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*Original Article*

# Diagnosis significance of single high frequency ultrasonography and mammography and their combined examination on breast cancer

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**Abstract:** Objective: to evaluate the diagnosis significance of single high frequency ultrasonography and mammography and their combined examination on breast cancer. Methods: 352 female patients diagnosed with breast cancer were selected in this study from The First Affiliated Hospital of Zhengzhou University from January 2012 to December 2014. Among them, 124 cases only received high-frequency ultrasonography examination, 102 cases only mammography, and the rest 126 patients received both. Results: the patients with single mammography examination had the coincidence rate of 79.4%, misdiagnosis rate of 10.8%, and missed diagnosis rate of 9.8%; the patients with single high frequency ultrasonography examination had the coincidence rate of 83.9%, misdiagnosis rate of 9.7%, and missed diagnosis rate of 6.5%; and patients with combined examination had the coincidence rate of 89.7%, misdiagnosis rate of 6.3%, and missed diagnosis rate of 4.0%. The differences of the detection rate and missed diagnosis rate between the combination diagnosis and single examinations had statistical significance, but the misdiagnosis rate had not. Conclusion: Mammography and high frequency ultrasonography have their own advantages, and it is complementary to adopt both in the diagnosis of breast cancer, which can significantly improve the detection and accuracy rate, and also decrease the misdiagnosis and missed diagnosis rate.

**Keywords:** Breast cancer, high frequency ultrasonography, mammography, combination of high frequency ultrasonography and mammography

## Introduction

The incidence rate and fatality rate of breast cancer increase year by year, and the patients are getting younger and younger. As the primary prevention method can not meet the needs of most breast cancer patients, the secondary prevention has become the main way to improve the prognosis of breast cancer. Meanwhile, the early detection, diagnosis and therapy of breast cancers are required for better quality of life of the patients. In this study, the clinical data of the breast cancer patients in The First Affiliated Hospital of Zhengzhou University during January 2012 to December 2014 were retrospectively analyzed. The aim of this study was to investigate the clinical value of the normal detection methods (e.g. high frequency ultrasonography and mammography), and to provide a better detection method for early clinical prevention, diagnosis, and treatment of breast cancer.

## Materials and methods

### *General materials*

352 female patients diagnosed with breast cancer in The First Affiliated Hospital of Zhengzhou University from January 2012 to December 2014 were recruited in this study. And their age ranged from 25 to 66 years old (an average age of 48.5±2.6 years old). 124 patients received single high frequency ultrasonography detection, 102 patients received single mammography detection, and 126 patients received both detections. Their main clinical manifestations were breast lumps, nipple discharge, nipple hemorrhage, breast pain, skin thickening, nipple retraction, etc.

**Table 1.** Comparison of different examination methods for breast cancer detection

| Method | Cases (n) | Diagnosis coincidence population [n (%)] | Misdiagnosis population [n (%)] | Missed diagnosis population [n (%)] |
|---|---|---|---|---|
| High frequency ultrasonography | 124 | 104 (83.9)* | 12 (9.7) | 8 (6.5)* |
| Mammography | 102 | 81 (79.4)* | 11 (10.8) | 10 (9.8)* |
| Combined diagnosis | 126 | 113 (89.7) | 8 (6.3) | 5 (4.0) |
| $X^2$ value | | 8.357 | 3.941 | 6.353 |
| *P* value | | 0.019 | 0.143 | 0.027 |

Note: *$P<0.05$, compared to combined diagnosis method.

**Table 2.** Comparison of high-frequency ultrasonography and X-ray mammography in diagnosing 126 cases

| Mammography | High frequency | | Total |
|---|---|---|---|
| | + | - | |
| + | 86 | 14 | 100 |
| - | 17 | 9 | 26 |
| Total | 103 | 23 | 126 |

Note: (+) indicates the test was positive, (-) indicates the test was negative; (Total) indicates the total cases of positive and negative; $x^2=5.012$, $p=0.021$.

