoma (EA) is the most common gynecologic malignancy. Traditional factors associated with its prognosis include patient’s age, tumour grade, stage, histologic type, and the depth of myometrial invasion. Two histologic types of EA-endometrioid and papillary serous—are associated with different biologic behavior p53 alteration may be an early event in the development of UPSC and may be related to its clinical aggressiveness, while it is a late event in UEC. Early detection of p53 nuclear accumulation may help to recognize precursor lesions of UPSC. Bcl-2 persistence is frequently associated with endometrial carcinoma, and failure to inactivate bcl-2 expression probably is related to the development of endometrial carcinoma.

The goals of this study were to evaluate the differences in the immunohistochemical expression of p53, bcl-2 in endometrioid and serous carcinoma and to correlate the results with tumour grade and stage.

The differences in immunohistochemical expression of p53, bcl-2, were quantified in 34 endometrioid and 16 papillary serous carcinomas of endometrium and were in touch with known predictors of survival, such as grade and stage. All cases were studied immunohistochemically by using a combination of the avidin-biotin complex peroxidase method (ABC kit; Vector Laboratories, Burlingame, CA) and microwave antigen retrieval (15 min-0.01 N citrate buffer, pH 6) in archival paraffin-embedded tissue. The antibody was a mouse, antihuman monoclonal antibody, clone D07 (DAKO, Copenhagen, Denmark).

Results: Uterine papillary serous adenocarcinomas (UPSA) had significantly higher p53 expression than did uterine endometrioid adenocarcinomas (UEA) (74.5% versus 35.5%); No difference in p53 overexpression was detected between tumours of early and late stages of UPSC; On the contrary, in UEC, there was an important difference in p53 immunostaining between tumours of early and late stages (P=0.01); For bcl-2 immunostaining, UEC had a significantly higher immunohistochemical staining score than did UPSC (P=0.005). Generally, the staining intensity of bcl-2 decreased progressively from proliferative phase and hyperplastic endometrium to UEC and then to UPSC, with 3 of 16 (18.7%) UPSC being negative.

Conclusion: These results mean that p53 alteration may be an early event in the development of UPSC and may be related to its clinical aggressiveness, while it is a late event in UEC. Early detection of p53 nuclear accumulation may help to recognize precursor lesions of UPSC. Bcl-2 persistence is frequently associated with endometrial carcinoma, and failure to inactivate bcl-2 expression probably is related to the development of endometrial carcinoma.
Objective. The aim of the study was to evaluate the outcome of a combined neoadjuvant treatment in 54 patients with inflammatory breast cancer (IBC).

Methods: 54 patients with histologically verified IBC (T4dN1-3M0) received 6 courses of intraarterial polychemotherapy (IAC) with docetaxel 75mg/m², endoxane 600 mg/m². Preliminary angiography was performed to determine tumour arterial blood supply and to guide chemotherapy infusion. Prior to IAC an arteriogram of subclavian, internal mammary, and lateral thoracic arteries was obtained, to determine the most appropriate vessels that supplies the tumour area. Patients were evaluated for complete response (CR) and partial response (PR). After the response had been achieved, a radical mastectomy was performed. A prerequisite for performing the operation was to achieve «clean margins» of the removed breast. In the absence of a clean edge, skin flaps were mobilized according to the methods of Hadenheim and Beck.

Results: Four patients showed stabilization of the process, another 4 progressing of the process, the remained 46 showed regression of the tumour: the total effectiveness rate (CR + PR) was 85.1%. At the same time, complete response was observed in 7 patients (rate 12.9%), and in 39 - partial response rate 72.2%. In 32 patients with PR, the tumour size was reduced by more than 50%. All 46 patients with objective response performed radical mastectomies with mandatory «clean margins». Twenty-four months after treatment, 8 patients showed progression of the disease (rate 17.4%), with no local recurrence (rate 0%). Transient systemic toxicity was observed in 12 cases (rate 26.1%, all-bone marrow depression).

Conclusion: A combination of IAC with radical mastectomy with «clean margins» provides an acceptable objective response, excellent local control even in the case of the treatment of IBC.

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IMMUNOHISTOCHEMICAL CHARACTERISTICS OF ENDOMETRIAL CANCER

Endometrial cancer, being the most common malignant neoplasm of female genital organs in the world, remains one of the most urgent problems of modern oncology.

The purpose of this study is to study the expression of markers of apoptosis, neoangiogenesis and p53 in endometrial tumour in association with clinical manifestations of uterine body cancer.

Data from 28 patients with cancer of the uterus body were studied. Expression of the protein p53, anti-apoptotic protein Bcl-2, estrogen (ER) and progesterone (PR) receptors was studied. An evaluation of angiogenesis in the tumour was performed by counting the number of microvessels stained with antibodies to endothelial cells (CD31).

According to the proto-oncogene Bcl-2, the entire group of patients was divided into 2 subgroups: Bcl-2-positive tumours (n=17), Bcl-2-negative tumours (n=11). The study showed that about a third of tumours, both Bcl-2-positive and Bcl-2-negative, had mutant p53.

In Bcl-2-positive tumours, a highly developed vasculature was predominantly detected (in more than 75% of cases), whereas in Bcl-2 negative tumours of the endometrium, a low vascular density was mainly detected. Tumours expressing Bcl-2 generally contained PR receptors unlike Bcl-2 negative endometrial tumours. Correlation analysis revealed statistically significant correlations between Bcl-2 expression and PR receptors (r = 0.459, p=0.008), Bcl-2 expression and microvessel density in the tumour (r=0.469, p=0.006). Bcl-2-positive tumours mostly carried PR, but with receptors of ER the picture was mosaic and most tumours did not express ER. The absence of ER in the endometrioid adenocarcinoma of the uterus body is accompanied by an increase in relapses from 11.5% to 27% and is generally associated with a more unfavorable prognosis. Thus, the combination of the results obtained indicates a more unfavorable prognosis in a group of patients with Bcl-2 expression, a moderate and high density of microvessels in the tumour, and the absence of ER.
THE IMPORTANCE OF SOME ENDOCRINE INDICATORS IN THE PROGRESS OF ENDOMETRIAL CANCER

Today, endometrial cancer (EC) occupies one of the leading places in the structure of oncogynecological morbidity and has become one of the most actual problems in oncogynecology.

Goal of research: to learn and evaluate the condition of reproductive and adrenocorticoiod hormones during endometrium atypical hyperplasia (EAH) and EC.

Material and methods: the study included 38 patients aged 35 to 45 years. All patients were divided into 2 groups: with diagnosis EAH – 11 patients, with histological verified diagnosis of endometrium adenocarcinoma – 27 patients. All patients before treatment were examined for adrenocorticotropic hormone (ACTH) and cortisol in peripheral blood, and also the level of estrone, estradiol, estriol, pregnandiol, androsterone excreting with daily urine.

Results: no relation was found between main representatives of reproductive steroid hormones and displacement of their equilibrium. The value of estradiol/pregnandiol was increased in both groups thus evidencing the relative hyperestrogenemia as a main factor of hyperplasia and cancer behaviour. Also there was an imbalance between separate forms of female reproductive hormones with the dominance of estriol fraction, which served stimulator of hyperplastic processes in endometrium. At the same time, the fault of production of reproductive steroids of the most patients, independently upon containing the EAH or EC, was supporting by hypercorticism condition. The level of cortisol in peripheral blood was increased on average by 1.3 times.

