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Original Article

Diagnostic efficacy of ultrasound elastography and dynamic contrast-enhanced MR in benign and malignant breast masses

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Abstract: Objective: To analyze the diagnostic efficacy of ultrasound elastography (UE) and dynamic contrast-enhanced MR in benign and malignant breast masses. Methods: From August 2016 to May 2019, the medical records of 98 patients with breast masses in the Zhuji Sixth People's Hospital were retrospectively analyzed, including 45 cases of benign tumor and 53 cases of malignancy diagnosed by pathology. All patients were examined by UE and dynamic contrast-enhanced MR imaging. The pathologic results were used as the gold standard, and the detection results of benign and malignant masses under different examinations were observed and compared with pathology to analyze the specificity and sensitivity. Results: The specificity and sensitivity of diagnosis by UE were 94.44% and 86.89% respectively. The specificity and sensitivity of diagnosis by dynamic contrast-enhanced MR imaging were 96.30% and 91.80%, respectively. The specificity and sensitivity of joint diagnosis were 98.36% and 90.74%, respectively. Conclusion: Joint diagnosis can improve the sensitivity in the diagnosis of benign and malignant breast masses. This improves the diagnostic value for breast tumors.

Keywords: Ultrasonic elastography, dynamic contrast-enhanced MR imaging, breast mass, diagnosis

Introduction

Breast cancer (BC) is the most common non-skin cancer among women all over the world. It is also a main cause of cancer-related death among women all over the world, with the second highest mortality [1]. According to statistics, there were about 2.1 million newly diagnosed cases in 2018, accounting for 11.6% of all new cancer cases. The total number of BC deaths in 2018 accounted for 15% of all cancer-related deaths worldwide [2]. With aging of the Chinese population, the morbidity and mortality of BC in China have also increased. In 2020, data showed that the age-standardized morbidity and mortality in China were 36.1 per 100,000 people and 8.8 per 100,000 people respectively [3]. Therefore, early detection of BC is helpful to treat it, reduce the risk of death, and improve the survival rate of patients.

Because early BC does not show obvious clinical symptoms, it is mostly diagnosed by imaging examination [4]. Clinical research shows that the elasticity of the diseased tissue is closely related to the benign versus malignant state. A malignant mass is composed of hard tissue, the boundary of which is mostly star-shaped or crab-like edged. Most of them show invasive growth, adhesion to nearby tissues, and reduced activity and elasticity during palpation, unlike a benign mass [5, 6]. Ultrasound elastography (UE) technology is widely used in clinical examination of the breast, because it can objectively reflect the relative hardness of tissue according to the color displayed in the image. At the same time, this technology has the advantages of being non-traumatic, no radiation, real-time dynamics, low cost, high efficiency, simplicity, and convenience [7, 8].

Magnetic resonance imaging (MRI) is an emerging imaging technique with good soft tissue resolution, and the time-dynamic contrast-enhanced curve can well show the hemodynamic characteristics of breast masses [9]. Many studies have revealed that with the wide clinical application of MRI, MRI of the breast plays a complementary role to other imaging techniques, because it can detect occult early BC that cannot be detected by other imaging techniques [10]. Dynamic contrast-enhanced MR is characterized by multi-orientation, multi-parameters, high resolution, and can detect small lesions, which has gained use in the diagnosis of BC [11]. After the injection of contrast agent, subtraction technology can be realized to improve the examination accuracy by analyzing the shape and blood flow of the lesion [12]. However, some studies have also concluded that MR is deficient in the diagnosis of breast masses. In the study by Satake et al. [13], the ability of UE and MR to diagnose 115 breast masses classified as BI-RADS category 4 or 5 was analyzed by multifactorial logistic regression analysis, and their study showed that UE provided a more reliable predictive value for malignancy compared to MR. Therefore, to explore the value of MR and UE, this study compared the diagnostic efficacy of these two diagnostic modalities for breast masses.

In order to effectively utilize the advantages of the two examination methods to improve the accuracy of the diagnosis of benign and malignant breast masses, this study was designed to use postoperative pathology as the gold standard, and compare the different advantages and limitations of UE and dynamic contrast-enhanced MR examination, aiming to provide a valuable reference for clinical diagnosis.