*High frequency ultrasonography detection*

Ultrasonic diagnosis instrument (Philips, Netherlands) with 15,000 pixels resolution and 5-12 MHz of the probe was used in this study. Patients laid themselves flat with arms lifted so as to fully expose bilateral breasts. Two-dimensional ultrasonography was applied to detect the location and features (e.g. size, edge shape, internal echo, vertical and horizontal diameters and sound, etc.) of tumors in each quadrant. Color Doppler was used to investigate the blood morphology and distribution inside the tumor and surrounding areas. Adler semi-quantitative method was adopted to analyze blood flow and resistance index (RI) [1]. The bilateral axillary tissues of the patients were detected regularly, including the lymph node size, quantity, morphology, edge, internal echo and blood supply, etc.

*Mammography detection*

Digital mammary gland machine (PlanmedOy, Finland) was adopted in this study. It could automatically and fully expose the bilateral breasts from the general and oblique position, but the photograph needs to be compressed and enlarged when necessary. The optimal inspecting time is during the 3rd day to the 10th day after the menstruation is completely over. The focus, size, quantity, form, calcification (size, shape, quantity and distribution), blood flow, and lymph node of the breast were observed.

*Diagnosis standard of high frequency ultrasonography*

The patients can be detected by two-dimensional diagnosis with rough edge, uneven internal echoes, rear echo attenuation, and irregular tumor shape with a ratio of vertical diameter to horizontal diameter greater than 1. Also, the patients can be detected as II level color Doppler flow imaging (CDFI) or above, and no less than 12 cm/s of the $V_{max}$ arterial blood flow by color Doppler. The patients who are diagnosed with breast cancer should have either 3 items of two-dimensional manifestations, or 2 items of color Doppler manifestations [2].

*Diagnosis standard of mammography*

The direct signs in the patients checked by mammography are shadows of the lump and nodular, tiny calcified lesions, lobulation sign, spicule or horn lesions on the edge, and blur edge. The indirect signs include skin change, structural disorder, vascular lesions and catheter sign. The patients who are confirmed with breast cancer should have 2 direct signs, or 1 direct sign and 2 indirect signs [3].

*Combined diagnosis standard*

Any one of the malignant signs of high frequency ultrasonography or mammography was required for determining whether or not the patient has breast cancer.

*Statistical method*

In this study, misdiagnosis refers that the findings were inconsistent with the imaging and

**Table 3.** Comparison of detection rate between high-frequency ultrasonography and mammography [n (%)]

| Pathological features | High frequency ultrasonography (n=225) | Mammography (n=206) | $X^2$ value | *P* value |
|---|---|---|---|---|
| Lump | 202 (89.8%) | 144 (69.9%) | 27.856 | <0.001 |
| Microcalcification | 72 (32.0%) | 142 (68.9%) | 51.318 | <0.001 |
| Abnormal blood vessels and blood flow signal | 142 (63.1%) | 69 (33.5%) | 36.837 | <0.001 |
| Enlarged axillary lymph node | 88 (39.1%) | 52 (25.2%) | 6.845 | 0.002 |

Note: the numbers (percentage) indicate the proportion of each pathological feature in the total cases.

pathological results. Missed diagnosis means that the patients were not able to detect with breast cancer. Diagnosis coincidence indicates that the detected manifestations were coincident with the pathology results. SPSS13.0 software was adopted for statistical analysis, and chi-square test was used to check the enumeration data, and $P<0.05$ was considered statistical significant.

## Results

*Invasion site*

All the included 352 cases had unilateral breast cancer, 184 cases with disease on the left breast (52.23%), and 168 cases on the right breast (47.77%). Among them, there were 215 cases with disease in the outer upper quadrant (61.08%), 49 cases in the inner upper quadrant (13.92%), 26 cases in the inner lower quadrant (7.39%), 48 cases in the outer lower quadrant (13.64%), and 14 cases in the rear areola(3.98%). The tumor diameters were range from 0.7-5.4 cm, with an average of 2.6±0.3 cm.

