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Value of real-time tissue elastography diffusion quantitative analysis combined with tumor markers for differential diagnosis of benign and malignant breast nodules

Vrednost elastografije mekih tkiva u realnom vremenu sa kvantitativnom analizom u kombinaciji sa tumorskim markerima za diferencijalnu dijagnozu benignih i malignih nodusa dojke

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Abstract

Background/Aim. Serum tumor markers (TMs) are commonly combined with imaging examinations to differentiate benign and malignant breast nodules (BNs), but there are still limitations. The aim of the study was to determine the value of real-time tissue elastography (RTE) diffusion quantitative analysis combined with serum TMs for the differential diagnosis of benign and malignant BNs. **Methods.** A total of 149 patients with BNs were included in this study. They were assigned to the benign BN group (n = 87) and malignant BN group (n = 62). All patients were examined using RTE diffusion quantitative analysis. Venous blood was collected to detect the levels of TMs carcinoembryonic antigen-CAE, cancer antigen (CA) 153, and CA 199. The value of RTE diffusion quantitative analysis parameters, TMs, and their combination for the differentiation of benign and malignant BNs was analyzed using the receiver operating characteristic-ROC curve. **Results.** Among all the above indicators, the area ratio of the blue region (AREA%) had the highest differential value, with an area under the curve (AUC) of 0.916 [95% confidence interval (CI): 0.812–0.967], while sensitivity and specificity were 88.90% and 86.79%, respectively ($p < 0.05$). Compared to RTE diffusion quantitative analysis parameters or TMs alone, the combination of the two showed the highest value for the differentiation of benign and malignant BNs, with an AUC of 0.957 (95% CI: 0.834–0.982), while sensitivity and specificity were 95.50% and 94.33%, respectively ($p < 0.05$). **Conclusion.** RTE diffusion quantitative analysis combined with TMs has a high value for the differentiation of benign and malignant BNs.

Key words:
breast, neoplasms; biomarkers, tumor; diagnosis, differential; elasticity imagine techniques; sensitivity and specificity.

Apstrakt

Uvod/Cilj. Za razlikovanje benignih i malignih nodusa (čvorića) dojke (ND) često se kombinuju serumski tumorski markeri (TM) i analize snimaka nodusnih promena, mada ograničenja još uvek postoje. Cilj rada bio je da se utvrdi korisnost elastografije mekih tkiva u realnom vremenu (EMTRV) sa kvantitativnom analizom u kombinaciji sa serumskim TM za diferencijalnu dijagnozu benignih i malignih ND. **Metode**. Ukupno 149 žena sa ND bilo je uključeno u ovu studiju. Bolesnice su podeljene na grupu sa benignim ND (n = 87) i grupu sa malignim ND (n = 62). Sve bolesnice su bile ispitane primenom EMTRV sa kvantitativnom analizom. Iz venske krvi, određivani su nivoi TM: karcinoembrionskog antigena-CAE, karcinomskog antigena (*cancer* antigen – CA) 153 i CA 199. Za diferencijalnu dijagnozu benignih i malignih ND, analizirane su vrednosti parametara EMTRV sa kvantitativnom analizom, TM i njihove kombinacije, korišćenjem *receiver operating characteristic*-ROC krive. **Rezultati**. Među navedenim pokazateljima, najveću diferencijalnu vrednost imala je *area ratio of the blue region* (AREA%) sa površinom ispod krive (*area under the curve* – AUC) od 0,916 [95% *confidence interval* (CI): 0,812–0,967], dok su senzitivnost i specifičnost iznosile 88,90% i 86,79%, redom ($p < 0,05$). U poređenju sa

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EMTRV sa kvantitativnom analizom ili samo sa TM, njihova kombinacija je pokazala najvišu vrednost za razlikovanje benignih i malignih ND, sa AUC 0,957 (95% CI: 0,834–0,982), dok su senzitivnost i specifičnost iznosile 95,50% i 94,33%, redom. **Zaključak**. EMTRV sa kvantitativnom analizom u kombinaciji sa TM ima veliku vrednost za razlikovanje benignih i malignih ND.

Ključne reči:
dojka, neoplazme; tumorski markeri; dijagnoza, diferencijalna; elasticitet, tehnike snimanja; osetljivost i specifičnost.

