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Original Article

Combined diagnosis of ultrasonic elastography and BI-RADS classification increases diagnostic value in female patients with breast neoplasms

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Abstract: Objective: This study was designed to investigate the clinical value of ultrasonic elastography combined with the Breast Imaging Reporting and Data System (BI-RADS) classification in patients with breast neoplasms. Methods: A retrospective observational study was conducted on 89 patients with breast neoplasms hospitalized from June 2017 to June 2018. All the enrolled patients had received ultrasound examinations. The diagnostic value of ultrasonic elastography, BI-RADS classification, and the combined diagnosis for breast neoplasms was analyzed. Results: The postoperative pathological examination showed 51 cases of benign lesions and 38 cases of malignant lesions among the 89 cases. The detection of the focal zone revealed 75 benign and 44 malignant lesions. Ultrasonic elastography misdiagnosed 8 malignant lesions as benign and 17 benign lesions as malignant; BI-RADS classification misdiagnosed 7 malignant lesions as benign and 15 benign lesions as malignant; The combined diagnosis misdiagnosed 2 malignant lesions as benign and 4 benign lesions as malignant. The sensitivity of the combined diagnosis was higher than that of ultrasonic elastography ($P<0.05$). The specificity and positive- and negative predictive values of the combined diagnosis were all higher than those of ultrasonic elastography and BI-RADS classification (all $P<0.05$). Conclusion: Ultrasonic elastography combined with BI-RADS classification has high clinical application value in the diagnosis of breast neoplasms, especially the sensitivity to benign and malignant lesions. And compared with the mono-detection of either ultrasonic elastography or BI-RADS classification, the combined detection yields significantly higher diagnostic accuracy.

Keywords: Breast neoplasms, benign and malignant lesions, BI-RADS classification, ultrasonic elastography

Introduction

With the rapid economic development and changes in lifestyles, young people are facing increasing pressure and health issues in daily living. Prior studies pointed out that breast cancer causes an annual death of 500,000 worldwide, with a rising incidence in the young population in recent years [1-4]. Imaging is the mainstay of the diagnosis of breast diseases, among which mammography and ultrasound are the basic methods for detecting breast cancer. However, the sensitivity and specificity of mammography for the detection of early breast cancer are less than satisfactory. The Breast Imaging Reporting and Data System (BI-RADS), on the other hand, can effectively distinguish between benign and malignant breast masses by classifying breast images [5-8]. Through the application of the BI-RADS system, breast feature terminology and reporting terms are standardized, thus avoiding confusion in imaging interpretation. Nonetheless, two-dimensional ultrasound cannot accurately distinguish between benign and malignant breast tumors as the system mainly relies on the morphological characteristics of tumors for classification and diagnosis. As to ultrasound, it is a conventional therapy for patients with breast cancer, which is appreciated for non-radiation, non-invasiveness, low costs, and real-time dynamic observation. As a noval

