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Study of the Value of Hyperechogenicity and Related Acoustic Features in the Diagnosis of Breast Cancer in Breast Nodules

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Abstract: To invest the diagnostic value of hyperecho and related acoustic features in break schedules in break cancer. The ultrasonic features of 90 cases of hyperechoic break schedules confirmed by pathology were retrospectively analyzed, including 49 cases of the sign group and 41 cases of the minor group. The ultra-graphic features of the two groups were compared and observed, including morphology, orientation, edge, calibration, interior echo, blood supply, hyperechoic Corona, etc. Multivariate Logistic regression model was used to screen the risk ultra sound signals of hyperechoic break schedules. ROC curve was drawn to evaluate the diagnostic validity of ultrasound for hyperechoic break rules by AUC. There were statistically significant differences in the morphology, orientation, margin, calibration, and echo halos between the two groups (x^2= 14.504, 5.511, 42.643, 9.870, 26.071, all $P<0.05$). There were no statistically significant differences in the posterior echo and blood supply (x^2= /, 2.089, $P>0.05$). The Multivariate Logistic regression model was shown that margin unbalances and microcalculation were the risk ultra sound signals of hyperechoic break schedules. The ROC curve was drawn based on the probability value of this model to predict hyperechoic break cancer, and the AUC was 0.912, the sensitivity was 0.829, the specificity was 0.918. Marginal unconsolidation and microcalcification are important ultra-signs of hyperechoic break nodules, which have high value in predicting hyperechoic break cancer.

1. Introduction

The global cancer statistics in 2020 show that breast cancer accounts for 11.7% of all cancers [1]. Breast cancer has become the most common cancer among women in the world and the second most common cause of cancer deaths among women [2]. At present, the pathogenesis of breast cancer is not completely clear, and there is no effective etiological prevention measures [3-4]. A large number of literature [5-7] reports that the prognosis of breast cancer is closely related to its clinical classification. breast cancer is divided into 4 types in clinical practice, and the 5-year survival rate of patients with type I to IV is reduced from 99.7% to 14.0%. It can be seen that early screening, detection, diagnosis and treatment are of great significance for improving the survival rate and clinical management of breast cancer patients [8]. Breast molybdenum target X-ray imaging and color Doppler ultrasound imaging technology are important screening methods, among which color Doppler ultrasound imaging can vividly reflect the growth characteristics of breast tumors and preliminarily distinguish between benign and malignant, which is an important imaging method [9]. In 2013, the American College of Radiology (ACR) released the 5th edition of the Breast Imaging Reporting and Data System (BI-RADS) [10], which has been widely used for the risk assessment of benign and malignant breast nodules. In the imaging dictionary of this system, the internal echoes of breast nodules can be divided into five types by comparing them with the echoes of breast fat: anechoic, hyperechoic, hypoechoic, isoechoic, and mixed echoic. Previous studies [11-16] have shown that high echogenicity of breast nodules is a characteristic benign manifestation, while low echogenicity is a prominent feature of malignancy. However, recent studies have found that a few breast cancer can also show hyperechogenicity [16, 17]. Based on this, this study aims to analyze the ultrasound imaging manifestations of breast hyperechoic nodules and explore their potential for predicting malignant ultrasound features.

2. Materials and methods

2.1 General information

A retrospective analysis was conducted on 90 female patients (90 nodules) who underwent color Doppler ultrasound examination at the First Affiliated Hospital of Hainan Medical College from September 2017 to September 2022. The preoperative ultrasound images showed high echogenicity, and the postoperative pathological results were confirmed. Based on pathology as the gold standard, it is divided into benign group and malignant group. 49 cases (49 nodules) in the benign group, aged 20-56 years, with an average age of (34.84 ± 10.69) years; There were 41 cases (41 nodules) in the malignant group, ranging in age from 33 to 84 years old, with an average age of (49.93 ± 14.01) years. This study has been reviewed and approved by the Ethics Committee of our institution.

2.2 Instruments and methods

Using LOGIQ E9 from GE in the United States, Acuson S2000 from SIEMENS in Germany, and DC-8 color Doppler ultrasound diagnostic instrument from Mindray in China, with a linear array probe frequency of 10-13MHz.