*Pathological types*

8 cases had intraductal carcinoma (2.27%), the rest 344 cases had invasive nonspecific carcinoma (97.73%). Meanwhile, in these 344 cases, 208 cases (59.09%) of invasive ductal carcinoma in, 74 cases (21.02%) of invasive lobular carcinoma, 41 cases (11.65%) of papillary carcinoma, 15 cases (4.26%) of carcinoma simplex, and 6 cases (1.70%) of medullary carcinoma were found.

*Comparison of different examination methods for breast cancer detection*

It had statistical significance in the detection rate and missed diagnosis rate among the three methods for breast cancer (high frequency ultrasonography, mammography, and combined diagnosis), but had no statistical significance in the missed diagnosis rate. See in **Table 1**.

*Comparison of high-frequency ultrasonography and X-ray mammography in diagnosing 126 cases*

Positive results of high frequency ultrasonography and mammography had statistical significance compared with the negative ones, as shown in **Table 2**.

*Comparison of pathological characteristics between the single high frequency ultrasonography and single mammography*

The difference of pathological characteristics detected by single high frequency ultrasonography and single mammography was statistically significant. The detection rates of lump, abnormal blood flow and axillary lymph nodes by high frequency ultrasonography were higher than those by mammography. But the detection rate of microcalcifications by single high frequency ultrasonography was lower than that by mammography, as shown in **Table 3**.

## Discussion

There are many methods to inspect breast cancer, such as ultrasonography, mammography, magnetic resonance (NMR), etc. Ultrasonography and mammography are the most commonly used ones clinically. In this study, the coincidence rates of mammography and high frequency ultrasonography were 79.4% and 83.9%, respectively ($P>0.05$), which are consistent with the findings reported in previous literature [4]. The breast cancer is very complex which includes noninvasive carcinoma, early-stage invasive carcinoma, invasive specific car-

cinoma and invasive nonspecific cancer, inflammatory breast cancer, eczema-like breast cancer and invasive ductal carcinoma (accounting for 65%~85%). In our study, the patients with invasive ductal carcinoma accounted for 59.09%. Although the complex pathological features can be shown as different image features by mammography and high frequency ultrasonography, the same image also can indicate different pathological types. Therefore, it is difficult to make the breast cancer diagnosis only based on imaging performances, and more difficult to exclude the false negative expression if apply mammography singly. One literature in China reported that the patients with false negative expression can be about 5%-15%, even up to 15%-25%. In this study, there were 20.59% (21/102) false negative expressions which included 11 cases of misdiagnosis and 10 cases of missed diagnosis by single application. Among them, 3 cases accompanied by severe mammary gland hyperplasia (<2 cm) were misdiagnosed as breast atypical hyperplasia; 6 cases with high density mammary gland were misdiagnosed as dysplastic nodules; 2 cases with oval shaped medullary carcinoma with smooth boundary were misdiagnosed as fibroma; 2 cases with tumor near chest wall were missed diagnosis because of the blurring tumor (<2 cm) and its low density; 2 cases were missed diagnosed because of oppression; 1 case was misdiagnosed as ductal carcinoma because of the clear tumor and non-calcification; 3 cases were missed diagnosed because of the dense breast. However, another international literature reported that the false negative expression was only 8%-10% [8]. In their study, 12 cases with misdiagnosis and 8 cases with missed diagnosis were found by single application of high frequency ultrasonography. Among them, 2 cases with tumor size (<1 cm), 2 cases with medullary carcinoma, 2 cases with simplex carcinoma (with unsharp sphere and smooth boundary and misdiagnosed as fibroma), 2 cases were misdiagnosed as atypical hyperplasia; 3 cases were misdiagnosed as dysplastic nodules, and 1 case was missed diagnosed (re-examined by the ultrasonography with acoustic shadow at the rear of the nipple). The tumors of the 2 missed diagnosis cases were located at the end of the mammary gland with a diameter less than 1 cm. 5 cases were miss-diagnosed because of the unclear tumor and two obese and big mammary gland patients. Therefore, the combined inspection can prevent from some bad effects and increase the diagnosis rate, especially in the early stage, and it has become the hot topic of among scholars [2, 3, 9].

