REPORT

Evaluation on diagnosis significance of single high frequency Ultrasonography and mammography and combination on Breast Cancer

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Abstract: **T**o evaluate the diagnosis significance of single high-frequency ultrasonography and mammography and combination therapy of both on breast cancer. 352 cases of female breast cancer patients were selected from The First Affiliated Hospital of Zhengzhou University from January 2012 to December 2014. Among the 352 patients, 124 patients had only performed high-frequency ultrasonography detection, 102 cases of patients were only conducted mammography, and 126 patients had applied the combination detection of high-frequency ultrasonography and mammography. The coincidence rate of single mammography detection was 79.4%, the misdiagnosis rate was 10.8%, and the missed diagnosis rate was 9.8%; the coincidence rate of single high frequency ultrasonography detection was 83.9%, the misdiagnosis rate was 11.5%, the missed diagnosis rate was 4.6%; the coincidence rate of combination of high frequency ultrasonography detection was 89.7%, the misdiagnosis rate was 6.3%, the missed diagnosis rate was 4.0%. The detection rate and missed diagnosis rate of combination diagnosis had statistical difference with single high frequency ultrasonography and single mammography. There was no statistical difference on misdiagnosis rate. mammography and high frequency ultrasonography respectively had their own advantages. The combination application of both had better diagnosis complementary, and could significantly improved the detection rate and accuracy rate on breast cancer, and decreased the misdiagnosis rate and missed diagnosis rate.

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

INTRODUCTION

Breast cancer incidence rate and fatality rate increased year by year, and also had a younger age trend. It has become one of the most common malignant tumor of women, which has become the first or second malignant tumors of women in China's major cities, and early diagnosis and treatment has major significance (Wang, Li and Wang, 2014) Early diagnosis of breast cancer is the key to effective treatment and patient prognosis, and the rapid development of medical imaging technology has made important contributions to the early diagnosis of breast cancer detection. In the clinic, patients with breast cancer diagnosis using high-frequency ultrasound and X-ray mammography imaging, and diagnostic method is simple and effective (Chen, 2016). Since the development and wide application of the ultrasonic diagnostic apparatus, as well as digital mammography technology matures, the detection rate of breast imaging has been significantly improved (Wu, Peng and Wei, 2011). Two diagnostic methods have its own characteristics, and how to apply, is currently a hot issue in diagnosing breast diseases, and the key to improve breast cancer survival (Wu *et al*., 2010). While, the primary prevention method was no satisfactory. The secondary prevention was the main way to improve the prognosis of breast cancer. In order to achieve early detection, early diagnosis and early treatment of breast cancer and improve the quality of life, this study retrospectively analyzed the clinical data of patients with breast cancer who were pathological diagnosed and confirmed by surgery in The First Affiliated Hospital of Zhengzhou University. It aimed to investigate the difference and application significance of breast cancer diagnosis through high frequency ultrasonography and mammography, which was the normal breast disease detection method and provided reliable imaging basis for clinical prevention and early diagnosis of breast cancer.

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MATERIAL AND METHOD

General Material

There were 352 cases of breast cancer female patients who were selected from The First Affiliated Hospital of Zhengzhou University from January 2012 to December 2014. The age was from 25~66 years old, average age was (48.5±2.6) years old. 124 patients only performed high frequency ultrasonography detection, 102 patients

only had mammography and 126 cases received the combined therapy of both detection. The main clinical manifestations were breast lumps, nipple discharge, nipple hemorrhage, breast pain, skin thickening, nipple retraction, etc which were physical examined and without symptom.

High frequency ultrasonography detection

Ultrasonic diagnosis was the Philips HD 15000 color ultrasonic diagnostic instrument, with linear array probe, 5~12 MHz frequency, the center frequency of high frequency probe was more than 7.5 MHz. Patients was in supine position with arm lifted, in order to fully expose bilateral breasts. Two-dimensional ultrasonography was applied to detect breasts each quadrant to confirm the location of tumor. Meanwhile, many tumor features were observed, such as tumor size, edge shape, internal echo, the ratio of vertical and horizontal diameter and whether the sound had attenuated or not, etc. Color Doppler was used to investigate the blood morphology and distribution of tumor inner side and surrounding area. Adler semi-quantitative method was adopted to detect blood flow classification and blood flow resistance index (RI) value (Adler *et al*., 1990). Normal detection were bilateral axillary examination, the axillary lymph node size, quantity, morphology, border, internal echo and blood supply, etc.