Introduction

Breast cancer (BC) is a common disease that affected about 2.26 million people in 2020 worldwide, which accounted for 11.7% of all malignancies [1]. The global 5-year survival rate is 82% [2] and the global mortality rate is 17.7 *per* 100,000 people [1]. Although the incidence rate of BC in China is lower than the global value [3], it is increasing annually and poses serious threats to women's lives and health. Breast nodules (BNs) are the common manifestations of benign and malignant breast lesions, and the treatment and prognosis of the two types of BNs vary considerably [4]. Therefore, the early identification of benign/malignant breast lesions is of great significance for timely treatment, contributing to an obvious reduction in the mortality rate and improvement of women's quality of life [5].

Presently, many methods are used to differentiate benign and malignant BNs, mainly including imaging and serum tumor markers (TMs), the latter of which refer to special substances that cause some functional abnormalities and, thus, change in the presence of malignant lesions [6, 7]. TMs play vital roles in the screening, adjuvant diagnosis, treatment, and prognosis of BC [8]. However, the detection of serum TMs is prone to influences by external factors during tests [9].

Real-time tissue elastography (RTE), as a novel ultrasound diagnostic technique, can closely monitor tissue elasticity using diffusion quantitative analysis [10, 11]. It has been used in the differential diagnosis of various benign and malignant diseases, which contributes to evaluating the nature of lesions [12–14]. Xu et al. [15] reported that RTE had a high diagnostic rate for BC with axillary lymph node metastasis. In addition to a diagnostic tool for BC, Fang and Yang [16] also proved the predictive role of RTE in the effect of neoadjuvant chemotherapy on patients with BC. Nevertheless, there are few studies regarding the differentiation of benign and malignant BNs using RTE.

Therefore, the aim of this study was to determine the value of RTE diffusion quantitative analysis used to analyze the tissue parameters of lesions in patients with benign and malignant BNs, combine their results with TMs to accurately differentiate benign and malignant BNs, and improve the treatment and prognosis.

Methods

Subjects

A total of 149 patients with BNs, who were admitted to our hospital from April 2020 to April 2021, were included in this study. The patients were all females, aged 25–70 years (mean 47.89 ± 5.63 years). RTE diffusion quantitative analysis was performed and serum TMs were measured before pathological examination; then, the ultrasound-guided needle biopsy was performed. The subjects were then assigned to the benign and malignant BN groups using pathological examination results as the gold standard. Informed consent was obtained from all patients and this study was reviewed and approved by the Ethics Committee of the Huzhou Maternal and Child Health Hospital, China (from April 4, 2020).

Inclusion and exclusion criteria

Inclusion criteria were as follows: 1) patients with a single BN; 2) no contraindications to imaging examination; 3) no previous treatment of breast lesions; 4) normal expressive and cognitive abilities of the patients allowing a normal description of symptoms and cooperation with examinations; 5) complete clinical records.

Exclusion criteria involved the following: 1) patients with a previous history of malignancy; 2) breast implants; 3) history of resection of the breast mass; 4) pregnancy or lactation to avoid the influence of hormone changes; 5) calcified lesions in the breast; 6) cardiovascular or cerebrovascular diseases to avoid the occurrence of sudden cardiac or cerebral adverse events; 7) poor compliance and patients unable to cooperate to affect examinations.

Real-time tissue elastography diffusion quantitative analysis

All patients were examined by the HI VISION Ascendus ultrasound platform using an L-52 linear array probe (Hitachi Aloka Medical, Ltd., Japan) with a frequency of 6–13 MHz. The size and location of BNs were observed following the routine ultrasound examination. Then, the instrument was switched to an elastography mode to observe the gray-scale echogram and elastogram using the dual-view display function, and the position of the probe was adjusted to ensure that the BN was in the center of the screen. During the examination, the pressure was manually applied. After a slight jitter, the stable and repeatable dynamic elastogram was displayed and obtained when the pressure value was within the range of 3–4. Images were analyzed using Strain Histogram Measurement software along with the platform. With the largest rectangular area not exceeding the extent of the lesion as the sampling location, 11 RTE parameters, including mean strain (MEAN), standard deviation (SD),

area ratio of the blue region (AREA%), complexity (COMP), kurtosis (KURT), skewness (SKEW), contrast (CONT), entropy (ENT), inverse difference moment (IDM), angular second moment (ASM), and correlation (CORR), were acquired. The examination was repeated three times to take the corresponding mean value.

