



Risk Factors for Breast Cancer

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Abstract: Breast cancer occupies a leading place among malignant neoplasms in women in all economically developed countries. Breast cancer is a serious medical and social problem for most developed countries of the world. Analysis of the qualitative characteristics of diagnosis, staging and treatment of breast cancer will routinely confirm the achievability of reducing the risk of cancer recurrence with an appropriate standard of treatment.

Keywords: breast cancer, diagnosis, qualitative indicators of cancer, HER2 status.

Relevance. Breast cancer occupies a leading place among malignant neoplasms in women in all economically developed countries. Thus, in EU countries the risk of the disease is 6-10 times higher than in Asian countries. In the United States, one in 28 women dies from breast cancer, and one in 8 is at risk for the disease. In the CIS countries, more than 50 thousand new cases of breast cancer are registered annually, and mortality from this pathology ranks first. According to EUSOMA, over the past twenty years in the United States and some developed European countries, mortality from breast cancer has decreased annually by 1-2%, thanks to early screening and constant improvement of diagnosis and treatment [9]. In Uzbekistan, there is an increase in the number of patients with primary breast cancer per 100,000 women, which in the Republic of Uzbekistan as a whole was 6.6. In the regions of Uzbekistan, the largest increase in incidence was noted in the Republic of Karakalpakstan - 1.7 times, and in the city of Tashkent - 1.5 times. In 2018, 3,578 women with breast cancer were registered in Uzbekistan. Today, approximately 18,000 women are diagnosed with breast cancer. The 5-year survival rate is currently 45% and the 1-year mortality rate is 1.1% [5]. Breast cancer mortality also increased from 1985 to 2004, and this increase was greater in Bukhara and Surkhandarya. area -3.9; 3.8 times respectively. [9] Another important factor is the rejuvenation of the disease in our republic. According to European scientists, about 90% of newly diagnosed cancers are epithelial forms of cancer, among them, one of the most common.

Material and methods. Diagnosis of breast cancer EUSOMA, with the participation of 24 leading experts "Quality indicators for the provision of services to patients with breast cancer " experts identified 17 main characteristics to assess the quality of care provided to patients with breast cancer: 7 for diagnosis, 4 for local surgical treatment, 2 for systemic treatment and 4 for cancer staging. Below is an abbreviated version, developed by EUSOMA experts, of the summary quality indicators for the diagnosis of breast cancer, which are recommended to all mammology departments in Europe to monitor the quality of services provided. Monitoring of quality indicators will make it possible to justify the medical and economic costs of each service in relation to the clinical outcome. Indicators of mandatory breast cancer testing methods: 1. Proportion of patients who have undergone a complete clinical and radiological diagnosis (preoperative mammography, ultrasound and clinical examination). 2. Proportion of patients who received specific diagnostic procedures (benign/malignant ratio). 3. Proportion of patients with invasive or in situ breast cancer who were diagnosed before surgery. 4. Proportion of patients with invasive cancer and prognostic/predictive

factors parameters (PPP) - histological type, histological degree of maturity, estrogen receptors (ER), progesterone receptors (PR), HER2 status; Proportion of patients with invasive cancer and with complete PPP - histological type, histological degree of maturity, ER, PR, HER2 status, pathological stage (T and N), size in mm (for invasive component), peritumoral vascular invasion and distance to the closest radial margin; Proportion of patients with invasive cancer and with PPP - dominant histological pattern, size in mm, (best pathological and radiological assessment if stage 2), histological maturity and distance to the closest radial margin. 5. Proportion of patients whose waiting time (between the date of the first diagnostic examination in the breast department and the date of surgery or the date of initiation of treatment) is within 6 weeks. 6. Proportion of patients who underwent MRI (at least 5% of cancers examined preoperatively). 7. Proportion of patients who received genetic advice.