Methods and materials

Patients data

From August 2016 to May 2019, the medical records of 98 patients with breast masses who underwent UE and dynamic contrast-enhanced MR imaging admitted to the Zhuji Sixth People' s Hospital were retrospectively analyzed. Using pathologic diagnosis as the gold standard, 45 patients were diagnosed as benign, with a total of 54 masses, and 53 cases were malignant, with a total of 61 masses. This study has been approved by the Medical Ethics Committee (Lot No. 20220308).

Inclusion and exclusion criteria

Inclusion criteria: Before use of UE and MR dynamic enhancement imaging, the patient had not undergone breast-related therapy. Both UE and dynamic contrast-enhanced MR imaging examinations were performed, and the time difference between the two detection methods was less than one week. All lesions underwent puncture biopsy or surgical resection, and specimens were obtained and sent for pathologic diagnosis, with pathologic diagnosis results as the gold standard. Patients received an accurate diagnosis of benign or malignant nodules. All patients had complete medical data, including medical records, past medical history, laboratory, and imaging findings.

Exclusion criteria were as below: Those with comorbid malignant tumors; congenital malformation of the chest that can affect the diagnosis of imaging; coagulation dysfunction; patients who were unable to cooperate with the examination; pregnant and lactating patients; patients with breast implants that may affect the imaging diagnosis.

Examination methods

UE: The IU22 intelligent ultrasonic equipment system produced by Philips Electronics Group in the Netherlands was selected for examination, and the probe frequency was 6-13 MHz. The first examination was a two-dimensional ultrasound. The patient was placed in supine position and lateral position if necessary. The arms were raised to fully expose the whole breast. With the nipple as the center point, circular scanning was done from the edge of the breast to the nipple direction to observe each quadrant of the breast and the axillary lymph nodes. If a tissue mass was detected, the position, size, blood flow, and frequency spectrum of the mass were measured and recorded from multiple sections. Then, the new mode of elastography technology preset by the instrument was entered, and the region of interest (ROIs) in the lesion area was further processed. An elastography technology scan was usually completed on the degree of spontaneous breathing and the amplitude of heartbeat of the patient. UE

technology inspection was designed to use real-time double-amplitude imaging, namely, the combined mode of two-dimensional image and elastography image, which showed the characteristics of an elastography image and gray-scale image respectively. The sampling frame of the elastography images should be 1.5 to 2 times larger than the range of the breast mass. The elastography images were color-coded to indicate the elastic hardness of different tissues. According to the hardness score of elastography (5-point scoring scheme) combined with the characteristics of the instrument, the elastography images were graded by color coding, and all information was recorded and stored on the spot. The final result was determined by two doctors.

Dynamic contrast-enhanced MR imaging: Avanto magnetic resonance imaging system (Siemens, Germany) was used for examination. The nipple was perpendicular to the ground, so that all breast tissues were located in the coil. MR plain scan was designed to select the fat inhibition sequence (T2WI: slice thickness 4.0 mm, TR4 300 ms, TE 105 ms, interval 1.0 mm) and T1WI non-fat inhibition sequence (T1WI: TR 775 ms, TE 12 ms, interval 1.0 mm, slice thickness 4.0 mm) for imaging. The scanning parameters of dynamic contrast-enhanced MR were TE 1.63 ms, TR 4.42 ms and slice thickness 1.2 mm. Magnevist was injected through the median cubital vein and compared by three-dimensional volume ultra-fast multi-phase dynamic sequence. The normal saline (15 mL) was used for scouring, so that the scanning time was gradually enhanced. Siemens Leonardo VD10B workstation was used for data processing. The ROIs was defined in the part with the largest lesion area and the most significant enhancement, which was slightly smaller than the lesion area, avoiding the lesions such as bleeding, necrosis, and a liquefied capsule. Dynamic enhancement was to make a perfusion curve according to the ROIs. The b value = 0.500 s/mm^2, 0.800 s/mm^2 and 0.1000 s/mm^2 were selected respectively to generate the corresponding ADC image. Each lesion was measured for 3 times, and the average value was the ADC value of the lesion. On T1WI of non-fat inhibition sequence, the composition of mammary gland tissue was described, and the signal intensity of lesion was expressed by high, slightly high, or low signal. The final result was determined by two doctors.