The patient's age, height, weight, family history of breast cancer, whether the nodule can be touched or painful, whether the nipple has effusion, whether the breast skin has edema, whether the axillary has swollen lymph nodes and other clinical data were recorded. During the examination, the patient selects a supine position, removes the pillow, and fully exposes the breast. The upper arms are extended at right angles to the trunk, and the forearms are flexed at right angles to the upper arms. High frequency ultrasound probes are used to repeatedly scan radially from the nipple to the outer edge of the breast in quadrants. The direction of the probe is always perpendicular to the breast skin layer. After determining the location of the lesion, the shape, orientation, and edge of the lesion are observed and determined through multiple longitudinal, transverse, and oblique sections 8 features including internal echo, calcification, posterior echo, blood supply, and surrounding tissue. Representative images are stored on a computerized storage workstation during the examination.

2.3 Image analysis

Two ultrasound physicians with more than 10 years of experience in breast ultrasonography selected all images from a computerized storage workstation for retrospective analysis (unaware of previous ultrasound and pathological diagnoses). When there is disagreement, a consensus is reached through discussion between two people and a diagnostic explanation is provided. The shape of the lesion (oval, circular, irregular), orientation (parallel to the skin, not parallel to the skin), edge (smooth, blurry, angular, lobulated, hairy), internal echo (uniform, uneven), and comparison with breast fat echo can be divided into 5 types: no echo, high echo, low echo, equal echo, and mixed echo, calcification (microcalcification, coarse calcification) Rear echo (no change, enhancement, attenuation), surrounding tissue echo (increase, no change, attenuation), blood supply is classified into four categories: no, small, moderate, and large (no blood flow signal within the nodule is defined as no blood vessel distribution; a small amount of blood flow signal is defined as displaying 1-2 vessels simultaneously on the optimal section; a moderate amount of blood flow signal is defined as displaying 3-4 vessels simultaneously on the optimal section; and a large amount of blood flow signal is defined as displaying 5 or more vessels simultaneously on the optimal section).

2.4 Statistical methods

SPSS 26.00 statistical analysis software was used. The econometric data that conforms to the normal distribution is represented by $\bar{x} \pm s$, and the comparison between groups is conducted using two independent sample t-tests; Counting data is represented as an example (%), and inter group comparisons are made using x^2Test or Fisher exact probability method. The correlation between preoperative clinical data and lesion pathology was analyzed using Spearman rank correlation analysis. Multivariate logistic regression model was used to screen the risk ultrasound signs of hyperechoic breast cancer. ROC curves were plotted and the diagnostic efficacy of ultrasonography for breast hypoechoic nodules was evaluated by AUC. The difference was statistically significant with bilateral P<0.05.

3. Results

3.1 Comparison of general information, ultrasound features, and pathological distribution between the 2 groups

Table 1: Comparison of general information and ultrasound features between the 2 groups of sufferers

	Number of cases	Age	BMI	family history		Touching nodules		pain		Overflow		Skin edema		Touching lymph nodes	
				nothing	have	nothing	have	nothing	have	nothing	have	nothing	have	nothing	have
Benign group	forty-nine	34.84 ± 10.69	20.92 ± 2.54	forty-nine	0	twenty	twenty-nine	twenty-three	twenty-six	forty-nine	0	forty-nine	0	forty-eight	one
Malignant group	forty-one	49.93 ± 14.01	21.60 ± 3.30	forty	one	three	thirty-eight	thirty-six	five	thirty-six	five	forty	one	twenty-four	seventeen
t/x^2		-5.407	-1.106	/		thirteen point one six seven		sixteen point five one zero		four point two one six		/		twenty-one point six eight two	
P-value		<0.001	zero point two seven two	0.456*		<0.001		<0.001		zero point zero four zero		0.456*		<0.001	

Table 2: Comparison of general information and ultrasound features between the 2 groups of sufferers

