

Screening, prevention and early diagnostic of breast cancer

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Summary. This article represents data aimed at providing health care professionals with practical rules on screening, preventive examinations and assessment of pathological neoplasms of breast. The presented methodology of prevention and early diagnostic of breast cancer allows applying it at all levels of practical health care, starting with the sick observation rooms of total hospital network.

Key words: breast cancer, screening, preventive examinations, risk groups of cancer, early detection of cancer.

In the structure of cancer morbidity in women in Ukraine, the breast cancer takes the first place [1]. On the registration of oncological institutions at the beginning of 2011 were more than 140,000 women with the breast cancer. Every year in Ukraine are recorded more than 16,5 thousand new cases of the breast cancer, including 25% of women of reproductive age and every year die more than 7,8 thousand women, of whom more than 20% – in the reproductive age. The incidence of the breast cancer during the last 20 years has increased in 2,5 times, the annual growth is more than 2%. Peak values of the incidence of the breast cancer are at the age of 50-75 years [1].

Taking into consideration the following statistics, are particularly relevant issues of screening, prevention, diagnosis and treatment of patients with the breast cancer in organization of which there are still significant shortcomings. Despite the fact that malignant neoplasms of breast relate to visual locations, neglected cases are in 2012, 20,5%, and in some regions it is over 30%. During the preventive examinations in 2011 were found 47,6 % of patients with the breast cancer, but the value of this indicator in some regions is up to 25 %. 83,4 % of newly diagnosed patients got special

treatment (from 70,6 % to 97,4% in some regions) [1]. Shortcomings in the organization of medical diagnostic process cause the death from this pathology during the first year in 10.8% of patients (for comparison – in the USA this indicant is less than 2 %). Treatment of patients with generalized forms of the breast cancer leads to increasing of costs in 25-30 times in comparison with when the tumor is detected at early or preclinical stages. That is why great significance has early detection, which improves 5-year survival of patients with the breast cancer and reduces the costs of anticancer treatment [2-4].

Effective way of improvement the case of detection of malignant breast neoplasms may be the implementation of effective programs of screening, prevention and early detection. It is known that through the introduction of state screening programs in developed countries over the last 15 years have been reduced death rates from the breast cancer on 25-30 % [4].

Early detection of the breast cancer is possible due to the fulfillment of programs of:

- a) self-examination;
- b) medical preventive examinations, monitoring and treatments of precancerous pathology;
- c) screening examinations and mammography diagnoses (now in European countries and the USA the widespread use of screening mammography is recommended for women at the age of 50-69 years). Screening examinations of breast in women are conducted without the presence of symptoms of breast cancer, in order to detect the disease earlier.

For proper planning of arrangements with the purpose of active identifying of patients with the breast cancer is necessary clear definition of “screening”, “preventive examination”, “periodic examination”.

Screening (literally – bolting) – a system of organizational measures for bulk periodic studies of healthy people for early (pre-clinical) detection of cancer, for example, the breast cancer. Screening examinations of breast cancer in women are conducted without the presence of symptoms of breast cancer, in order to detect the

disease earlier. The main goal of all programs of screening is to reduce mortality rates through early detection of the breast cancer.

Preventive examination – active detection of the disease of breast with mandatory participation of medical worker. Individual preventive examination is conducted by nurse practitioner of pre-doctor service room of feldsher-midwife station. The purpose – to identify visual forms of cancer. When suspected the breast cancer, the patient goes to the obstetrician-gynecologist, therapeutic, surgeon, mammologist. Objective preventive examination is conducted by mammologist to detect the breast disease. Complex preventive examination is conducted by a group of physicians to identify various nosological forms of cancer pathology, including the breast cancer.

Periodic examination – periodic examination of women who were registered by mammologist due to the high risk of the development of breast cancer as well as those who received treatment with benign and malignant breast tumors.

In some cases, screening, preventive examination and periodic examination may be combined or be the stages of diagnostic route of patient. For example, is conducted screening → formed “group of risk” → prevention examination at the group of risk → is detected a woman with the adjusted diagnosis of breast cancer disease → treatment → periodic examination.