Tumor marker tests

Fasting venous blood was drawn from each subject in the early morning. The serum was then separated, followed by the detection of the levels of TMs carcinoembryonic antigen (CEA), cancer antigen (CA) 153, and CA199 using the E411 electrochemiluminescence analyzer (Roche, Switzerland).

Observation of indicators

Firstly, the patients were assigned to the benign BN group (n = 87) and malignant BN group (n = 62) with pathological examination results as the gold standard, and the RTE diffusion quantitative parameters and TM levels were compared between the two groups. Secondly, the differences in RTE diffusion quantitative parameters and TM levels were compared among patients with different degrees of differentiation (poor, moderate, and good) and different stages (I, II, III, and IV) of malignant BNs. Thirdly, the value of RTE diffusion quantitative analysis and TMs in differentiating benign and malignant BNs was analyzed using pathological examination results as the gold standard.

Statistical analysis

The SPSS software version 22.0 was used for statistical analysis. The Kolmogorov-Smirnov test was applied to determine whether the data conformed to normal distribution. Normally distributed measurement data were expressed as mean ± SD and analyzed by the independent samples *t*-test for comparison between groups. If the data did not conform to normal distribution, they were expressed as a median and interquartile range [M (Q1, Q3)] and analyzed by the Wilcoxon test to compare between groups. Count data were expressed as numbers (percentages) and analyzed using the Chi-square (χ^2). The value of RTE diffusion quantitative parameters, TMs, and the combination of the two in the differentiation of benign and malignant BNs was analyzed by plotting receiver operating characteristic (ROC) curves. With the area under the curve (AUC) > 0.7 representing the differential value, a larger AUC corresponded to a higher differential diagnosis value. The value of $p < 0.05$ was considered statistically significant.

Results

Among 149 pathology-proven BNs, there were 87 benign lesions and 62 malignant lesions (Table 1).

Considering the 11 obtained RTE diffusion quantitative parameters, all of them had statistically significant differences between benign and malignant BN groups, except for COMP and CORR. Specifically, the MEAN, SD, CONT, and ENT were lower and the AREA%, KURT, SKEW, IDM, and ASM were higher in the malignant nodule group than those in the benign BN group ($p < 0.05$). Compared with those in the benign BN group, the levels of TMs CEA, CA153, and CA199 were higher in the malignant BN group ($p < 0.05$) (Table 2).

The nine RTE diffusion quantitative parameters with statistically significant differences between benign and malignant BNs were further analyzed. It was found that patients with poor differentiation of malignant BNs showed lower MEAN, SD, CONT, and ENT and higher AREA%, KURT, SKEW, IDM, and ASM than those with moderate/good differentiation of malignant BNs ($p < 0.05$). The levels of TMs CEA, CA153, and CA199 were also compared among patients with different degrees of differentiation of malignant BNs, and it was seen that patients with poor differentiation had higher CEA, CA153, and CA199 levels than those with moderate/good differentiation ($p < 0.05$) (Table 3).

With the increasing stage of malignant BNs, the MEAN, SD, CONT, and ENT declined gradually and the AREA%, KURT, SKEW, IDM, and ASM rose gradually

Table 1

Pathological examination results

Pathological finding	n (%) of nodules
Benign breast nodules (n = 87)	
mammary inflammatory granuloma	19 (21.84)
intraductal papilloma	17 (19.54)
fibroadenoma	24 (27.59)
breast adenopathy	21 (24.14)
usual-type ductal epithelial hyperplasia	6 (9.68)
Malignant breast nodules (n = 62)	
invasive ductal carcinoma	18 (29.03)
invasive lobular carcinoma	20 (32.26)
ductal carcinoma in situ	14 (22.58)
medullary carcinoma	10 (16.13)

n – number.