Summary: the research showed the containing of general pathogenetic factors by changing of level of reproductive steroid hormones and hypothalamic-adrenocortical system in progress of EAH and EC, and testify the reasonability of usage of this data along with clinical indicators for the formation of the group of risk of progress EC among patients with EAH.

EPIDEMIOLOGICAL STUDIES OF CERVICAL CANCER IN UZBEKISTAN

Relevance: The problem of malignant neoplasms (MN) of female genital system, including cervical cancer (CC), continues to be extremely pressing given the fact of increasing morbidity and mortality and the tendency for further growth.

Aim: Epidemiological study of incidence and prevalence of cervical cancer in Uzbekistan.

Materials and methods: Data analysis and calculation of indicators based on forms of statistical accounting and reporting (Form No. 7-SSV MOH Republic of Uzbekistan).

Results: Study of CC incidence and mortality has revealed a necessity to analyse the overall growth trend in Uzbekistan from epidemiological point of view. Such a focus was primarily justified by the endorsement of the National Program on Combating Cancers aimed to ensure prevention and early diagnostics of MN, with a main emphasis was on the population screening and epidemiological research.

The conducted studies have brought the following findings: CC ranks 4th in the structure of MN in Uzbekistan, and 2nd among female pathologies after breast cancer, with an incidence of 5.5, death rate of 2.5, and peak incidence at the age of 50-64 (median value - 53 years old). In spite of accessible location and suitability of visual methods of examination, the majority of patients are referred to a specialized cancer centres at advanced stages of CC.

To date, the relevant epidemiological studies were aimed at the analysis of CC causality factors. Epidemiological analysis included the study of interrelationship between the incidence and the affecting factors of external and internal environment, such as primarily associated genetic (hereditary) and ecological (exogenous and endogenous) factors.

The literature provides data on the genes with established essential role in the development of hereditary forms of ovarian cancer. However, no relevant data was found for CC. There are also studies of the role of HPV in the development of premalignant CC, as well as the hormonal and hypothalamic-pituitary-ovarian system status leading to genital cancer.
We studied the inter-regional differences of CC incidence in the Republic of Uzbekistan. These differences might have been caused by both ethnic factors and various endogenous and exogenous factors, as well as by the growing labour migration in the region. The available data evidences some differences in cancer morbidity among indigenous ethnic groups (Uzbek, Kazakh, and Kyrgyz) and other ethnic groups inhabiting Central Asia. In particular, some observations over the Russian population show a higher frequency of MN of female genital system with a relevant trend in morbidity and mortality.

Conclusion: Follow up epidemiological studies and analysis are required in order to ensure a rational approach to CC prevention and screening. In this respect, an information system development was initiated with the aim to track the CC screening programs, to set up a relevant database for comprehensive coverage of population, and to provide subsequent scientific evidence for the implementation of targeted programs.

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CHOICE OF CHEMOTHERAPY REGIMEN IN PATIENTS WITH BREAST CANCER STAGE I-II OVER 60 YEARS

Breast cancer is one of the main causes of morbidity from malignant tumours. 30-45% of breast cancer cases occur in women aged 60 years and over. The patient's age is an important prognostic factor at the time of diagnostics of the primary breast cancer tumour.

Material and methods. During 2009-2015, we examined 50 women over 60 years with breast cancer. After radical surgery, they were divided into 2 groups and received different regimens of adjuvant chemotherapy. First group received 4 cycles of adjuvant chemotherapy according to the scheme AC (doxorubicin, cyclofosfamide), second group received 4 cycles of adjuvant chemotherapy according to the scheme TC (docetaxel, cyclofosfamide).

Results. Long-term results have shown significant advantage of the TC combination compared with the combination of AC 5 year disease free survival were 81% and 75% respectively. It is important to note that the TC treatment was equally effective, regardless of receptor status of the tumour and the status of regional lymphatic nodus (р>0,05). Improvement in survival was achieved without enhanced toxicity and complications. That was particularly important patients over 60 years who had comorbidities and contraindications to anthracyclines.

Conclusion. Adjuvant chemotherapy in patients over 60 years with breast cancer stage I-III with TC scheme is effectively in terms of 5-year disease-free survival and it is important for elderly patients due to the presence of concomitant diseases.

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TACTICTS OF TREATMENT OF PATIENTS OVER 60 YEARS WITH BREAST CANCER STAGE I-II AFTER RADICAL SURGICAL TREATMENT

30-45% of breast cancer cases occur in women aged 60 years and over. Hormon positive cancers account for 70-80% of all breast cancers, but distribution of subtypes Luminal A and B is not the same in different populations of women.

Material and methods. We have examined 45 women over 60 years old with breast cancer stages I-III treated between 2010 and 2015 at the Tashkent city oncological centre. We identified ER,PR, HER 2 neu, ki 67 by immunohistochemistry and all patients were divided into 2 group: Group 1 had a defined Luminal type A, Group 2 - luminal type B with HER 2 neu negative, but high levels of ki 67. All patients underwent radical surgery treatment. Group 1 received only adjuvant endocrine therapy with tamoxifen, Group 2 received adjuvant chemotherapy according to CAF scheme with endocrine therapy.
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FEATURES OF SURGICAL TREATMENT OF PHYLLOID BREAST TUMOURS

Relevance. Fibroepithelial tumours of mammary gland are quite rare in oncological practice. According to various authors, they make from 0,3-2,6% of all tumours of mammary glands therefore this pathology is insufficiently studied. The etiology and a pathogenesis of phylloid tumours aren’t clear. Fibroepitelial tumours are two-component tumors with a prevalence of connective tissue component which dominates in sarcomas. The foliaceous tumour is quite rare neoplasm and despite the available arsenal of modern diagnostic methods the principles of surgical treatment are insufficiently studied.

Research objective: Improvement of results of treatment by the choice of radical volume of surgical intervention at various types of foliaceous tumours.

Material and methods: during 2010-2017, we observed 72 (100%) patients with various types of the above-mentioned tumoral pathology at Tashkent City Oncological Dispensary. From them, 58 (80,5%) patients had benign tumour type I, 12 (16,6%) had borderline tumour type II, and 2 (2,7%) patients had malignant tumour type III. The age of women ranged from 15 to 70 years.

Material and methods : A study of expression immunohistochemical marker Ki-67 in 28 patients with CIN of various degrees. CIN I - 11 patients, CIN II and CIN III 8 - 9 patients. The age of patients ranged from 24 to 52 years.

The results and discussion : In CIN I the level of expression of Ki-67 ranged from 0-20%, i.e. a low degree of expression in CIN II, this figure was in the range of 20-50%, while in CIN III, there was a gradual increase in the expression molecular biological marker Ki 67 50% and above

Conclusion: Determination of the expression of molecular-biological marker Ki 67 can be used as a reliable prediction method precancerous diseases of the cervix.

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NEW APPROACHES IN PREVENTION AND EARLY DIAGNOSTICS OF CERVICAL CANCER

Cervical cancer for many decades continues to be in the center of attention of leading foreign and Russian oncologists. In 2015, our the Republic among the General population revealed more than 21 thousand malignant tumours, including cervical cancer in 1496 women (from 9.0 per 100 thousand women of the population).