Planning and conduction of screening is not fixed and depends on the specific demographic, institutional and economic conditions of the state health care and even certain regions of one country (for example, the influence of population density, age, sex structure of the population in the region of screening).

Analyzing the results of randomized researches on screening the breast cancer, International Agency for Research on Cancer (IARC, Lyon) and the Department of Cancer of WHO recommend the conduction of screening for all women who are in “targeted” cohort 50-69 years with the help of a single test – mammography, which is repeated in every 2 years [2].

The program of prevention and early detection of the breast cancer has two main directions: primary prevention (etiopathogenetical) and secondary prevention, which aims at the diagnosis and treatment of precancerous diseases. As etiopathogenesis of the breast cancer is not completely elucidated, the possibility of primary prevention of

the breast cancer limited [2,3]. Major efforts of researches are currently focused on improving the system of secondary prevention of the breast cancer.

Preventive examination of patients should start with risk assessment. After collecting of anamnestic data regarding risk factors are formed groups of patients who are subjected to mandatory referral for mammography.

The most obvious risk factor is age – the incidence of the breast cancer increases with increasing of age. Familial history should include information about the immediate family (mother, sister, daughter), who had the breast cancer and the age when they were sick. The patient, an immediate relative of whom was diagnosed with premenopausal breast cancer, has a greater risk (in 4-5 times) to disease than others. If the immediate relative has cancer of both breasts or, if the immediate relative had the breast cancer, the risk for such woman may in 8-10 times exceed the risk in the general population. During the examination, the physician should obtain detailed information about pregnancy and childbirth in women, in particular, the number of childbirths and age at which a woman first gave birth to a child. A woman who had no children, or had a baby after 30 years, has a greater risk of become sick.

The main risk factors of the breast cancer currently are considered (see Table 1) [4]:

Risk factors of the development of the breast cancer.

Table 1

Risk factor	Відносний ризик
Mutations in genes BRCA1 or BRCA2*	10,0-32,0
Cancer in the family history (without known mutations)*	
1 immediate family (the first degree of blood)	1,5-2,0
2 immediate family	3,0
3 or more immediate family	4,0
1 relative of the second degree of blood	1,2-1,5
The use of radiation therapy in the area of chest at the age of 30 years**	7,0-17,0
Hormonal factors	
Late (at the age over 30 years) birth of the first child or	1,2-1,7

the inability to childbirth	
Early (at the age less than 12 years) onset of menarche or late menopause (at the age over 55 years)	1,2-1,3
Combined hormone replacement therapy (e.g., during 10 years or longer period)	1,5
Postmenopausal obesity	1,2-1,9
Use of alcohol	1,2
Smoking before the first childbirth	1,2
Sedentary lifestyle	1,1-1,8
Representatives of European race	1,1-1,5
Density of the breast (very dense in comparison with the breast mostly with adipose tissue)	5,0
Atypical ductal or lobular hyperplasia or lobular carcinoma in situ as result of preliminary biopsy of breast tissue	4,0

After the polling, patients are divided into zones of risk, they get recommendations.

I zone of risk. Mandatory examination by operating surgeon or gynecologist. In identifying pathology – treatment and periodic examination. Examination by mammologist at least once every 12 months with the use of sonography in women under 40 years. Sonography once a year + 1 mammography once in every 2 years for women older than 40 years, study the rules of self-examination.

II zone of risk. Annual mandatory examination by mammologist, gynecologist, therapeutic, surgeon or district oncologist once in 6 months and sonography for women under 40 years. Mammography for women older than 40 years once a year, study the rules of self-examination.

III zone of risk. Examination by obstetrician-gynecologist, therapeutic, surgeon or district oncologist once a year, at the age of 40 years – sonography once in 6 months, older than 40 years 1-2 times per year; older than 40 years – mammography

once a year, study the rules self-examination. Explanation of influence of “risk factors” that increase the likelihood of breast disease, recommendations for dealing with them and treatment.

The low percentage of detection of breast tumors by physician during preventive examinations is associated with the practical absence of specialists – mammologists who can correctly assess the state of breast, make the appropriate treatment of precancerous diseases and observe patients at risk groups.