Mammography

Planmed Digital Nuance global digital mammary gland machine from Finland was adopted in this study. It could fully automatic expose the general detected bilateral breasts axial view and oblique position, the photograph need to be compressed and enlarged when necessary. The detection time was within the 3rd days to 10th day after the menstruation completely over. It needed to observe breast disease focal size, quantity, form, presence of calcification, which included calcification size, shape, quantity and distribution and whether the abnormal blood or axillary lymph nodes.

Diagnosis standard of breast cancer high frequency ultrasonography

Two-dimensional ultrasonography included rough edge, uneven internal echoes, rear echo attenuation, irregular tumor shape, the ratio of vertical and horizontal diameter which was more than 1; color Doppler detection included CDFI blood flow classification α and above, or arterial blood flow Vmax not less than 12cm/s. Breast cancer was diagnosed and confirmed for patients to have either 3 items of two-dimensional manifestations, or 2 items of color Doppler manifestations (Shi, Zhang and Chen, 2005).

Diagnosis standard of breast cancer mammography

The direct signs were lump and nodular with shadows, timy calcification focal, lobulation sign, spicule or horn change on edge, blur edge. Indirect signs were skin change, structural disorder, blood vessels change and catheter sign. Breast cancer was diagnosed and confirmed for patients to have 2 direct signs, or 1 direct sign and 2 indirect signs (Yuan *et al*., 2005).

Combined diagnosis standard on breast cancer

Breast cancer was diagnosed and confirmed for patients to have either one malignant signs of high frequency ultrasonography and mammography.

STATISTICAL ANALYSIS

In this study, misdiagnosis was for the inconsistent of imaging results and pathological results. Missed diagnosis was for the non-detected patients. Both was the negative manifestation. Diagnosis coincidence was that the negative manifestation was coincident with pathology results. SPSS13.0 software was adopted for statistical analysis, and chi-square test of enumeration data, $P<0.05$ was for the difference with statistical significance.

RESULTS

Invasion site

In352 cases of breast cancer patients, 184 cases of patient had disease on left breast (52.23%), and 168 cases had disease on right breast (47.77%), all are unilateral breast cancer. 215 cases had disease on outer upper quadrant (61.08%), inner upper quadrant for 49 cases (13.92%), inner lower quadrant 26 cases (7.39%), outer lower quadrant 48 cases (13.64%), rear areola for 14 cases (3.98%). Tumor diameter 0.7~5.4cm, average (2.6±0.3) cm.

Pathological type

Apart from the 8 cases of intradutal carcinoma (2.27%), the rest 344 cases were invasive nonspecific carcinoma, accounting for 97.73%, which included 208 cases of invasive ductal carcinoma (59.09%), 74 cases of invasive lobular carcinoma (21.02%), 41 cases of papillary carcinoma (11.65%), 15 cases of carcinoma simplex (4.26%) and 6 cases of medullary carcinoma (1.70%).

Comparison of different inspection methods

The detection rate and missed diagnosis rate of the three methods for breast cancer had statistical significance, the missed diagnosis rate between the three did not have statistical significance; The statistical significance existed on detection rate and missed diagnosis rate of the single usage of high frequency ultrasonography and mammography and combined diagnosis treatment, as seen in table 1.

Comparison of the combined diagnosis of high frequency ultrasonography and mammography

Results on high frequency ultrasonography and mammography in combined diagnosis had statistical

Table 1: comparison of different examination methods for breast cancer detection [n(%)]

Method	Cases	Diagnosis coincidence population	Misdiagnosis population	Missed diagnosis population
High frequency ultrasonography	124	104 (83.9)	12 (11.5)	8 (4.6)
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	3.789	5.557
p value		0.019	0.006	0.007

Compared to combined diagnosis method, $^*P < 0.05$.

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

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

$X^2=5.012$, P=0.021

Table 3: Comparison of detection rate of case characteristics between high-frequency ultrasonography and mammography

Pathological features	high frequency ultrasonograpny (n=225)	Mamography (n=206)	X^2 value	P value
lump	202(89.8%)	144(69.9%)	27.856	<0.001
Micro calcification	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

significance, as shown in table 2. For 126 cases of patients, 86 cases had a positive diagnosis of ultrasound and mammography at the same time, while 9 patients have the diagnosis of negative. Ultrasound diagnosis was positive and X-ray mammography diagnosis was negative with 17 cases, and X-ray mammography diagnosis was positive while the ultrasound diagnosis of negative with 14 cases and $X^2= 5.012$, P = 0.021.