Table 2

Real-time tissue elastography (RTE) diffusion quantitative parameters and tumor marker levels of patients with benign and malignant breast nodules (BNs)

Parameter	BNs group		*t*	*p*-value
	benign (n = 87)	malignant (n = 62)		
RTE diffusion quantitative parameters				
MEAN	84.53 ± 10.19	24.53 ± 2.13	45.620	0.001
SD	39.18 ± 3.20	28.29 ± 2.19	23.190	0.001
AREA%	42.32 ± 2.89	84.43 ± 1.09	109.200	0.001
COMP	24.31 ± 1.89	24.35 ± 1.20	0.147	0.883
KURT	3.12 ± 0.67	5.64 ± 1.12	17.130	0.001
SKEW	0.68 ± 0.12	1.42 ± 0.28	22.000	0.001
CONT	28.97 ± 3.42	17.78 ± 1.10	24.840	0.001
ENT	3.12 ± 0.29	2.25 ± 0.21	20.150	0.001
IDM	0.31 ± 0.07	0.58 ± 0.12	17.280	0.001
ASM	0.03 ± 0.01	0.09 ± 0.03	17.370	0.001
CORR	5.62 ± 0.89	5.69 ± 0.72	0.511	0.610
Tumor marker levels				
CEA (ng/mL)	5.32 ± 1.09	11.23 ± 2.54	19.360	0.001
CA153 (U/mL)	23.41 ± 2.39	42.31 ± 5.62	28.040	0.001
CA199 (U/mL)	20.19 ± 2.32	37.64 ± 3.12	39.160	0.001

MEAN – mean strain; SD – standard deviation; AREA% – area ratio of the blue region; COMP – complexity; KURT – kurtosis; SKEW – skewness; CONT – contrast; ENT – entropy; IDM – inverse difference moment; ASM – angular second moment; CORR – correlation; CEA – carcinoembryonic antigen; CA – cancer antigen. All values are given as mean ± SD.

Table 3

Real-time tissue elastography (RTE) diffusion quantitative parameters and tumor marker levels of patients with different degrees of differentiation of malignant breast nodules

Parameter	Degree of differentiation			*F*	*p*
	good (n = 20)	moderate (n = 24)	poor (n = 18)		
RTE diffusion quantitative parameters					
MEAN	37.75 ± 2.31	26.31 ± 3.89[a]	18.97 ± 1.65[ab]	42.810	0.001
SD	32.42 ± 4.52	28.78 ± 2.11[a]	25.63 ± 2.10[ab]	8.741	0.001
AREA%	79.98 ± 6.12	86.75 ± 7.85[a]	92.31 ± 9.06[ab]	7.442	0.001
KURT	4.10 ± 0.42	5.90 ± 0.78[a]	7.89 ± 1.13[ab]	20.971	0.001
SKEW	1.18 ± 0.21	1.50 ± 0.12[a]	1.87 ± 0.14[ab]	17.670	0.001
CONT	20.19 ± 2.23	17.85 ± 1.96[a]	14.53 ± 1.20[ab]	14.375	0.001
ENT	2.89 ± 0.28	2.10 ± 0.23[a]	1.67 ± 0.15[ab]	24.705	0.001
IDM	0.40 ± 0.03	0.59 ± 0.10[a]	0.70 ± 0.15[ab]	13.146	0.001
ASM	0.06 ± 0.02	0.08 ± 0.03[a]	0.11 ± 0.03[ab]	9.153	0.001
Tumor marker levels					
CEA (ng/mL)	8.77 ± 1.09	11.32 ± 2.31	15.63 ± 2.45	17.025	0.001
CA153 (U/mL)	32.42 ± 2.31	40.51 ± 3.42[a]	45.64 ± 3.41[ab]	21.180	0.001
CA199 (U/mL)	30.92 ± 2.39	36.73 ± 2.19[a]	42.31 ± 4.78[ab]	14.154	0.001

[a] $p < 0.05$ vs. good differentiation; [b] $p < 0.05$ vs. moderate differentiation.
For abbreviations, see Table 2.
All values are given as mean ± SD.

($p < 0.05$), while the levels of tumor markers CEA, CA153, and CA199 were elevated gradually ($p < 0.05$) (Table 4).