Evaluative criteria of UE results

The hardness score of elastography (5-point scoring scheme) was used in this study. 1: The whole or most of the lesion was green; 2: The lesion was shown as blue in the center and green at the periphery; 3: The proportion of green and blue in the lesion was similar; 4: The whole lesion was blue or there was a little green inside; 5: The lesion and surrounding tissues were all blue, with or without green inside [14]. A score of 1-3 was diagnosed as benign, while scores of 4 and 5 were diagnosed as malignant.

Evaluative criteria of MR results

The images of all cases were analyzed, and the MR shape and dynamic contrast-enhanced scan points of the lesions were divided into 1-8 points. Finally, it was concluded that lesions with a round and flaky shape were benign, while those with irregular shape and spiculated margins were malignant.

Outcome measures

Using the final pathologic diagnosis results of patients as the gold standard, the diagnostic results of benign and malignant breast masses by two diagnostic methods and joint diagnosis were observed. The joint diagnosis was made by parallel test, and two tests were used at the same time. If one of the test results turned out to be positive, the test was regarded as positive. The specificity and sensitivity of each diagnostic method were calculated and compared, and ROC curves were drawn to evaluate their diagnostic efficacy. Sensitivity = true positive/(true positive + false negative) × 100%; specificity = true negative/(true negative + false positive) × 100%.

Statistical methods

All the data were calculated by SPSS 26.0 (SPSS Inc., Chicago, IL, USA), and the chi-square test was used to compare the rates, expressed as χ^2. All the measuring materials were in accordance with the normal distribution. The ROC curve was drawn to detect the diagnostic value of various diagnostic methods

Table 1. Pathologic results

Benign mass (n = 54)		Malignant mass (n = 61)	
Fibroadenoma	21 (38.89)	Invasive ductal carcinoma	36 (59.02)
Mastopathy	17 (31.48)	Intraductal carcinoma in situ	14 (22.95)
Intraductal papilloma	11 (20.37)	Intraductal papillary carcinoma	7 (11.48)
Breast inflammatory disease	3 (5.56)	Invasive lobular carcinoma	3 (4.92)
Benign phyllodes tumor	2 (3.70)		

Table 2. Score results of UE diagnosis

Pathologic diagnosis	Benign mass (n = 54)	Malignant mass (n = 61)
Benign diagnosed by UE		
1 point	12 (22.22)	4 (6.56)
2 points	24 (44.44)	2 (3.28)
3 points	15 (27.78)	2 (3.28)
Malignant diagnosed by UE		
4 points	2 (3.70)	22 (36.07)
5 points	1 (1.85)	31 (50.82)

Note: UE: ultrasound elastography.

for benign and malignant breast masses. The specificity and sensitivity of different diagnostic methods were compared by the three-dimensional chi-square test. The area under the ROC curve of each detection method was compared and analyzed by Z test. GraphPad Prism 7 (GraphPad Software, Inc., San Diego, CA, USA) was used to draw pictures. $P<0.05$ was regarded as statistically significant.

Results

Pathology results

A total of 115 breast masses were collected from 98 patients, including 54 benign masses and 61 malignant masses. The pathologic results after operation are shown in **Table 1**.

Score results of UE diagnosis

The diagnostic results of breast masses by UE diagnostic score and pathology comparative analysis are shown in **Table 2**. With pathologic diagnosis as the gold standard, 54 benign masses and 61 malignant masses were diagnosed. The 56 malignant breast masses were diagnosed by UE, among which 53 were correctly diagnosed and 3 were misdiagnosed. The 59 benign breast masses were diagnosed by UE, among which 51 cases were correctly diagnosed and 8 cases were misdiagnosed.

