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Original Article

Differential diagnosis of benign and malignant breast tumors using elasticity score, strain rate ratio, and area ratio methods: a comparative analysis

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Abstract: Purpose: To investigate the differential diagnosis and diagnostic values of the elasticity score, strain rate ratio, and area ratio methods in ultrasonic elastography for benign and malignant breast lesions. Methods: We retrospectively analyzed the medical records of 165 patients with breast cancer and assessed and compared the diagnostic values of the elasticity score, strain rate ratio, and area ratio methods. Results: The elasticity score, strain rate ratio, and area ratio methods showed differences in mean diagnostic values for benign and malignant breast tumors ($P<0.05$; sensitivities, 80.6%, 74.5%, and 50.3%, respectively; and specificities, 85.5%, 95.2%, and 97.6%, respectively). The accuracies of the elasticity score and strain rate ratio methods were higher than those of the area ratio method ($P<0.05$). The specificity of the elasticity score method for the diagnosis of breast lesions was lower than that of the strain rate ratio and area ratio methods ($P<0.05$). The areas under the receiver operating curve for the diagnosis of breast lesions were 0.903, 0.858, and 0.744 for the strain rate ratio, elasticity score, and area ratio methods, respectively. Conclusion: The differential diagnostic value of the strain rate ratio method in ultrasonic elastography was high for benign and malignant breast tumors.

Keywords: Ultrasonic elastography, breast lesions, sensitivity, specificity, accuracy

Introduction

Breast cancer that forms in breast cells can occur in both men and women but is more common in women than in men and jeopardizes the health and life of patients. The incidence of breast cancer has increased rapidly in recent years (378.6 per 1 million individuals) and comprises 17% of all malignant gynecological tumors. The breast cancer mortality rate has been reported to be 114 per 1 million individuals, and breast cancer is ranked fourth among the causes of gynecological cancer-related mortality [1, 2]. Because of an increase in the incidence of tumors, diagnosis has become increasingly important.

Tests and procedures used to diagnose breast cancer comprise breast examinations, mammography, breast ultrasonography, and breast magnetic resonance imaging (MRI). In recent years, ultrasonic elastography has emerged as a useful method for diagnosing tumors. Compared with conventional sonography and mammography, MRI visualizes tissue elasticity (stiffness) in vivo and provides further additional information regarding breast lesions. The application range of MRI is greater than that of conventional ultrasonography, and compared with conventional B-mode ultrasound (US), MRI can offer improved specificity in tumor evaluation to help better characterize and differentiate benign from malignant breast masses, thus offering a clear advantage in diagnosis [3-5].

Ultrasonic elastography is a valuable tool in the diagnosis of breast lesions; however, different methods of diagnosis result in corresponding differences in the diagnostic results [6]. Ultrasonic elastography involves many different criteria, and there is no consistent standard in relation to ultrasonic elastography. The most commonly used analysis techniques include the elasticity score, strain rate ratio, and area ratio methods [7-9]. The elasticity score method is an early ultrasonic elastography technique used to identify benign and malignant tumors by measuring the degree of deformation in the lesion tissue. Elasticity imaging provides complementary information by adding stiffness as another measurable property to the current conventional ultrasound imaging techniques.

The strain rate ratio method is a relatively objective indicator used to identify benign and malignant tumors according to the differences in hardness between the lesion tissue and normal tissue at the same level. Strain elastography is a qualitative technique in which relative differences in stiffness are displayed in insonified tissue. However, the current strain rate ratio method lacks unit criteria for differentiating the critical point between benign and malignant tumors [3]. The area ratio method is used to compare lesion areas measured on ultrasonic elastography and grayscale imaging maps because the area ratio of a malignant tumor is larger [10].

In this study, we retrospectively analyzed the medical records of 165 patients with breast lesions, compared them to the pathological diagnostic criteria, and explored the diagnostic value of the elasticity score, strain rate ratio, and area ratio methods for breast lesions.

