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Original Article

Combination of color Doppler ultrasound and CT for diagnosing breast cancer

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Abstract: Objective: This research aimed to estimate the diagnostic value of the combination of color Doppler ultrasound (CDU) and computed tomography (CT) in breast cancer (BC). Methods: Among the 90 BC patients treated in our hospital from May 2018 to December 2020, 43 were examined by CDU before surgery and they served as the control group (CG), while the other 47 were examined with CDU and CT and were considered as the research group (RG). Lesions were confirmed as BC by postoperative pathological examination. The diagnosis rate for BC in the two groups was recorded, and the diagnostic value was analyzed by the receiver operating characteristic (ROC) curve. The imaging features were compared. The diagnostic accuracy for T, N and M stages was evaluated, as well as the diagnosis rate for axillary lymph node metastasis (ALNM) in BC. Results: The RG showed a higher diagnosis rate for BC ($P<0.05$) and sharper imaging features, with an area under the curve (AUC) of 0.843 ($P<0.05$). The diagnostic accuracy for T, N and M stages and the diagnosis rate for ALNM in the RG were higher than those in the CG ($P<0.05$ for each comparison). Conclusion: The combination of CDU and CT has a high diagnostic value in BC, which is worthy of clinical promotion.

Keywords: Color Doppler ultrasound, computed tomography, diagnosis, breast cancer, staging

Introduction

Breast cancer (BC) is a frequent malignancy in women, acting on the glandular epithelium of the breast [1]. It is rare in men, accounting for only approximately 1% [2]. In recent years, the rapid social and economic development in China has changed people's daily habits, leading to an increase in the incidence of BC; It has been reported that more than 10,000 women die of BC every year [3]. The prevalence of BC ranks first in Chinese women, and lymph node metastasis (LNM) occurs at an early stage, resulting in poor prognosis and threatening the health of female patients [4, 5]. The clinical treatment guidelines follow "early diagnosis and treatment" [6]. Therefore, early and accurate diagnosis is of great significance to reduce the mortality of BC patients.

Clinically, color Doppler ultrasound (CDU) [7], computed tomography (CT) [8], magnetic resonance imaging (MRI) [9], fiberoptic ductoscopy (FDS) [10], positron emission tomography (PET) [11] and high-frequency X-ray mammography [12] are the main options for BC diagnosis. Among them, CDU and CT are preferred. CDU has simple operation, higher resolution, less radiological damage and cost effectiveness [13]. CT also presents high spatial and density resolution, which clearly illustrates the changes in masses and surroundings [14]. However, both CDU and CT have limitations [15-17]. As the mechanism of the occurrence and development of BC is not yet understood, it is vital for diagnosing early patients, in order to improve the rate. We combined CDU with CT to improve the diagnostic accuracy for BC, and to estimate the value of this testing in BC diagnosis using surgical and pathological results as the diagnostic criteria.

Data and methods

Participant selection

A total of 90 patients with BC admitted to the Dongying Shengli Hospital of Shangdong Pro-

vince from May, 2018 to December, 2020 were included. Among them, 43 were randomly designated as the control group (CG), averagely aged 45.26±3.15 years, and 47 were regarded as the research group (RG), 45.81±3.03 years old on average. Inclusion criteria are as follows: patients suffering from breast lump, breast pain and nipple discharge; patients with complete clinical imaging data; patients with pathologically confirmed BC. Exclusion criteria are as follows: pregnant women; those with communication or mental disorders; those who have received adjuvant radiotherapy and chemotherapy. All patients signed an informed consent form, and ethics approval was granted by the Ethics Committee of our hospital.

Methods

Patients in the CG were examined by CDU before surgery. The specific steps were as follows: Firstly, the frequency of the probe (10-13 MHz) on the ultrasonic instrument (GE-E9) was set. Ultrasonic coupling agent was applied and the breast and axilla were fully exposed. All quadrants of the whole breast were scanned with two-dimensional ultrasound (vertical and horizontal and radial scanning). Afterwards, the location, shape and echogenicity of lesions were recorded according to the images. Next, CDU was performed.

Patients in the RG received CDU plus CT. The specific steps were as follows: Before surgery, patients' data were strictly inspected. They were positioned in a supine position with both hands raised. The area from clavicle to the lower edge of the breast was scanned following the principle of BCT scan first and then enhanced scan. Plain BCT parameters are as follows: tube current: 150-170 mA; tube voltage: 100-120 kV; layer interval: 3 mm; layer thickness: 5 mm. Ultravist (90 mL) was injected (monophasic bolus) into the cubital vein using a high-pressure injector at a rate of 3.5 mL/s. The enhanced scan was executed after a 10-s delay of the injection of contrast agent.

Outcome measures

The diagnosis rate for BC in the two groups was recorded, and the diagnostic value was analyzed by the receiver operating characteristic (ROC) curve.

