COMBINED USE OF MAMMOGRAPHY AND ULTRASOUND IN THE DIAGNOSIS OF BREAST CANCER IN WOMEN WITH HIGH TISSUE DENSITY

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Introduction. Breast cancer (BC) is the most common malignancy in women worldwide and is a leading cause of cancer-related mortality [1,2]. According to the World Health Organization, more than 2 million new cases are registered annually, and early diagnosis remains a key factor determining patient survival [1].

Mammography is currently recognized as the "gold standard" for breast cancer screening and has a high sensitivity, reaching 80–98% in women with predominantly fatty breast tissue [3,4]. However, the effectiveness of the method is significantly reduced in women with high breast density (BI - RADS 3–4), where sensitivity can decrease to 30–48% [4–6]. This is due to the fact that fibroglandular tissue and tumor formations have similar radiographic density, which complicates their differentiation and can lead to false-negative results [5,7].

High breast density not only reduces the diagnostic accuracy of mammography but is also considered an independent risk factor for breast cancer [6,8]. This increases the likelihood of so-called "interval cancers" detected between screening examinations, which worsens the prognosis of the disease [8].

Ultrasound examination (US) is widely used as an additional imaging method, allowing for more effective differentiation between cystic and solid lesions, as well as the detection of pathological changes not visualized by mammography [9–11]. Unlike mammography, the diagnostic effectiveness of ultrasound is less dependent on breast tissue density [10,12].

According to a number of studies, the combined use of mammography and ultrasound can increase the overall sensitivity of breast cancer diagnosis from 63% to 90–95%, as well as increase the detection of tumors that are not detectable by radiographic examination [11,13]. However, the additional use of ultrasound is accompanied by an increase in the number of false-positive results and the number of invasive procedures, which requires a balanced approach to its use [12,14].

In clinical practice in Tashkent, it was noted that mammography alone does not always provide sufficient diagnostic effectiveness, especially in women with dense breast tissue. Despite this, the combined use of imaging techniques in Uzbekistan remains understudied and requires further analysis.

The aim of this study is to evaluate the diagnostic value of ultrasound in addition to mammography in women with dense breasts in a retrospective analysis.

Materials and methods. This study is a retrospective analysis conducted at medical institutions in Tashkent between 2022 and 2024. The study included 200 women aged 35 to 78 years who sought breast examination as part of screening or diagnostic search. Inclusion criteria were the presence of dense breast structure (BI - RADS 3-4) and mammography. Patients with a previously established diagnosis of breast cancer were excluded from the study. Mammography was performed using standard projections (craniocaudal and mediolateral oblique). Breast

density assessment and interpretation of the results were carried out in accordance with the BI - RADS classification (American College of Radiology).

Patients with negative or questionable mammography results underwent additional breast ultrasound examination. Ultrasound was performed using high-frequency linear transducers (7–12 MHz). The echogenicity of the lesion, its contours, shape, orientation, the presence of acoustic shadowing or enhancement, and vascularization using color Doppler mapping were assessed. If suspicious lesions (BI - RADS ≥4) were detected, morphological verification of the diagnosis was performed. Biopsy was performed in 50 patients, followed by cytological and/or histological examination. Descriptive and analytical statistics were used for statistical processing of the data. Quantitative data are presented as the mean (M) and standard deviation (SD), while qualitative indicators are presented as absolute and relative frequencies (%). In some cases, the indication for biopsy was the presence of a palpable lesion with negative results of radiographic methods.

The diagnostic performance of the methods was assessed by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). A comparison of the diagnostic performance of mammography and the combined approach (mammography + ultrasound) was performed using the χ^2 (chi-square) test. Differences were considered statistically significant at $p < 0.05$. Statistical data processing was performed using SPSS software (version 25.0, IBM Corp., USA).

Results. The study included 200 women with dense breast structure (BI - RADS 3-4) aged 35 to 78 years. The diagnosis of breast cancer was established based on a combination of mammography, ultrasound, clinical examination and morphological verification when indicated. Based on the results of a comprehensive examination (mammography, ultrasound and morphological verification when indicated), breast cancer was diagnosed in 77 patients (38.5%), while benign changes were detected in 123 patients (61.5%). Diagnostic efficacy of mammography: using mammography alone, malignant tumors were detected in 29 of 77 patients, which corresponds to a sensitivity of 37.7%. In 48 patients with confirmed cancer, mammography gave a false-negative result. The specificity of the method was 91.9%, while false-positive results were noted in 10 cases. The overall diagnostic accuracy was 71.0%.

Diagnostic efficacy of ultrasound: The use of ultrasound as an adjunct allowed the detection of 32 cases of breast cancer not visualized by mammography. The sensitivity of ultrasound was 41.6%; however, an increase in the number of false-positive results (n = 25) was noted, resulting in a decrease in specificity to 79.7%.