Materials and methods

Study participants

We retrospectively analyzed the medical records of 165 patients diagnosed with breast cancer based on surgical pathology in the breast surgery department at The First Affiliated Hospital of Anhui Medical University Hospital in China. The patients' age ranged from 25 to 60 years and had 248 lesions, of which 83 and 165 were malignant and benign lesions, respectively. The inclusion criteria were all patients who underwent pathological diagnosis and ultrasonic elastography examination at our hospital, except male patients with breast cancer. Patients presenting with no other tumors or no previous tumor history were included. Preoperative patients with no organ dysfunction, such as liver or kidney dysfunction, were included, and none of the patients had abnormal bleeding or coagulopathy before surgery. Exclusion criteria were patients with incomplete data, and patients with mental or learning disabilities. No tumors were excessively large, and no patients underwent chemotherapy or had recurrent breast masses. This study was approved by The First Affiliated Hospital of Anhui Medical University, and the patients or their families provided written informed consent for participation in this study.

Methods

Elastic diagrams were obtained using the following steps. We used a Siemens color doppler ultrasound diagnostic instrument. The probe frequency was set to 7.0-13.0 MHz. All patient examinations were performed using the conventional compression elastography method by highly qualified physicians with Level 2 National Vocational Qualification Certificates. The breast lesions were first examined using two-dimensional ultrasound. The diameter, mass shape, lesion location, internal echo, borders, and blood flow signals at the edge were carefully observed and measured using multiple sections. Following the initial diagnosis of the breast mass, the instrument was switched to elastography mode. The examiner detected the lesion using the probe, which was positioned perpendicular to the patient's skin. The lesion color was allowed to stabilize and freeze. The elastography and grayscale imaging maps were observed in real time. The sampling frame was approximately twice the size of the mass positioned in the center of the sampling frame. The lesions were then scored using the elasticity score method. The length and area of the grayscale imaging and elastography maps were measured, and the area ratios were calculated.

Statistical analysis

Statistical analyses were performed using SPSS 19.0 (Asia Analytics, formerly SPSS China). The enumeration data were expressed as rates, and the rates were compared using χ^2 tests. The measurement data were expressed as mean ± standard deviation. *Kolmogorov*-Smirnov tests were used for comparison between the benign and malignant tumor groups. Variance analysis was used for analyzing among the three methods, and the least significant difference test was used for comparison between the two groups. Receiver operating characteristic (ROC) curve analysis

Table 1. Patient clinical data

	General information (n = 165)
Age (Year)	42.3±7.9
Benign mass [n (%)]	165 (66.5)
Fibroadenoma	64 (58.2)
Sclerosing adenosis	19 (17.3)
Itraductal papilloma	16 (14.5)
Chronic inflammation of the breast and proliferation of granulation tissue	11 (10.0)
Malignant mass [n (%)]	83 (33.5)
Invasive ductal carcinoma	34 (61.8)
Intraductal carcinoma in situ	14 (25.5)
Invasive lobular carcinoma	4 (7.3)
Mucinous carcinoma	3 (5.5)
TNM staging	
I stage	16 (29.0)
II stage	26 (47.2)
III stage	13 (23.6)
Tumor diameter [n (%)]	
<2 cm	183 (73.8)
≥2 cm	65 (26.2)
Menopausal status [n (%)]	
Non-menopause	106 (64.2)
Postmenopausal	59 (35.8)

Table 2. Results of the elasticity score

	Benign mass	Malignant mass	Statistic	*P*-valued
Number	165	83		
Avg score	2.71±0.77	3.89±0.69	10.677	<0.001
1 [n (%)]	8 (4.8)	0 (0.0)	8 (3.2)	
2 [n (%)]	56 (33.9)	4 (4.8)	60 (24.2)	
3 [n (%)]	77 (46.7)	12 (14.5)	89 (35.9)	
4 [n (%)]	24 (14.5)	55 (66.3)	79 (31.9)	
5 [n (%)]	0 (0.0)	12 (14.5)	12 (4.8)	
Itoh ≤3	141 (85.5)	16 (19.3)	101.281	<0.001
Itoh >3	24 (14.5)	67 (80.7)		

was used to assess the diagnostic value of the elasticity score, strain rate ratio, and area ratio method. *P*-values of <0.05 were considered statistically significant.