Comparative analysis of morphological diagnosis and pathology comparative of breast tumor by dynamic contrast-enhanced MR examination

Comparative analysis of diagnostic morphology and pathology of breast tumors by dynamic contrast-enhanced MR examination is shown in **Table 3**. With pathological diagnosis as the gold standard, 58 malignant breast masses were diagnosed by dynamic contrast-enhanced MR, among which 56 cases were correctly diagnosed and 2 cases were misdiagnosed. 57 benign breast masses were diagnosed by dynamic contrast-enhanced MR, among which 52 cases were correctly diagnosed and 5 cases were misdiagnosed.

Analysis of results of the two diagnostic methods and joint diagnosis

Totally 54 benign masses and 61 malignant masses were diagnosed by pathologic gold standard; 56 malignant masses were diagnosed by UE; 58 malignant masses were diagnosed by dynamic contrast-enhanced MR imaging; and 61 malignant masses were jointly diagnosed, as shown in **Table 4**.

Comparison of diagnostic efficiency between the two diagnostic methods and joint diagnosis

The ROC curve showed that the AUC of UE diagnosis was 0.907, that of dynamic contrast-enhanced MR imaging was 0.940, and that of joint diagnosis was 0.946; so, there was significant difference between UE and dynamic contrast-enhanced MR in AUC ($P<0.05$), but there was no significant difference between joint diagnosis and both UE and dynamic contrast-

Table 3. Results of dynamic contrast-enhanced MR examination

Pathologic diagnosis	Benign (n = 54)	Malignant (n = 61)
Benign diagnosed by dynamic contrast-enhanced MR examination		
Round shape	34 (62.96)	3 (4.92)
Flaky shape	18 (33.33)	2 (3.28)
Malignant diagnosed by dynamic contrast-enhanced MR examination		
Irregular shape	1 (1.85)	27 (44.26)
Spiculated margin	1 (1.85)	29 (47.54)

Note: MR: Magnetic resonance.

Table 4. Joint diagnosis results

Diagnostic mode	Pathologic diagnosis		Total
	Malignant	Benign	
UE			
Malignant	53	3	56
Benign	8	51	59
Total	61	54	
Dynamic contrast-enhanced MR imaging			
Malignant	56	2	58
Benign	5	52	57
Total	61	54	
Joint diagnosis			
Malignant	60	5	65
Benign	1	49	50
Total	61	54	

Note: UE: ultrasound elastography; MR: Magnetic resonance.

enhanced MR in AUC (P>0.05). In addition, there was no statistical difference in specificity and sensitivity among the three groups (P>0.05) as shown in **Tables 5**, **6**, and **Figure 1**.

Discussion

Ultrasound elastography (UE) imaging is based on the difference in elasticity coefficient between human tissues. The higher the elasticity coefficient of the tissue, the greater the hardness of the tissue. By superimposing two-dimensional sound images of different tissues and codes with different elastic coefficients, the obtained image can show the hardness of the lump objectively [15]. The changes in echo signals of the breast tissue before and after compression can be transformed into real-time color images. In these images, those tissues with larger displacement and smaller elastic coefficient after compression are displayed in red. The breast tissues with small displacement and large elastic coefficient after compression, are displayed in blue. Those breast tissues with medium elasticity coefficient are displayed in green. Therefore, the hardness of the patient's tissues can be visually observed according to the color of the image [16]. Two-dimensional gray scale images and color Doppler imaging are generally easy to overlook some minimal lesions in the breast, and the benign and malignant lesions are very similar and difficult to distinguish [17]. However, UE can better detect minimal breast lesions, and can accurately distinguish benign and malignant breast lesions. The reason is that, regardless of the size of tumor lesions, there are fundamental differences in hardness and tissue elasticity coefficients. Moreover, when the volume of malignant lesions is small, they are not prone to liquefaction and necrosis inside the lesions, so the probability of a false positive or false negative is low [18]. According to the scoring results of this UE diagnosis, 56 malignant masses and 59 benign masses were detected in 115 masses, so the specificity, sensitivity and accuracy of UE diagnosis were 94.44%, 86.89% and 90.43%, respectively. However, some sources of error exist in the diagnosis of UE. The reason may be that when a patient has a long course of disease, the hardness may increase due to calcification, and a large size of the lesions in the catheter and an increase in fibrous composition may also lead to the increase of hardness and affect the score.

