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ORIGINAL RESEARCH

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Value of ultrasonic shear wave elastography combined with vascularization-flow index in differential diagnosis of benign and malignant breast tumors in the elderly

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Abstract

Background: The study aimed to investigate the value of ultrasound shear wave elastography (SWE) combined with vascularization-flow index (VFI) in the differential diagnosis of benign and malignant breast tumors in the elderly. **Methods**: A retrospective analysis and examination of 122 elderly patients with breast tumors (54 benign and 68 malignant) admitted to our hospital from January 2021 to November 2023 was conducted using SWE and Color Doppler ultrasound (CDU) index. Using postoperative pathological examination results, the SWE index, CDU index, SWE classification and the diagnostic efficacy of the combined examination were compared between both groups. Different diagnostic methods were further compared using receiver operating characteristic curves. **Results**: The maximum elasticity, mean elasticity, minimum elasticity, AveT1, AveR, Ratio1, Fibrosis Index (FI), Vascular Index (VI) and VFI indexes in the malignant group were significantly higher than those in the benign group ($p < 0.05$). Compared to the benign group, the proportion of classification 1 was significantly lower in the malignant group. The proportion of classifications 4, 5 and 6 in the malignant group was significantly higher ($p < 0.05$). The receiver operating characteristic (ROC) curve showed that the largest area under the ROC curve of the combination of both was 0.935; for both, the difference was significant when compared to a single diagnosis ($p < 0.05$). **Conclusions**: Breast tumors can be diagnosed more effectively using SWE integrated with CDU than with SWE alone. Breast tumor clinical diagnosis can be improved when SWE and CDU are combined.

Keywords

SWE; VFI; Breast tumor; Diagnosis

1. Introduction

Breast tumors refer to neoplastic lesions arising in breast tissue [1], including benign and malignant tumors. Based on incomplete statistics, urban Chinese women with breast cancer are about 30~50 cases/100,000, while elderly women, especially those over 60, are about 100~150 cases/100,000 [2]. As patients age, prevalence and harm also increase. Early symptoms of breast cancer are often not apparent, so many patients are already in the middle or advanced stages when they are diagnosed and are too late for effective treatment. Breast tumor growth and development are closely related to angiogenesis. Vascular changes in early breast tumors are subtle, with a low diagnostic yield using conventional diagnostic modalities (palpation, ultrasound flow imaging) [3]. Therefore, the rapid and effective diagnosis of malignant breast tumors has emerged as a priority in clinical medicine. SWE is a novel sonoelastography technique [4] that uses emitted ultrasound radiation pulses to generate shear waves in tissues based on the characteristics of malignant breast tumors with higher stiffness than benign tumors. By comparing shear wave propagation speeds in tissues of different stiffnesses [5], it quantifies tissue stiffness. For certain types of breast tumors, SWE is accurate, non-invasive and real-time. CDU can reflect the density, scattering intensity or energy distribution of red blood cells in blood [5]. It can also analyze and demonstrate the distribution, morphology and blood perfusion of blood vessels. As malignant breast tumors induce more and more complex neovascularization [6], CDU has some reference value in diagnosing breast tumors. CDU is intuitive and three-dimensional with rich information, but susceptible to external interference. The purpose of this study is to investigate how SWE combined with VFI can improve the diagnostic accuracy of elderly patients with breast tumors. Detailed information is provided below.

2. Materials and methods

2.1 Clinical data

Clinical data of 122 elderly patients with breast tumors admitted to our hospital from January 2021 to November 2023

were analyzed retrospectively. Patients were aged 54~76 years, with a mean of (61.85 ± 6.21) years; Body Mass Index (BMI) 17~24 kg/m^2, with a mean of (21.38 ± 2.37) kg/m^2. Postoperative pathological results divided the patients into two groups: benign (n = 54) and malignant (n = 68).

2.2 Inclusion and exclusion criteria

2.2.1 Inclusion criteria

① Mass tissue presence confirmed by breast ultrasonography, and breast tumor confirmed by postoperative pathological results; ② Female; ③ First treatment; ④ Age ≥60 years old; ⑤ Patients agreed to participate and signed the informed consent.