The purpose of the study: The study of the expression of molecular-biological marker Ki 67 cervical intraepithelial neoplasia (CIN) of varying degrees.

Material and methods : A study of expression immunohistochemical marker Ki-67 in 28 patients with CIN of various degrees. CIN I -11 patients, CIN II and CIN III 8 - 9 patients. The age of patients ranged from 24 to 52 years.

The results and discussion : In CIN I the level of expression of Ki-67 ranged from 0-20%, i.e. a low degree of expression in CIN II, this figure was in the range of 20-50%, while in CIN III, there was a gradual increase in the expression molecular biological marker Ki 67 50% and above

Conclusion: Determination of the expression of molecular-biological marker Ki 67 can be used as a reliable prediction method precancerous diseases of the cervix.

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FEATURES OF SURGICAL TREATMENT OF PHYLLOID BREAST TUMOURS

Relevance. Fibroepithelial tumours of mammary gland are quite rare in oncological practice. According to various authors, they make from 0,3-2,6% of all tumours of mammary glands therefore this pathology is insufficiently studied. The etiology and a pathogenesis of phylloid tumours aren’t clear. Fibroepitelial tumours are two-component tumors with a prevalence of connective tissue component which dominates in sarcomas. The foliaceous tumour is quite rare neoplasm and despite the available arsenal of modern diagnostic methods the principles of surgical treatment are insufficiently studied.

Research objective: Improvement of results of treatment by the choice of radical volume of surgical intervention at various types of foliaceous tumours.

Material and methods: during 2010-2017, we observed 72 (100%) patients with various types of the above-mentioned tumoral pathology at Tashkent City Oncological Dispensary. From them, 58 (80,5%) patients had benign tumour type I, 12 (16,6%) had borderline tumour type II, and 2 (2,7%) patients had malignant tumour type III. The age of women ranged from 15 to 70 years. Diagnostics of tumours was based on objective survey, a palpation of mammary glands, these Ultrasound, mammographies, a cytologic research of smears.

Results and their discussion: At a preoperative stage the diagnosis was established at 10 (12,8%) patients. Tumours of type I were 1,5 to 6,5 cm in the diameter, II-from 4,5 to 8 cm, primary tumours of type III reached 7-10 cm and more in the diameter.

All patients with tumours type I had a tumour enucleation and local recurrence. After sectoral resection of a mammary gland no recurrence was observed. Sectoral resection was made only to 40 (68,9%) patients, of them, the recurrence in 9 (15,5%) patients could
be due to the larger size of the primary tumour. At 12 (16.6%) patients the II type, after asectoral resection of a mammary gland was taped; the recurrence was observed at 3 (4.15%) patients in 6 months, it made a repeated sectoral resection. At 2 patients the III type of a tumour after a sectoral resection of amammary gland was taped, the recurrence of a disease is noted at both patients in a year, from them at one patient concerning a recurrence the radical mastectomy on Mädnea was made (the tumour size in the diameter of 25 cm). At the same patient in 6 months after operation the metastatic lesion of a lung is taped.

Thus, thebigger is the size of tumour and the higher is its histological type, the higher is the probability of local recurrence and metastases of the tumoural process.

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CONSERVATION THERAPY OF CERVICAL CANCER. THE EXPERIENCE OF N.N. ALEKSANDROV REPUBLICAN RESEARCH AND PRACTICAL CENTRE FOR ONCOLOGY AND MEDICAL RADIOLOGY

Relevance. The statistics shows a steady increase in the frequency of detection of cervical cancer (CC) in young women worldwide. In the Republic of Belarus, the peak of CC morbidity in the last 5 years has moved to a younger age, with an overall increase in morbidity among women aged 30 to 45 years. Standard treatment of early CC (various types of hysterectomy and/or radiation therapy) results in the loss of reproductive function, the development of psycho-sexual disorders, the reduction of quality of life of treated women. Therefore, the preservation of fertility is an acute problem and one of the most important directions in the treatment of these patients.

Aim. To improve the efficacy of treatment of younger patients with IA1-IB1, IIA1 stages of CC through the implementation of new technologies ensuring the preservation of fertility.

Material and methods. 54 patients aged 22 to 43 years (median is 31 years) with IA1LVSI+, IA2, IB1 and IIA1 stages were included in the prospective study in accordance with the developed selection criteria. The patients were stratified into three subgroups depending on the oncological risk: 7 patients of low risk underwent a cervical amputation and pelvic lymph node dissection; 40 patients of moderate risk underwent radical abdominal tracheotomy; 7 patients of high risk received a complex treatment including 3 neoadjuvant courses of polychemotherapy, the assessment of effect and surgical treatment in the volume of radical abdominal trachealudy.

52 patients after radical hysterectomy with IA1LVSI+, IA2, IB1 and IIA1 stages were retrospectively analysed to compare the oncological results after organ-resecting surgery. The groups were comparable by their main clinical characteristics.

Results. The performed treatment allowed to save the organ in 47 (87%) patients. In 7 patients, radical hysterectomy was conducted due to various pathomorphological findings during surgery.

The menstrual function has recovered in 96% of patients with a saved organ (45 out of 47). Pregnancy occurred in 3 (16%) of 19 patients who were observed for more than 3 years; it resulted in delivery in 2 (11%) of them; one patient had a spontaneous abortion at week 16.

47 patients were observed for 6.5 to 75.2 months (median – 22.1 months). No CC mortality was observed during the study period, 1 patient died from ovarian cancer after 36.8 months. The adjusted and overall 3-year survival rate was 100%. 4 (11%) patients had a relapse within 3 years after surgery: 3 patients – after 6, 8, or 19 months; one had distant metastases after 20 months.

In the group receiving organ-resecting surgery, the adjusted 3-year survival rate was 93.3% (the difference with the group of conservation therapy is statistically insignificant, p = 0.67). 3 patients had recurrences within 3 years after the surgery: after 13, 14, or 24 months, respectively. Metastases appeared in 2 patients after 3 or 28 months. One patient had both recurrence and metastases. In total, 4 (8%) patients had the relapse (the difference with the group of conservation therapy is statistically and clinically insignificant, p = 0.83).

Conclusion. Use of the method of step-by-step examination described in this study, the selection criteria for conservation therapy and new conservation technologies in the treatment of IA1-IB1, IIA1 stages of CC allows preserving fertility in 87% women and does not worsen oncological results in comparison with organ-resecting surgery.
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**ASSESSMENT OF ADJUVANT CHEMOTHERAPY REGIMENS FOR TRIPLE NEGATIVE BREAST CANCER TREATMENT**

Relevance. Triple negative breast cancer (TNBC) occurs in about 10-20% of all cases of cancer in young patients aged 22-44 years. It has a more aggressive course and low sensitivity to chemotherapy. The inhibitors of TNBC (CDX-011) that improve the TNBC treatment outcome have been recently studied in clinical trials.

Materials and methods. The trials included 102 female patients aged 24-44 years with newly diagnosed TNBC who received polychemotherapy (PCT) from 2007 till 2012 at the Tashkent City Oncological Dispensary. The patients were divided in 4 groups. Group 1 included 23 women who received 6-8 cycles of PCT by FAC regimen (fluorouracil, cyclophosphamide, doxorubicin). Group 2 included 31 patients who received 6-8 cycles of PCT by TC regimen (paclitaxel, cisplatin). Group 3 included 21 patients who received 8-10 cycles of monochemotherapy with cisplatin. Group 4 included 27 patients who received 8-10 cycles of paclitaxel by “sealed” (dose-dense) regimens, with a decrease in intervals between cycles.

