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The Role of Magnetic Resonance Imaging and Molecular Features in the Diagnosis of Breast Cancer

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Authors' contributions

This work was carried out in collaboration among all authors. Author YN designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author IJ managed the analyses of the study. Author SK managed the literature searches. All authors read and approved the final manuscript.

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Short Research Article

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ABSTRACT

Aims: To study the importance of differential diagnosis of breast cancer using Magnetic resonance mammography.
Study Design: Cohort Study.
Place and Duration of Study: The study was conducted Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology between 2017 and 2019.
Methodology: The study included a clinical and instrumental examination of 70 women with suspected breast cancer. The age of the patients was 26-75 years (average age - 49.0 ± 2 years). All patients underwent core biopsy. The procedure was performed in a horizontal position of the patient, a needle was brought in and a "shot" was performed, during which a tissue sample was taken from the focus of interest. In 5 (7.1%) cases, the second stage of verification of the diagnosis was carried out through sectoral resection with an urgent histological examination. The resulting material is sent for cytological and histological studies.
Results: The sensitivity of x-ray mammography in detecting breast tumors was 83.4%, specificity 60.0%. The sensitivity of ultrasound in the diagnosis of breast cancer was 86.4%, specificity -

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44.8%. In our observations of breast MRI, the sensitivity was 97.5%, specificity 87.2%. Magnetic resonance mammography is considered a more effective method in the early diagnosis of breast cancer.

Conclusion: Breast MRI is highly sensitive, specific and accurate in assessing the prevalence and differential diagnosis between a benign and malignant process.

Keywords: Breast cancer; radiation; indications; MRI; immunohistochemical.

1. INTRODUCTION

Today, the diagnosis of preclinical forms of breast cancer is impossible without the use of modern radiation research methods. The widespread use of X-ray mammography (MG) in the general population has indeed significantly improved the detection of breast tumors (MF). The methodically correct use of mammography studies can reduce mortality from breast cancer in the age group from 40 to 49 years by 18%, and in women older than 50 years by more than 30% [1,2]. However, the authors report low MG efficacy in high-risk women. MG sensitivity in young women was only 40–60% and was lower in comparison with the results of screening of the general population in women aged 50–75 years. Harmlessness and ease of use of ultrasound allow you to use it as the first diagnostic method for diseases of the breast in young, pregnant and lactating women, with developed fibroglandular complex and fibrocystic mastopathy. But numerous studies of diagnostic methods for breast cancer in high-risk women have shown that ultrasound has low sensitivity and specificity: 43% and 33–96%, respectively [3,4]. The advantage of magnetic resonance imaging (MRI) is the ability to detect clinically and radiologically hidden formations. Some studies [5], in which the annual MRI was compared with MG in women at high risk of developing breast cancer, it was found that its sensitivity is almost twice that of MG. Using MRI, it is possible to detect 2.7 times more tumors than with MG. The combination of these 2 methods increases detection by 20% [6,7,8]. Studies have shown that early detection and appropriate treatment of breast cancer significantly increase the chances of survival [9]. They also showed that early detection of small lesions improves prognosis and leads to a significant reduction in mortality. However, the interpretation of the mammogram is not easy due to the small difference in the density of various tissues in the image. As a traditional method of obtaining medical images, ultrasound (ultrasound) for many years plays a very important role in the detection of breast cancer, biopsy with visual monitoring and diagnosis of lymph nodes. Breast magnetic resonance imaging (MRI) is an integral component of breast imaging protocols, and in recent years its importance has increased. The overall sensitivity of MRI to breast cancer is relatively high, with an estimated 85% to 100% [10]. In cases of invasive ductal carcinoma, its sensitivity approaches 100%. The sensitivity of MRI to invasive lobular carcinoma and ductal carcinoma in situ is lower and still not well defined [11]. The expression of hormone receptors (estrogen receptors - ER and progesterone - PR), as well as over-expression or amplification of human epidermal growth factor receptor 2 (HER2), have been identified as important predictors in patients with breast cancer [12]. Currently, these markers are usually used to determine treatment and to establish a prognosis of the disease associated with clinical and pathological variables, such as lymph node lesions, tumor size, histological type, tumor degree and surgical fields [13,14]. This study was undertaken to determine the diagnostic effectiveness of MRI with dynamic contrast enhancement for various histological and molecular biological types of breast cancer.