2.2.2 Exclusion criteria

① Combined with other malignant tumors; ② Suffering from mental disorders; ③ Suffering from serious organ dysfunction.

2.3 Method

SWE and CDU examinations were performed by the same team of physicians for all patients.

2.3.1 SWE inspection

Patients were scanned using a Philips EPIQ 7C Diagnostic Ultrasound System (Philips, Andover, MA, USA) with 3-dimensional probe frequencies set at 4 to 10 MHz and 2-dimensional probe frequencies set at 7 to 15 MHz. (1) Patient preparation: In a supine position, patients' breasts were fully exposed and their arms were raised. (2) Instrument setting: Select SWE function mode. Probe frequency, depth, gain and other parameters were then adjusted to keep the image clear and accurate. (3) Routine ultrasound scanning: Routine ultrasound probe was used to perform all-round scanning of bilateral breasts, covering multiple sections such as transection, longitudinal section and oblique section. We observed breast tissue's overall structure to find suspicious lesions. (4) Localization of the lesion: Suspected tumor lesions were found, and key features including location, size and shape were accurately recorded. (5) Image acquisition: Switch to SWE mode. Probe was placed on the lesion smoothly and precisely until the image stabilized. At least 3 SWE images with a representative image were collected. (6) Data analysis: Elastic modulus value of the tissue inside and around the lesion was accurately measured, and the color distribution in the elastic image was observed.

Lesions were classified according to examination findings. Among them, classification 1 (homogeneous type): the elasticity value distribution in the tumor area is more uniform, without significant elasticity difference; classification 2 (peripheral high central low type): the elasticity value in the tumor peripheral area is higher, while the elasticity value in the central part is lower; classification 3 (central high peripheral low type): the elasticity value in the central part is higher, while the elasticity value in the periphery is lower; classification 4 (mixed type): the elasticity value distribution in the tumor is disorganized, and the height is uneven; classification 5 (low elasticity type): the elasticity value in the whole tumor area is low, suggesting that the tissue is softer; classification 6 (high elasticity type): the elasticity value of the tumor as a whole is higher, indicating that the tissue hardness is large.

2.3.2 CDU check

(1) Patient preparation: In a supine position, patients' breasts were fully exposed and their arms were raised. (2) Instrument setting: Start the color Doppler ultrasonic diagnostic apparatus. High-frequency linear array probe, and 7.5~12 MHz frequency was used. Next, 50%~70% initial gain, 3~5 cm depth, and 500~1000 Hz pulse repetition frequency, 50~100 Hz wall filter, and 1~2 mm sampling volume were set. (3) Breast scanning: Two-dimensional ultrasound scanning was performed to observe the overall breast structure. It was then switched to color Doppler mode to observe blood flow in and around the tumor. (4) Blood flow parameter measurement: 3-5 vessels, blood flow velocity, resistance index, *etc.* were measured. (5) Angiogenesis assessment: Angiogenesis characteristics were assessed according to blood flow signals distribution and morphology.

2.4 Outcome measures

(1) SWE index: The maximum, mean and minimum elasticity, AveT1, AveR and Ratio1 indexes were compared between both groups.

(2) CDU index: FI, VI and VFI were compared between both groups.

(3) SWE classification: The number and proportion of each type were compared between both groups.

2.5 Statistics

Data were analyzed by t and χ^2 tests using SPSS 27.0 (IBM, Armonk, NY, USA). $p < 0.05$ indicated statistically significant differences. ROC (receiver operating characteristic) curves were plotted with SPSS to further compare diagnostic methods differences.

3. Results

3.1 SWE index comparison

The maximum, mean and minimum values of elasticity, AveT1, AveR and Ratio1 in the malignant group were significantly higher than those in the benign group ($p < 0.05$) (Table 1). The outcomes were shown in Table 1.

3.2 Comparison of CDU parameters

FI, VI and VFI indexes in the malignant group were notably higher than those in the benign group ($p < 0.05$) (Table 2).

3.3 SWE classification comparison

Compared to the benign group, the proportion of classification 1 was significantly lower in the malignant group. The proportion of classifications 4, 5 and 6 in the malignant group was significantly higher ($p < 0.05$) (Table 3).