	Number of cases	position		quadrant				Maximum diameter (cm)	form		azimuth	
		Left	right	Externally superior	Externally inferior	Inner inferior	Internally superior		rule	Irregular	parallel	Non parallel
Benign group	forty-nine	twenty-three	twenty-six	twenty-six	eight	seven	eight	2.96 ± 1.40	forty-three	six	forty-nine	0
Malignant group	forty-one	nineteen	twenty-two	twenty-eight	four	two	seven	4.71 ± 2.74	twenty-one	twenty	thirty-five	six
t/X ²		zero point zero zero three		three point seven three zero				-3.715	fourteen point five zero four		five point five one one	
P-value		zero point nine five five		zero point two nine two				<0.001	<0.001		zero point zero one nine	

Table 3: Comparison of general information and ultrasound features between the 2 groups of sufferers

	Number of cases	edge		calcification			posterior echo		Hyperechoic halo		Blood supply	
		Finishing	Not smooth	nothing	small	Bulky	No changes, enhancements	attenuation	nothing	have	None, small amount	Medium and large quantities
Benign group	forty-nine	forty-one	eight	thirty-two	fourteen	three	forty-nine	0	forty-seven	two	twenty-nine	twenty
Malignant group	forty-one	six	thirty-five	fourteen	twenty-five	two	thirty-nine	two	twenty	twenty-one	eighteen	twenty-three
X ²		forty-two point six four three		nine point eight seven zero			/		twenty-six point zero seven one		two point zero eight nine	
P-value		<0.001		zero point zero zero seven			zero point two zero five		<0.001		zero point one four eight	

Note: * represents Fisher's exact probability method

Table 4: Distribution of pathological properties of two groups of lesions

Pathological type	Number (%)
Benign nodules	49 (100.00)
Fibroadenoma	21 (42.86)
Adenopathy with adenomatous hyperplasia	8 (16.33)
Adenosis	8 (16.33)
Solitary fibrous tumor	4 (8.16)
Intraductal papilloma	4 (8.16)
inflammation	1 (2.04)
Benign lobular tumor	1 (2.04)
Hamartoma	1 (2.04)
lipoma	1 (2.04)
Malignant nodules	41 (100.00)
Ductal infiltrating carcinoma	15 (36.60)
Ductal non invasive carcinoma	5 (12.20)
other	21 (51.20)

There were statistically significant differences in age, palpation of nodules, pain, discharge, palpation of lymph nodes, and length between the benign and malignant groups ($P<0.05$); There were statistically significant differences in morphology, orientation, edge, calcification, and hyperechoic halo in the characteristics of ultrasound images ($P<0.05$); There were no statistically significant differences in BMI, family history, skin edema, location, quadrant, posterior echo, and blood supply (all P>0.05), as shown in Table 1~3. High echo breast malignant nodules are often characterized by irregular morphology, orientation not parallel to the skin, blurred edges, and microcalcifications on ultrasound images, as shown in Figure 1. The pathological distribution of 90 cases of breast hyperechoic nodules (90 nodules) is shown in Table 4.

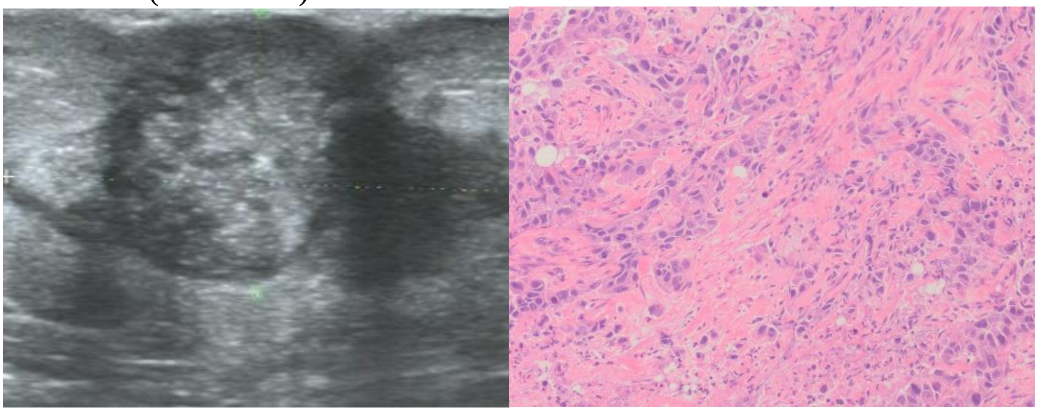

Figure 1: Patient female, 45 years old, with infiltrating carcinoma of the left breast. A. seen in the left breast -3.7cm × 2.5cm × 1.7cm, high echogenic nodule with irregular shape, blurry edges, uneven internal echoes, and a few punctate strong echoes visible; B. Pathology: Breast infiltrating carcinoma (HE × 200)

