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The Role of Screening in Early Diagnosis of Breast Cancer

Allaberganova Khadicha Muradkhanovna
Khorezm branch of Republican specialized scientific and practical Medical center of oncology and radiology of the Ministry of Health of the Republic of Uzbekistan

Gafur-Akhunov Mirza-Ali Allayarovich
Center for the development of professional qualifications of medical workers of the Ministry of Health of the Republic of Uzbekistan

Yigitaliyev Alisher Bakhodirovich
Fergana Medical Institute of Public Health

Abstract: The article presents data on early diagnosis of breast cancer. A comprehensive analysis of statistical data and risk factors for breast cancer, the use of self-examination, mammographic screening and the determination of tumor markers is carried out. Early detection of breast cancer reaches 80% with mammographic screening and, accordingly, the mortality rate is reduced by 20-30%.

Keywords: breast cancer, screening, tumor markers, risk factors, mortality reduction, survival, mammography.

Introduction.

Breast cancer statistics : Breast cancer accounts for 28.8% of all oncological diseases. In 2022, more than 2.3 million new cases of breast cancer were registered worldwide, with about 46,000 such cases being diagnosed annually in Russia. As of 2016, there were >2.8 million women with breast cancer in the United States (including women undergoing and those who have completed treatment). The upward trend in incidence is observed primarily among the urban population and in overweight women. More than half of all patients are women aged 50–69, and 11% are patients under 45 [41].

The incidence of breast cancer (BC) is steadily increasing by 1–2% every year . In Russia, it ranks first in the structure of malignant neoplasms among the female population. In 2020, the share of breast cancer was 21.7% of all cases of malignant neoplasms in women, and in the age group of 30-59 years, this figure was 28.9%. The absolute number of cases in 2020 was 64,951 per 100 thousand population, with 1,289 at the age of 30-34 years, and 2,726 at the age of 35-39 years (29.75% of the total)

The probability of developing breast cancer increases with age. The risk of breast cancer over 10 years is 1:72 for women aged 40–49, 1:36 for women aged 50–64, and 1:29 for women over 70. Breast cancer is the most common cause of death in women compared to other forms of malignant neoplasms. In Western Europe and North America, it is the leading cause of death in women aged 35–54 (reaching 20%), and after 50 years, it is the second cause of death after cardiovascular diseases. In Russia, mortality from breast cancer is approximately 2 times lower than the incidence, while in most EEC countries and North America it is 3 times lower.

Breast cancer is most common in the United States (99.4%), where this pathology develops in every eighth woman , and in Western European countries (82.5%), where every tenth woman gets sick. Lower rates (30%) are typical for most countries in Africa and Asia (Parkin D., Fernandez L., 2006). In China, with an indicator of 18.7%, the annual increase in breast cancer incidence is 5%, in Russia 3.3%. In the United States, breast cancer is more common in white women than in blacks - 79% and 47%, respectively. The incidence rates of breast cancer in white and Japanese women are 92.8% and 47.6%, respectively (Ferlay J . et al .,1998).

According to statistics from the World Health Organization, in 2020, breast cancer was diagnosed in 2.3 million women, with 685,000 deaths from this disease registered worldwide. All women in the world at any age who have reached puberty are at risk. But it should be noted that the incidence rate increases with age.

The significant decline in breast cancer mortality in the United States from 1975 to 2000 is attributed to continued improvements in both screening mammography and treatment. According to the World Health Organization (WHO), improving breast cancer outcomes and survival through early detection remains the foundation of breast cancer control policies.

About 46% of breast cancer cases in economically developed countries occur in the elderly, and by 2050 this figure is projected to increase to 71%. Breast cancer is more common in developed countries: the incidence rate in Western Europe is 89.7 per 100,000 women, while in East Africa it is 19.3 per 100,000. These differences are determined by several factors: the age of the woman at the birth of the first child (pregnancy and childbirth before the age of 35 reduce the risk of developing breast cancer); lactation (a long period of breastfeeding helps protect the female body - for every 12 months of feeding, the risk decreases by 4.3%); insufficient early detection of the disease [1 1].

Risk **factors .** Screening programs are designed for early detection of existing breast cancer , but not for its prevention. The main risk factors for the development of breast cancer begin to be realized at the age of up to 30 years, but its prevention, as a rule, is thought about after menopause .

Selective screening, i.e. examination of women with an increased risk of developing breast cancer, is especially relevant. This requires:

1. formation of high-risk groups development of breast cancer;
2. identification of persons with genetic disease among them predisposition to developing breast cancer,
3. dispensary observation of patients with benign diseases of the mammary glands, including periodic examinations by a mammologist, instrumental and laboratory tests [12].

To determine the relative risk of developing breast cancer, many different methods have been proposed with an assessment of each risk factor in points, grouping of factors taking into account age, various variants of precancerous pathologies [2] .

Breast cancer detected at early stages has a more favorable prognosis and high rates of relapse-free and overall survival. Thus, at stage I, the 5-year overall survival rate is >90% with radical treatment

Tumors detected in patients under 40 years of age have a more aggressive course and worse survival rates compared to breast cancer detected in patients over 40 years of age (odds ratio (OR) 1.52; confidence interval (CI) 1.37–1.74). Such tumors are characterized by a larger tumor node size, a higher degree of malignancy (grade III), lack of expression of hormone receptors, and more frequent invasion of the lymph nodes ($p < 0.01$) [2].