3.4 Analysis results of ROC curve

According to the ROC curve, the largest area under the ROC curve of the combination of both was 0.935; for both, the

TABLE 1. SWE index comparison ($\bar{x} \pm s$).

Group	Case	Elastic Maximum (kPa)	Elastic Mean (kPa)	Elastic Minimum (kPa)	AveT1 (kPa)	AveR (kPa)	Ratio1
Benign group	54	44.81 ± 15.52	23.09 ± 9.31	11.19 ± 4.92	38.37 ± 16.44	8.97 ± 1.90	14.19 ± 5.53
Malignant group	68	57.81 ± 15.52	38.38 ± 16.06	16.16 ± 7.40	59.79 ± 31.46	11.66 ± 3.86	22.07 ± 8.63
t value	—	3.654	6.213	4.250	4.532	4.704	5.828
p value	—	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

TABLE 2. CDU parameters comparison ($\bar{x} \pm s$).

Group	Case	FI	VI	VFI
Benign group	54	28.13 ± 5.81	2.05 ± 1.20	0.53 ± 0.25
Malignant group	68	35.83 ± 9.18	3.20 ± 1.42	0.89 ± 0.39
t value	—	5.367	4.745	5.996
p value	—	<0.001	<0.001	<0.001

FI: Fibrosis Index; VI: Vascular Index; VFI: vascularization-flow index.

TABLE 3. Comparison of clinical efficacy between both groups (n, %).

Group	Case	Classification 1	Classification 2	Classification 3	Classification 4	Classification 5	Classification 6
Benign group	54	27, 50.00	22, 40.74	3, 5.56	1, 1.85	1, 1.85	0, 0.00
Malignant group	68	1, 1.47*	0, 0.00*	13, 19.12	13, 19.12*	21, 30.88*	20, 29.41*
χ^2 value	—	100.578					
p value	—	<0.001					

*Note: *Compared with the benign group, $p < 0.05$, the difference was significant.*

difference was significant when compared to a single diagnosis ($p < 0.05$) (Tables 4,5, Fig. 1).

4. Discussion

Breast tumor diagnosis was complicated by their diverse characteristics, such as benign and malignant divisions, growth rates and morphological changes. Conventional detection methods have low diagnostic efficacy. Moreover, breast tumors exhibit nonspecific early clinical symptoms that can be overlooked and misdiagnosed. Therefore, it is of great significance to identify benign and malignant breast tumors as soon as possible and accurately develop an effective treatment plan to improve patients' quality of life. Activated cell proliferation [7] and fibrous hyperplasia resulted in hard breast tumors. Meanwhile, blood must supply their growth and development, which will result in the formation of new blood vessels with complex structure [8]. Therefore, assessment of tissue stiffness changes and VFI can provide a reference for breast tumor diagnostic evaluations. SWE can determine tissue elasticity values [9, 10], which were higher in malignant breast tumors than in benign tissues. CDU can reflect VFI. Compared with benign tissue, malignant breast tumors had a higher number of blood vessels, an irregular shape, accelerated blood flow velocity and increased blood perfusion.

This study showed that the maximum elasticity, mean elasticity, minimum elasticity, AveT1, AveR, Ratio1, FI, VI and VFI indexes were significantly higher in the malignant group ($p < 0.05$). These results suggested that both SWE and CDU were both found to be useful for differentiating breast tumors. Reasons were as follows [11]: Active cell proliferation, increased stromal components and fibrous hyperplasia contribute to increased hardness in malignant breast tumors. SWE can quantitatively measure the elastic modulus value of the tissue [12] and provide a basis for judging the nature of the tumor. Malignant breast tumors form a rich and abnormal vascular network to grow rapidly, and observing the vascular supply can evaluate the tumor growth and metastasis and other related conditions. CDU can stereoscopically and comprehensively show the vascular distribution, shape, and number in and around the tumor and provide more basis for differential diagnosis.

This study demonstrated that the proportion of classification 1 was significantly lower in the malignant group. The proportion of classifications 4, 5 and 6 in the malignant group was significantly higher ($p < 0.05$). SWE appeared to reflect the complexity and heterogeneity of malignant tumors' internal

TABLE 4. ROC Curve analysis results.