The mechanism of the high frequency ultrasonography was the usage of acoustic impedance that will reflect different echoes against different tissues. And it has different absorption attenuation of X-ray in the imaging of mammography from which we can see their own advantages, and disadvantages in diagnosing the tissues [10]. 11 cases were detected as no specific lesion by the combined inspection, but were misdiagnosed and missed diagnosed by single high frequency ultrasonography or single mammography. Among them, 7 cases were detected with malignant calcification through mammography, 4 cases were misdiagnosed through mammography because of the local structural disorder and irregular dense shadows. In these 4 cases, 1 case was diagnosed with fibroma accompanied by calcification via single high frequency ultrasonography. Also, there were 12 cases which were not detected with tumor by single mammography, but were detected with tumor by the high frequency ultrasonography, and 8 cases of them had abnormal II-III blood flow, 1 case had axillary lymph nodes and 2 cases with invasion into the chest wall. 2 cases with tiny lesion detected by mammography and ultrasonography and were diagnosed with fibroma. The following re-examination showed that this fibroma had the risk of developing into axillary lymph nodes for its fibroids changes on the surface. The findings had been verified in their operations. Calcification is an important index of benign and malignant tumor for examination. The calcification can exist in both early and late (malignant) tumors and it is typically small with a diameter of 10~500 μm. The mammography can detect the minimal calcification of 200 μm [7], while the current ultrasonography can detect 100~500 μm [11].

This research showed that mammography had a higher detection rate on calcification than high frequency ultrasonography. The microcalcification, a key sign for breast cancer diagnosis, including sand-like microcalcification, tiny rod-like microcalcification, Y-shape calcification, and pin-like microcalcification, are usually seen in the invasive ductal carcinoma. The

results in this study showed that the detection rates of abnormal blood flow signal and axillary lymph nodes by high frequency ultrasonography were higher than that through mammography. The blood flow is sufficient to judge whether the tumor is malignant or not. The blood vessels distribution and structure were central type and penetration type. Some researches classified the mammary gland malignant degree into four types based on the tumor's distribution and structure, including angionecrosis, blood vessels diameter, twisted blood vessels, and arteriovenous vessels. The blood vessels of fibroadenoma usually go though the upper of the tumor and nodes [12]. There are a lot of fat in axillary site, so the tumor structure is complex. The enlarged lymph node in the breast cancer patients might be hyperplasia, and can transfer. The two inspections can easily detect the lymph node. While, to the transfer diagnosis, the accuracy and sensitivity of them are significantly different. In this study, the coincidence rate of axillary lymph node by single mammography and high frequency ultrasonography were 26.2% and 38.6%, respectively. The diagnosis criteria of transferred lymph nodes are as follows: the diameter is greater than 0.5 cm; the ratio of length to widthis less than 1.7; nolymph nodes gate; cortical asymmetric thickening and increased peripheral blood flow. The cortical asymmetric thickening and increased peripheral blood flow of small lymph node (<1 cm) are different from those of normal lymph nodes [13].

Combined detection has advantages of both single methods and can reflect the pathological characteristics more accurately. Ultrasonography detection is suitable for people of all ages, especially the young, pregnant and lactating women. Mammography is not suitable for pregnant women, lactation women and acute mastitis because of its radiation, and it should not be done frequently [14]. Mammography detects the whole mammary gland, which would bring less misdiagnosed cases. However, ultrasonographyis easy to have missdiagnosed cases because of the small and light echo [15].

The calcification detected by mammography is more clear than ultrasonography. The accuracy of high frequency ultrasonography is not affected by the type of gland, but is not high in the obese patients and patients with big breasts. Also, mammography is difficult to detect the mammary glands with high density. This might be one of the reasons that there were more false negative expressions in China. Ultrasonography can scan from different angles, including the small breast cancers in the inner quadrant or near the edge or chest wall where the current mammography cannot reach. Ultrasonography is more suitable for the young patients, while mammography is more suitable for the elder patients because of their low fat density [16].