There is no convincing scientific evidence that can specify the optimal age for research using mammography. Research results [4-7] confirm the feasibility of making mammography for women at the age from 50 to 70 years. There is controversy regarding the frequency of examinations in women of 75 years and over. Conduction of routine mammographic examination of women under the age of 40 has a high efficiency [4-7].

It is known that periodic screening mammographic examination of women who have no complaints reduces mortality from the breast cancer.

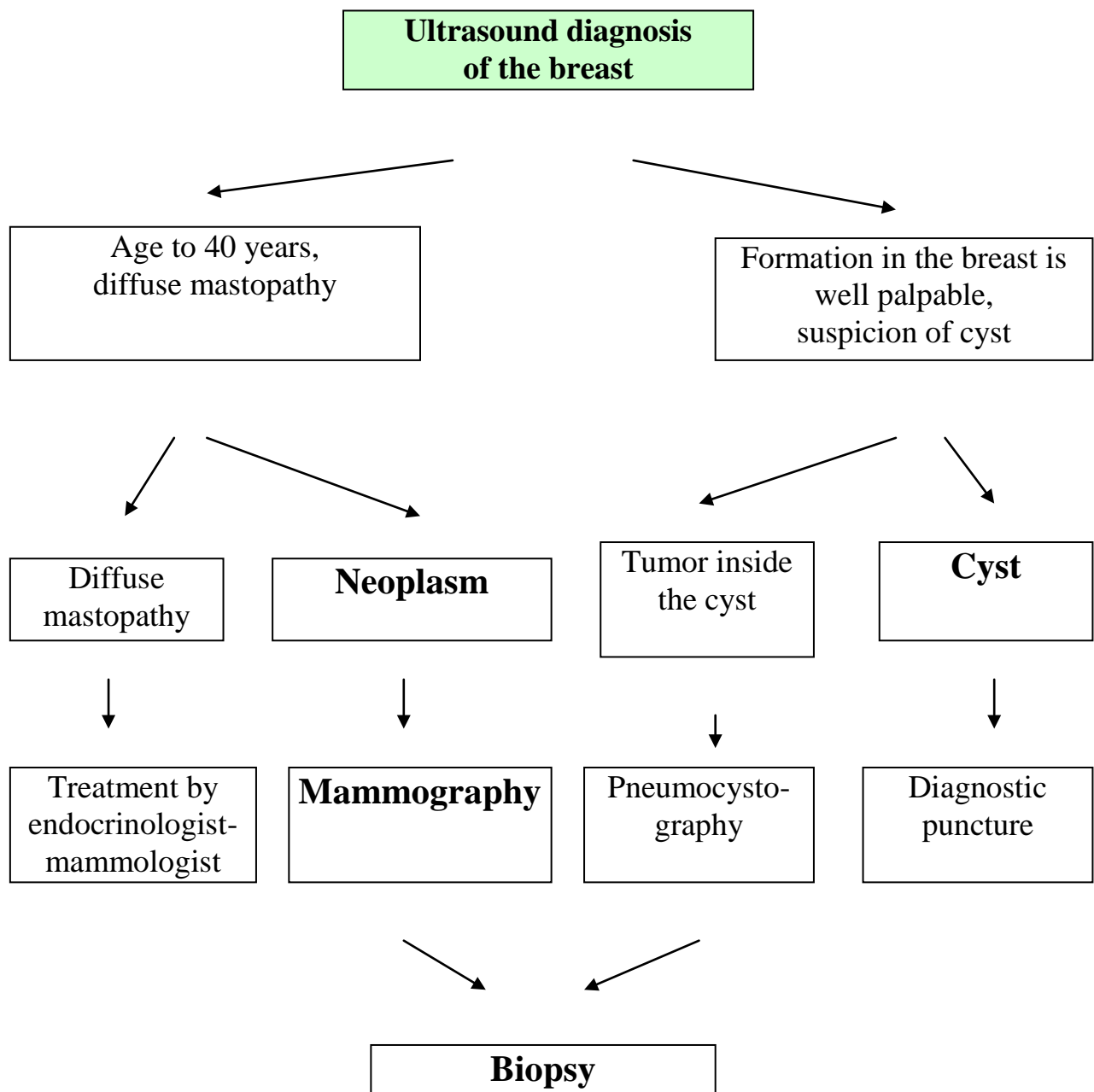
In areas where there are enough mammologists, screening mammography is a radiological research to identify at an early stage “hidden” breast cancer in women who have no symptoms. In addition, the research aims at dividing the patients into two groups of women – with low and high risk of disease. Results can convince most women that no significant abnormalities were found in them, while others must be said that abnormalities are and they need further examination. Of course researches are limited by angular projections of craniocaudal and mediolateral area of every breast. Sometimes, for optimal visualization of breast tissue are necessary additional projections, but they must not be done routinely. When there is a suspicion of pathology, one can offer further visual researches, diagnostic mammography or biopsy.