When determining risk factors for the development of malignant neoplasms for various organs, it is necessary to take into account the patient's family history and probable polygenic risks [22]. The presence of several patients with malignant neoplasms among relatives, especially of the same localization, may indicate the presence of a hereditary mutation, which increases the risk of developing cancer in a healthy relative at a relatively young age.

Unfortunately, there are no real ways to prevent the occurrence of breast cancer, because it is a multifactorial disease. However, if breast cancer is recognized in the preclinical period with a tumor size of up to 1 cm^3 , when the probability If the number of metastases is small, then most patients can be cured (although 10–15% of patients at this stage will subsequently develop metastases). Therefore, practicing physicians should be oriented toward identifying tumors measuring 1 cm3 or less.

According to the well-known model, the period of the "natural history of growth" of breast cancer (Schwartz J., 1961) is the time from the appearance of the hypothetical first cancer cell to the death of

the patient. The tumor reaches the size of 1 cm3 after 30 doublings, i.e. over a period of 2 to 18 years, depending on the doubling time (DT) of the tumor. The rate of tumor growth and metastasis determines the "natural history" of the disease.

Women with early onset of menstruation (before age 12), cycle disorders, late menopause, dysfunction of the thyroid gland and adrenal glands are more likely to get sick. Mutations in the BRCA1 and BRCA2 genes, long-term hormonal therapy and a history of breast cancer significantly increase the risk, while early childbirth, an increased number of births and a long period of breastfeeding have a protective effect.

According to the National Cancer Institute (NCI) , mammographic examinations help to reduce mortality in women over 50 by 1/3. Randomized controlled trials in women aged 40-74 years due to early detection of the disease note a relative reduction in mortality of 15-20%. The absolute reduction in mortality in women examined annually for 10 years is about 1% (in 4 out of 10 thousand women who began diagnostics at the age of 40, in 50 out of 10 thousand , first examined at the age of 50).

The impact of risk factors that cannot yet be prevented in menopausal women is currently estimated as follows: mutation of the BRCA1 and BRCA2 genes – about 5% of all cases of breast cancer; height of the woman and age at menarche – 9%; age at first birth and number of children born – up to 18% of cases of breast cancer [25].

According to research, in the US, 17% of cases could be prevented by maintaining optimal body weight; women who have undergone bariatric surgery are less likely to develop breast cancer during menopause after adequate weight loss.

5% of breast cancer cases can be prevented by eliminating alcohol consumption. The role of active and passive smoking in the development of breast cancer has been studied for a long time, but no clear links between these factors have been found.

Early initiation of preventive measures (in the 3rd–4th decade of life) can reduce the risk of breast cancer by 50%, and if they are started in childhood by 68%.

Approximately 5-10% of breast cancer cases are associated with gene mutations [25]. Currently, much attention is paid in the scientific literature and the press to new developments in the field of carcinogenesis, especially breast cancer. DNA research in families with breast cancer has confirmed the genetic cause in some of these families. The first gene for breast cancer has been identified (BRCA1) on chromosome 17 and the second gene (BRCA2) on chromosome 13.

Despite the fact that breast cancer is a visual localization and is easily accessible for examination, stage I and II breast cancer is diagnosed in only 57.6% of patients, and the mortality rate in the first year of life from the moment of diagnosis is about 12.6% of cases. Patients with advanced forms of breast cancer make up a high percentage of observations. Analysis of the causes of advanced disease showed that to a large extent, advanced disease is associated with the low medical culture of the population: 42% of patients postponed their visit to the doctor, citing their busy schedule, unfavorable situation at work, family circumstances, etc., in 10.9% of patients the reason was the fear of going to the doctor, in 6.5% of cases women self-medicated, which led to a sharp progression of the disease. However, in 32.5% of cases, advanced disease is the fault of general practitioners due to their low oncological literacy and lack of oncological alertness. In 51.7% of patients, 1 to 6 months passed from the moment of the appearance of clinical signs of breast cancer to diagnosis.

Female patients under 40 years of age are more likely to have a family history of breast cancer than female patients over 60 years of age: 24% versus 17% [24]. Mutations in the BRCA1 and BRCA2 genes increase the risk of developing breast cancer by 5 times, with the maximum peak of breast cancer diagnosis observed in carriers of BRCA1 mutations at the age of 35–39 years [7].

The development of this pathology can be caused by various general factors: age (breast cancer occurs more often with age), obesity, alcohol consumption, hereditary predisposition, radiation exposure, tobacco use, and hormone therapy during the postmenopausal period. Unlike other cancers that occur

due to infection (for example, cervical cancer), adenocarcinoma of the mammary gland is not associated with infection and the influence of certain pathogens.

Uncertain etiology and lack of specific preventive measures are the main reasons for the popularity of this disease.

Frequently encountered tumors producing estrogen and progesterone receptors are explained by a certain rhythm of life of modern times, which includes birth control, obesity. The absence of regular pregnancies and lactations in reproductive age disrupts the physiological functions of the mammary gland, which leads to a violation of fluctuations in the level of steroid hormones and cell renewal. And life in conditions of unlimited access to food has led to the fact that obesity has become one of the most significant and popular diseases of our time. It is also worth noting that after menopause, adipose tissue is a particularly important source of circulating estrogens. The emergence of ER / PgR -positive tumors is often associated with the age of patients, i.e. this type of tumor occurs in older women. ER+/ PgR + is characterized by a sluggish course and sensitivity to endocrine therapy. Risk factors for other types of breast cancer, such as triple-negative breast cancer or HER2-associated tumors, have been studied to a much lesser extent. For example, about 20% of ER/ PgR -negative breast cancer is detected in women who have mutations in the BRCA1 gene. Such BRCA1-associated cancers are typical for young women and are practically not associated with lifestyle. But they are characterized by a tendency to an aggressive course. Such typical diversity of breast cancer cannot but affect the effectiveness of screening and treatment of this disease.

self-examination . Breast self-examination as an independent method is not sufficient, but still an important element in detecting cancer at an early stage. It is a cheap method, generally available and does not require complex technical training, as it can be performed at home.