3.2 Correlation between preoperative clinical data and pathological changes of lesions in two groups

The Spearman rank correlation analysis results showed a significant positive correlation between age (r=0.447, P<0.001), palpable mass (r=0.382, P<0.001), pain (r=-0.428, P<0.001), overflow (r=0.265, P<0.012), abnormal axillary lymph nodes (r=0.491, P<0.001), longest diameter (r=0.409, P<0.001), and pathological malignancy of breast nodules.

3.3 Multi factor Logistic regression model to screen risk ultrasound signs of hyperechoic breast cancer

Table 5: Characteristics and assignments of high echo breast nodules on ultrasound images

Audiovisual features	Variable name	Assignment Description
form	X1	Rule=0, Irregular=1
azimuth	X2	Parallel to skin=0, not parallel to skin=1
edge	X3	Smooth=0, not smooth=1
calcification	X4	No calcification=0, microcalcification=1, coarse calcification=2
Hyperechoic halo	X5	None=0, Yes=1

To eliminate confounding bias and overlapping effects between various ultrasound features, statistically significant ultrasound features (morphology, orientation, edge, calcification, hyperechoic halo) were used as independent variables in univariate analysis, and pathological results of breast nodules were used as dependent variables. A logistic regression model was established and stepwise regression analysis was performed using forward likelihood ratio method. The results showed that edges and calcification were dangerous ultrasound signs of hyperechoic breast nodules, as shown in Tables 5 and 6.

Table 6: Regression model screening for high-risk ultrasound features of high echo breast nodules

Audiovisual features	Partial regression coefficient	Standard error	Wald χ^2 value	P-value	OR value (95% CI)
Edge (X3)	two point nine seven	zero point six nine	eighteen point six zero	<0.001	19.49 (5.05-75.14)
Calcification (X4)	one point zero two	zero point five two	three point nine four	zero point zero four seven	2.79 (1.01-7.66)
Constant term	-2.95	zero point six eight	eighteen point six five	< 0.053	zero point zero five three

3.4 ROC curve and AUC

The ROC curve (Figure 2) is drawn based on the probability value of the model to predict hyperechoic breast cancer. AUC is 0.912, standard error is 0.034, 95% CI is 0.844~0.979, P<0.001, sensitivity is 0.829, and specificity is 0.918. This suggests that the Logistic regression model established based on the ultrasonic characteristics of uneven edges and microcalcification has high value in predicting hyperechoic breast cancer.

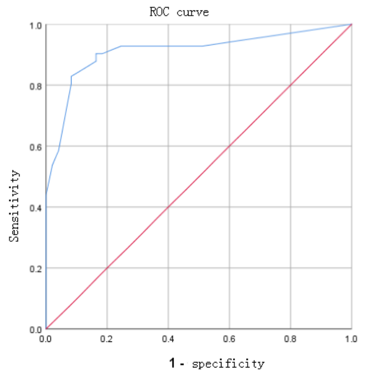

Figure 2: ROC curve of logistic regression model for prediction of hyperechoic breast cancer

4. Discussion

Previous studies [12-17] suggest that breast nodules with high internal echogenicity are predicted to be benign. Although some studies [18] show that the negative predictive value of hyperechoic breast nodules is 100%, however, with the deepening of research, it is found that a few breast cancer can also be hyperechoic. Wang Xinyi et al. [17] analyzed 848 cases of breast nodules and found that 8 cases (0.9%, 8/848) exhibited hyperechogenicity, with 2 cases (25.0%, 2/8) being malignant. Linda et al. [12] analyzed 4511 cases of breast nodules and found that 25 cases (0.6%, 25/4511) exhibited hyperechoic breast nodules, among which 9 cases (36.0%, 9/25) were malignant. Sang et al. [19] analyzed 16416 cases of breast nodules and found that there were 103 cases (0.6%, 103/16416) with high echogenicity, including 27 cases (26.2%, 27/103) with malignancy. From this, it can be seen that high echo is not an absolute feature for predicting benign breast nodules, and it should be differentiated between benign and malignant.