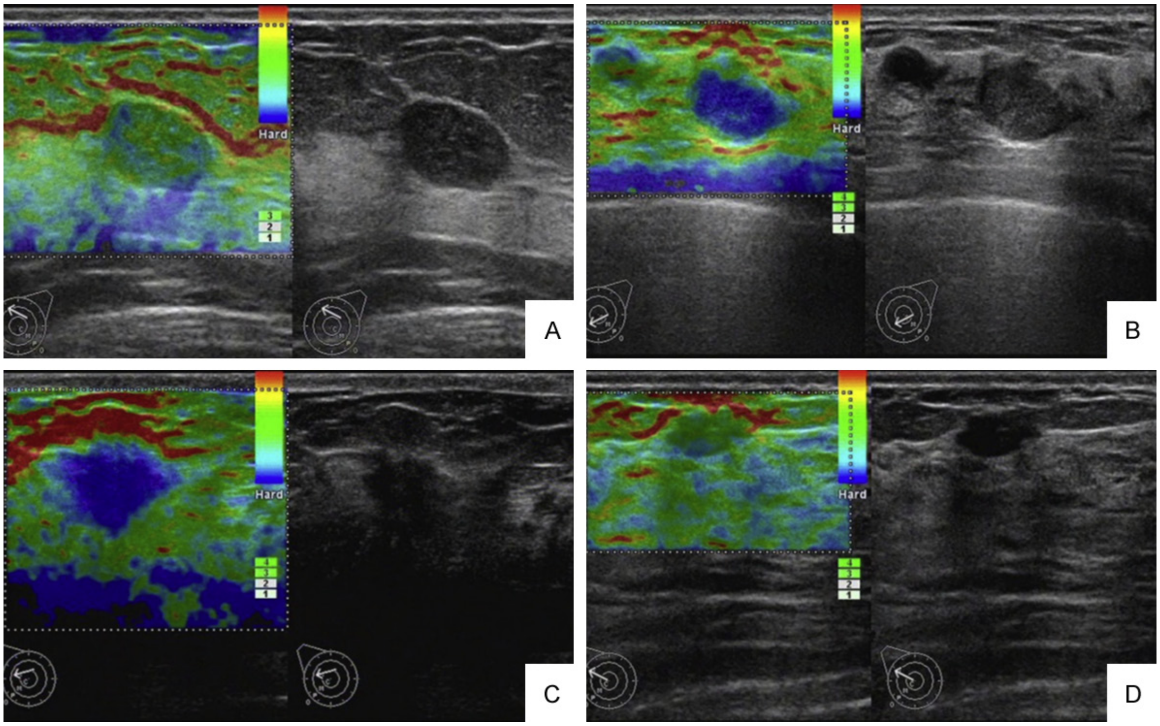

Figure 1. Typical pictures of the Ultrasonic Elastography and BI-RADS Classification. A: Fibroadenoma in a 35-year-old woman. Left, ultrasonic elastography reveals entire lesion to be evenly shaded in green (score: 1 point). Right, B-mode ultrasound classified lesion as BI-RADS category 3. B: Intraductal papilloma in a 38-year-old woman. Left, ultrasonic elastography reveals almost all of lesion to be blue (score: 4 points). Right, B-mode ultrasound classified lesion as BI-RADS category 3. C: Invasive ductal carcinoma in a 55-year-old woman. Left, ultrasonic elastography reveals entire lesion and its surrounding area to be blue (score: 5 points). Right, B-mode ultrasound classified lesion as BI-RADS category 5. D: Fibroadenoma in a 22-year-old woman. Left, ultrasonic elastography reveals entire lesion to be shaded in green (score: 1 point). Right, B-mode ultrasound classified lesion as BI-RADS category 4A.

Table 1. Pathological examination results of patients with breast masses (n, %)

	Cases	Tumor types	Number of lesions
Benign lesions	51	Adenosis	29 (24.37)
		Fibroadenoma	21 (17.65)
		Intraductal papilloma	12 (10.08)
		Cyst	7 (5.88)
		Inflammation	6 (5.04)
Malignant lesions	38	Invasive ductal carcinoma	24 (20.17)
		Intraductal carcinoma	10 (8.41)
		Papillary carcinoma	6 (5.04)
		Lobular carcinoma	2 (1.68)
		Mucinous carcinoma	2 (1.68)
Total	89		119 (100.00)

ultrasonic technique, ultrasonic elastography can reflect the hardness of breast tissue effectively. Given the promising effect of ultrasonic elastography in identifying intraductal carcinoma of the breast and distinguishing breast lesions from benign breast masses, it is considered to be superior to conventional ultrasound in comprehensive diagnosis. Herein, 89 patients with breast neoplasms admitted to our hospital from June 2017 to June 2018 were retrospectively analyzed to further explore the diagnostic value of ultrasonic elastography combined with BI-RADS classification for breast neoplasms.

Materials and methods

General materials

The clinical data of 89 female patients with breast neoplasms admitted to our hospital from June 2017 to June 2018 were analyzed retrospectively. The postoperative pathological

Table 2. Results of ultrasonic elastography diagnosis

	1 point	2 points	3 points	4 points	5 points	χ^2	P
Malignant lesions (n=44)	1	2	5	25	11	41.14	<0.001
Benign lesions (n=75)	28	16	14	12	5		

Table 3. Diagnostic sensitivity and specificity of ultrasonic elastography diagnosis

		Pathological examination		
		Negative	Positive	Total
Ultrasonic elastography	Negative	58	8	66
	Positive	17	36	53
	Total	75	44	119

examination showed 51 benign and 38 malignant lesions. The mean age of patients was 46.7±8.24 years (range: 23-70 years) and the mean diameter of masses was 20.1±5.3 mm (range: 8-45 mm). The study protocol was ethically approved by the Medical Science Research Ethics Committee of Nanjing Medical University (Nanjing, Jiangsu, China; License No. LC 2016-8345).

