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PECULIARITIES OF THE MAMMOGRAPHIC DENSITY OF THE SYNCHRONIC BILATERAL BREAST CANCER**ОСОБЛИВОСТІ МАМОГРАФІЧНОЇ ЩІЛЬНОСТІ СИНХРОННОГО ДВОСТОРОННЬОЇ РАКУ МОЛОЧНОЇ ЗАЛОЗИ****Cheshuk V.E.**

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Summary. In this article it was made an analysis of the case history out-patient medical records of 30 patients with synchronic bilateral breast cancer (SBBC), 34 patients with unilateral breast cancer (BC) and 32 healthy patients. The obtained results show the higher mammographic density in patients having the synchronic BBC in comparison with the healthy patients and lesser density compared with the unilateral BC. The 2nd grade of the mammographic density is 60% in the group of the synchronic BBC and is higher on 34-35% than that of the two other groups. The presence of the 2nd grade of the mammographic density of the mammary gland requests the more thorough examination (Ultrasonic examination, MRT) for excluding the synchronic BBC.

Key words: synchronic bilateral breast cancer, mammographic density.

Резюме. В статті проведено порівнювальний аналіз даних мамографічної щільності в 30 пацієнток із синхронним двостороннім раком молочної залози (ДРМЗ), 34 пацієнток з одностороннім раком молочної залози (РМЗ) та 32 здорових жінок. Отримані результати виявили більший ступінь мамографічної щільності у жінок із синхронним ДРМЗ в порівнянні з здоровими пацієнтками і в незначній мірі в порівнянні з хворими на односторонній РМЗ. Другий ступінь мамографічної щільності становить 60% в групі з синхронним ДРМЗ, що на 34-35% більше в порівнянні з обома іншими групами. Наявність 2 ступеня мамографічної щільності молочної залози вимагає більш уважного обстеження (УЗД, МРТ) для виключення наявності синхронного ДРМЗ.

Ключові слова: синхронний двосторонній рак молочної залози, мамографічна щільність.

Synchronic bilateral breast cancer (SBBC) and metachronous bilateral breast cancer appear in 10-20% of cases. The relevance of its forms is made up of the fact that in the prognostic sense the bilateral breast cancer has more aggressive disease course compared with the unilateral process. The essentially aggressive course has been established in the cases when the pathology is developing under 40 years of age and the interval between the primary and secondary tumors is very short – up to 1-3 years. The disease course is more aggressive for the SBBC in contrast with the metachronous one.

Concerning the problem of bilateral breast cancer (BBC) diagnostics, the special significance is devoted to the early secondary tumor detection, which has an effect on the disease prognosis. The early metachronous BBC diagnostics is a crucial point for this sphere. About a half of the bilateral breast cancer cases are hereditarily determined, thus, the specification of the BRCA1 and BRCA2 genes mutation could be an alternative variant of the preliminary diagnostics. But, therethrough, there could not be covered all the cases.

A substantial point is the identification of such patients for the early detection of the secondary tumors in another breast. There are papers which show that the greater risk of the BBC development was specified in patients with the body weight more than 60 kg (three times as much as other); more typical was the development of BBC in patients with the blood group AB(IV) and positive progesterone receptors in the tumor [1]. It is possible to prognosticate that the tumor's multicentric growth in one mammary gland suggests a tendency to the metachronous process beginning in the contralateral breast. Insofar as the basic method of the breast cancer (BC) diagnostics is the mammography. It is important to screen the secondary breast too, i.e. to diagnose BC on the preclinical phase.

Now is known, that the high tissues' mammographic density (TMD) is associated with the BC development risk increasing by 1,8 – 6 times [2, 3, 4], and besides, among all risk factors, in spite of the large body of research, it is the less studied one [5]. It has never been resolved the open question of the mammographic diagnostic method sensitivity and specificity decreasing while diagnosing the women with high TMD, the problem of so-called interval cancer [6, 7, 8].

TMD is defined as the proportion of radiodense fibroglandular tissue in the breast [9]. The two component parts of the breast tissue – fibroglandular tissue and fat – look in a different way. The fat has the lower X-rays transmission coefficient, thus, some parts of the fatty tissue look darker on the shadow gram. The lighter parts, represented by the fibroglandular tissue, specify the mammographic density [2].