Results. A higher and long-term effect of therapy was achieved in accordance with the principle of “bigger tumour requires bigger therapy” and the use of modern chemotherapy regimens in Groups 2 and 4 subject to compliance to the scope and regimen of treatment.

Conclusions. A more toxic effect on the ovaries was observed in the group of women who received treatment by TC regimen (paclitaxel, cisplatin) (64%) compared with patients who received paclitaxel chemotherapy by “sealed” (dose-dense) regimes with a decrease in intervals between cycles (36%).

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**ENDOMETRIAL CANCER: ANALYSIS OF EPIDEMIOLOGICAL DATA**

Endometrial cancer (EC) ranked third in the structure of cancer morbidity in Ukraine in 2000-2016, with a specific share of 7.6-9.1%. EC ranked first in the structure of female cancer morbidity, accounting for 37.6-43% of cases. According to the data of the National Cancer Registry, the standardized morbidity from EC in 2015 was 17.6 per 100,000 people (6,383 cases), with the mortality of 4.4 per 100,000 people (1,596 cases) (without Donetsk and Lugansk regions, the Autonomous Republic of Crimea and the city of Sevastopol). More than 80% of EC cases are revealed at stages I-II. During 2000-2014, the number of EC patients has increased from 7,082 (2001) to 7,777 (2013), with a stable mortality rate – 4.4 in 2000 and 4.2 in 2013. There is an increase in the detection of EC patients during preventive examinations – from 26.2 to 38.6 (2000 vs. 2015). The coverage of primary patients with special treatment has increased from 80.1 to 86.1 (2000 vs. 2015). The distribution of patients with EC by stages in 2015 was: 81.3% of patients with EC stage I-II, 7.9% - with EC stage III, 3.2% - with EC stage IV. The International Agency for Research on Cancer (IARC) has expected about 319,000 new EC cases worldwide in 2012, and about 99,000 new cases in Europe.

EC ranks 14th among causes of death worldwide. In Europe, EC ranks 9th among causes of death from cancers in women; in 2012, it caused the death of about 23,700 women.

In North America, the morbidity is about 23.3 per 100,000 people.

In the UK, 8,475 new cases of EC were detected in 2011; EC caused the death of 2,025 patients. The EC morbidity is 26.3 per 100,000 people. Most patients are over 50 years. About 95% of patients with EC have a survival rate of more than 5 years.

Purpose of the study was to analyse the dynamics of morbidity, mortality and the account of patients receiving treatment from EC in the National Cancer Institute.

The analysis covered personal data of patients with EC from the National Cancer Institute cancer registry who received treatment in 2000-2015 as per the programs of the register.

Results. During this period (2000-2015), 3,546 patients with malignant neoplasms (MN) of the
uterus body were treated at the National Cancer Institute. Most of the women (90%) were above 45 years. Stage I was established in 2,290 patients (66%), stage II – in 444 (15%) patients, stage III – in 375 (16%) patients, stage IV – in 145 cases (4%).

By morphological structure, the MN of the uterus body included: adenocarcinoma – in 2,769 (78.2%) patients, squamous cell cancer - in 42 (11.8%) patients, papillary adenocarcinoma – in 50 (1.4%), clear-cell carcinoma – in 24 (0.67%), glandular papillary cancer – in 146 (4.1%), sarcoma – in 290 (8.2%) cases, and others. The tumour differentiation was high in 307 (8.7%) patients with MN of the uterus body, moderate – in 1,382 (39%) patients, low – in 572 (16.1) patients, and 15 (0.4%) patients had undifferentiated tumours. In 1,270 (35.8%) patients, the degree of differentiation was not established.

Methods of treatment of patients with MN of the uterus body included: surgery – in 1,378 (38.9%) cases, radiological therapy – in 116 (3.3%), combined treatment (surgery + radiological therapy) – in 1,129 (31.8%), surgery + chemotherapy – in 313 (8.8%), complex treatment – in 440 (12.4%), chemoradiological therapy – in 42 (1.2%), chemotherapy – in 36 (1%) cases, and others.

Thus, among patients with MN of the uterus body treated at the National Cancer Institute during 2000-2015, 90% were above 45 years, the majority (81%) had stage I-II of the disease; and adenocarcinomas with different degrees of differentiation dominated by morphological structure (78.2%).

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HORMONAL HOMEOSTASIS IN PATIENTS WITH RECURRENT SEROUS OVARIAN CANCER, PECULIARITIES OF HORMONAL RECEPTOR STATUS, THE EXPRESSION OF VEGF, HER 2/neu IN SEROUS CANCER AND FUNCTIONAL OVARY CYSTS

Purpose of study: to study and compare the hormonal homeostasis of patients with recurrent ovarian cancer (OC) (control group) and the patients with surgical menopause after surgery for non-malignant uterine pathology (control group); to study and compare the hormonal receptor status, the expression of HER-2/neu and VEGF in serous OC cells and the ovaries of patients from the control group.

Materials and methods of study: The prospective study involved 41 female patients with recurrent serous OC (main group) and 35 female patients with surgical menopause after surgery for non-malignant uterine pathology (control group). The hormonal homeostasis of the patients from the two groups was studied and compared by immunochemical method in the Synevo laboratory. The surgical material of patients from the two groups was morphologically-analysed; the frequency of concomitant hyperplastic endometrial processes, in particular, of complex non-atypical endometrial hyperplasia was studied. Paraffin blocks of surgical material of patients from the two groups underwent immunohistochemical study. The hormonal receptor status (oestrogen receptor (ER), progesterone receptor (PR), testosterone receptor (TR)), expression of HER-2/neu and VEGF in serous OC cells and ovaries of patients from the control group were studied and compared. The correlation between the age and the expression of steroid receptors, HER-2/neu and VEGF in OC cells and ovaries of patients from the control group was analysed.

Results. The frequency of a complex non-atypical endometrial hyperplasia as a result of chronic dishormonal disorders was similar in patients with recurrent OC and the control group (58.6 and 51.5%, respectively).

The hormonal homeostasis parameters had no significant differences in patients with recurrent OC and the control group (p <0.05) and corresponded to the reference levels of sex hormones in the postmenopausal period.

In the control group, the expression of steroid hormone receptors, HER-2/neu and VEGF was observed only in the cells of functional ovarian cysts. Those markers were highly expressed both in the serous OC cells (oestrogen receptor – 65.9%, progesterone receptor - 63.4%, testosterone receptor-56.1%, HER-2/ neu - 65.9 and VEGF - 48.8%) and the functional ovarian cysts (follicular cysts: oestrogen receptor – 75.0%, progesterone receptor – 50.0%, testosterone receptor – 25.0%, HER-2/neu – 75.0 and VEGF – 50.0%; corpus luteum cysts: oestrogen receptor – 61.5%, progesterone receptor – 76.9%, testosterone receptor - 61.5%, HER-2/neu - 92.3 and VEGF - 69.2%). However, those mark-
The patients with recurrent OC in the postmenopausal period had the greatest proven number of oestrogen-, progesterone- and testosterone-receptor positive tumours (63.6%, 61.5 and 65.2%, respectively), whereas the patients of fertile age had the lowest frequency of receptor-positive serous OC (14.8%, 11.6 and 13.1%, respectively). The expression of HER-2/neu, VEGF was not found to correlate with the age of patients with recurrent OC (r=-0.014, p=0.85 and r=-0.036, p = 0.73, respectively). Still, there was a significant direct correlation between the expression of HER-2/neu and VEGF in serous OC cells (r=0.925, p=0.001).