Inclusion criteria

a) Patients with benign or malignant tumors confirmed by pathological examination; b) Patients receiving ultrasonic elastography; c) Patients with neither history of chemotherapy/radiotherapy nor distant metastasis; d) Patients with complete clinical case reports; e) Patients were fully informed of the study and signed the informed consent.

Exclusion criteria

a) Patients with lesions of the brain, heart, kidney, liver, or other organs; b) Patients with simple breast cyst or acute breast inflammation; c) Patients with mental or other cognitive impairment or refused to cooperate; d) Patients with multiple lesions.

Methods

All patients underwent routine ultrasound examinations. Specifically, the high-frequency linear array probe was set to 6-15 MHz, and continuous real-time scanning was performed after applying the coupling agent. The scanning was started at the nipple to locate the mass. The diameter, shape, boundary, uniformity, aspect ratio, presence of capsule, type of calcification, changes of posterior echo, echo type, and axillary lymph node abnormality were observed and recorded [9-11]. Then Color Doppler flow imaging (CDFI) was carried out using the HI VISION Ascendus ultrasound system (GE730, GE, USA) to detect the morphology, distribution, spectral morphology, and blood flow signals of the neoplasms. The selected images were then frozen and saved for the elastography procedure. The setting range of the sampling box was not less than the focal zone displayed by double-contrast. The images with good repeatability and stability were comprehensively evaluated and classified by the BI-RADS. Typical pictures of the Ultrasonic Elastography and BI-RADS Classification are shown in **Figure 1**.

Outcome measures and diagnostic criteria

Ultrasonic elastography score of breast cancer: Blue with a small amount of green in the overall image of the lesion was 4 points, and blue in the lesion and surrounding tissue was 5 points; breast cancer was indicated when the score was 4-5 points. BI-RADS classification of breast cancer: IV-VI of BI-RADS classification was defined as breast cancer. IV: the possibility of malignant is 2-95%, requiring histological examination; V: the possibility of malignant is above 95%, and histological examination is required; VI: confirmed malignancy by pathological examination. When the mass was diagnosed as malignant by ultrasonic elastography and/or BI-RADS classification, it was also confirmed as malignant by the combined diagnosis. Image analysis and diagnosis were performed by the same team of experienced doctors.

Statistical analysis

All analyses were carried out using SPSS, version 20, and Graphics drawing was carried out using GraphPad Prism, version 7. Count data were expressed as [n, (%)] and analyzed by the χ^2 test, while measurement data were expressed as ($\bar{x}$ ± sd) and analyzed by the t-test. A normality test was adopted for data conforming to a normal distribution. Differences were considered statistically significant at P<0.05.

Table 4. Results of BI-RADS classification

	Category 0	Category I	Category II	Category III	Category IV	Category V	Category VI	X^2	P
Malignant lesions (n=44)	0	0	3	4	23	13	1	52.68	<0.001
Benign lesions (n=75)	27	14	10	9	11	3	1		

Table 5. Diagnostic sensitivity and specificity of BI-RADS classification

		Pathological examination		
		Negative	Positive	Total
BI-RADS classification	Negative	60	7	67
	Positive	15	37	52
	Total	75	44	119

Table 6. Diagnostic sensitivity and specificity of ultrasonic elastography combined with BI-RADS classification

		Pathological examination		
		Negative	Positive	Total
Combined diagnosis	Negative	71	2	73
	Positive	4	42	46
	Total	75	44	119

Results

Pathological diagnosis results of breast neoplasms

The postoperative pathological examination showed 51 cases of benign lesions and 38 cases of malignant lesions among the 89 cases. The detection of the focal zone determined 75 benign and 44 malignant lesions. Among the 75 benign lesions, 29 were adenosis, 21 were fibroadenoma, 12 were intraductal papilloma, 7 were cysts, and 6 were inflammation. Of the 44 benign lesions, there were 24 invasive ductal carcinoma, 10 intraductal carcinoma, 6 papillary carcinoma, 2 lobular carcinoma, and 2 mucinous carcinoma, **Table 1**.

Ultrasonic elastography score

The score and the number of malignant lesions by ultrasonic elastography were as follows: 1 point (1), 2 points (2), 3 points (5), 4 points (25), and 5 points (11). The score and the number of benign lesions by ultrasonic elastography were as follows: 1 point (28), 2 points (16), 3 points (14), 4 points (12), and 5 points (5). There were significant differences in the distribution of the ultrasonic elastography score between the two groups (P<0.001), as shown in **Table 2**. Ultrasonic elastography misdiagnosed 8 malignant lesions as benign and 17 benign lesions as malignant, as shown in **Table 3**.

