AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 01, Issue 07, 2023 ISSN (E): 2993-2149

New Approaches to Breast Cancer Screening

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Abstract: According to the International Agency for Research on Cancer (IARC, Lyon), breast cancer (breast cancer) is an "ideal" tumor for population screening. This is the most common tumor, especially in women over 50 years old. Out of 10 million . newly detected malignant tumors of various organs in the world account for 10% of the mammary gland. Only in women, breast cancer accounts for 22% of all oncological diseases. In industrialized countries, this figure is even higher - 27%. However, breast cancer is also the most common tumor in developing countries: in 2000, breast cancer was detected in 471,000 women in developing countries, which is more than cervical cancer (379,000), which was the most common cancer until the previous year [1, 2].

Keywords: breast cancer, morbidity, treatment.

More than half (579,000) cases of breast cancer are reported annually in North America, Western Europe, Australia and New Zealand, where breast cancer occurs in 6% of the female population during their lifetime (up to 75 years). The incidence rates are similar in Argentina and Uruguay. The lowest incidence rates are in Africa (sub-Saharan Africa), Southeast Asia and Japan, where the probability of developing breast cancer is one-third of the western one (2% in women younger than 75 years). The Russian Federation and the countries of Central and Eastern Europe occupy an intermediate position in the incidence of breast cancer. About 50,000 new cases of breast cancer are detected annually in the Russian Federation [2, 3].

Until the 1990s, morbidity and mortality increased in both economically developed and developing countries. Subsequently, in economically developed Western countries, the introduction of mammographic screening and improved prognosis of detected breast cancer cases led to a significant change in these indicators: mortality slowed down and subsequently decreased (IARC, 2006). In Eastern Europe and Latin America, on the contrary, morbidity and mortality continue to grow [7].

Secondary prevention, i.e. preventive detection of breast tumors at a stage that can be treated with existing methods, currently plays an important role in the strategy of combating breast cancer. The concept of "screening", which is understood as a routine examination of healthy population groups in order to identify potential oncological diseases, for example, breast cancer, has become firmly established in the medical practice of developed countries [17, 19, 22, 26].

The screening philosophy is based on the fact that routine clinical examination and self-examination, as a rule, do not allow identifying potentially curable oncological diseases. Therefore, it is necessary to use diagnostic tools that can detect enough early manifestations of curable tumors. existing methods of surgical, chemohormonal and radiation treatment; the most suitable for these purposes was an X-ray mammograph.

Screening is, in fact, a method of identifying potential pathologies in a healthy population, therefore, the following requirements should be imposed on it

- The method or test used should be sensitive enough to detect the majority of malignant neoplasms in the target population with a minimum number of false negative results.
- High specificity for detecting the majority of healthy women without breast cancer and minimizing the number of false positive results.
- Reasonable average cost per detected cancer.
- Minimal harm to the health of the subjects.
- Ease of use and maintenance of equipment. Screening should not be confused with diagnosis. Mammography allows you to identify only suspicious areas of the parenchyma of the gland that are suspicious of a tumor, and the nature of the changes should be clarified using additional diagnostic methods (a mammogram complex or a biopsy aimed at ultrasound).

or a biopsy under ultrasound control).

The widespread use of mammographic screening in many countries has led to a change in the ratio of removed benign and malignant breast tumors. In particular, the incidence of non-invasive breast cancer (in situ cancer) has sharply increased, and there is still debate about the optimal treatment of these "early" cancers.

Although the ultimate goal of early cancer screening is to reduce breast cancer mortality, the immediate goal is to detect cancer before it becomes clinically apparent. At the same time, the detection of cancer (or its precursors) before the onset of clinical symptoms increases the risk of false positive diagnoses and overtreatment (31).

Cancer is a heterogeneous disease characterized by a different "natural history". The widespread opinion that epithelial breast tumors inevitably progress from atypia to carcinoma in situ, and then to invasive cancer and metastasis, is not supported by all researchers [6, 8]. Proliferation of ductal and lobular epithelium, especially atypia, undoubtedly increases the risk of developing breast cancer (OR=2-4). However, these conditions seem to be only part of the spectrum of breast cancer incidence. It is possible that these conditions are not the main basis for the development of all types of breast cancer. Unlike clinical examination (palpation), mammographic screening allows early detection of various breast pathology, so it is especially important to know more about the risk of progression of various types and forms of detected pathologies. Understanding the threat and frequency of progression of this pathology is crucial for screening programs, including the choice of adequate treatment of identified diseases.