Using pathological examination results as the gold standard, it was revealed that the sensitivity, specificity, and accuracy of RTE diffusion quantitative analysis in differentiating benign and malignant BNs were 88.71% (55/62), 88.51% (77/87), and 88.59% (132/149), respectively (Table 5). The sensitivity, specificity, and accuracy of TMs in differentiating benign and malignant BNs were 79.03% (49/62), 78.16% (68/87), and 78.52% (117/149), respectively (Table 6). Besides, the sensitivity, specificity, and accuracy of RTE diffusion quantitative analysis combined with TMs

Table 4

Real-time tissue elastography (RTE) diffusion quantitative parameters and tumor marker levels of patients with different stages of malignant breast nodules

Parameter	Stage I (n = 15)	Stage II (n = 20)	Stage III (n = 17)	Stage IV (n = 10)	*F*	*p*
RTE diffusion quantitative parameters						
MEAN	30.97 ± 4.55	27.53 ± 3.16[a]	22.94 ± 2.25[ab]	17.63 ± 1.12[abc]	13.547	0.001
SD	34.24 ± 3.15	30.12 ± 2.89[a]	27.89 ± 2.11[ab]	22.31 ± 2.07[abc]	15.780	0.001
AREA%	71.42 ± 4.51	80.32 ± 5.63[a]	88.06 ± 8.94[ab]	97.68 ± 9.12[abc]	14.396	0.001
KURT	3.99 ± 0.78	5.13 ± 0.43[a]	6.98 ± 1.24[ab]	8.12 ± 1.69[abc]	12.440	0.001
SKEW	1.03 ± 0.12	1.56 ± 0.13[a]	1.93 ± 0.16[ab]	2.35 ± 0.21[abc]	30.060	0.001
CONT	24.53 ± 2.18	20.31 ± 2.23[a]	17.85 ± 2.18[ab]	15.63 ± 1.12[abc]	17.775	0.001
ENT	2.78 ± 0.32	2.34 ± 0.15[a]	2.00 ± 0.19[ab]	1.78 ± 0.13[abc]	13.994	0.001
IDM	0.42 ± 0.03	0.54 ± 0.04[a]	0.65 ± 0.04[ab]	0.79 ± 0.05[abc]	34.800	0.001
ASM	0.05 ± 0.02	0.07 ± 0.02[a]	0.10 ± 0.03[ab]	0.13 ± 0.04[abc]	9.968	0.001
Tumor marker levels						
CEA (ng/mL)	7.85 ± 0.97	13.42 ± 1.10[a]	16.98 ± 2.31[ab]	19.74 ± 2.41[abc]	25.905	0.001
CA153 (U/mL)	30.21 ± 2.19	39.09 ± 3.42[a]	46.64 ± 4.51[ab]	50.98 ± 6.12[abc]	18.210	0.001
CA199 (U/mL)	28.38 ± 2.11	36.64 ± 4.51[a]	38.97 ± 2.19[ab]	45.53 ± 6.76[abc]	13.887	0.001

[a] $p < 0.05$ vs. stage I; [b] $p < 0.05$ vs. stage II; [c] $p < 0.05$ vs. stage III.
For abbreviations, see Table 2.
All values are given as mean ± SD.

Table 5

Value of real-time tissue elastography diffusion quantitative analysis for differentiating benign and malignant breast nodules (BNs)

BNs	Gold standard		Total
	malignant BNs	benign BNs	
Malignant	55	10	65
Benign	7	77	84
Total	62	87	149

Note: Gold standard means pathohistological finding.

Table 6

Value of tumor markers for differentiating benign and malignant breast nodules (BNs)

BNs	Gold standard		Total
	malignant BNs	benign BNs	
Malignant	49	19	68
Benign	13	68	81
Total	62	87	149

Note: Gold standard means pathohistological finding.

Table 7

Value of real-time tissue elastography (RTE) diffusion quantitative analysis combined with tumor markers for differentiating benign and malignant breast nodules (BNs)

BNs	Gold standard		Total
	malignant BNs	benign BNs	
Malignant	60	6	66
Benign	2	81	83
Total	60	6	66

Note: Gold standard means pathohistological finding.

in differentiating benign and malignant BNs were 96.77% (60/62), 93.10% (81/87), and 94.63% (141/149), respectively (Table 7). Overall, the value of RTE diffusion quantitative analysis combined with TMs was optimal in differentiating benign and malignant BNs.