Women in menopause should also examine their breasts once a month, preferably on the same day of each month. There is also evidence of low sensitivity of the method - 12-14%. Its disadvantage is the high level of false positive results and overdiagnosis. [31].

According to the results of the largest domestic study conducted within the framework of the educational program on self-examination, in which 123,746 patients took part, it was shown that puncture biopsy was performed more often in the self-examination group (7.5%) compared to the control group (3.5%), $p < 0.01$. Also, in the self-examination group, the frequency of detection of benign (1.1%) and malignant (0.85%) tumors was higher than in the control group (0.5 % and 0.69%, respectively), $p < 0.05$. At the same time, the difference in detection of tumors at an early stage (T1N0M0, Tis) in the main and control groups was insignificant - 23% and 17.6%, respectively. The authors also did not note a significant difference in mortality rates in both groups [11] .

In another study, which involved 266,064 women working in 519 factories in Shanghai, patients were randomly assigned to either a self-examination training and active self-examination group (132,979 women) or a control group (133,085 women). There were 135 (0.10%) breast cancer deaths in the study group and 131 (0.10%) in the control group. Cumulative breast cancer mortality rates after 10–11 years of follow-up were similar in both groups (OR 1.04; 95% CI 0.82–1.33; $p = 0.72$). In addition, breast self-examination increased the number of mammograms and ultrasound examinations performed and the number of biopsies with a negative (benign) result [37].

A decrease in sensitivity was noted from 41% in women aged 35–39 years to 21% among patients aged 60–74 years. Self-examination training increases physician attendance.

The results of self-examination in St. Petersburg (1985) of 120,310 women aged 40–64 years were analyzed [10]. The training group consisted of 60,221 women, the control group – 60,098 women. BSE training was carried out in small groups of 5–20 women by nurses and doctors. After 5 years, 493 cases of breast cancer were diagnosed in the BSE group and 446 in the control group, with 157 deaths in the BSE group and 164 in the control group. To date, no study has shown a decrease in breast cancer mortality in the self-examination group.

Breast cancer screening. Mass examinations of the population for the purpose of early detection of the disease are referred to as screening studies. The effectiveness of the latter is determined by the reduction of mortality rates. In 1963–1994, in different countries 8 randomized studies of breast cancer screening were conducted. The study results reveal the value of mammography, clinical examination (CBE – Clinical Breast Examination) and self-examination (BSE – Breast Self - Examination) of the mammary glands on the incidence of mortality from breast cancer [22] It is known that breast cancer has an asymptomatic phase that can be detected using mammography. Mammographic screening is a sensitive (77 to 95%) and specific (94 to 97%) method of examination and can be used in most women [27]. Screening means preventive examination of healthy population groups in order to detect the disease at an early stage.

The main goal of screening programs for early detection of breast cancer is to reduce mortality rates from this disease by diagnosing early stages of breast cancer. Screening for detection of malignant neoplasms of the mammary glands is carried out at the age of 40 to 75 years inclusive in the form of mammography of both mammary glands in 2 projections with double reading of radiographs once every 2 years [28]

According to a number of authors, among carriers of BRCA mutations, screening measures aimed at diagnosing tumors in target organs are optimally started at the age of 25 to 30 years. To assess patterns of disease manifestation time in several studies, the age of onset of familial malignant neoplasms was analyzed. One study was aimed at studying various familial syndromes, another at studying the age of disease onset in one first-degree relative, and a third at studying the age of disease onset only in carriers of BRCA1 or BRCA2 mutations [8]. Knowledge of the probable age of malignant neoplasm manifestation will allow optimization of the initiation of screening and preventive measures.

According to ESMO recommendations, if a healthy carrier of a germline mutation in the BRCA1, BRCA2 or PALB2 genes has a germline mutation, screening measures should begin 5 years before the age of cancer manifestation in the youngest family member, but no later than 30 years.

In BRCA1 mutation carriers, regardless of age, no effect of additional mammographic screening was observed, but in carriers of other penetrant mutations, its benefit for early detection of breast cancer was noted [15]

The creation of mobile complex mammological groups is one of the forms of implementing early diagnostics of breast cancer in the conditions of Russia by bringing specialized oncomammological care closer to the female population of areas remote from specialized medical institutions. To effectively solve the problem of early diagnostics of breast cancer, a new approach to training personnel capable of mastering the most complex diagnostic equipment is needed.

Frequent false positive results cause anxiety in patients, lead to the use of additional diagnostic methods and increased costs . The justification for screening correlates with the patient's age. In 6-46% of cases, patients with breast cancer may have negative test results , especially with dense breast tissue, in which case additional examinations and comparative assessment of the data obtained help . [9]

Mammographic screening for breast cancer has reduced mortality from this disease in developed countries. In particular, in Norway and Denmark, where breast cancer screening has been carried out most extensively and comprehensively, mortality from breast cancer has decreased by 10% and 25%, respectively [30].

A review of more than 5.6 million screening mammograms from the U.S. National Mammography Database from 2008–2014 found no significant age-related reasons for stopping mammographic breast cancer screening. With continued screening in women over age 75, there was an increase in the detection rate of breast cancer per 1,000 mammograms and an increase in the positive predictive values for recommended and performed biopsies.