2. MATERIALS AND METHODS

The study involved 70 women with suspected breast cancer who were examined and treated at the Department of Radiology in Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology between 2017 and 2019. The age of the patients is 26-75 years (mean age - 49.0 ± 2 years). MRI - mammography was performed on a PHILIPS 3.0 Tesla device, in T1 WI, T2 WI, STIR modes. The study was carried out in the supine position with hands pressed to the body using a special surface coil. A catheter was inserted into the elbow vein and a woman was warned of undesirable movement during the study. For an initial assessment of the structure of the mammary glands, images were obtained using impulse sequences to obtain T1 WI and T2 WI with the suppression of the MR signal from fat, since the intense MR signal from adipose tissue presented in milk glands, does not allow

differentiating pathological changes, especially of small size. In addition, impulse TIRM sequences are used with the suppression of the MR signal from free water, which allows us to evaluate the structure of the gland.

2.1 Pathomorphological Diagnosis

All patients underwent immunohistochemical (IHC) core biopsy with a Medax apparatus with a 14 G needle. The procedure was performed in a horizontal position of the patient, a needle was brought in and a "shot" was performed, during which a tissue sample was taken from the focus of interest. In 5 (7.1%) cases, the second stage of verification of the diagnosis was carried out by sectoral resection with an urgent histological examination.

3. RESULTS

According to the results of a comprehensive examination, benign formations were more common in the age group from 25 to 45 years (mean age - 39.0 ± 2.5 years). Among benign changes in the mammary gland, cysts (N60.3) (40.0%) were most often diagnosed, fibroadenomas (D24) (33.3%), a nodular form of mastopathy (local fibrosis) were detected much less often (16.7%), fibrolipomas (6.7%), also a phyloid tumor in 1 patient (3.3%). The defeat of the right mammary gland was noted in 37 (52.9%) cases, the left - in 33 (47.1%). The average size of breast tumors was 4.8 ± 1.2 cm. Tumor masses up to 2.0 cm in size were detected in 10 (14.3%), from 2.1 to 5.0 cm - 47 (67.1%) , more than 5.0 cm - in 13 (18.6%) women. The defeat of the right mammary gland was noted in 37 (52.9%) cases, the left - in 33 (47.1%). Based on the clinical and morphological studies, the histological type of the tumor and its prevalence with an assessment of TNM and stages were established in all patients.

An analysis of the data in Table 1 shows that the largest number of patients was in stages IIIa - 54.3% and IIa - 21.4%, IIb –17.1%; the number of patients was the smallest - in stage III b - 2.9%. According to the histological form, breast cancer patients had invasive ductal cancer - 85.7%; invasive lobular cancer –8.5%; other forms: 2.9% and 2.9%, respectively. Grade G for the mammary gland determines the degree of tumor differentiation, the higher the differentiation of cells, the less aggressive the tumor and a better prognosis (Table 2).

A study of the expression of RE and RP in patients with breast cancer showed that positive expression of RE and RP (RE +/RP +) was detected in 23 (32.9%); negative RE and positive RP (RE-/RP +) in 14 (20%); positive RE and negative RP (RE +/RP-) in 12 (17.1%); negative RE and RP (RE-/RP-) - in 21 (30.0%) patients. Her-2/neu receptor expression was studied in 70 patients, depending on the level of expression, the patients were divided into 4 groups, while in 31 patients did not have Her-2/neu (-), which amounted to 44.3%; in 12, the weakly positive phenotype Her-2/neu (1+) was determined - 17.1%; Her-2/neu (2+) positive phenotype in 11 - 15.7%; Her-2/neu (3+) three times positive in 16 - 22.9%.

During MR – mammography, skin and internal architectonics were evaluated: thickening of the skin was found in 2.9% of women. Skin deformation over education was found in 2.9% of women. Concerning the surrounding tissues, the formations were divided into two types of growth: infiltrating and expansive. In 82.9% of women, formations were characterized by an infiltrating

Table 1. Distribution of patients by stages and TNM system

Stage	TNM	Number of patients n=70 (%)	
		abs	%
Stage I	$T_1N_0M_0$	3	4,3
Stage IIa	$T_1N_1M_0$	4	5,7
	$T_2N_0M_0$	11	15,7
Stage IIb	$T_2N_1M_0$	12	17,1
Stage IIIa	$T_2N_2M_0$	25	35,7
	$T_3N_1M_0$	13	18,6
Stage IIIb	$T_4N_1M_0$	2	2,9
Total		70	100,0%

Table 2. The distribution of patients depending on the degree of tumor differentiation