According to the ROC curve analysis, among all the RTE diffusion quantitative parameters and TMs, AREA% had the highest differential value, with an AUC of 0.916 [95% confidence interval (CI): 0.812–0.967], while sensitivity and specificity were 88.90% and 86.79%,

respectively ($p < 0.05$). In contrast to RTE diffusion quantitative parameters or TMs alone, the combination of the two showed the highest value in the differentiation of benign and malignant BNs, with an AUC of 0.957 (95% CI: 0.834–0.982), while sensitivity and specificity were 95.50% and 94.33%, respectively ($p < 0.05$) (Figure 1).

The typical RTE diffusion quantitative analysis images are exhibited in Figures 2 and 3.

Discussion

Many TMs are currently available in differentiating benign and malignant BNs, among which CEA, CA153, and CA199 are most commonly used [17]. The combination of CA153 and CA199 has the highest value in diagnosing BC and identifying benign and malignant BNs. Additionally, Can et al. [18] reported that CEA positivity was related to the

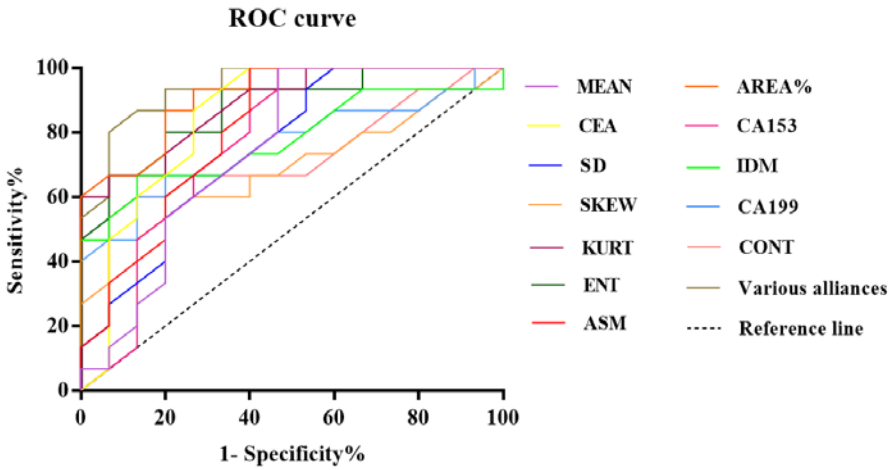

Fig. 1 – Receiver operating characteristic (ROC) curve analysis of real-time tissue elastography diffusion quantitative parameters and tumor markers in differentiating benign and malignant breast nodules. For abbreviations, see Table 2.

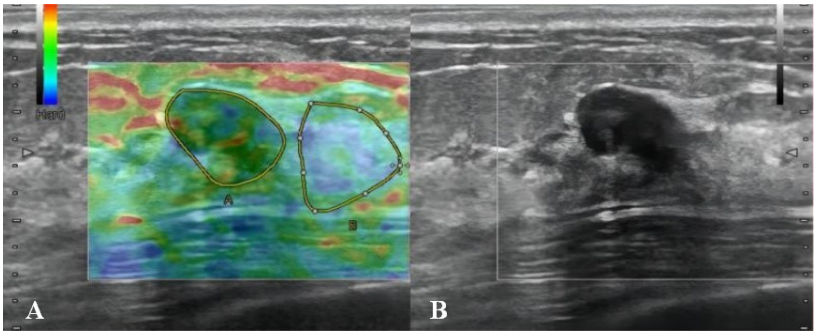

Fig. 2 – A 30-year-old female presented with a right breast nodule. Real-time tissue elastography diffusion quantitative analysis showed an area ratio of the blue region (AREA%) of 21.89 and soft tissues, suggesting it was a benign breast nodule (A and B).

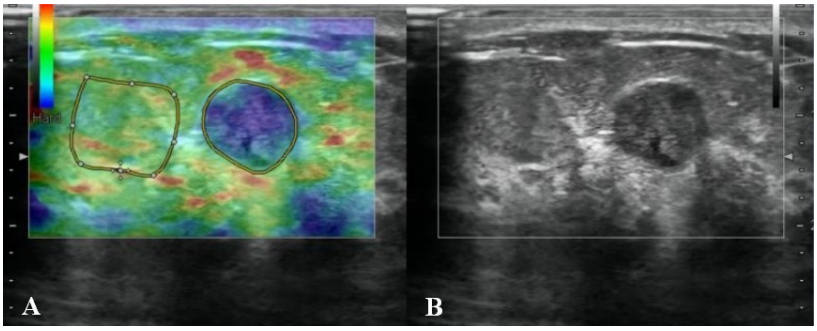

Fig. 3 – A 28-year-old female with a right breast nodule identified by physical examination. Real-time tissue elastography diffusion quantitative analysis revealed an area ratio of the blue region (AREA%) of 89.72 and hard tissues, suggesting it was a malignant breast nodule (A and B).