World experience shows that due to active implementation of screening programs in Western Europe and North America, it has become possible to detect stage I of the disease in 70-80 % and , accordingly

, to recover from breast cancer in 60-80 % of women . If in the Russian Federation mortality from breast cancer continues to increase , amounting to 50 % of the incidence rate , then in most countries of Europe and North America there is a tendency towards a decrease in mortality from breast cancer (up to 30% of the incidence rate). Mammography is the main element of breast cancer screening . The effectiveness of using mammography as the main screening test has been tested in numerous randomized trials conducted in the USA . When conducting a multivariate analysis , N. Boyd et al . (2014) noted that the main reason for false-negative breast cancer is not the optical density of the tissue, but a larger volume of dense tissue in relation to the entire area of the gland. The second significant risk factor was young age [1 6] . Based on this work N. Boyd (2014) proposed a standardized criterion – the percentage of mammographic density (percent mammography density). The risk of breast cancer in women with a mammographic density percentage of 75% is 4–6 times higher compared to those with this parameter of 10% [17] . Several methods can be used to calculate breast density. The American College of Radiologists (College of Radiology (ACR) proposed a uniform reporting form for mammographic examinations Breast Imaging – Reporting and Data System (BI - RADS), which includes 4 degrees - a, b, c, d. It is significantly subject to subjective assessment, but is easy to use and applicable in the context of screening. According to the meta-analysis of J. Melnikow et al . (2014) , in 12-18.7% of women, the degree of breast density will be reclassified into a fundamentally different category during screening (for example, from "non-dense" to "dense"), which has a fundamental impact on determining the risk group and the intensity of preventive examination.

The mammographic picture of early breast cancer is highly variable. The characteristic signs include the presence of clusters of calcifications , nodes with pointed edges, and multinodular dense formations. However, in a significant proportion of patients, radiological signs of the disease are less pronounced and the diagnosis is made on the basis of minimal signs of the disease - the presence of one dilated duct, local heterogeneity of the gland's architecture, asymmetry, signs of increased tissue density [33]

Making a correct diagnosis often requires the radiologist to perform a non-standard diagnostic search and a subjective, non-standardized assessment of the observed picture. Microcalcifications (microcalcifications) are often the only manifestation of early invasive breast cancer and ductal carcinoma in situ . At the same time, calcifications are most often a sign of benign processes in the mammary gland, and even in the presence of suspicious calcifications that require a biopsy, the diagnosis of breast cancer is confirmed only in 1/3 of patients [40]

According to localization, calcifications are lobular, ductal and stromal . The first are most often found in benign changes and are most often detected in sclerosing adenosis , cysts and fibrocystic mastopathy. In the latter, calcifications are usually located bilaterally in the form of "cups"

The detection rate of breast cancer was 0.2% of all examined patients and corresponded to the average level of tumor detection during mammographic screening in the Russian Federation [8]. Among the patients with breast cancer detected in 2013 during mammographic screening, 86.6 % of women (2011 – 78.8%) had tumors in the early stages of the disease – I and II. At the same time, mortality from breast cancer decreased from 27.6 to 20.7 per 100 thousand people from 2009 to 2013, which confirms the effectiveness of mammographic screening. Thus, the detection rate of early stages of breast cancer during mammographic screening is significantly higher than when women self-referral for an appointment, in which stage I and II in 2013 amounted to 75.3%.

screening is carried out as part of a preventive medical examination, which is carried out annually. It includes a clinical examination of the mammary glands by a gynecologist , ultrasound examination of the mammary glands for all women aged 30 and over, and X-ray mammography for all women over 40 (once every 2 years in the absence of pathology). If necessary, the examination can be carried out more often (monitoring the condition), and can also be supplemented with other examination methods - targeted mammography, MRI examination. (Vysotskaya I.V.)

Women with detected or suspected breast pathology after undergoing a preventive medical examination are referred to a specialized oncologist who has specialized in mammology, who clarifies the diagnosis and determines the patient's management tactics.

Analysis of the work of the medical and sanitary unit on breast cancer screening convincingly shows positive results, since the diagnosis of breast cancer in the early stages (I-II) was on average 90% (in the Russian Federation this figure is 25-30%).

1. Comprehensive work aimed at early diagnostics of breast cancer, including rational and consistent use of clinical and paraclinical diagnostic methods, conducting a dispensary examination, as well as oncological alertness made it possible to diagnose breast cancer at the initial stage of tumor development. Early diagnostics of this disease, in turn, made it possible to apply an organ-preserving type of surgical treatment (lumpectomy) to the patient, significantly improving the rehabilitation prognosis and quality of life.
2. The experience gained convincingly proves the correctness of the chosen approach to diagnosing breast cancer and the advantage of active tactics in relation to patients with non-palpable forms of breast pathology at the preclinical stage with the wide use of clarifying examination methods (targeted mammography, puncture of the formation under ultrasound or mammography control, blood testing for tumor markers).