The purpose of all mammographic studies is to help identify preclinical forms of the breast cancer but, unlike mammography screening, mammographic breast research to solve specific problems (diagnostic mammography and ancillary procedures) is directed to provide special analytical research of patients with abnormalities, which were detected clinically or by screening. Diagnostic research of breast should lead the

doctor to the final conclusion on the clinical findings, to verify the diagnosis that allows providing specific recommendations for treatment.

During the preventive examinations of young women (under 40 years) making the mammographic examinations may be replaced by sonographic examination. As a result of ultrasound diagnostic, was reported an absolute increase up to 20% level of detection the invasive breast cancer in women with dense breasts, where mammography sensitivity is reduced, and the risk of the breast cancer increases [6]. Algorithm for referral of patients is shown in Scheme 1. If during the ultrasound diagnostic of breasts the doctor does not see any nodal tumors, the patient is sent to the doctor endocrinologist-mammologist (in the presence of diffuse mastitis) or is recommended control ultrasound examination 1 per year (in the absence of pathology in the breast).

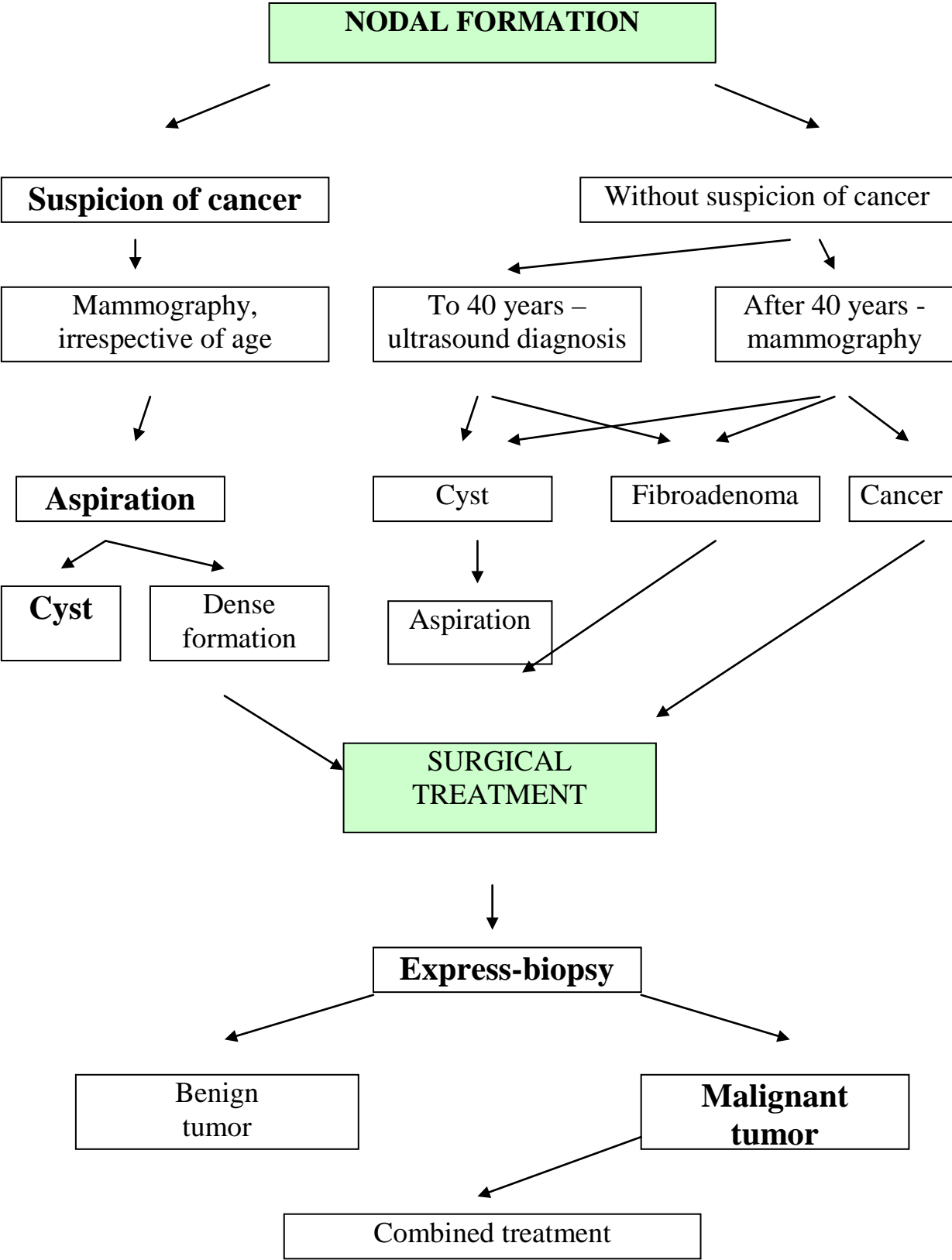
Scheme 1. Algorithm of referral the patients of juvenile age