Indicators	AUC	Standard error	*p* value	95% Confidence interval	
				Lower limit	Upper limit
SWE	0.865	0.033	<0.001	0.801	0.929
CDU	0.870	0.032	<0.001	0.807	0.933
Combined	0.935	0.023	<0.001	0.891	0.980

AUC: Area Under the Curve; SWE: shear wave elastography; CDU: Color Doppler ultrasound.

TABLE 5. Pairwise sample region differences under ROC curve.

Test results	Asymptotic		AUC difference	Standard error difference b	Asymptotic 95% confidence interval	
	z	*p* value			Lower limit	Upper limit
SWE-CDU	−0.115	0.908	−0.005	0.254	−0.088	0.078
SWE-Combined	−2.798	0.005	−0.070	0.234	−0.119	−0.021
CDU-Combined	−2.472	0.013	−0.065	0.233	−0.117	−0.014

AUC: Area Under the Curve; SWE: shear wave elastography; CDU: Color Doppler ultrasound.

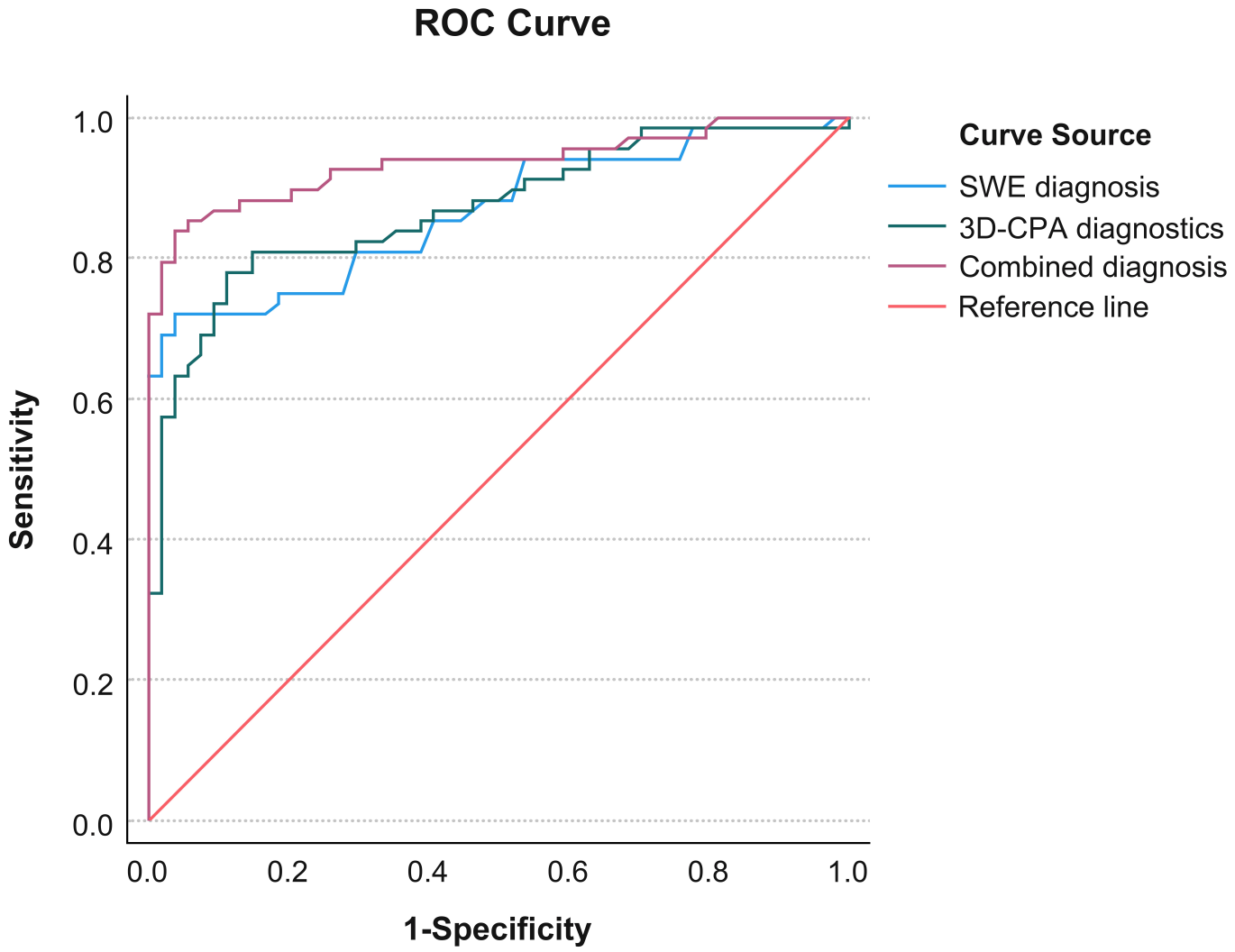

FIGURE 1. ROC Curve. ROC: receiver operating characteristic; 3D-CPA: Three-Dimensional Contrast-Enhanced Perfusion Analysis.

tissue structures [13]. This can be explained as follows. Cell growth in malignant breast tumors was rapid and disordered, cellular density increased, and interstitial components were diverse, resulting in differences in mechanical properties and uneven internal hardness distribution. SWE can detect differences in hardness [14], indirectly reflecting their internal complexity. Malignant breast tumor cells were disorganized, resulting in different elastic properties of their tissues from healthy cells. During the continuous growth of breast tumors, interstitial pressure inside the tumor will change [15]. SWE can detect this elastic change derived from alteration in interstitial pressure.

Based on ROC curves, the combined diagnosis of the two had the largest area under the curve, and the difference was significant ($p < 0.05$). Combining the two led to the best diagnostic result and the highest predictive value. Compared to a single diagnosis, a combined diagnosis provided more advantages. There were several main reasons for this. Combined detection can integrate information into multiple dimensions. SWE can reflect the hardness of tumor tissue, and CDU can reflect the vascularity and blood flow of tumor [16]. Combination of the two allowed a more comprehensive and multidimensional description of tumor characteristics based on physiological and pathological characteristics. SWE was sensitive to fibrosis and tissue compactness inside the tumor [17, 18]. CDU had unique advantages in estimating tumor's blood supply and angiogenesis characteristics. Combining the two can compensate for their limitations. As malignant tumors change tissue structure and angiogenesis, combined detection can accurately capture these