Combined approach (mammography + ultrasound): the combined use of methods ensured the detection of 61 cases of cancer, which increased the sensitivity of diagnosis to 79.2% (p < 0.001 compared to mammography). In 16 patients (20.8%), malignant tumors were not detected by radiation methods and were diagnosed on the basis of morphological examination.

Morphological verification: Biopsies were performed on 50 patients with suspicious lesions. Histological and/or cytological examination confirmed malignancy in 16 patients (32.0%), while benign changes were detected in the remaining 34 cases (68.0%).

Table 1. General characteristics under study groups

Indicator	Meaning
General number female patients	200
Age (range)	35–78 years old
Revealed Cancer	77 (38.5%)
Benign changes	123 (61.5%)
Biopsy completed	50 (25.0%)

malignant (by biopsy)	16 (32.0%)
benign	34 (68.0%)

Table 2. Diagnostic indicators methods visualizations

Indicator	Mammography	Ultrasound	MG + ultrasound
Sensitivity	37.7%	41.6%	**79.2%**
Specificity	**91.9%**	79.7%	75.6%
PPV	74.4%	56.1%	67.0%
NPV	70.2%	68.5%	**85.3%**
Accuracy	71.0%	65.0%	**77.0%**

Discussion. The results of the study demonstrate the limited diagnostic efficacy of mammography in women with dense breast structure. The sensitivity of mammography in our study was 37.7%, which is significantly lower than the values described in the literature for women with predominantly fatty tissue, where it can reach 80–90% [3,4]. The decrease in sensitivity is explained by the high density of fibroglandular tissue, which masks tumor formations and complicates their visualization [5,7]. The additional use of ultrasound examination allowed us to increase the detection of breast cancer. In our study, ultrasound detected 32 additional cases of cancer not diagnosed by mammography, which confirms its significant role as a second-line method. The sensitivity of ultrasound was 41.6%, which is consistent with the data of other studies indicating its ability to detect mammographically occult tumors [9,11].

The most significant results were obtained with the combined use of mammography and ultrasound. The sensitivity of the combined approach reached 79.2%, more than twice that of mammography alone. These data are comparable with the results of previously published studies, which noted an increase in overall diagnostic sensitivity to 90–95% with the use of combined methods [11,13].

At the same time, a decrease in specificity should be noted when using ultrasound and the combined approach, which is due to an increase in the number of false-positive results. In our study, the specificity of mammography was 91.9%, while with ultrasound it was 79.7%, and with the combined approach it was 75.6%. This confirms the need for cautious interpretation of ultrasound results and its use primarily in patients with increased risk or dense breast structure [12,14].

Of particular note is the fact that in 16 patients (20.8% of all cancer cases), malignancies were not detected by any imaging method and were diagnosed only after morphological examination. This result highlights the limitations of both mammography and ultrasound, as well as the need for clinical vigilance and a comprehensive approach to diagnosis.

Our study also noted a high frequency of benign changes (61.0%), predominantly represented by cysts and fibroadenomas, which is consistent with literature data [9]. This explains the increase in the number of invasive interventions using ultrasound, since the differentiation of benign and malignant formations requires morphological verification.

The obtained results have important practical implications for clinical practice in Uzbekistan. The introduction of a combined approach (mammography and ultrasound) in women with dense breast tissue significantly increases the detection of cancer in its early stages, potentially improving prognosis and reducing mortality.

Thus, despite the increase in the number of additional examinations and a decrease in specificity, the combined use of imaging methods is justified and appropriate in the diagnosis of breast cancer in this category of patients.

Despite the findings, this study has a number of limitations that should be considered when interpreting the data.

Firstly, the study is retrospective in nature, which may lead to certain systematic errors associated with the selection of patients and incompleteness of the initial data.

Secondly, the relatively small sample size (200 patients) limits the generalizability of the results to a wider population.

Third, ultrasound is an operator-dependent method, and its diagnostic effectiveness may vary depending on the experience of the specialist, which could affect the results obtained.

In addition, the study did not conduct a detailed analysis of risk factors (age, hormonal status, family history) that may influence the likelihood of developing breast cancer.

It should also be noted that not all patients underwent morphological verification, which may lead to potential underestimation or overestimation of diagnostic indicators.

Finally, the lack of long-term follow- up does not allow us to assess the frequency of missed cancer cases and long-term clinical outcomes.

Conclusion. The results of this study showed that mammography has limited diagnostic efficacy in women with dense breast tissue, demonstrating low sensitivity in detecting malignant lesions. The addition of ultrasound significantly increases breast cancer detection, especially in cases not detected by mammography. The highest diagnostic efficacy rates were achieved with the combined use of mammography and ultrasound, confirming the feasibility of this approach in patients with dense breast tissue.

Despite decreased specificity and an increased rate of false-positive results, combined diagnostics enables earlier detection of malignant tumors, which is essential for improving prognosis and choosing treatment strategies. Thus, the introduction of a combined approach (mammography + ultrasound) into clinical practice in Uzbekistan is a justified and promising direction in breast cancer diagnostics.

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