## Conclusion

High frequency ultrasonography and mammography are simple and low-costed, without causing trauma in the patients with breast cancer. Since it had no significant difference in the diagnosis coincidence rate between the patients with single high frequency ultrasonography or mammography, clinicians should choose one suitable for the patients based on their diseases. Also, combined application of both methods can obviously increase the detection rate and accuracy rate of breast cancer, decrease misdiagnosis rate and missed diagnosis rate. Therefore, the combined inspection plays an active role in the early-stage diagnosis of breast cancer.

## Disclosure of conflict of interest

None.

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## References

[1] Adler DD, Carson PL, Rubin JM and Quinn-Reid D. Doppler ultrasound color flow imaging in the study of breast cancer preliminary findings. Ultrasound Med Biol 1990; 16: 553-559.

[2] Shi CY, Zhang LT and Chen Y. Study of mammography and color Doppler ultrasound in diagnosis of early breast cancer. Journal of Harbin Medical University 2005; 39: 531-533.

[3] Yuan ST, Zhao ZH, Lu XL, Wang J and Ling GL. The clinical value on diagnosis of early breast cancer by mammography combined with high frequency ultrasound. Shandong Medical Journal 2009; 49: 21-23.

[4] Meng QC, Tian YX, Gao LF and Ma AF. Analysis on breast cancer mammography imaging

signs. Hebei Medical Journal 2012; 34: 520-521.
[5] Zhou Q, Liu SR and Huang J. Analysis of two-dimension and high-frequency color Doppler ultrasonography for breast cancer. Journal of Jinan University (Medical Edition) 2009; 30: 441-444.
[6] Liang RB, Shi RX, Guo ZZ and Li X. Comparative analysis of BI-RADS III~IV lesions imaging by X-ray mammography and ultrasound. BME Clin Med 2011; 15: 37-40.
[7] Wang JL, Qin SC and Cui KF. Comparison of micro-pure imaging system of ultrasonography and mammography on microcalcification of breast tumor. Chinese Journal of Medical Imaging Technology 2012; 28: 297-300.
[8] Jackson EF, Barboriak DP, Bidaut LM, Jackson EF and Meyer CR. Magnetic resonance assessment of response to therapy: tumor change measure, truth data and error sources. Transl Oncol 2009; 2: 211-215.
[9] Masroor I, Ahmed MN and Pasha S. To evaluate the role of sonography as an adjunct to mammography in women with dense breasts. Pak Med Assoc 2009; 59: 298-301.
[10] Li QY and Wang Y. The value of ultrasonography and mammography combination diagnosis on breast tumor. Modern Journal of Integrated Traditional Chinese and Western Medicine 2011; 20: 85-86.
[11] Li YF and Liu HG. Comparison of breast lumps diagnosis of color ultrasonography and mammography. Shanghai Medical Imaging 2010; 20: 141-142.
[12] Guo SR, Li XX and Wu RX. New development about comprehensive application of breast cancer ultrasonic diagnosis. Hebei Medical Journal 2012; 34: 582-584.
[13] Leng ZP and Hua Y. Application progress of ultrasonography on breast cancer lymph node detection. Chin J Med Ultrasound (Electronic Edition) 2010; 7: 94-97.
[14] Wu SQ, Zhao ZH, Li PC, Liao HH and Liu JJ. Diagnostic significance of ultrasonography, mammography and combination of both on breast cancer. Journal of Modern Oncology 2010; 18: 1323-1325.
[15] Zhang J. Analysis on mammography and ultrasonography combined diagnosis on breast carcinoma in situ in 21 cases. Chin J Misdiagn 2011; 11: 4002-4002.
[16] Song SQ. Mammography combined with high-frequency ultrasonography for the diagnosis of early breast cancer. Journal of Qiqihar University of Medicine 2011; 32: 1730-1731.