Results. The efforts of EUSOMA experts are aimed at ensuring that, through routine measurements and evaluation of available indicators, the final result is achieved, which will ensure the quality of medical services provided with appropriate standards of diagnosis and treatment. Annual mammography screening and magnetic resonance imaging (MRI) of the breast are recommended for women at “very high risk” of developing breast cancer: positive BRCA-1 or BRCA-2 mutations, as well as other gene predispositions that increase the risk of developing breast cancer; untested carriage of a gene mutation, in carriers of the first degree of relationship; hereditary breast cancer syndrome, when the total personal lifetime risk is more than 25%. Mammography and MRI screening are, with lesser evidence, recommended for women with high marker risk, based on biopsy findings (atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ) and after chest radiotherapy (under 30 years of age or at least for the previous 8 years). ESMO experts recommend annual breast MRI and mammography in order to diagnose cancer at a more favorable, preclinical stage, for women with a family history of breast cancer, regardless of proof of carriage of the BRCA mutation. In case of test confirmation of BRCA carriage, patients are recommended to undergo preventive procedures.

The pathological diagnosis of breast cancer is based on an initial puncture biopsy obtained under ultrasound or stereotactic guidance. The pathological report should include: determination of the histological type; histological degree of maturity; immunohistochemical (IHC) assessment of estrogen receptor (ER) status using standard Allred or H-core methods; assessment of cancer aggressiveness by IHC assessment of progesterone receptors (PR) and HER2 expression. Routine cancer identification is aimed at determining the local spread of cancer, so it is not necessary for all patients to undergo comprehensive laboratory and radiological staging of cancer, since distant metastases are very rarely asymptomatic [7,9,10]. Additional studies, such as computed tomography (CT) of the chest, abdominal ultrasound or CT and x-ray bone examination, are necessary for patients: with clinically positive axillary nodes; with a large tumor formation (>5 cm); with clinical symptoms or laboratory data suggesting the presence of metastases [4,9].

A method of functional and anatomical characterization, such as positron emission tomography (PET)/CG, is necessary when conventional methods do not provide a definitive diagnosis. The use of PET/CT for staging local regional spread of cancer is not advisable due to limited specificity compared to the “gold standard” of axillary breast cancer staging: sentinel lymph node biopsy (SLNB), which is recommended unless involvement of axillary nodes is proven [5,8,13]. Routine methods for determining the status of HER2 gene amplification are fluorescent, chromogenic and silver in situ hybridization of histological material from the primary tumor. The choice of a reliable method for determining the status of the HER2 gene is very important to prevent overdiagnosis and overtreatment with anti-HER targeted agents. In case of ambiguous HER(2+) IHC results, analysis by one of the in situ hybridization methods is recommended. In case of negative results of ER/PR and HER2 in the puncture biopsy material, it is necessary to retest ER/PR and HER2 on surgical material after tumor resection. A complete postoperative pathological evaluation of the surgical specimen should be performed according to the pTNM system. The final pathological diagnosis should be made according to the World Health Organization Classification with analysis of the entire volume of the resected tumor. ER/PR and HER2 status are the most reliable and effective predictors

of response to hormonal and anti-HER2 therapy. In addition, high ER expression may predict less benefit from chemotherapy. A proliferation marker such as the Ki67 index can provide additional useful information about the aggressiveness of the process. After neoadjuvant systemic treatment, cancer response to treatment and amount of residual disease are important prognostic factors, but more convincing standardized biological markers are still needed. To date, there are no universal recommendations for assessing response to neoadjuvant treatment. Although there are many published results of scientific studies devoted to the study of the molecular panel of predictors of response to breast cancer treatment. Although they note the great importance of circulating cancer cells in predicting the development of the disease and survival in some forms of metastatic cancer. The authors of the publication caution that there are no proven definitive results in the literature indicating the possibility of changing therapy and improving treatment outcomes based on circulating cancer cells.

It is noted that the sensitivity of circulating cancer cells is relatively lower than that of some imaging methods. In addition, the authors of the document argue that there is no data confirming the greater effectiveness and clinical benefit of circulating cancer cells over other cancer biomarkers and it is possible that the results of the expected numerous ongoing clinical trials will determine the clinical role and value of circulating cancer cells in the treatment of cancer. The importance of micro-metastatic dissemination and isolated circulating cancer cells for optimal management of the cancer process is a matter of ongoing research. Determination of the prognostic index - Nottingham Prognostic Index (NPI), which depends on clinical parameters (tumor size, lymph node involvement and the degree of histological maturity of cancer), will predict the likelihood of relapse and mortality from breast cancer.

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