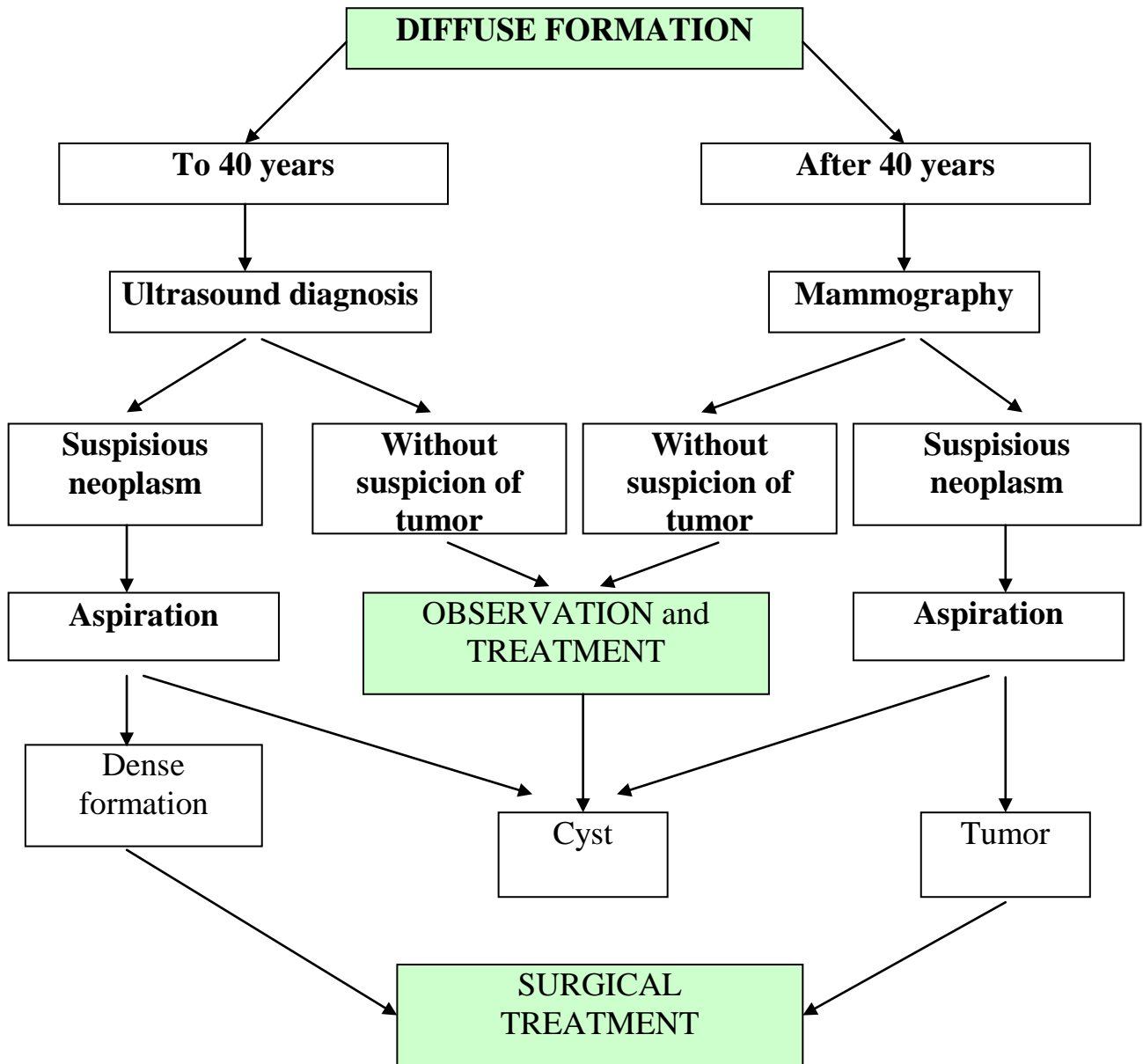
Upon detection of nodal tumors (fibroadenoma, cyst, etc.) the patient should be investigated by mammographic or pneumocystotomographic diagnosis (Scheme 2, 3). If fibroadenoma is detected – is recommended surgical intervention with histological examination, during the presence of cysts – needle aspiration with cytological examination of the exudate, during the suspicion of proliferative and malignant processes – is required surgical intervention with histological examination. If cyst is