Comparison of detection rate for different pathological characteristics

The detection rate of two detection methods had statistical significance on tumor pathological characteristics. The detection rate of high frequency ultrasonography on lump, abnormal blood flow and axillary lymph nodes were higher than the results of mammography. The detection rate of micro calcifications was lower than that of mammography, as seen in table 3.

DISCUSSION

Breast cancer had many detection, such as ultrasonography, mammography, magnetic resonance (NMR), of which the ultrasonography and mammography were commonly used in clinical field. In this study, the coincidence rate of mammography and high frequency ultrasonography were respectively 79.4% and 83.9%, between which there was no statistical significance, which was coincident to literature (Meng *et al*., 2012). The Breast pathological type of caner was complex which included noninvasive carcinoma, early stage invasive carcinoma, invasive specific carcinoma and invasive nonspecific cancer, there were few inflammatory breast cancer, nipple eczema-like breast cancer, *et al*. The invasive ductal carcinona was the most common one, accounting for 65%~85%. The invasive ductal carcinoma in this group accounted for 59.09%. Although the complex pathological type of breast cancer could enable mammography and high frequency ultrasonography had different image features, the same image feature may indicate different pathological types. Therefore, it was difficult to make the breast cancer diagnosis only based on imaging performance. It had a great difference on the false negative expression of the single application of mammography. Domestic literature reported that the false negative expression was 5%~15%, even up to 15%~25%. In this group, the misdiagnosis of single application of mammography was 11 cases, missed diagnosis was 10 cases, false negative expression was 20.59% (21/102), among which there were 3 cases with combination of severe mammary gland hyperplasia, the tumor size was less than 2cm, which was misdiagnosed as breast atypical hyperplasia; 6 cases of high density mammary gland were misdiagnosed as dysplastic nodules; 2 cases of oval

shaped medullary carcinoma with smooth boundary were misdiagnosed as fibroma. The missed diagnosis were 2 cases near chest wall tumor, which was because the size was less than 2cm, the density was low and tumor was blurring; Therefore, only the imaging performance was difficult to make the breast cancer diagnosis. It had a big difference on the domestic and abroad literature on the false negative expression of single application of mammography. In domestic literature, there were 5%~15% of false negative expression (Liang *et al*., 2011), even up to 15%~25% (Wang, Qin and Cui, 2012); The X-ray mammography was not visible in the dense breast shape of breast cancer, while high-frequency ultrasound was able to clearly show the tumor edges or burrs small Lobulation signs and blood flow through the center of the tumor, and to make a clear diagnosis, the patient in this case was the X-ray mammography missed. For clustered calcifications in breast cancer, sand-like calcification, can be detected by X-ray mammography and ultrasound can not be detected by ultrasound had become undetected (Jia *et al*., 2003). 2 case of missed diagnosis were due to oppression; 1 case of missed diagnosed ductal carcinoma was because the clear tumor and the calcification were not found; 3 cases of missed diagnosis were the dense breast. The aboard literature reported false negative expression was only 8%~10% (Jackson *et al*., 2009). In this experiment, there were 12 cases of misdiagnosis and 8 cases of missed diagnosis in the single application of high frequency ultrasonography, among which there were 2 cases of breast cancer with tumor size less than 1cm, 2 cases of medullary carcinoma and 2 cases of simplex carcinoma with unsharp sphere and smooth boundary, which were misdiagnosed as fibroma; 2 cases was miss-diagnosed as atypical hyperplasia; 3 cases was miss-diagnosed as dysplastic nodules; 1 case was missed diagnosed, as the ultrasonography had formed the acoustic shadow at the rear of the nipple. The 2 cases of missed diagnosis located at the end of the mammary gland and the size was less than 1 cm; 5 cases was miss-diagnosed, as the tumor was not clear; 2 cases of patients were obesity and with big mammary gland. Therefore, the proper understanding of this two detection methods, it could avoid the bad effect and increase the diagnosis rate of breast cancer, especially the breast cancer early stage, which was the explored hot topic in domestic and aboard scholars (Shi, Zhang and Chen, 2005; Yuan *et al*., 2005; Masroor, Ahmed and Pasha, 2009).