The patients of fertile age had the highest frequency of expression of oestrogen receptor, progesterone receptor, testosterone receptor, HER-2/neu, VEGF in granulosa lutein cells of functional ovarian cysts (100%, 91.7% 88.9%, 86.7% and 90.9%, respectively). At that, we have established proven correlations between all steroid receptors in the cells of functional ovarian cysts; the age of women and the expression of all steroid receptors; the expression of oestrogen receptor, progesterone receptor with the expression of HER-2/neu and VEGF.

Conclusions. We have shown that the assessment of hormone levels in the blood serum of postmenopausal women does not provide a complete information on possible variants of pathological developments since the hormonal impact requires the presence of a sufficient level of steroid receptors in the cells of target tissues. The presented results represent the existence of common risk factors and mechanisms of hormonal pathogenesis of hormone-dependent benign diseases of reproductive organs and OC.

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THE IMPACT OF NEURO-PRESERVING RADICAL HYSTERECTOMY (RHE-C1) ON BLADDER CONTRACTILE FUNCTION IN PATIENTS WITH INFILTRATIVE CERVICAL CANCER

Aim: To evaluate the bladder contractile function in post-surgery patients with infiltrative cervical cancer.

Materials and methods. The patients with cervical cancer treated in the oncogynecological department of the National Cancer Institute in 2014-2016 were examined in order to evaluate some functions of the urinary system and the impact of neuro-preserving radical hysterectomy (RHE-C1). 50 patients with infiltrative cervical cancer (mean age of patients is 32.7 ± 4.9 years) underwent RHE followed by cystomanometry. In 25 cases, (Group 1) RHE was performed with the preservation of the pelvic vegetal nerve plexus (PVNP), in other 25 cases (Group 2, control arm) RHE was conducted by standard method without the preservation of PVNP. The patients were divided into groups according to the pathological type and histological differentiation of the tumour. Group 1 included 3 people (3%) with adenocarcinoma and 22 (88%) – with squamous cell cervical cancer. Histological differentiation of the tumour: GX-2(8%); G1-9(36%); G2-5(20%); G3-9(36%). Group included 4 people (16%) with adenocarcinoma and 21 (84%) – with squamous cell cervical cancer. Histological differentiation of the tumour: GX-2(8%); G1-8(32%); G2-6(24%); G3-9(36%).

Results and discussion. The female patients in both groups were examined for the main symptoms of urinary system disorders, such as: difficulty in urinary bladder emptying (DUBI); involuntary urination of different degree of manifestation (IUDMM). Group 1 was divided into 2 subgroups: sub-group A – the patients with the stage IB and preserved PVNP on both sides (18 people,72%) and sub-group B – the patients with the stage IIA, with the preserved PVNP on one side (7 people, 28%). DUBI was diagnosed in 1 (4%) patient of sub-group A and in 2 (8%) patients of subgroup B, altogether – 12%. IUDMM was diagnosed in 1 (4%) patient of sub-group B, which was 4%. In total, the main symptoms of urinary system disorders were detected in 16% of cases. The catheter in patients with the stage IB and preserved PVNP on both sides was removed after 3-4 days. At that, the hospital stay was 6-7 days. The urinary catheter in patients with the stage IIA, with the preserved PVNP on one side was removed after 5-7 days; the hospital stay was 10-12 days.

Group 2 was divided into 2 sub-groups by the stage of the process: I B (9 people, 36%) and II A (16 people, 64%). DUBI was diagnosed in 6 (24%) patients with IB stage and 9 (36%) patients with IIA stage, altogether – 60%. IUDMM was diagnosed in 1 (4%) patient with IB stage and in 4 (16%) patients with IIA stage, altogether – 20%. In total, the main symptoms of urinary system
disorders were detected in 80% of cases. The catheter in patients with IB stage was removed after 8-14 days. The hospital stay amounted to 15-16 days. In stage II A patients, the urinary catheter was removed after 15-21 days; the hospital stay was 22-25 days.

Conclusion: Thus, Group had 16% of complications in the functions of the urinary system vs. 80% in the control group. It proves the positive impact of RHE-C1 on these functions and a significant improvement of the quality of life of patients.

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NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER: TWO RANDOMISED STUDIES

Background: In Uzbekistan, women with cervical cancer are often diagnosed in advanced stages of the disease. Cervical cancer is the leading cause of death among patients with malignant tumours in Uzbekistan. Most women with locally advanced cervical cancer are candidates for chemotherapy or radiotherapy. http://ascopubs.org/doi/full/10.1200/JCO.2014.58.4391

Gynecologic Oncology Group (GOG) protocol 204 established double therapy of cisplatin and paclitaxel as the standard of care. This combination had an overall response rate of 29.1%. Then, GOG-240 demonstrated an improvement in both PFS, and OS endpoints from this doublet with the addition of bevacizumab. By harnessing this anti-angiogenic agent, there was an addition of 3.4 months to OS. However there were no established treatment options in locally advanced cervical cancer.

Vinorelbine has moderate activity in advanced or recurrent squamous cell carcinoma of the cervix.

Carboplatin has been reported to be a less effective platinum analog than cisplatin for cervical cancer. Carboplatin induces milder nephropathy, less nausea/vomiting, and lower neuropathy than cisplatin. http://ascopubs.org/doi/full/10.1200/JCO.2014.58.4391

The objective of this phase II study was to assess the efficacy and toxicity of vinorelbine + carboplatin in the treatment of chemo-naive cervical cancer patients.

Materials and Methods: Between August 2014 and January 2016, 184 patients with squamous cell carcinoma of the cervix, FIGO stage II B IV A were randomised (study 1) to receive either two cycles of intravenous (i.v.) vinorelbine 30 mg/m² infused over 20 min on day 1, 8, 15 every 4 weeks; carboplatin 360 mg/m² by intravenous injection on day 1 every 4 weeks (VP). Chemotherapy (CT) followed by radiotherapy (RT). No prior chemotherapy or radiotherapy was allowed.