only punctured, the patient should be examined once more in 1-1,5 month to see if there is any recurrence of the cyst. If the cyst after aspiration recurs rapidly, the patient should be referred for surgery.

Scheme 2. Algorithm of referral the patients with nodal formation



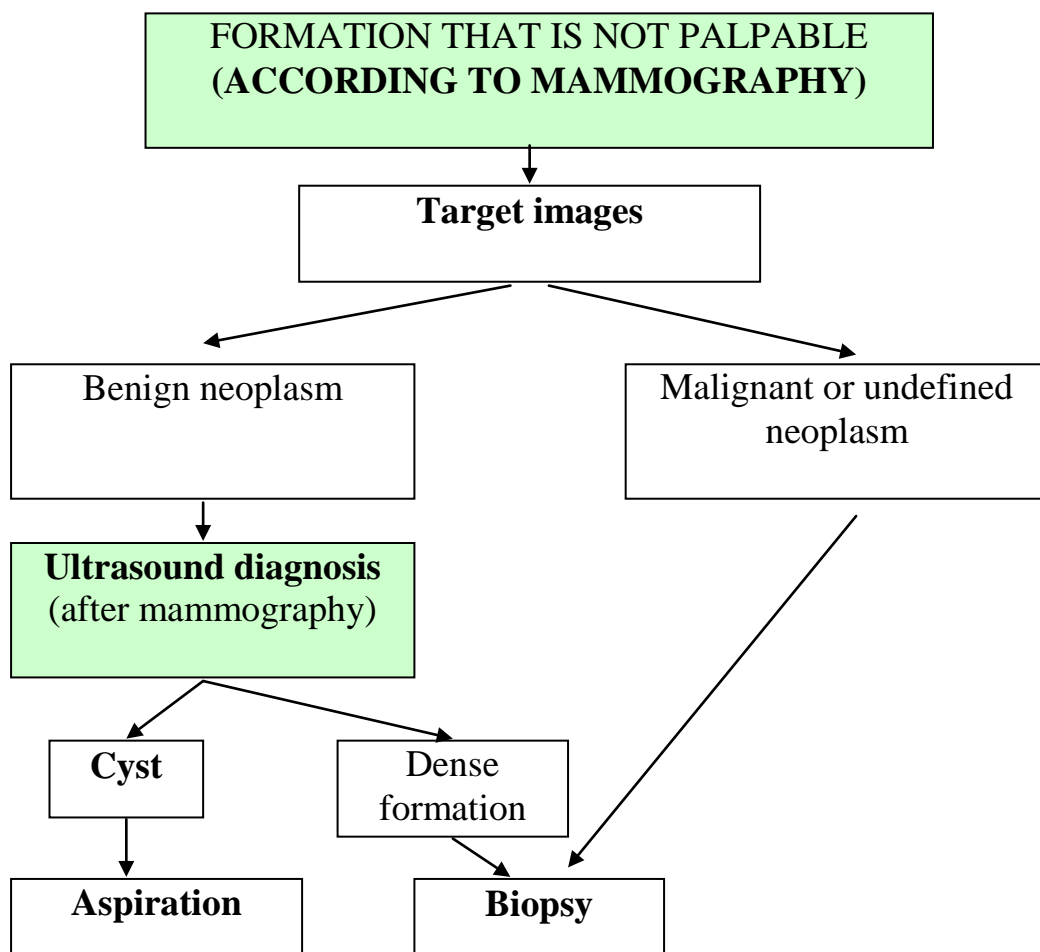
Scheme 3. Algorithm of referral the patients with diffuse forms