The basis for early detection of breast cancer is mammographic screening, which is recommended by the International Agency for Research on Cancer (IARC, WHO) for women aged 50-70. Mammography allows us to detect tumors from 2 mm in the early stages of the disease, which are often not detectable by touch. X-ray mammography is the most sensitive and gentle technique for detecting breast cancer. That is why it was chosen as the main research method. But its information content depends not only on the quality of the images, but also on the interpretation (qualified specialists are important). Depending on the stage of the disease, the sensitivity of the PET method in the primary detection of breast cancer ranges from 48 to 96%, specificity - from 73 to 100%, as in the case of using MRI, the sensitivity of PET depends on the size of the pathological lesion. In the diagnosis of breast disease, the radiothermometry method is also actively used , the sensitivity of which reaches 85-92%, and the specificity - 70-75%. But, unfortunately, high sensitivity and often insufficient specificity of the above methods can lead to false positive results. Therefore, it may be necessary to perform an invasive diagnostic procedure - taking a tissue sample and examining it using microscopic analysis . Despite such a wide variety of diagnostic methods, 80% of women accidentally discover breast cancer, which most often corresponds to late stages . Thanks to mammographic screening, MRI, PET-CT and ultrasound, it is possible to detect a tumor at an early stage, but it is worth noting that, according to statistics, only 59% of the female population undergo such types of diagnostics in the Russian Federation. As a result, stage 1 breast cancer is detected in only 10-15% of patients. OSO followed by radiation therapy is the "gold standard" in the treatment of early breast cancer.

Screening involves the use of a method for identifying hidden pathology in a large group of apparently healthy individuals and therefore must meet the following requirements:

High sensitivity of the method or test used, which detects most malignancies in the population being examined with a minimum number of false negatives. z $_{z}$ High specificity of the method, which excludes most healthy women who do not have breast cancer and minimizes the number of false positives . Acceptable average cost per detected case of cancer. Minimal harm to health of the person being examined. Ease of operation and maintenance of the equipment.

Screening should not be confused with diagnostics. Mammography only allows detecting areas of the gland parenchyma that are suspicious of a tumor, the nature of the changes of which requires clarification using additional diagnostic methods (stereotaxis biopsy using the Mammotome-Mammotest complex or directed biopsy using ultrasound).

X-ray mammography as a method of obtaining a tumor image is focused on its minimum size or minimal (preclinical) manifestations (microcalcifications , disruption of the ductal architecture, etc.), but not on its biological characteristics. It is generally believed that the smaller the size of the detected tumor, the better the prognosis of the disease and the higher the effectiveness of screening. However, it is now becoming clear that not all minimal (less than 1 cm) tumors detected through screening are characterized by a good prognosis.

A number of large studies in the last 1.5 years have presented long-term treatment results for breast cancer patients with tumors smaller than 1 cm (T1a-bN0M0), i.e. tumors that screening is ideally aimed at detecting. It turned out that in the presence of HER2 expression, 5-year relapse-free survival was only 77% versus 94% (in the group of patients with HER2-negative tumors). Patients with pT1abN0M0 breast cancer with HER2 positivity had a 7.8-fold higher risk of distant metastasis compared to patients with ER+/HER2-negative disease.

The IARC guidelines, based on 25 years of screening experience in Europe and North America, are simple and clear: 1) one screening test is used, mammography; 2) women are screened every 2 years and over many years; 3) all women aged 50-69 years (regardless of risk group membership) are screened and invited to screening; 4) all women invited to participate in screening should be informed that no other screening tests except mammography (self-examination , physical examination, ultrasonography , etc.) lead to a reduction in mortality from breast cancer; 5) in countries where nationwide mammographic screening and standard treatment are not practiced, no reduction in mortality from breast cancer has been observed .

Screening is a mass screening of a healthy population with the aim of identifying a disease at such an early stage that it will reduce mortality.

Screening should ultimately lead to a reduction in mortality from the cancer for which it is used to detect preclinically . Indirect signs of effectiveness include a reduction in the detection rate of common forms, an increase in the detection rate of early cancers, and an improvement in survival.

It is not advisable to screen for those forms of cancer that, despite active detection at preclinical stages and appropriate treatment, progress, metastasize and lead to the death of the patient. Eight randomized trials of breast cancer screening were conducted between 1963 and 1994. The results of these studies provided information on the effects of mammography, clinical examination (CBE) Breast Examination) and self-examination (BSE – Breast Self-Examination) of the mammary glands on mortality from breast cancer [23]

Today, the leading method of screening for breast cancer is mammography, which has reduced mortality from breast cancer to 30%.

The key factor in achieving the main result of breast cancer screening is the high quality of the entire screening program process. And the radiologist plays a key role here, taking full responsibility for the quality of the mammographic examination and its diagnostic interpretation. Full knowledge and understanding of the risk/benefit of mammographic breast cancer screening requires the organization of infrastructure, the formation of a team including clinical and non-clinical specialists involved in this process (epidemiologist, physicist, surgical oncologist, pathologist , radiologist, radiologist).

A critical analysis of the experience of the European Community countries demonstrates the existence of a certain balance between desirable and undesirable effects even in organized high-quality programs. The sensitivity and specificity of mammographic examination and its interpretation must be optimal. In Russia, there is no state program for breast cancer screening. Currently, in 80% of cases, breast cancer is detected by the patient independently, in 10% - during a medical examination, and only in 10% - during mammography.

Mammographic screening of women aged 50–69 years reduces mortality from breast cancer by 20–25%. The International Agency for Research on Cancer (IARC) and the WHO Cancer Department recommend only one test, proven in 7 prospective studies – mammography (preferably digital) for all

(excluding risk groups) women included in the targeted cohort aged 50–69 years. With the introduction of mammographic screening, significantly the number of detected intraductal cancers has increased mammary gland in situ . The proportion of detection of non-palpable breast cancer is also high. In this case, the radiographic picture has its own characteristics, due to the small size of the tumor, the absence of stringiness along the edges of the node and hypervascularization .