Results

General information

There was no significant difference in the location of benign and malignant masses (P>0.05) (**Table 1**).

Results of the elasticity score method

There was a statistically significant difference between the benign and malignant masses when using the elasticity score method (P<0.05). The detailed results of the elasticity score method for benign and malignant masses are shown in **Table 2**.

Results of the strain rate ratio method

T-test results showed that the difference in the strain rate ratios between benign and malignant masses, measured using ultrasonic elastography, was statistically significant (P<0.05) (**Figure 1**).

Results of the area ratio method

Ultrasonic elastography showed statistically significant differences in the length and length change rate of grayscale imaging and elastography for benign and malignant tumors and in

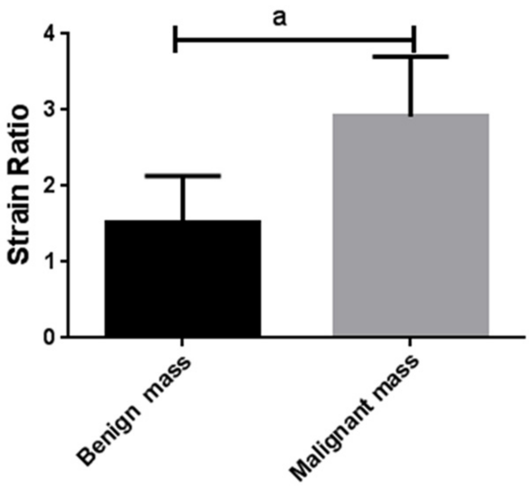

Figure 1. Analysis results of the strain ratio method; a: P<0.05.

the areas and area ratios of grayscale imaging and elastography (**Table 3**).

ROC results regarding the diagnostic values obtained from the three methods for breast lesions

The accuracy of the elasticity score and strain rate ratio methods was higher than that of the area ratio method (P<0.05). The specificity of the elasticity score method for the diagnosis of breast lesions was lower than that of the strain rate ratio and area ratio methods (P<0.05). The sensitivity of the area ratio method for the diagnosis of breast lesions was lower than that of the elasticity score and strain rate ratio methods (P>0.05) (**Table 4**; **Figure 2**).

Discussion

Breast cancer is a common gynecological malignancy. In recent years, the incidence of breast cancer has increased, and the age of onset has decreased [11, 12]. With the introduction of ultrasonic elastography in the 5^{th} edition of the Breast Imaging Report and Data System [13], the use of ultrasonic elastography for the diagnosis of breast lesions has become more widespread [6]. The detection principle of ultrasonic elastography is to press the detected tumor toward the probe, calculate the elastic coefficient distribution and the strain distribution of the tumor according to the displacement of the detected tumor, and form an image [14]. This study analyzed the diagnostic values of the elasticity score, strain rate ratio, and area ratio methods for breast lesions to provide a reference for the clinical diagnosis of breast lesions using ultrasonic elastography.

The results of this study showed that the mean diagnostic value of the elasticity score method for malignant masses was significantly higher than that for benign masses. ROC results showed that the elasticity score method had a diagnostic value of 3.5 points, with ≥4 points indicating a malignant lesion and <4 points indicating a benign lesion, which is similar to that reported in other studies [4, 15]. In our study, the sensitivity, specificity, and area under the curve (AUC) of the elasticity score method for the diagnosis of breast lesions were 80.6%, 85.5%, and 0.858, respectively. This method provided differential diagnostic values with respect to benign and malignant breast lesions. Previous studies have reported that the sensitivity and specificity of the elasticity score method for the diagnosis of benign and malignant breast masses ranged from 70.0% to 98.0% and from 45.0% to 98.0%, respectively, with both parameters fluctuating significantly [16, 17]. Some benign and malignant breast lesions may overlap, and the internal tissues of the breast lesions are more complicated. As a result, some elastic images may be difficult to match to any of the five points [18, 19], which may explain why the elasticity score method for the diagnosis of benign and malignant breast cancer has varied in different reports. Although an improved elasticity score method has been reported [20], the challenge in using this method is in distinguishing the color changes of tumor imaging, which remains a deficiency. The complexity of the scoring method prevents its widespread use in clinical practice.