When suspicion of malignancy of tumors is necessary an urgent section resection of breast with histological examination (the operation should be performed under conditions of oncology center and cancer institute). Upon confirmation of the diagnosis of the breast cancer it is necessary to conduct radical surgery followed by combined treatment.

If during the mammographic or sonographic diagnosis of patient were diagnosed diffuse tumors (Scheme 4) in the breast, treatment and surveillance are carried out by an outpatient basis. Among diffuse forms are discharged fibrous forms of dysplasia with ovarian failure of various genesis and cystic forms of mastitis with different comorbidities. The physician has the ability to identify laboratory the hormones ground during the diffuse form of breast hyperplasia. After this are formed drug complexes that are assigned depending on the level of estrogen, progestin and clinical form of dishormonal hyperplasia. Assessment of the situation should be done individually. For example, at low levels of estrogen seem to be found hypoestrogenisation with the development of mastitis. In fact it appears that concomitant hyperthyroidism, liver dysfunction, dysfunction of corpus luteum results in clinical hyperestrogenisation with the development of cystic components of fibrosing adenosis. This situation encourages searching a new approach to building treatment strategy based on clinical, radiological, cyto-histological data and data of hormonal diagnosis assessed for their clinical implementation. This suggests the possibility of an integrated approach to the evaluation of form of dishormonal hyperplasia and assignment of differential treatment.