Results: ‘CT-RT Group’ n=94 or RT alone, RT Group n=90. In the ‘CT-RT Group’, of evaluable 89 patients, 64 responded: complete response (CR) four (4.5%) and partial response (PR) 60 (67.5%). Of the remaining 25 patients 23 had stable disease and two progressed. Eighty of 89 patients completed RT as planned. Following RT 56 (70%) achieved CR, 19 (23.7%) had residual disease and five (6.3%) had progressed. Patients aged >45 and those with Hb > 10 gm/dL had significantly better response to CT. Further, CT responders had a better response to RT; 83% (49/59) vs 33.3% (seven/21), p<0.01. In the ‘RT Group’ 88 patients were evaluable; 61 (69.3%) patients achieved CR, 25 had residual disease and two progressed. The estimated overall survival at 48 months in the ‘CT-RT Group’ and the ‘RT Group’ is 38% +2.01 (SE) and 36% +1.85 (SE), p=0.59 respectively. In a subsequent randomised study (study 2) 36 patients with stage III B cervical cancer received two cycles of VP (as above) followed by RT vs 36 patients who received RT alone. In the ‘CT-RT Group’ 29 patients responded; CR-8 (22.2%), PR-21 (58.3%). Six patients had no response to CT and one patient died of CT toxicity. Following RT-24 of 35 (68-6%) patients achieved CR, eight had residual disease and three patients progressed while on RT. In the ‘RT Group’-11 of 36 (58.4%) achieved CR, 8 had residual disease and three progressed. Estimated survival was 71% in the ‘CT-RT Group’ and 39% in the ‘RT Group’; p = ns. Granulocytopenia was the major toxicity, with 47% of patients exhibiting grade 3 or 4 toxicity. Dose reduction and/or treatment delay was necessary in 28 patients (78%). Peripheral neuropathy reported in 10 patients was mild (grade 1 in 9 patients and grade 2 in 1 patient). Cystitis, proctitis and local skin reaction after RT occurred equally in the two groups in both the studies.

Conclusion: In conclusion, VP CT prior to RT in patients with locally advanced cervical cancer results in a high response rate. Response to CT predicts response to RT. There is no increase in the toxicity to subsequent RT. Our studies have demonstrated significant difference in overall and disease-free survival when neoadjuvant CT is added prior to the standard RT regimen.
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PRESERVATION OF REPRODUCTIVE FUNCTION IN PATIENTS WITH INVASIVE CERVICAL CANCER

WHO reports about 500,000 of new cases of cervical cancer (CC) worldwide every year, and about 250,000 deaths from this disease. The CC morbidity and mortality are growing since 1990s. The National Cancer Registry of Ukraine registers an increase in CC incidence at the young age: at the age of 20-24 years – from 1.7 to 2.3 cases per 100,000 women; at the age of 30-34 years – from 14.6 to 25.5 cases per 100,000 women. We witness redistribution in the age structure of the disease towards a younger age. The morbidity is rejuvenated, and this trend will be preserved in the next 10 years. In spite of the visibility of CC, organ preservation in the treatment of invasive CC (T1B) remains one of the most urgent problems of modern oncogynecology.

Aim: To study the results of using radical abdominal trachelectomy (RAT) in the treatment of patients of fertile age with stage T1a1-b1 invasive CC.

Materials and methods. Since 2008 to 2016, 96 patients of fertile age (23 to 30 years, mean age – 27.7±3.4 years) with invasive CC (T1aN0M0 - T1b-N0M0) treated in the oncogynecological department of the National Cancer Institute received conservative surgery in the form of RAT including iliac lympho-dissection, removal of the cervix and the creation of uterovaginal anastomosis. In all cases, squamous cell carcinoma was morphologically confirmed.

RAT methodology: a bilateral pelvic lymph node dissection was performed after laparotomy and revision of the abdominal cavity and pelvis organs. The uterine cervix with parametrial tissue and upper third of vagina were removed, with the formation of uterovaginal anastomosis.

64 patients underwent electrocauterizing conization during previous treatment. In one case, the intraoperative urgent histological test detected the signs of carcinoma with infiltrative growth in sections of the proximal cervix/uterine body. This patient underwent Wertheim’s hysterectomy. RAT went on for 130±15 minutes, and the blood loss was less than during Wertheim’s hysterectomy and amounted to 270±50 ml. The average hospital stay was 9±1.2 days.

In 12 patients, lymphocysts in the postoperative period required conservative treatment. The longest observation period was 107 months. During the observation period, the recurrence of the disease was detected in 2 patients (0.5%) 14 months after the intervention. Other patients had no recurrence. All patients had the recurrence of menses.

Conclusion: RAT as a method of surgical treatment of patients with CC allows preserving not only the ovaries but also the uterus thus fully preserving the reproductive function of the woman. The usage of RAT in treatment of patients of fertile age with T1b1 stage infiltrative CC allows preserving reproductive and menstrual function in women, gives the opportunity to improve their psychoemotional condition and the quality of life of patients. RAT can serve as an alternative to Wertheim’s surgery in treatment of patients with early stages of CC wishing to preserve their reproductive function.

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THE SPECIFICS OF CLINICAL MANIFESTATIONS AND DIAGNOSTICS OF MALIGNANT TROPHOBLASTIC TUMOURS TRIGGERED BY MOLAR PREGNANCY, IN ADOLESCENTS

Trophoblastic disease of pregnancy is a rare disease diagnosed mainly in women of fertile age.

Purpose of this study is to study the specifics of clinical manifestations and diagnostics of malignant trophoblastic tumours (MTT) triggered by molar pregnancy (MP), in adolescents.

Materials and methods. The study included 158 women with malignant trophoblastic tumours triggered by MP who were examined and treated in the Oncogynecological Department of the National Cancer Institute (NCI). The main group included 28 (17.7%) adolescent women, and the control group – 130 (82.3%) women aged 20 to 40 years.

According to WHO definition, adolescence is the period from 10 to 19 years. In this study, the adolescent group included patients aged 16 to 19, aver-
age age – 17.8±1 year. The average age in the control group was 26.7±5 years. The majority of patients in the control group (66.9%) were aged 20 to 27.

Staging in both groups was performed according to the anatomical classification of FIGO-WHO (2002). Prior to treatment, all patients were assigned to the group of low risk of resistance to methotrexate, so their comparative analysis was eligible.

Results and discussion. In both groups, MTT development was in most cases initiated by a complete HM: in 92.9% of cases among adolescents, and in 88.5% among adult women (p>0.05).

Ovarian cysts more than 6 cm in diameter were one of the risk factors for MP malignancy. In the study, the cysts were diagnosed in 65 patients, of them, only in 1 case (1.5%) in the adolescent group.

The main criterion for preclinical diagnostics of MTT after removal of MP was the level of chorionic gonadotropin (hCG) in serum. The baseline level of hCG was higher in the adolescent group (37,457±130.7 mIU/L vs. 16,439±81.4 mIU/L, respectively, p<0.05).

Stage I of the disease was diagnosed in most cases in both groups: 78.6% - in the adolescent and 85.4% - in the control group. MTT at the preclinical stage was diagnosed only in 7.1% of adolescents and 11.5% of adult women (p>0.05). At the same time, MTT with a massive lesion of myometrium (tumour nodes ≥5 cm in diameter) were diagnosed in 53.6% of adolescents and only in 9.2% of adult women (p<0.05). Anaemia as a result of bleeding from the tumour nodes in the uterus was more often (p<0.05) observed in women of the adolescent group (28.6% of cases).

In 89.3% of cases, late diagnostics of MTT in adolescent women was due to the breach of hCG level monitoring requirements by the patients.

Conclusions. The late diagnostics of MTT in adolescent women indicates the need for health education among adolescents to prevent the development of locally advanced and disseminated forms of malignant trophoblastic tumours triggered by molar pregnancy.