A systematic review and independent expert assessment found a significant reduction in breast cancer mortality of 15–21% among women aged 50–69 who were screened [20].

Humphrey LG et al. (2012) reported a significant reduction in breast cancer mortality in screened women younger than 50 years of age in addition to a clear reduction in mortality in women older than 50 years [28].

There are works in the literature indicating the shortcomings of mammographic screening in a number of cases. These situations are described in detail in the review article by V. F. Semiglazov (2014) [9].

In Norway, women aged 50–69 undergo mammography every two years. An evaluation of this approach suggests that mortality from breast cancer is reduced by approximately 20% in this group of women [24]. It has also been shown that the more women participate in mammography screening, the more economically beneficial it is for health care [39]. In the case of breast cancer, early stage treatment and screening are much cheaper than treating patients with advanced stages.

However, in recent years, some epidemiologists and other researchers in the field of medical statistics have questioned the success of mammographic screening, considering suboptimal randomization in some randomized trials, as well as the contribution of effective adjuvant measures to reducing mortality from breast cancer [36]

The organization and implementation of measures for the early diagnosis of cancer is also considered as a component of secondary prevention, and the prevention of cancer recurrence as tertiary cancer prevention. Secondary prevention of breast cancer includes early detection and treatment of precancerous diseases of the mammary glands - various forms of mastopathy, fibroadenomas, other benign tumors and diseases, as well as endocrine disorders system, diseases of the female genital organs, liver dysfunction. The organization of the weekend developed by us The mammography complex and mobile appointments with oncology specialists increases the availability of specialized oncological care for remote rural areas of the region.

The development of effective methods for diagnosing the MC process in patients with breast cancer is of great clinical importance, since it largely determines the tactics of surgical and radiation treatment. In accordance with the recommendations of the TNM system, the MC process is defined as a special type of cancer growth, which is represented by two or more nodular formations located in different quadrants of the breast.

The density of breast tissue was determined according to the BI-RADS system: A- completely fatty, B- fatty with scattered fibroglandular tissue, C- heterogeneously dense and D- extremely dense. In accordance with the international recommendations of the ACR (American College of Radiology) the mammary gland was assessed as dense in C and D variants of the mammographic picture. In our study, increased X-ray density of mammary gland tissue was found in 171 (39%) of 437 women with suspected breast cancer.

The final decision on the presence or absence of the MC process was made on the basis of a morphological examination of the surgical material.

In particular, our studies indicate that women with dense breast tissue mSG increases the sensitivity in the diagnosis of early breast cancer by 82% [23]. Other authors also point out the potential of using mSG to detect breast cancer in women with dense breast tissue [36].

When a population of women is screened, not all cases of breast cancer are detected during the initial round of screening; some tumors are diagnosed in the post-screening period using a clinical method (palpation). These are the so-called "interval" or interscreening breast cancers detected in women with

negative screening results. Typically, the proportion of interval breast cancers ranges from 15% to 25%. The higher the frequency of interval (missed during screening) breast cancers, the less reason to expect a decrease in mortality in this population. The probability of detecting cancer during screening depends on the duration of the "preclinical detection time" of the tumor (length time detectable preclinically). The longer this interval, the greater the chance of detecting a tumor. Thus, many tumors detected during screening are characterized by slow growth and a good prognosis.

The diagnostic accuracy of digital and analog (film) mammography, projected onto the entire population, gives comparable results. However, the accuracy of digital mammography is significantly higher than that of film mammography in the following cases: • when examining women of the age group up to 50 years; • when examining women with heterogeneously dense or very dense mammary glands; • when examining women in the period before menopause or early menopause (G.P. Korzhenkova , 2006).

Magnetic resonance imaging (MRI) can effectively detect tumors in high-risk women with a BRCA 1 or BRCA 2 mutation, but it is not an acceptable screening test due to its high cost and the lack of uniform standard approaches to its implementation. In addition, MRI of the breast is highly sensitive but not specific, which results in a large number of false-positive results, which in turn can lead to unnecessary biopsies. For women with a normal risk of developing breast cancer (and there are over 90% of these), mammography is still the best screening method.

The effectiveness of using mammography as a primary screening test has been tested in numerous randomized trials conducted in the United States (Shapiro , 1966), Scotland (Alexander, 1999), Canada (Morrison and Miller , 1992), Sweden (Tabar , 1999; Andersson , 1997; Nystrom ,

In the Russian Federation, about 50 thousand new cases of breast cancer are registered annually. About 25 thousand die from this disease. One third of these losses could be avoided if screening were carried out - preventive mammographic examination of healthy women, allowing to detect early, curable forms of tumors.

According to the European standard, 60 examinations should be performed daily on one mammograph, and the number of studies per year (210 working days) is 12,600 screening mammograms only. Taking this information into account, 486 mammographs are needed to conduct mammographic screening in Russia.

If analog (film) mammographs are already available or are being purchased, then another 486 developing units, special X-ray film and chemical reagents are needed. If digital technologies are used, then systems for digitizing mammograms or digital converters (digital pacs) – 111 pieces.

High-quality mammographic screening ultimately leads to a significant (up to 30%) reduction in mortality from breast cancer. Women who, for various reasons, do not participate in mammographic screening should be informed that there are no other screening methods (physical [palpatory] examination, self-examination) that could also effectively reduce mortality from this disease.