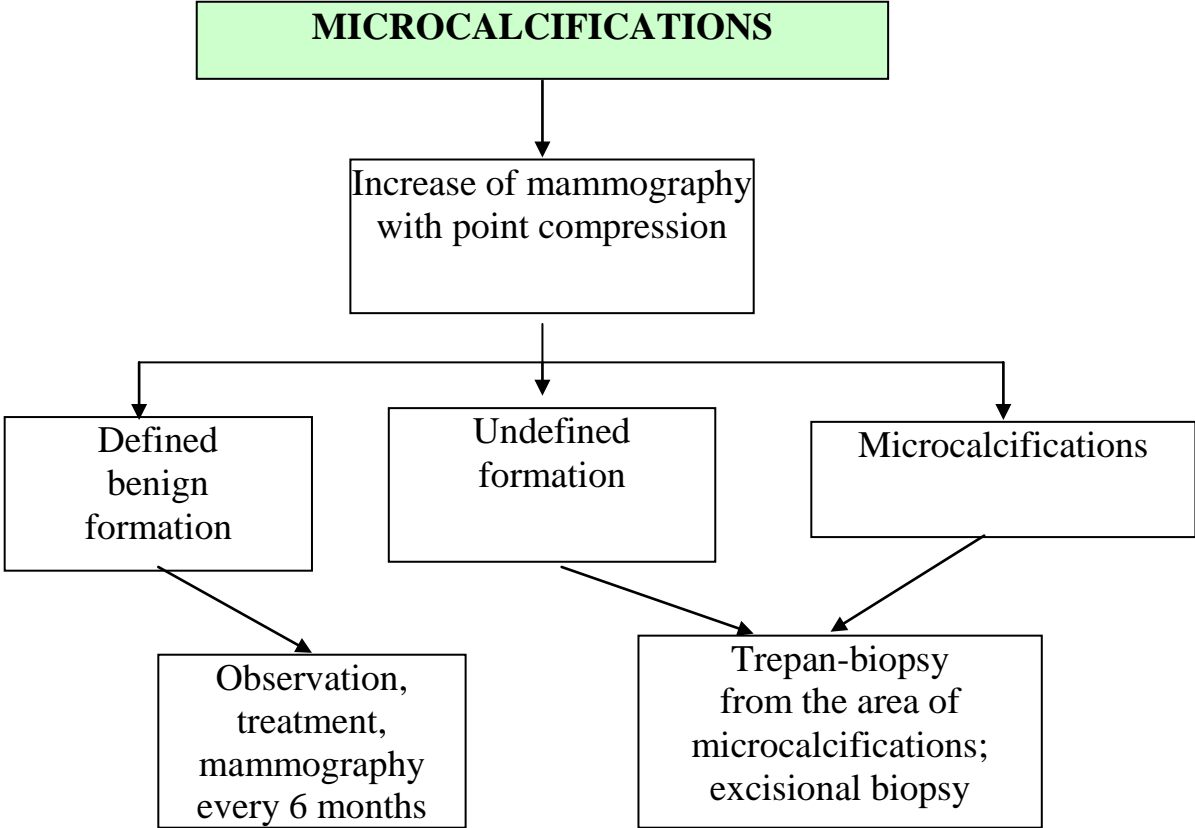
Scheme 4. Algorithm of referral the patients with preclinical forms



It is proposed to distinguish such forms of dishormonal hyperplasia, reflecting simultaneously degrees of its development and significantly differ in tactic of treatment: fibrous form, fibro-cystic form, adenose form, fibrous-adenomatous, involutive-fibromatous, mastopathy with galactophoritis or galactorrhea, mixed diffuse forms, nodal forms of dishormonal hyperplasia. Treatment of patients with dishormonal hyperplasia requires an individual approach based on the pathogenesis of disease, comorbidities, female phenotype, the nature of disease in breasts (clinical, radiographic data), accompanied by certain changes in the hormonal homeostasis. Algorithms of direction of motion of patients with diffuse, nodular mastitis, tumors that are not palpable, and microcalcifications in breast are shown in Schemes 3, 4, 5. Biopsy is mandatory for a solid, dominant and persistent tumor process. Patients with solid tumor should be referred to a surgeon, even if the result of mammography is negative. In tumors that are not palpable (see algorithm in Scheme 5), but detected on

mammography, should be made target images and if possible puncture or trepan-biopsy under the control of ultrasound diagnosis. Upon receipt conclusion after biopsy, confirming the benign process, the patient is examined and treated outpatiently, when certain suspicion or “malignant process” – it is necessary surgical treatment.

Scheme 5. Algorithm of referral the patients in the presence of microcalcifications



When detection on mammographic images microcalcifications or macrocalcifications (see algorithm of Scheme 5), it is obligatory to conduct target mammography with increasing and compression. If while increasing the process is seen as benign, it is necessary to get X-ray control in 1 month to find out the tactic of further treatment. If the pattern remains controversial, it is necessary to carry out partial resection with urgent histological examination and carry out further treatment depending on the histological report. All nodal forms of dishormonal hyperplasia are subjected to cytological or histological biopsy and when suspected in proliferative processes – surgical treatment with urgent histological examination in terms of

oncological institution as treatment of cancer in general medical network worsens the prognosis in more than 3 times. Assessment of the effectiveness of received results is related to the specific recommendations for practical actions with respect to patients at both individual and group / population levels.

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