increased preoperative tumor burden of malignant BNs, which was beneficial to the diagnosis. In this study, the differences in the levels of these serum TMs between patients with benign and malignant BNs were analyzed using pathological examination results as the gold standard, and the results showed that CEA, CA153, and CA199 levels in malignant BNs were higher than in benign BNs, being consistent with the literature mentioned above. Moreover, we found that CEA, CA153, and CA199 levels were significantly higher in poorly differentiated and stage IV patients than in patients with moderate to good differentiation and stages I to III. Hence, CEA, CA153, and CA199 may be involved in the progression of malignant BNs.

Ultrasound and color Doppler ultrasound are usually employed to diagnose benign and malignant BNs. However, they are unsuitable for BC with no or small masses, because no image is obtained or the image is obscure [19]. Thus, RTE diffusion quantitative analysis was used to differentiate benign and malignant BNs in this study to improve the accuracy of evaluating differentiation. The results exhibited that, except for COMP and CORR, all the diffusion quantitative parameters obtained by RTE diffusion quantitative analysis had statistically significant differences in differential diagnosis of benign and malignant BNs. Specifically, lower MEAN, SD, CONT, and ENT indicated higher tissue stiffness, while higher AREA%, KURT, SKEW, ENT, IDM, and ASM represented higher tissue stiffness. Besides, in comparison with benign BNs, MEAN, SD, CONT, and ENT were lower and AREA%, KURT, SKEW, ENT, IDM, and ASM were higher in malignant BNs, which were associated with the degree of differentiation and stage of patients with malignant BNs. Similarly, Guo et al. [20] conducted an RTE diffusion quantitative analysis and found that except for COMP and CORR, the other nine characteristic parameters showed statistically significant differences in the differentiation of benign and malignant prostate nodules. Theoretically, it may be explained by the tissue stiffness of malignant breast lesions higher than that of benign lesions, and such tissue stiffness gradually increases as the disease progresses.

With pathological findings as the gold standard, the value of RTE diffusion quantitative analysis in differentiating benign and malignant breast lesions was analyzed. The results indicated that 55 out of the 62 malignant nodules were identified by RTE diffusion quantitative analysis. The remaining seven cases of medullary carcinoma were misdiagnosed as fibroadenoma and usual-type ductal epithelial hyperplasia, probably because medullary carcinoma has less collagen content, small amounts of fibrous tissues, and abundant cancer cells, making the texture relatively soft [21]. Besides, 77 out of the 87 benign nodules were identified by RTE diffusion quantitative analysis, and the remaining ten were misdiagnosed as fibroadenoma, possibly because fibroadenoma principally presents as mesenchymal hyperplasia, and the complex mesenchymal hyperplasia may increase the stiffness of tissues [22].

In this study, ROC curves were plotted to analyze the values of RTE diffusion quantitative analysis and TMs for the differentiation of benign and malignant BNs. AREA% had the highest differential value, probably because it reflects the area of the blue region, of which the proportion has a positive relationship with the tissue stiffness [23]. However, RTE diffusion quantitative analysis still needs to be combined with other methods to reduce the misdiagnosis rate in the clinical differentiation of benign and malignant BNs [24]. We found that the value of RTE diffusion quantitative parameters combined with TMs was markedly higher than that of RTE diffusion quantitative parameters or TMs alone, suggesting that the combination may improve the detection accuracy and prognosis.

Conclusion

In conclusion, real-time tissue elastography diffusion quantitative analysis combined with tumor markers is effective in differentiating benign and malignant breast nodules and has a highly differential diagnosis. Nonetheless, this study is limited because this study was, first of all, a single-center study with a small sample size. Second, we did not consider other histopathological parameters such as tumor type, size, and dissemination. Therefore, additional multicenter studies with large sample sizes are still needed for further validation.

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Conflict of interest

The authors declare no conflict of interest concerning authorship and/or publication of this article.

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