The high frequency method used the acoustic impedance in different tissues. The imaging principle of mammography was that different density tissues had different absorption attenuation on X-ray (Li and Wang, 2011). For the imaging principle, two methods had their own advantages and also had diagnostic difficulties. In the tumor cases, which did not happen in clinical field, there were 11 cases without specific focal from the combined detection, high frequency ultrasonography had misdiagnosed cases and missed diagnosed cases. In these cases, 7 cases were detected with malignant calcification through mammography, 4 cases were confirmed through mammography due to the local structural disorder and irregular dense shadow. In this 4 cases, 1 case was diagnosed to be fibroma combined with calcification through high frequency diagnosis. In the 12 cases which the mammography did not found the tumor, the high frequency ultrasonography had observed the tumor and found 8 cases was detectable and abnormal II~III stage blood flow, 1 cases was confirmed in the axillary lymph nodes and 2 cases were found the chest wall got invaded. 2 cases of small scale focal was diagnosed to be fibroma through mammography and ulstrasonography. In the following re-examination, the tumor had fibroids changes on the surface, and could reached at axillary lymph nodes. It was confirmed in the surgery. As both the begin and malignant tumor had calcification. The calcification was often smaller, around 10~500μm in diameter. Normally not more than 1000μm. The minimal calcification was 200μm through mammography detection (Wang, Qin and Cui, 2012). As the current ultrasonography could detect the tiny calcified points in hypoechoic tumor with size of 100~500μm (Li and Liu, 2010). The calcification was the important index of benign and malignant tumor judgment for both detection.

This research showed that mammography had higher detection rate on calcification than high frequency ultrasonography. While, the micro calcification included sand-like micro calcification, tiny rod-like micro calcification, Y-shape calcification, pin-like micro calcification, which was the key sign on breast cancer diagnosis and usually seen in invasive ductal carcinoma. This study posed that the detection rate of high frequency ultrasonography on tumor, abnormal blood flow signal and axillary lymph nodes was higher than that through mammography. The blood flow was sufficient in the malignant tumor. The blood vessels distribution and structure were central type and penetration type. Related research had classified the mammary gland malignant degree into four types based on distribution and structure, including dead end blood vessels, different diameter blood vessels, twisted blood vessels and arteriovenous vessels. The blood vessels of fibro adenoma usually went though the coating and nodes (Guo, Li and Wu, 2012). There were a lot of adipose tissue in axillary site, and the structure was complex. The enlarged lymph node for breast cancer patients might be the reactive hyperplasia, and may transfer. Two detection could easily detect at the lymph node site. While, for the transfer diagnosis, the accuracy and sensitivity of both had big difference. In this study, the axillary lymph node coincidence rate of mammography and high frequency ultrasonography were respectively 26.2% and 38.6%. Although both had statistical difference, it was not high. The diagnosis standard of transferred lymph node, which met the study

reports included that diameter was more than 0.5cm, ratio of length and width was less than 1.7, lymph nodes gate disappeared, asymmetry of cortical thickening and increased peripheral blood flow. In small lymph node (<1cm), it had significant difference for the cortical asymmetric thickening and increased peripheral blood flow than normal lymph nodes (Leng and Hua, 2010).

Combined detection utilized the imaging advantages and emphasis of both to reflect the pathological characteristics of lesions from different aspects. It had a good diagnosis complementary. Ultrasonography detection was suitable for any age, especially young women, pregnant women and lactating patients. Mammography had certain X-ray radiation, the frequent examination was not welcomed, and not suitable for pregnant women, lactation women and acute mastitis (Wu *et al*., 2010). Mammary gland mammography was the whole detection, which included the entire breasts. It was not easy to misdiagnose. The examinee's subjective factors were smaller than ultrasonography and the ultrasonic integral feeling was poor, and could easily be miss-diagnosed for the focal with little or not oblivious echo changes; This had higher requirement for surgeon technique and experience (Zhang, 2011).

Mammography could expressed the calcification more highly than ultrasonography and expressed more lowly tumor than ultrasonography. High frequency ultrasonography was not affected by gland type, while was not sensitive on tumor in obesity patients and patients with big breasts. While, mammography was difficult to detect the high-density mammary glands. This might be one of the reason why the false negative expression was high in China. Ultrasonography could scan in different angle and dimention and could make up the limitation of mammography technique, which could not display the small breast cancer in inner quadrant and near the edge or chest wall. For young patients, it shall emphasized on the ultrasonography. The mammography expression of elderly patients lard type was low density, most tumor was high density. The mutual dependence was good. The mammography detection shall be emphasized (Song, 2011).

CONCLUSION

In a word, two detection methods were simple, no trauma and low-costed. As the single application had no statistical difference for the diagnosis coincidence rate, it could be applied according to their advantages and the specific conditions of patients. The combined application could obviously increase the detection rate and accuracy rate on breast cancer, increase misdiagnosis rate and missed diagnosis rate. It had important significance on early stage breast cancer.

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