MR has a high resolution of soft tissue and a high sensitivity for BC. It can be imaged in multiple directions to observe areas that cannot be

Table 5. Diagnostic efficacy

	Specificity	Sensitivity
UE	94.44%	86.89%
Dynamic contrast-enhanced MR imaging	96.30%	91.80%
Joint diagnosis	90.74%	98.36%
X^2	1.492	5.724
P	0.474	0.057

Note: UE: ultrasound elastography; MR: Magnetic resonance.

Table 6. Comparison of area under the curve

	Z	P
UE vs. Dynamic contrast-enhanced MR imaging	-2.021	0.043
UE vs. Joint diagnosis	-1.598	0.110
Dynamic contrast-enhanced MR imaging vs. Joint diagnosis	-0.223	0.823

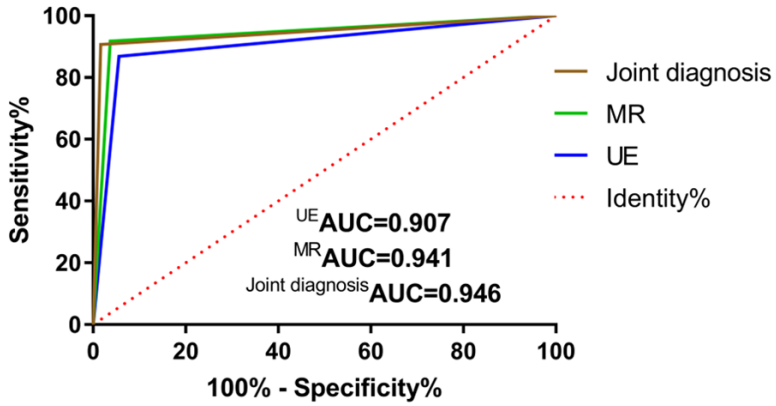

Figure 1. ROC curves of two diagnostic methods and joint diagnosis. UE: ultrasound elastography; MR: Magnetic resonance; ROC: receiver operating characteristic; AUC: area under the curve.

shown by mammography molybdenum target, such as armpits and the deep part of the breast near the chest wall [19]. Dynamic contrast-enhanced MR can reflect the blood flow velocity in the lesion by contrast agent, and then diagnose the lesion by combining its morphologic characteristics [20]. The blood flow in normal glands or benign lesions is weak, and the signal intensity changes slowly with time. However, due to the abundant blood supply and the lack of normal capillaries in malignancies, the contrast agent flows out faster, which makes the MR signal fade faster. Benign lesions tend to grow slowly, and are characterized by smooth edges, clear boundaries, and uniform enhancement, mainly by pushing and pressing the surrounding tissues. Malignancies tend to show lobulation, unclear boundaries, and a spiculated margin, which are related to their invasive growth [21, 22]. In this study, 61 malignant masses and 54 benign masses were diagnosed by dynamic contrast-enhanced MR, and the specificity, sensitivity, and accuracy were 96.30%, 91.80% and 93.91%, respectively. The reason for misdiagnosis may be that not all patients with ductal carcinoma in situ have neoplastic new capillaries, so the enhancement shows diversity [23]. Gilles et al. also revealed that dynamic contrast-enhanced MR showed poor calcification in some lesions [24]. The specificity, sensitivity, and accuracy of UE combined with dynamic contrast-enhanced MR examination were 96.30%, 96.72%, and 96.52%, which were higher than those of a single examination method, indicating that the combined examination had higher diagnostic value for breast tumors. Gao et al. also revealed that the diagnostic rate of MR in BC could be improved by combining UE, which is similar to our research [25].

There are also some shortcomings in this study. First, for the selection of the ROIs, we placed them at the most uniform part of the early enhanced parenchyma of the lesion, but the parameter results obtained by different placement methods may be different. Whether this arrangement is optimal needs to be further studied. Second, the technique and experience of the doctor who conducted the examination may also cause variation in research results. Finally, the number of individual pathologic types of mass included in the study was small, so the research results may not be comprehensive.

To sum up, joint diagnosis could improve the sensitivity of diagnosis, which has higher diagnostic value for breast tumors.

Disclosure of conflict of interest

None.

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