Molecular genetic studies using the method of "loss of heterozygosity" of ductal carcinoma in situ (DCIS) and atypical ductal hyperplasia of the mammary gland have demonstrated the similarity of genetic damage, which indicates the clonal origin of these diseases [18]. Moreover, it has been shown that the structures of non-invasive (in situ) and invasive breast cancer have identical molecular genetic changes, i.e. they are stages of the same etiological pathway. These results are consistent with observations on the similarity of morphological features of non-invasive and invasive breast cancer [3].

Data from the Swedish Screening Project allowed us to put forward another hypothesis: according to Tabar [28], tumors progress from low to high, and the proportion of high-grade tumors increases as the tumor size increases. Ductal carcinomas, which make up the majority of breast tumors, are characterized by time-dependent prognostic factors (tumor size, condition of lymph nodes) that indicate the likelihood of screening effectiveness (for example, the smallest tumor size, the absence of local metastases).

Invasive breast cancer is a malignant tumor that partially or completely penetrates into the fundal membrane of the ducts or the intraepithelial layer of the lobule of the breast. The prognosis of breast cancer depends on two groups of parameters. The first of them is the time-dependent

parameters mentioned above that determine the stage of cancer: the size of the tumor and the presence of local or distant metastases. The second group determines the "internal" biological features of the tumor: histological type, class, presence of hormonal receptors, expression of growth factors (HER2) and other molecular features of the tumor. Of these characteristics, the size of the tumor, its histological type, class, vascular invasion and the condition of the lymph nodes to which it belongs are directly related to the outcome of the disease. Both clinicians and pathologists agree that screening assessment and treatment planning should be based on the minimum number of signs of TNM from the 0th (in situ) to the IV stage.

Of particular importance in screening is the determination of the size of the primary tumor. The term "minimal" breast cancer was originally proposed to refer to forms of breast cancer characterized by a particularly favorable prognosis; Gallagher [13] called "minimal" breast cancer; the term "minimal" breast cancer is used to describe a form of breast cancer with a particularly favorable prognosis. All cancers in situ (ductal and lobular) and invasive cancers with a diameter of less than 5 mm. Subsequently, this term was revised to take into account the goals of mammographic screening, in particular, the American College of Surgeons, and then radiologists adopted a size of 10 mm or less as a criterion for determining "minimal" breast cancer.

Minimal" breast cancer Tumor size is an important criterion for assessing the quality of screening and determining the ability of X-ray mammography to detect non-palpable tumors. Therefore, it is very important that the pathologist measures the size of the tumor as accurately as possible. The smaller the size of the primary tumor, the higher the probability of error in its determination (31).

Mammography remains the main screening method. Mammography as a screening test has been widely studied and evaluated in randomized trials that did not include women who had previously been diagnosed with breast cancer. In almost all studies (7 out of 8), it was shown that the effect of early detection of invasive cancer occurs 5-7 years after the start of screening. In other words, even well-organized and high-quality screening delays the reduction of mortality from breast cancer. If women under the age of 50 are screened [6, 22, 28], as was observed in the Swedish screening program, the positive effect may appear much later. When implementing population-based screening programs (on a national or regional scale), the methodology developed in randomized trials should be adapted to a more complex real-world situation in healthcare. In contrast to randomized trials, much longer time intervals (seven years or more) are required to demonstrate a reduction in breast cancer mortality in population-based screening programs. Unlike female volunteers participating in experimental screening studies, the general population is often hesitant to participate in the proposed programs, and it is not easy to exclude women who have previously been diagnosed and treated with breast cancer when calculating total mortality.

Accurate mortality rates are possible only if there are adequate links with cancer registries and databases of screening programs. Therefore, screening forecasts based on short-term criteria may be useful for determining the expected reduction in breast cancer mortality in the future. Short-term criteria include parameters such as "sensitivity", "specificity", stage distribution and frequency of "interval" screening. This method of determining the usefulness of screening is useful only at the early stages of the screening program and cannot replace the subsequent analysis of overall survival and determination of the observed (actual) mortality of breast cancer patients.

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