The strain rate ratio method was developed in response to deficiencies in the elasticity score method for diagnosing breast lesions and to more objectively reflect the status of breast lesions. The results of our study showed that the mean diagnostic value of the strain rate ratio method for malignant masses was significantly higher than that for benign masses. ROC results showed that the cut-off point of the strain rate ratio method was between 2 and 3 points, and its sensitivity, specificity, and AUC were 74.5%, 95.2%, and 0.903 respectively, showing good differential diagnostic value for

Table 3. Results of the area ratio method

	Benign mass	Malignant mass	Statistic	*P*-valued
Number	165	83		
Gray scale image length (cm)	1.91±0.38	2.14±0.69	3.385	0.001
Elastic image length (cm)	2.22±1.01	2.72±0.91	3.800	<0.001
Long path rate	0.82±0.42	1.29±0.51	7.727	<0.001
Gray-scale imaging area (cm^2)	2.08±1.13	3.43±1.28	8.487	<0.001
Elastic image area (cm^2)	3.29±1.59	5.07±2.70	6.520	<0.001
Area ratio	1.17±0.32	1.69±0.85	6.950	<0.001

Table 4. Diagnostic values of the three methods for breast lesions

	Itoh	Strain ratio	Area ratio	Statistic	*P*-value
Accuracy rate [% (n)]	82.3 (204)	81.5 (202)	66.1 (164)	22.865	<0.001
Specificity [% (n)]	85.5 (71)	95.2 (79)	97.6 (81)	10.061	0.007
Sensitivity [% (n)]	80.6 (133)	74.5 (123)	50.3 (83)	39.312	<0.001
Diagnostic level	3.5	2.3	1.7		
95% CI	0.807-0.909	0.859-0.946	0.670-0.819		
AUC	0.858	0.903	0.744		

benign and malignant breast lesions. Currently, there is no recognized critical cut-off point for the strain rate ratio method to identify benign and malignant breast masses [3]. Kim et al. [21] reported that the best cut-off point for the diagnosis of breast lesions using the strain rate ratio method was between 2 and 3 points (sensitivity, 77.5%; specificity, 93.2%), similar to our study; however, Patel et al. [22] reported that the strain rate ratio method using a critical cut-off point of 2.5 resulted in a sensitivity of 92% and a specificity of 95.6%, which were higher than those observed in our study. Patel et al. used a Samsung RS80A ultrasound system with a 6.5-MHz linear probe to detect and analyze 50 patients with breast lesions. In contrast, we used a Siemens color doppler ultrasound diagnostic instrument with a probe frequency between 7.0 and 13.0 MHz to analyze 248 tumors in 165 patients with breast lesions. These differing approaches may explain the variations in the results besides any differences in relation to the study patients. Another reason for the variation may be that Patel et al. made a comparison with glandular tissue, whereas we made a comparison with surrounding fatty tissue. However, these varying results still showed that the strain rate ratio method was effective in diagnosing breast lesions.