In 2011, the effectiveness of mammological examination in the Chelyabinsk region doubled and amounted to 0.67% of the number of those who underwent mammography. Breast cancer was diagnosed in 740 women, 67.3% of whom had stage 1-II tumors. For comparison, early-stage breast cancer among the entire female population of the region in 2011 was detected in 63.7%, which is less than the screening results.

CA 15–3 and CA 27.29 as markers of breast cancer (BC). CA 15–3 and CA 27.29 tests allow to determine the circulation of MUC-1 antigen in the peripheral bloodstream. Since the release of the latest ASCO recommendations, several studies have been published confirming the prognostic significance of these circulating markers in early stages of BC [13], who conducted a study involving 1046 patients, report that CA 15–3 predicts a worse outcome in univariate but not multivariate analysis, which evaluates factors such as tumor size, lymph node status, histological grade of malignancy, and estrogen receptor status. M. Gion et al . [13] reported high prognostic value of CA

15–3 in a COX regression model that included parameters such as age, estrogen status, and tumor size in 362 node-negative patients. Although serum markers CA 15–3 and CA 27.29 seem to have prognostic value, their role in the diagnosis of early breast cancer remains unclear [29]

Several well-designed studies have shown that increases in CA 15-3 and CA 27.29 after primary and/or adjuvant therapy can predict relapse 5 to 6 months before the onset of other symptoms or positive test results. Although several studies have been reported since the last publication of the ASCO guidelines to determine the value of these serum markers in predicting relapse [20]

There is currently no basis to recommend CA 15–3 and CA 27.29 for use in routine practice. In one study of 53 women with metastatic breast cancer, CA15-3 and CEA were elevated in 94% and 69% of cases, respectively. CEA was elevated in only 1 case where CA 15-3 was not elevated [38]. This suggests that it is reasonable to measure both MUC-1 and CEA in a patient with metastatic disease. If MUC-1 is elevated, there is no need to monitor CEA.

A total of 13 categories of breast tumor markers were considered. The following categories proved to be reliably clinically applicable and were recommended for practical use: CA 15–3; CA 27.29; CEA (in metastatic breast cancer); ER; PR; human epidermal growth factor receptor 2 (HER2 neu), UPA and PAI-1, as well as several tests of multiparameter gene expression studies.

Thus, early diagnostics of breast cancer is one of the urgent problems of clinical oncology. Early diagnostics is based on a comprehensive examination of healthy women . taking into account age, reproductive function, the particular development of risk factors and screening studies using X-ray mammographic examination once every 2 years taking into account age and risk factors. This allows increasing the number of patients diagnosed with early-stage breast cancer by 20-30% and, accordingly, reduces the mortality rate.

List of references.

1. Высоцкая И. В. Скрининг рака молочной железы: ситуация в России // Онкология сегодня № 4–2013/№ 1–2014. С. 10.
2. Давыдов М. И., Ганцев Ш. Х. Онкология 2010, С. 42, С. 377
3. Давыдов М. И., Ганцев Ш. Х. Онкология 2010, С. 42, С. 377.
4. Доброкачественная дисплазия молочной железы. Клинические рекомендации. Министерство здравоохранения Российской Федерации, 2020.
5. Довгалюк А.З. рак молочной железы. С.-Пб., НТФФ “Полисан”;2001.с. 47-8
6. Любченко Л.Н. Наследственный рак молочной железы и/или яичников: ДНК-диагностика, индивидуальный прогноз, лечение и профилактика. Автореф. дис. … д-ра мед. наук, 2009. 281 с. Lyubchenko L.N. Hereditary breast and/or ovarian cancer: DNA diagnostics, individual prognosis, treatment, and prevention. Summary of thesis … of doctor of medical sciences, 2009. 281 p. (In Russ.)
7. Роль и место скрининговой маммографии в диагностике рака IN SITU. Л.Е. Комарова. ГУ РОНЦ им Н.Н. Блохина РАМН, Москва // Опухоли женской репродуктивной системы. – 2008. – № 3. – С. 20-23.
8. Семиглазов В. Ф. Что лучше: маммографический скрининг или системное лечение? // Злокачественные опухоли. – 2014. –№ 4. – С. 3 – 9.
9. Семиглазов В. Ф., Моисеенко В. М. Программа «Россия» (СанктПетербург) ВОЗ по оценке эффективности самообследования молочной железы // Матер. I съезда онкологов СНГ, г. Москва, 1996. – Ч. 2. – С. 41
10. Семиглазов В.Ф., Манихас А.Г., Моисеенко В.М. и др. Результаты проспективного рандомизированного исследования значения самообследования в раннем выявлении рака молочной железы. Вопросы онкологии 2003;(4):434–41.

11. Хайленко В.А. Ранняя диагностика рака молочной железы info@oncology.ru

12. Чёрная а.В., Канаев С.В., новиков С.н. и др. диагностическая значимость маммографии и маммосцинтиграфии с 99м Tc-MIBI при выявлении минимального рака молочной железы // Вопросы онкологии. — 2017. — Т. 63. — № 2. — С. 274-280.

13. Ebeling F., Stieber P., Untch M. et al. Serum CEA and CA 15–3 as prognostic factors in primary breast cancer // Br. J. Cancer. – 2002; 86:1217–1222.

14. Gotzsche P., Jorgensen K. Screening for breast cancer with mammography (review). The Cochrane collaboration. The Cochrane library 2013, issne G., pp. 1–17.