The significant role in the TMD visualization plays the stroma. The histological research of the breast tissues with higher TMD, compared with the lower one, on postmenopausal women, had revealed no essential difference in quantity of the lobular and ductal elements, but determined the higher collagen content, fibrosis dissemination and the expression of two stromal proteoglycans – the lumican and decorin, etc. The latest one correlates with the BC development [10, 11]. The collagen and stroma due to their mechanical properties promote the tumor invasion [12].

The reduction of the collagen and granulation tissue as well as fatty tissue growing with the increase of years – involution – are associated with the BC. In the majority of carcinoma cases (breast cancer in particular) the adhesive capacity of the stromal E-cadherins are essentially decreased and this leads to the disturbance of the cell junctions and facilitates the release of cells from the primary tumoral lump

[3]. It is proved that the reattachment of the tumoral cells to the laminin and fibronectin mediated by receptors indicates the subsequent invasion and metastatic procedures. Moreover, tamoxifen effect could be predicted via the changes in the mammary gland tissue density, which happened to be the only statistically significant prognostic risk factor. At decreasing the density of the mammary gland tissue by 10%, the risk of the BC development decreases by 52% [15].

In all age categories the TMD is higher in women who have the developed BC [12]. Whereas, the higher the BC development risk is at the increased TMD, the higher the TMD should be in patients with SBBC.

The object of the research was to determine the mammographic density in patients with SBBC and compare it with the density in patients with unilateral BC.

Materials and methods. An analysis of the case history out-patient medical records of 30 patients with SBBC, 34 patients with unilateral BC and 32 patients without any oncopathology was made. Before starting the special treatment the patients' mammograms were selected in the mammographic room of Kiev municipal oncology hospital. The mammograms that had been passed the neoadjuvant therapy – the hormonotherapy, chemotherapy and radiotherapy – were not evaluated. The conducting of the special treatment methods, according to the data from the literature, leads to the decrease of the mammographic density, which could testify for the treatment effectiveness. The chosen mammograms were evaluated using the planimetric analysis and the level of the mammographic density was defined. The content of the method was in the fact that the mammograms were inspected through the transparent net with the cell area of 1cm². It was calculated the relative area in per cent of the gland tissue density to the total area of the mammary gland. The classifications Wolfe and BI-RADS belong to the qualitative method. BI-RADS represents the standardized visual classification of the mammographic findings, which was designed by the American Radiology College. According to this classification there are 4 density categories:

Category 1 – almost completely fat tissue structure (dense structures occupy <25% of the gland area);

Category 2 – separate fibroglandular densities (dense structures occupy 25% -50% of the gland area);

Category 3 – heterogeneous density (dense structures occupy 51% -75% of the gland area);

Category 4 – expressed density (dense structures occupy >75% of the gland area).

Whereupon, the Categories 1 and 2 are defined as the low mammographic tissue density, and the Categories 3 and 4 – are the high mammographic tissue density.

The quantitative methods are based on the measurement of the dense structure area ratio to the whole mammary gland tissue area on the mammogram. To the quantitative methods are referred the following: the planimetry, the computer method and the visual classification. The result is represented on a percentage base or the total density area (pixels, square centimeters or millimeters) [8, 16].

The mammographic density was evaluated in patients with the synchronic BBC and was compared to the density in patients having the unilateral BC and with practically healthy patients.

Results and discussion. The average age of the patients with the SBBC was 63,47±12,5 years, in patients with unilateral BC it was 58,67±9 years, and in the healthy women group – the control group – 60,06±7,3 years. Thus, according to the age all the patient groups not differed from each other, which could testify for the opportunity

to conduct the mammographic density evaluation results comparison.

The obtained results show that the presence of BC manifests by increasing of the mammographic density, compared with the healthy women. The SBBC from its part manifests with the higher percentage level of the increased mammographic density in comparison with the healthy patients and that of having the unilateral BC.

The Table 1 shows that in the group of patients having the SBBC it was detected the lowest quantity of women with the low mammographic density – 6(20%) which is lesser by 24% than that of the group with the unilateral BC and by 40% lesser than that of the healthy patients group. The second level of the mammographic density was significantly manifested too in the group of patients with SBBC. In this group the quantity of patients having the 2nd grade of the mammographic density was 18 (60%) persons, which is on 34% higher than that of the group of patients having the unilateral BC and on 35% higher than in the healthy group. The 2nd grade of the mammographic density is characterized by

fibroglandular density by 25-50% of the gland tissue area. In other words, the SBBC peculiarity is, in 60% of cases, the presence of the denser image on the mammogram, which shows the specificity of this disease.