Diagnosis of breast masses by bi-rads classification

The BI-RADS classification showed a significant difference in the distribution of malignant and benign lesions (P<0.001), as shown in **Table 4**. BI-RADS classification misdiagnosed 7 malignant lesions as benign and 15 benign lesions as malignant, while the combined diagnosis misdiagnosed 2 malignant lesions as benign and 4 benign lesions as malignant, as shown in **Tables 5** and **6**.

Comparison of the diagnostic value of ultrasonic elastography, bi-rads classification, and the combined diagnosis

The sensitivity and negative predictive value of the combined diagnosis were higher than those of ultrasonic elastography (P<0.05). And the specificity and positive predictive value of the combined diagnosis were higher than those of the mono-detection of either ultrasonic elastography or BI-RADS classification (all P<0.05), as shown in **Table 7**.

Discussion

Breast cancer is recognized as a malignancy derived from the epithelium of mammary gland or duct. To date, breast cancer, with elusive pathogenesis, is considered to be related to genes, sex hormones, reproductive hormones, environmental factors, and dietary factors. The disease progresses from a painless lump in the early stage to adverse symptoms such as nipple retraction, axillary lymph node enlargement, mammary skin dimpling, or peau d'orange [12-15]. It is occasionally identified by health examination at the early stage as its symptoms are rather hidden. Therefore, early detection and early treatment are crucial to

Table 7. Comparison of the diagnostic value of ultrasonic elastography, BI-RADS classification, and the combined diagnosis

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Ultrasonic elastography	81.82 (36/44)	77.33 (58/75)	67.92 (36/53)	87.88 (58/66)
BI-RADS classification	84.09 (37/44)	80.00 (60/75)	71.15 (37/52)	89.55 (60/67)
Combined diagnosis	95.45 (42/44)*	94.67 (71/75)*,#	91.30 (42/46)*,#	98.63 (71/73)*,#
χ^2	5.098	9.435	7.865	5.658
P	0.043	0.004	0.034	0.021

*P<0.05 *vs.* Ultrasonic elastography; #P<0.05 *vs.* BI-RADS classification.

reduce mortality. Ultrasonic elastography, an emerging technique, has been transformed into a functional imaging technology compared with traditional ultrasound, which can improve the clinical assessment of tissue hardness with the application of tissue elasticity coefficient and digital signal-processing techniques [16-19]. In this study, the misdiagnosis rate of ultrasonic elastography for malignant lesions was 18.18%, and that for benign lesions was 22.67%, which indicates the occasional instability of ultrasonic elastography in the diagnosis of breast cancer. The misdiagnoses mainly stem from the following four reasons. a) The intensified hardness of the tissue by calcification inside the lesion. b) The impaired tissue elasticity of the lesion with the limited range of motion by the adhesion between the lesion and surrounding tissues. c) The partial overlap of the elastic coefficients of different tissues. d) The affected elastography results by lesion growth. BI-RADS classification is a semi-quantitative comprehensive evaluation method, which is mainly based on Color Doppler ultrasound and two-dimensional ultrasound to classify the echo of lesions. The mono-detection by either ultrasound elastic technique or BI-RADS classification yields a high misdiagnosis rate, while the combined detection can achieve complementation and mutual assistance to enhance diagnostic sensitivity and accuracy. The findings of this study are consistent with those of Anindita [20], who found that ultrasonic elastic technique and BI-RADS classification were both valuable in the diagnosis of breast masses, and their combination yielded better detection results. Therefore, the diagnostic value of ultrasonic elastography combined with BI-RADS classification for breast masses is encouraging. However, there were some deficiencies in this study. First, the procedure of ultrasonic elastography required patients to hold their breath for more than 5 s, which was difficult for some patients. Second, the reproducibility of the results of ultrasonic elastography was poor with low sensitivity. At last, this study did not adopt blind method, which may lead to selection bias in data processing.

Conclusion

To sum up, ultrasonic elastography combined with BI-RADS classification has high clinical application value in the diagnosis of breast neoplasms, especially the sensitivity to benign and malignant lesions. Compared with the mono-detection of either ultrasonic elastography or BI-RADS classification, the combined detection yields significantly higher diagnostic accuracy.

Disclosure of conflict of interest

None.

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