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SURGICAL TREATMENT OF LOCAL VULVA CANCER RECURRENTS

Relevance: Vulva cancer is a rare form of oncogynecological cancer. The recurrences of vulva cancer (VVC), in comparison with primary tumours, are characterized by an increased degree of malignancy and resistance to therapeutic intervention; they often lead to significant anatomical and topographical disorders in the area of occurrence and are the main cause of patients’ deaths. According to summarized statistics, VVC arise in 24-30% of cases after the initial definitive treatment. In 80% of cases, the recurrences are local in nature and occur primarily in the first 2 years of follow-up. The use of wide radical local excision (WRLE) is the main method of treatment of local recurrences and provides satisfactory results in many cases. Treatment of regional recurrences (in the lymphodissection zone) is less promising in terms of prognosis. It is also palliative in nature and is not considered in this paper. The repeated intervention, partial resection of the perineum central structures (urethra, vagina, particularly perineum) with subsequent neoplastics was performed in 20 (57%) cases. In 2 cases, a back pelvic evisceration was performed due to the involvement of rectum sphincter into the neoplastic process. The extensive defects were closed by the displacement of autogenous tissues after formation of fasciocutaneous flaps of various shapes or by a bi-, monolateral musculocutaneous graft. VVC surgery treatment outcomes (5-year survival of 71.4%) have significantly exceeded the similar parameters of treatment after radiation therapy.

Conclusions: regular follow-up of female patients allows identifying VVC at early and potentially curable stages. Surgical treatment of local vulva cancer recurrences (WRLE) is the most preferable and promising for patients since it allows achieving local control in 70% of cases. Surgical treatment of PVC presents a certain difficulty; it requires high qualification and skills of the surgeon in closing extensive defects.

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EPIEDEMOLOGY OF OVARIAN CANCER IN THE REPUBLIC OF KAZAKHSTAN IN 2004-2014

Relevance. According to Globocan 2012, ovarian cancer (OC) is the 7th most widespread form of cancer affecting female population globally. Over 238,000 new cancer cases were registered only during 2012. Currently, no explicitly recognized preventive tools are available in detection of early forms of OC. According to the statistics, in 70% of cases malignant neoplasms of the ovaries are detected at stages III-IV of the disease. OC ranks 3rd among malignant tumours in Kazakhstan. According on the national statistics, in 2014 the share of OC in the total incidence of cancers was 3.2%.


Findings. Rough intensive indicators of CC incidence revealed the increased detection of CC in 2004-2014. In 2004, the incidence rate was 10.2 per 100,000 of female population vs. 11.8 in 2014. Standardized indicators have shown a similar trend. Malignant neoplasms of the ovaries were registered in all age groups, with a marked increase at the age of 65-69 years.

The analysis of OC incidence broken down by the stage of disease has shown an increased detection at the I-II and III stages of the disease in 2004-2014 with a noticeable decline in the detection of advanced forms. I.e., 1520 stage IV OC cases were registered in 2004 vs. 106 advanced cases in 2014.

Conclusion. The increase of OC incidence was due to an increased registration of patients at the initial stage of the disease. It also resulted in a better 5-year survival rate of patients with malignant neoplasms of the ovaries. Such a progress was achieved thanks to the improvement of diagnostics, surgical techniques, as well as an upgrade in chemotherapy and the availability of targeted drugs.

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DYNAMICS OF INCIDENCE OF ONCOGINAECOLOGIC PATHOLOGY IN THE REPUBLIC OF KAZAKHSTAN IN 10 YEARS (2007-2016)

Timeliness. Malignant tumours (MT) of cervix uteri, corpus uteri and ootheca are in the top ten of all female oncopathologies. According to world data (GLOBOCAN 2012), cervical cancer amounts to 7.9% and ranks 4th in disease distribution among women, uterine corpus cancer – 4,8% and ovarian cancer – 3,6% (6 and 7 rank places respectively). Cervical cancer, uterine corpus cancer and ovarian cancer ranked 3 to 5 in distribution of MT among women in 2016 in the Republic of Kazakhstan and amounted to 9.1%, 5.9% and 5.6%, respectively, among all women oncopathology.


Materials and methods. Main medical report and account forms (Ф. №7, №35, №090/У) and database of cancer-register on malignant tumours (MT) and cervical cancer (CC), uterine corpus cancer (UCC) and ovarian cancer (OC) for 2007-2016, information about population size were used. Extensive (E), intensive (I) and standardized (SI) indicators were calculated.

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Results. Dynamic of disease incidence of three main nosology of malignant tumours of female reproductive organs for 10 years tends to increase. However trends of disease incidence are slightly different by present pathologies.

Adjusted incidence rate of cervical cancer in the RK was growing since 2007 till 2015 from 13,51 to 17,56‰ and went down to 16,2‰ in 2016. Rate of increase of disease incidence in the Republic for the last 10 years was 20,8%. Disease incidence with CC has reduced on 1,34‰ or 7,6% in 2016 in comparison with 2015. Maximum increase was observed in 2012 (1,44‰). Minimum increase was fixed in 2016 (-1,34‰).

Average value of CC incidence was 15,46‰ since 2007 till 2016. Rate of increase of analyzed indicator was 1,02 during the whole period. CC incidence has increased annually on 2,1% (on 0,3‰) in average. Stable linear increase of CC incidence was obtained during analytical equation of trend of disease incidence with trend rate 0,454 (t>2.306).
Disease incidence with uterine corpus cancer in the RoK tends to increase during 10 years period. UCC disease incidence in the RK has increased on 1,19‰/uniF655/uniF655 or on 12.3% in 2016 (10,66‰/uniF655/uniF655) in comparison with 2007 (9,47‰/uniF655/uniF655). Average value of UCC disease incidence was 10,14‰/uniF655/uniF655 since till 2016. In average UCC disease incidence in the RK has increased in each period on 0.13‰/uniF655/uniF655 or on 1.3%. Maximum growth is observed in 2012 (0.9‰/uniF655/uniF655), minimum – in 2016 (-0.68‰/uniF655/uniF655). Disease incidence of UCC has reduced on 0.68‰/uniF655/uniF655 or on 6% in 2016 in comparison with 2015. Rate of increase demonstrates that trend is decreasing and this is evidenced by deceleration of disease incidence of this pathology. However trend line is increasing and straight, with trend coefficient 0.22 (t>2,306).

Indicators of incidence rates of ovarian cancer have periods of growth and reduction during 10 years, however, growth of disease incidence of this pathology is observed. Disease incidence of OC in the RoK has increased on 0.29‰/uniF655/uniF655 or on 3.2% in 2016 (9,42‰/uniF655/uniF655) in comparison with 2007 (9,13‰/uniF655/uniF655). Disease incidence of OC has increased in average on 0.03‰/uniF655/uniF655 (on 0.4%). Disease incidence of OC has reduced on 1,32‰/uniF655/uniF655 or on 12.3% in 2016 in comparison with 2015. Minimum increase was in 2016 (-1,32‰/uniF655/uniF655).

Growing rates demonstrate that trend is increasing and this is evidenced by acceleration of OC in the RoK (Trend rate b = 0,123, t>2,306). Conclusion. So, analysis of disease incidence for the last 10 years of main clinical entity of oncogynaecological pathology demonstrates growth of present indicator. Growth rates in case of cervical cancer are the most expressed, then in case of uterine corpus cancer and then in case of ovarian cancer. Expressed increase of cervical cancer rate demonstrates necessity in performance of screening for detection of pretumour pathology and earlier forms of malignant tumour of cervix uteri with the purpose of increase of patients’ life expectancy.