15. Kuhl C., Weigel S., Schrading S. et al. Prospective multicenter cohort study to refine management recommendations for women at elevated familial risk of breast cancer: the EVA trial. J Clin Oncol 2010; 28(9):1450–7. DOI: 10.1200/JCO.2009.23.0839

16. Boyd NF, Huszti E, Melnichouk O et al. Mammographic features associated with interval breast cancers in screening programs. Breast Cancer Res 2014; 16 (4): 417.

17. Boyd NF. Mammographic density and risk of breast cancer. Am Soc Clin Oncol Educ Book 2013.

18. Brandt A., Lorenzo Bermejo J., Sundquist J. et al. Breast cancer risk in women who fulfill high-risk criteria: at what age should surveillance start? Breast Cancer Res Treat 2010; 121(1):133–41.

19. Claus EB, Risch N., Thompson WD Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. Cancer 1994; 73(3):643–51.

20. D'Alessandro R., Roselli M., Ferroni P. et al. Serum tissue polypeptide specific antigen (TPS): A complementary tumor marker to CA 15–3 in the management of breast cancer // Breast. Cancer. Res. Treat. – 2001; 68:

21. De La Lande B., Hacene K., Floiras J. et al. Prognostic value of CA 15.3 kinetics for metastatic breast cancer // Int. J Biol. Markers. – 2002; 17: 231–238.

22. Elmore JG, Barton MB, Moceri VM et al. Ten-year risk of false positive screening mammograms and clinical breast examinations // N. Engl. J. Med. – 1998. – Vol. 338, N 16. – P. 1089–1096. Tabar L., Chen HH, Fagerberg G. et al. Recent results from the

23. Elmore JG, Barton MB, Moceri VM et al. Ten-year risk of false positive screening mammograms and clinical breast examinations // N. Engl. J. Med. – 1998. – Vol. 338, N 16. – P. 1089–1096.

24. Forskningsrad N. Research-based evaluation of the Norwegian Breast Cancer Screening Program Final Report // Oslo: Norges forskningsrd , 2015.

25. Gion M, Boracchi P, Dittadi R, et al. Prognostic role of serum CA15.3 in 362 node-negative breast cancers: An old player for a new game // Eur. J. Cancer. – 2002; 38:1181–1188.

26. Hettipathirana T., Macdonald C., Xie J. et al. The value of clinical breast examination in a breast cancer surveillance program for women with germline BRCA1 or BRCA2 mutations. Med J Aust 2021; 215(10):460–4. DOI: 10.5694 / mja 2.51226

27. Humphrey LJ, Helfand M, Chan BK et al. Breast cancer screening: a summary of the evidence for the US preventive Services Task Force. Ann Intern Med. 2012 – Vol. 137(5). – pp. 347–360.

28. Humphrey L., Chan BKS, Detlefsen S., Helfand M. Screening for breast cancer: systematic evidence review. Ann Int Med 2002. DOI: 10.1059/0003-4819-151-10-200911170-00009

29. Khatcheressian JL, Wolff A, Smith T et al. American Society of Clinical Oncology 2006 update of the breast cancer follow-up and management guidelines in the adjuvant setting // J. Clin . Oncol . – 2006; 24:5091–5097.

30. Marmot MG. Altman DG. Cameron DA. et al. The benefits and harms of breast cancer screening: an independent review. Br J Cancer , 2013-vol. 108(11). – pp.2205–2240.

31. Profilaktyka raka szyjki macicy - NFZ [Internet]. [Cited 2021.

32. Sessa C., Balmaña J., Bober SL et al. ESMO Guidelines Committee. Risk Reduction and Screening of Cancer in Hereditary BreastOvarian

33. Sickles EA. Mammographic features of "early" breast cancer. Am J Roentgenol 1984; 143 (3): 461–4. 57. Kolyadina IV. Heterogeneity of early breast cancer: biological, population, and prognostic significance. Diss . … Dr. of Medicine. Moscow, 2015. [Kolyadina IV Geterogennost ' rannego raka dairy glands : biological , popular and prognostic znachenie . Dis. ... d- ra med. nauk . Moscow, 2015 (in Russian)..

34. Sidoni A., Cavaliere A., Bellezza G. et al. Breast cancer in young women: clinicopathological features and biological specificity. Breast 2003; 12(4):247–50. DOI: 10.1016/S0960-9776(03)00095-X

35. Silva O.E., Zurridia S. Breast cancer. A Practical Guide. Toronto; Novartis Oncology, 2005. p. 41-3.

36. Chessa F. et al. scintimammography with high resolution dedicated breast camera and mammography in multifocal, multicentric and bilateral breast cancer detection // QJ nucl . Med. Mol. Imaging. - 2009. - Vol. 53. - P. 133-143.

37. Thomas D., Gao D. Randomized trial of breast self-examination in Shanghai: final results. J Natl Cancer Inst 2002; 94(19):1445–57. DOI: 10.1093 /JNCI/ 94.19.1445

38. Tondini C., Hayes D., Gelman R. et al. Comparison of CA15–3 and carcinoembryonic antigen in monitoring the clinical course of patients with metastatic breast cancer // Cancer. Res . – 1988; 48:4107–4112.

39. Tornberg SA. Screening for early detection of cancer – ethical aspects // Acta Oncol . – 1999. – Vol.38. – pp. 77–81.

40. Villeirs G, Mortier M, De Potter C et al. Breast calcifications. J Belge Radiol 1995; 78 (1): 11–7.

41. Gofur-Okhunov , M. A., Yigitaliyev , A. B., & Karimov , O. M. (2024). Morphological Features and Methods of Treatment of the Diffuse Form of Breast Cancer. International Journal of Alternative and Contemporary Therapy , 2 (6), 20-29.