Degree of differentiation	Number of patients n=70	%
G1	9	12,8
G2	38	54,3
G3	23	32,8

Table 3. Phenotype classification based on biological features of breast cancer

Immunohistochemical status	Number of patients (n=70)	
	n	%
Luminal A	20	28,6
Luminal B type	22	31,4
Luminal B Her-2/neu negative	8	11,4
Luminal B Her-2/neu positive	14	20,0
Her-2/neupositive	11	15,7
Triple negative	17	24,3
Total	70	100

type of growth, which was often characteristic of ductal carcinoma. Expansive growth was found in patients with medullary cancer (17.1%). Analyzing data MR mammogram, 57 (81.4%) women had irregular shapes, in other cases, their shape was round and/or oval and lobulated, respectively 3 (4.3%) and 9 (12.8%); with uneven and fuzzy - 44 (62.9%), also tuberous 8 (11.4%) and spiculate contours were in - 13 (18.6%). Less often, their contours were smooth even in 5 (7.1%) cases. The kinetic changes in the MR signal depended on the size of the tumor, less commonly the histological types of breast cancer. Malignant tumors up to 10 mm HF were intensively accumulated in the central and peripheral regions, in the first minutes of the study with rapid leaching and the release of the "plateau" 60.0% and 40.0%, respectively. Breast cancer with histological type IPR, when they exceeded 11 mm, with contrast enhancement, had dynamic criteria typical of malignant tumors. Contrast method started faster on the periphery of the tumor. The MR signal increased rapidly, reaching a maximum by the 2 minutes after the introduction of gadolinium. Subsequently, the signal either reached a “plateau” (40.0%), or quickly began to decline from 2 to the 11 minutes after contrast enhancement (60.0%). In one patient, MR signal increased slowly, which was the reason for the error in the diagnosis. With sizes of 11–20 mm, in most cases (70.0%), contrasting of the pathological formation began centripetally from the first minutes. The discrepancy between MR-mammographic and histological data was observed in 6 patients: of these, in 3 patients, MRI data were false-positive and 3 were false-negative. False-negative results are because in 3 women (4.3%) the intensity of the MR signal from tumors did not increase significantly, thereby causing difficulties in the differential diagnosis of the nature of the tumor. Upon verification, this MR picture was characteristic of invasive ductal and mucinous carcinomas.

False-positive results were associated with hypervascularization of the tumor which as a result was evaluated as malignant mass in 3 (4.3%) cases. In two cases, there were fibroadenomas and a leaf-shaped tumor. Dynamic MRI revealed multicentric breast growth in 3 cases, which coincided with the data of histological examination. Next, we analyzed the main diagnostic, morphological, and molecular genetic factors that influence the outcome of the disease. In our study, the luminal A-subtype was noted in most patients (20 of 70 cases; 28.6%). But this group did not show any particular MR - signs of malignancy.

4. DISCUSSION

Considering the role of MRI in the diagnosis of breast cancer in women with a high risk of occurrence, it should be noted that certain types of tumors that are detected only by this method. Even with a retrospective review of ultrasound images of these patients in 39% of cases, the tumors remain unrecognized. Most of them are invasive ductal carcinomas - 62%, DCIS (ductal carcinoma in situ) - 38% [15]. Among the tumors that are detected by MRI and ultrasound, but remain hidden during mammography, even with retrospective image review (47%), invasive

ductal carcinomas account for 80%, ductal carcinomas DCIS - 20% [16]. The reason for poor visualization of tumors in women carriers of RP mutations by mammography is the fact that breast cancer occurs in them at a younger age than in the general population of women. It is also known that the mammographic density of the mammary gland is inversely proportional to the age of the woman. In carriers of RP mutations, the dense background of the gland hides additional formations in the structure, which, in addition, rarely display malignant morphological features, such as displacement of surrounding tissues, spicules, microcalcifications [17]. Every year, an increasing amount of knowledge about the manifestations of genetically determined breast cancer is changing the standard approaches to monitoring patients at high risk for breast cancer associated with mutations in the genes RP, BRCA2, etc. There is a high risk of developing synchronous and metachronic breast cancer, tumors with multicentric growth in this group of patients [18,19] require a more thorough examination. Due to the low efficiency of standard examination methods (MG and ultrasound), it became necessary to include an additional method that allows you to objectively characterize changes in the breast tissue. The non-ionizing MRI method showed high sensitivity in detecting early breast cancer regardless of the age of the patients. Our study showed how to confirm the feasibility of using an integrated approach in the diagnosis of hereditary breast cancer with MRI along with MG and ultrasound.