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DETERMINATION OF HIGH RISK HUMAN PAPILLOMA VIRUS IN CERVICAL CANCER

Relevance. Cervical cancer (CC) is one of the most widespread forms of cancer. In the Republic of Kazakhstan, it ranks 4th among female cancer diseases and 7th among all malignant tumours. According to Kazakhstan National Cancer Registry, in 2016 the standardized CC incidence rate was 18.2 per 100,000 population, and CC mortality rate was 7.1 per 100,000 population. The linkage between the human papilloma virus of high oncogenic risk (HPV HR) and CC, especially of pre-invasive and invasive forms, is well known. Based on the studies, a persistent HPV HR infection is the most significant risk-factor for invasive CC. Still, nothing is known today about the prevalence of HPV HR though it has a predominant importance in development of invasive CC in Kazakhstan. Therefore, the aim of our study was to assess the distribution of HPV types in biopsy material of Kazakhstani patients with diagnosed CC.

Methods: The study included 99 formalin-fixed and paraffin-embedded (FFPE) CC tissue samples gathered at the centre for morphological examination of Kazakh Research Institute of Oncology and Radiology. The archival material was cut into layers up to 10 μm thick in the department of pathology of Ljubljana University. DNA was extraction in the DNA Mini Kit (Qiagen, Hilden, Germany) following the protocol of the Institute of Microbiology and Immunology, Medical Faculty of Ljubljana University. The HPV HR detection was carried out using RealTime High Risk HPV Test (Abbott, Wiesbaden, Germany) to ensure a simultaneous HPV genotyping of types 16 and 18, and 12 other types: HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68.

Findings: Out of 99 samples, two (2.0%) were excluded from the study due to incorrect results of amplification with beta-globin. The total of 77/97 (79.4%) samples were positive for HPV HR. HPV 16, HPV 18 and other types of HPV HR were detected in 69/77 cases (89.6%), 3/77 (3.9%) and 6/77 (7.8%), respectively. Most of the samples (98.7%) had a single infection with one type of HPV HR.

Conclusion. As of today, it was the only study on the assessment of distribution of HPV HR types among Kazakhstani women diagnosed with CC. The prevalence of HPV HR in FFPE cervical tumours was slightly lower than in the similar studies performed in other countries. Most likely, it was due to the fixation technique and/or storage conditions of archive materials. However, approximately 80% samples were positive for HPV HR. Of them, HPV16 was detected in almost 90% cases. The study findings evidence that the introduction of vaccination against HPV could have a critical impact on CC incidence in Kazakhstan.
ON THE ASSESSMENT OF LOST LIFE POTENTIAL DUE TO BREAST CANCER MORTALITY IN KAZAKHSTAN

Relevance: Breast cancer (BC) mortality significantly affects the average life expectancy of female population and is of great socioeconomic importance. The life expectancy is the main integral indicator recommended by World Health Organization as a suitable criteria for health status and living standards of population in a specified area.

Aim of the study: Assessment of lost life potential (LLP) due to breast cancer mortality in Kazakhstan.

Materials and methods: The base-line material included the data of the Committee for Statistics of the Ministry of National Economy RK on the deaths from BC nationwide, and the tables on survival rates in 2010 and 2014. Indirect loss was calculated by V.V. Dvoirin and E.M. Aksel method (1990).

Results: In 2014, the total loss of female population due to BC mortality amounted to 13,983 life years (LLP), with a decline by 12.3% vs. 2010 (15,950 life years). The total loss due to premature mortality of women with BC has also decreased and amounted to 1.71‰ per 1,000 female population in 2014 compared to 2.07‰ in 2010. The age-standardized LLP (age range of 1-69 years) amounted to 1.59‰ in 2014 vs. 1.96‰ in 2010.

The total lost life years in productive age (20-54 years) amounted to 3378 life years in 2014 vs. 3980 in 2010 (15.1% less).

The life-years loss associated with premature mortality of women in productive age due to BC has also declined to 0.68 ‰ in 2014 per 1,000 population vs. 0.84‰ in 2010. A similar trend was observed in standardized LLP indicators in productive age (1.22‰ in 2014 vs. 1.50‰ in 2010).

In Kazakhstan, the average number of lost-life years per one woman died from BC amounted to 14.8 years in 2014 vs. 16.0 years in 2010. The average number of lost-life years in productive age due to premature death of one woman from BC amounted to 7.9 years both in 2010 and 2014.

Conclusion: Thus, a preliminary assessment of LLP shows a declining dynamics in socioeconomic losses due to BC mortality in the years of study what is definitely associated with a relevant improvement of diagnostics, treatment and prevention, as well as the implementation of BC screening in Kazakhstan.

THE RESULTS OF CERVICAL CANCER SCREENING IN KARAGANDA OBLAST

Relevance: Kazakh Research Institute of Oncology and Radiology reports the incidence rate of cervical cancer (CC) in Kazakhstan at the level of 9.7; 9.6 and 10.3 per 100,000 in 2012-2014, respectively. CC ranked 2nd among cancer pathologies in female population after breast cancer. The mortality rate was 0.9, 3.6 and 4 per 100,000 in 2012-2014, accordingly. In Karaganda oblast, the morbidity rates reached 10.3, 9.7 and 10 in specified years, respectively. The mortality rates in Karaganda oblast were 0.5, 4.8 and 4.4 per 100,000 in 2012-2014, accordingly. Thus, the morbidity and mortality in Karaganda oblast exceed the national level. It evidences the importance of timely diagnostics of CC as its early detection determines further success of prescribed therapy, rehabilitation and retention of life quality of patients with CC.

Aim: Analysis of results of CC screening in Karaganda oblast.

Materials: Reporting forms of the Centralized cytology laboratory of the regional oncology dispensary for 3 years (2012-2014).
Findings: The total of 120,912 smears from targeted groups underwent Pap-test (liquid cytology). The obtained results have revealed: the norm – in 87,263 (72.17%) cases, background pathology – in 24,495 (20.2%) cases, non-informative material – in 3,522 (2.92%) cases, and dysplasia – in 5,795 (4.8%) cases. HSIL accounted for 185 cases (0.15%). The suspected cancer and cancer were found in 21 cases (0.017%). Background processes prevailed in women aged 30 to 40 years, and the cases of pre-cancer and CC – in women aged 50 to 60 years. The coverage of women by routine inspections has increased from 92% in 2008 to 98% in 2014. The conducted activities have contributed to a decline in CC incidence in Karaganda oblast from 10.3 per 100,000 in 2012 to 10.0 per 100,000 in 2014. The share of stages I-II of CC has grown from 68.3% to 79.6%. 100% of CC cases were cytomorphologically verified in the years of study. The incidence and detection of stages I-II of CC have actually improved, with a high level of verification. The implementation of screening programs, including screening for CC, also improved the situation. Thus, the share of patients with stages I-II of CC detected during screening activities has improved from 73.7% in 2012 to 92.6% in 2014. At the same time, the number of patients with stage IV of CC has decreased from 5.3% to 3.7%, respectively.

Conclusion: The collaboration and well-organized work of cytologists and clinicians involved in early diagnostics and adequate therapy of CC pathology ultimately contributes to the reduction of CC incidence and the decline in CC morbidity and mortality. This also improves the course of rehabilitation, the disease prognosis and life quality of patients with CC.