In recent years, the area ratio method has also been reportedly used for the differential diagnosis of benign and malignant breast lesions [23]. This method detects the area of breast lesions using both elastography and grayscale imaging. The area ratio is then automatically analyzed using an ultrasound instrument calculation system [10]. Malignant tumors mostly infiltrate in the shape of crab-like claws. The area around the elastography is twice that of the grayscale ultrasound image. When the infiltration of an early stage malignant tumor is small, it cannot generally be detected using conventional grayscale ultrasound. Ultrasonic elastography can reflect the degree and extent of tumors by identifying differences in the stiffness between the infiltrating interface and normal tissue [24, 25]. Our study results showed that the area ratio method for the diagnosis of a malignant mass was significantly higher than that of a benign mass. ROC results showed that the diagnostic value of the strain rate ratio method was 1.7, with a sensitivity, specificity, and AUC of 50.3%, 97.6%, and 0.744, respectively. Compared to the elasticity score and strain rate ratio methods, the area ratio method offered relatively insufficient diagnostic value, although the specificity was higher than that of the elasticity score method; however, there was no difference compared with the strain rate ratio method. Lei et al. [26] reported a sensitivity, specificity, and AUC of 46.4%, 94.1%, and 0.70, respectively, for the diagnosis of breast lesions using the area ratio method. In that study, the diagnostic area for the area ratio method was 1.95 cm^2, which was similar to that noted in our study. Lin et al. [27] reported a sensitivity, specificity, and AUC of 76.19%, 98.88%, and 0.917, respectively, for the diagnosis of breast lesions using the area ratio method, with a diagnostic value of 1.43. Although Lin et al.'s diagnostic value was similar to that found in our study, the value of the diagnosis of breast lesions under

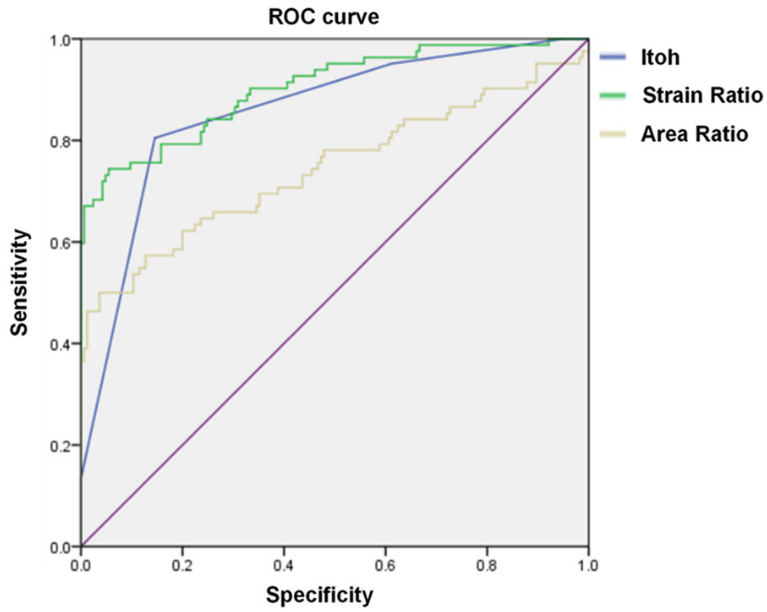

Figure 2. Three methods were used to diagnose the ROC of breast lesions. AUC (strain ratio) = 0.903, AUC (elasticity score) = 0.858, AUC (area ratio) = 0.744.

the area ratio method was significantly higher in their study. Their research method involved acoustic radiation force impulse imaging, which was performed using thrust impulses on the tissues. This method is less affected by human factors than conventional compression elastography, which was used in our study; therefore, it can produce small local changes in tissue during thrust pulses. This may be the main reason for the differences in the results.

The elasticity score, strain rate ratio, and area ratio methods are used to diagnose breast lesions. The strain rate ratio method had a better diagnostic value, and its specificity and sensitivity were not inferior to those of the elasticity score and area ratio methods. However, the detection technique used in the area ratio method requires further improvement. Moreover, many factors may affect accuracy. For example, some lesions grow faster and have a large volume, and the blood supply may be insufficient; therefore, liquefaction and necrosis occur, resulting in a very uneven hardness in the lesion. The location, type, depth of the lesion, and size of the region of interest will also have an effect. Additionally, the heterogeneity of breast cancer itself will make its internal hardness uneven and may affect the elasticity measurement. Future studies are needed to further improve the diagnostic methods and validate our results.

In summary, the strain rate ratio method in ultrasonic elastography was found to have a high value for the differential diagnosis of benign and malignant breast tumors, and its sensitivity and specificity were not inferior to those of the conventional elasticity score and area ratio methods. The strain rate ratio method is, therefore, worthy of clinical reference in the diagnosis of breast tumors.

Disclosure of conflict of interest

None.

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