5. CONCLUSION

Imaging is of great importance for the diagnosis and treatment planning of patients with breast cancer. As indicated earlier, the accuracy of assessing the degree of local spread of the tumor depends on many external and internal factors that can affect the resolution of radiation diagnostic methods. Therefore, at the first stage, we used the whole complex of diagnostic methods to determine the place of each of them in the algorithm for evaluating the effectiveness of diagnosis of breast cancer patients. Determining the level of expression of ER and RP in a tumor is mandatory; IHC method is preferred. The result of determining receptor status should include data on the percentage of RE + and RP + cells and staining intensity. At the same time, the expression levels of HER2 and Ki67, which are also taken into account when planning therapy, should be determined by the IHC method.

CONSENT

Written informed consent was obtained from the participants of the study.

ETHICAL APPROVAL

All experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Hamilton L.J., Evans A.J., Wilson A.R. et al. Breast imaging findings in women with BRCA1- and BRCA2-associated breast carcinoma. Clin Radiol. 2004;59(10):895–902.
2. Veltman J., Mann R., Kok T. et al. Breast tumor characteristics of BRCA1 and BRCA2 gene mutation carriers on MRI. Eur Radiol. 2008;18(5):931–8.
3. Kuhl CK, Schrading S, Leutner CC, et al. Mammography, breast ultrasound and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. J Clin Oncol. 2005; 23(33):8469–76.
4. Warner E, Plewes DB, Hill KA, et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. JAMA. 2004; 292(11):1317–25.
5. Riedl CC, Ponhold L, Flöry D, et al. Magnetic resonance imaging of the breast improves detection of invasive cancer, preinvasive cancer, and premalignant lesions during surveillance of women at

high risk for breast cancer. Clin Cancer Res. 2007;15(13):6144–52.

6. Kriege M, Brekelmans CT, Boetes C, et al. Magnetic resonance imaging screening study group. Efficacy of breast cancer screening with MRI and mammography in women with a familial or genetic predisposition. N Eng J Med. 2004;351(5): 427–37.
7. Lehman CD, Blume JD, Weatherall P, et al. International breast MRI consortium working group. Screening women at high risk for breast cancer with mammography and magnetic resonance imaging. Cancer. 2005;103(9):1898–905.
8. Lehman CD, Isaacs C, Schnall MD. Cancer yield of mammography, MR, and US in high-risk women: Prospective multi-institution breast cancer screening study. Radiology. 2007;244(2):381–8.
9. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA: A Cancer Journal for Clinicians. 2015;65:87–108.
10. Abdulkareem ST. Breast magnetic resonance imaging indications in current practice. Asian Pac J Cancer Prev. 2014; 15:569-75.
11. Lee CH. Problem solving MR imaging of the breast. RadiolClin North Am. 2004;42: 919.
12. Karger S, Freiburg G Kh. Recommendations for pathologists on immunohistochemical studies of estrogen and progesterone receptors in breast cancer. Breast Care (Basel). 2010;5(3): 185-7.
13. Carlos S, Vallejos HL, Gómez WR. Cruz Clinical Breast Cancer. 2010;10(4):294-300.
14. Lloyd MC, Allam-Nandyala P, Purohit CN, Burke N, Coppla D, Bull MM. Using image analysis as a tool to evaluate prognostic and prognostic biomarkers of breast cancer: How reliable is it? J PatholInform. 2010;1:29.
15. LaTrenta LR, Menell JH, Morris EA, et al. Breast lesions detected with MR imaging: utility and histopathologic importance of identification with US // Radiology. 2003; 227(3):856-861.
16. Causer PA. Breast cancers detected with imaging screening in the BRCA population: Emphasis on MR imaging with histopathologic correlation // Radio Graphics. 2007;27:165-182.
17. Tran B, Bedard PL. Luminal-B breast cancer and novel therapeutic targets. Breast Cancer Res. 2011;30;13(6):221.
18. Stomper PC, Herman S, Klippenstein DL, et al. Suspect breast lesions: findings at dynamic gadolinium-enhanced MR imaging correlated with mammographic and pathologic features // Radiology. 1995; 197:387-395.
19. Stoutjesdijk MJ, Boetes C, Jager GJ, et al. Magnetic resonance imaging and mammography in women with a hereditary risk of breast cancer // J. Natl. Cancer Inst. 2001;93:1095-1102.

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