This study found through univariate comparative analysis that there was a statistically significant difference in the shape, orientation, edge, calcification, and characteristics of hyperechoic breast nodules between the two groups (all P<0.05), while there was no statistically significant difference in the posterior echo ($P>0.05$). To eliminate the confounding bias and overlap effect between the various features on the ultrasound image, and further determine the relative importance of each feature on the ultrasound image, a binary logistic regression model was established with tissue pathology as the dependent variable. The results of the multivariate logistic regression model showed that irregular edges and microcalcifications were dangerous ultrasound signs of hyperechoic breast nodules. Using this model to predict the probability value of hyperechoic breast cancer, ROC curve is drawn, and AUC is 0.912 (95% CI 0.844~0.979), sensitivity is 0.829, specificity is 0.918. This shows that the analysis of the ultrasound image edge and calcification of hyperechoic breast nodules has a high diagnostic efficiency for the differentiation of benign and malignant breast nodules, which can significantly increase the confidence of examiners in the differentiation of benign and malignant breast nodules.

This study used a logistic regression model to obtain the OR values of two ultrasound feature independent variables, namely edge (19.49) and calcification (2.79), indicating that edge irregularity has the highest value in diagnosing breast hyperechoic nodules. This sign is mainly manifested on the ultrasound image as blurry, burred, angled, and lobulated nodules, which may be caused by factors such as interstitial reactions around the cancer, direct outward invasion and expansion of the cancer, expansion of cancer cells along the breast duct, or traction of the trabecular structure around the cancer towards the tumor direction. In this study, microcalcification is another important feature for distinguishing breast hyperechoic nodules. The reason may be due to the rapid growth rate of the tumor and insufficient blood supply leading to necrosis. In the univariate analysis of this study, 28.57% (14/49) of benign nodules with high echogenicity showed microcalcification, while 60.98% (25/41) of malignant nodules showed significant differences ($P=0.007$). In the multivariate logistic regression model, the OR value of microcalcification was 2.79, indicating that the malignant risk of microcalcification in hyperechoic nodules is 2.79 times higher than that without microcalcification, consistent with the results reported by Soo et al.

The differences in lesion morphology, orientation, and hyperechoic halo between the two groups of cases in this study were statistically significant in univariate analysis (all $P<0.05$). However, the above three sonographic features did not contribute to the multivariate logistic regression model, and may be related to mixed bias and overlap effects between multiple sonographic features. The echo situation behind the breast lesion reflects the internal structure of the breast lesion. When the cancerous tissue inside the tumor is dominant, its acoustic interface is less, the acoustic transmittance is better, and the posterior echo can be enhanced. If the collagen fiber composition in the tumor stroma increases and the arrangement is disordered, it shows attenuation of the posterior echo. In this study, there was no significant difference in the posterior echo of the two groups of high echogenic breast nodules ($P>0.05$); Zhu Qingli et al. pointed out that malignant tumors can secrete tumor angiogenesis factors, stimulate the production of new blood vessels in tumors and adjacent tissues. Therefore, using color Doppler ultrasound can help differentiate between benign and malignant breast tumors. However, this study showed no statistically significant difference in blood supply between the two groups of hyperechoic breast nodules ($P>0.05$). Therefore, it is inferred that the differential diagnosis of hyperechoic breast nodules cannot be made based on posterior echo and blood supply, and further research is needed.

This study still has certain limitations: ① the sample size is small and retrospective; ② Single center, geographically limited, with patients mostly coming from tropical Hainan Island; ③ Most high echo breast nodules with low BI-RADS classification choose regular follow-up and lack histopathological results, which may lead to selective bias. Therefore, further multicenter, wide regional, and large sample studies are needed to verify this.

In summary, this study established a binary logistic regression model and found that the ultrasound features of edge irregularity and microcalcification have high value in the diagnosis of benign and malignant breast nodules with high echogenicity. Understanding these two ultrasound features can reduce misdiagnosis and help improve the diagnostic efficiency of ultrasound physicians for high echo breast nodules.

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