Considering the frequency of the 3d grade of the mammographic density manifestation it was detected that the group of unilateral BC had the major quantity of the patients – 7(21%), and it was on 8% fewer patients having the SBBC - 4(13%), and the lowest quantity was noted in the group of practically healthy women – 6%.

The 4th grade of the mammographic density was manifested practically in all the groups of patients: in the group of the SBBC it worked out 2(7%) of women, in the group of unilateral BC it was 3(9%) and in the group of healthy patients it was 3(9%). In other words, it was no significant difference between the groups, although it seemed more logical that there should be more such cases among the patients with the SBBC.

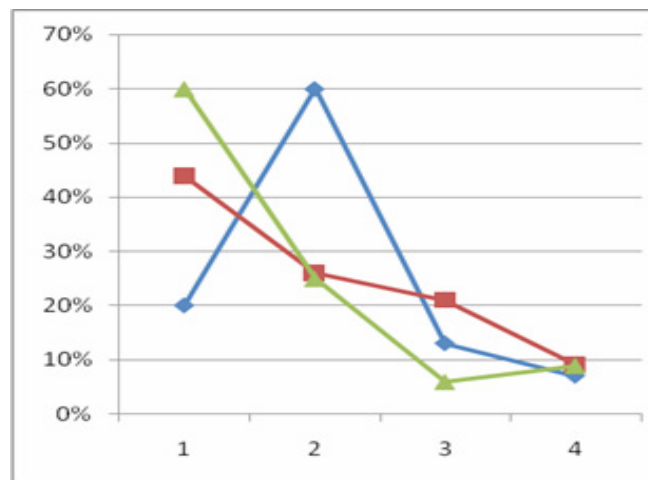
Table 1

The data of the mammographic density in the investigated groups

Mammographic density	Average age	1	2	3	4
Quantity of patients having the SBBC n=30, 31%	63,47 ±12,5	6(20%)	18(60%)	4(13%)	2(7%)
Quantity of patients having the unilateral BC n=34, 36%	58,67±9,0	15(44%)	9(26%)	7(21%)	3(9%)
Quantity of the healthy patients n=32, 33%	60,06±7,3	19(60%)	8(25%)	2(6%)	3(9%)

Picture 1.

The graphs of the mammographic density in the investigated groups



- ◆ The quantity of patients having the synchronic BC, n=30, 31%
- The quantity of patients having the unilateral BC, n=34, 36%
- ▲ The quantity of healthy patients, n=32, 33%

It is shown graphically the differences between the graphs of each group mammographic density grade. It is shown clearly that in the group of patients with the SBBC there are more cases of the increased mammographic density of 2nd grade and there are insignificant differences in the cases of 3d and 4th grades of the mammary glands density. The low grade of the mammographic density, comparing with the both groups, occurs very rarely, in other words it is not practically typical for this group of patients. The 2nd grade of the mammographic density was low both in the control group and in the group of patients having the unilateral BC.

The calculation of the mean grade of the mammographic density showed that it was 2,1 in the group of SBBC, 1,9 in the group of unilateral BC and 1,6 in the group of the healthy patients, healthy as of the time of examining.

The investigation that had been conducted by us showed the presence of the significant mammographic density profile changes in patients having the SBBC and healthy patients and lesser changes in the group of unilateral BC. The main specificity of this patient group

was the high percentage level (60%) of the 2nd grade of the mammographic density. The 3d and 4th grades were less manifested and did not differ statistically in all the groups. Thus, the presence of the 2nd grade of the mammographic density at the primary diagnostics of the BC specifies the necessity for conducting the additional investigation methods - ultrasonic diagnosis, MRT-mammography, - to exclude the possibility of the SBBC or for the early diagnostics of the metachronous BBC. Today, there are more and more uses of the MRT-mammography, especially for excluding the multicentric or multifocal process, which predicts the disease recurrence at the planning of the organ preserving surgeries, and reduces the quantity of the re-surgeries that are consequence of the incorrectly conducted nonoperative interventions. For the estimation the confidence of this hypothesis it is necessary to conduct the investigation of the mammographic density in patients having the metachronous BBC and increase the quantity of the supervisions in patients having the SBBC.

Conclusion. We found out that the grade of the mammographic density in patients with the SBBC is higher, compared with the healthy patients, and is lesser in comparison with the patients with the unilateral BC. The most abundant grade is the 2nd grade of the mammographic density in patients having the SBBC and works out 60%.

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