changes and improve diagnosis accuracy. A single diagnostic method may appear false positive (benign diagnosis as malignant) or false negative (benign diagnosis as benign) due to individual differences, special performance of the tumor or technical limitations [19]. Combining the results of the two methods can reduce the likelihood of false positives and false negatives by further analyzing and judging the inconsistent conditions.

5. Conclusions

In summary, SWE quantitative measurement can effectively reflect the differences in hardness caused by malignant breast tumor cell proliferation, increased stromal components and fibrous tissue proliferation. CDU can display the distribution, morphology and quantity of blood vessels inside and around the tumor. Both have certain diagnostic values in distinguishing malignant breast tumors. Through the ROC curve, it was found that the area under the ROC curve of SWE combined with CDU diagnosis is the largest, indicating that the combined diagnosis of the two can more comprehensively describe tumors, complement each other's limitations, and accurately capture subtle changes in the development of malignant tumors, thereby reducing misdiagnosis rates.

There were limitations to this study. As a retrospective analysis, the study was prone to selection bias; with only 122 cases, the sample size could not cover all tumor conditions. This study's results were not representative since it was a single-center study. Besides, no consideration was given to other potential factors such as family genetic history and hormone levels. Moreover, there was no in-depth description of SWE and Three-Dimensional Contrast-Enhanced Perfusion Analysis (3D-CPA) technology limitations. This study lacked long-term follow-up of patients and evaluation of the impact of different diagnostic results on treatment and prognosis. Consequently, generalizability and accuracy of the study results, along with the overall clinical value judgment, may be affected.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

JC, YBC—designed the study and carried them out. JC, YBC, NC, JJQ, XLL, CYX—prepared the manuscript for publication, reviewed the draft of the manuscript and supervised the data collection. JC, YBC, NC, JJQ, XLL—analyzed the data. JC, YBC, NC, JJQ—interpreted the data. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Nanjing First Hospital, Nanjing Medical University (Approval no. KY20230615-02-KS-01). Written informed consent was obtained from legally authorized representatives for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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