Imaging features of CDU and CT were compared. CDU criteria are as follows: (1) diagnostic features of BC: hypoechoic masses with calcified foci, abundant blood flow, irregular shape and ill-defined borders; (2) grading of blood flow: Grade 0, no flow signals; Grade I, short-linear flow signals; Grade II, dendritic flow signals with regular direction; Grade III, dendritic and reticular flow signals with irregular direction.

CT criteria are as follows: Lumps, calcified foci and burrs were observed by plain CT. The display of masses was more prominent in enhanced scan due to the strong iodine uptake and high iodine concentration of cancerous tissues.

The diagnostic accuracy for T, N and M stages was evaluated, as well as the diagnosis rate for axillary lymph node metastasis (ALNM) in BC.

Statistical analysis

SPSS 20.0 was used for statistical analysis, and GraphPad Prism 6 was used for graphing. The continuous data were expressed as Mean ± SD, and inter-group comparisons were performed with independent samples t-test, followed by a post-hoc LSD-t test for pairwise comparison. The categorical data were expressed as n, and inter-group comparisons were done with the χ^2 test. The diagnostic value of preoperative CDU and CT in BC was evaluated by receiver operating characteristic (ROC) curve. Statistical significance was assumed as $P<0.05$.

Results

The general data

Comparing the baseline data of patients in both groups, there was no statistically significant difference ($P>0.05$), which showed comparability (**Table 1**).

Diagnosis rate for BC in both groups

There were 32 patients in the CG and 43 in the RG pathologically diagnosed with BC, so the rate in the RG was higher than that in the CG (91.5% *vs.* 74.4%) ($P<0.05$) (**Table 2**).

Table 1. Comparing the baseline data of patients in both groups

	Age (years)	Site of disease (left breast/right breast)
Control group (n=43)	45.26±3.15	25/18
Research group (n=47)	45.81±3.03	27/20
χ^2/t	0.8440	0.0044
P	0.4009	0.9470

Table 2. Diagnosis rate for BC in both groups

	Patients meeting criteria for pathological diagnosis (n)	Diagnosis rate
Control group (n=43)	32	74.4%
Research group (n=47)	43	91.5%
χ^2/t		4.7121
P		0.0300

ROC curves for assessing diagnostic value of CDU and CT

The sensitivity of CDU combined with CT in diagnosing BC was higher than that of CDU alone (P<0.05) (**Figure 1** and **Table 3**).

Imaging features

The CDU images in the CG showed that most lesions were irregular shaped with ill-defined margins. The imaging features of CDU + CT in the RG: most of the lesions were round-like with burrs visible on margins, and a few showed irregularities. CT results documented that the distribution of radioactivity in soft tissue masses was concentrated in the upper quadrant (**Figure 2**).

Diagnosis rate for T, N, and M stages

In the CG, 25 patients were diagnosed at T stage, 11 at N stage and 7 at M stage. The diagnostic accuracy of CDU + CT for T, N and M stages (28, 14, 5) was higher than that of CDU alone (P<0.05) (**Table 4**).

Diagnosis rate for ALNM

ALNM was pathologically confirmed in 15 patients in the RG and 17 in the CG. The diagnosis rate for ALNM by CDU plus CT was higher than that by CDU alone (P<0.05) (**Table 5**).

Discussion

The quality and duration of survival of early BC patients are better than those in the late stage. Early BC is manifested by a solitary and painless mass whose boundary with surrounding tissues is blurred, usually leading to unnoticeable symptoms, thereby making patients fail to receive timely and effective treatment [18, 19]. Patients may develop breast tenderness and nipple discharge as BC progresses, which may threaten their lives if not diagnosed and treated at this time [20]. Therefore, early diagnosis is pivotal for patients with BC. Although it is the most effective clinical test for BC, pathological examination often requires tissue sampling. Because of the high plantability of tumor cells, the sampling generally removes the entire suspected tissue before testing, such that it cannot be widely used for general population screening [21]. In addition, there are non-invasive and easy ways for early and effective diagnosis such as ultrasound and CT; however, diagnostic accuracy must be improved and the rate of misdiagnosis must be reduced in order to achieve early treatment.

In the present study, the diagnostic value of the combination of CDU and CT was analyzed in BC patients. It turned out that the CDU + CT group showed a higher diagnosis rate for BC (P<0.05) and sharper imaging features (P< 0.05), with an AUC of 0.843 (P<0.05). Breast masses were irregularly shaped with ill-defined borders, heterogeneous echogenicity and absence of envelope coverage. If hemorrhagic necrosis had appeared inside the tumor, CDU is still feasible to find the changes in blood flow signals and determine the position, direction and number of blood vessels [22]. Nevertheless, the specificity of CDU in mass examination remains relatively low, along with the high requirements for doctors, deviation or even misdiagnosis are likely to occur [23]. CT collects images from many different levels, and allows thin-layer scanning upon the discovery of lesions to increase the resolution, which facilitates the accurate assessment of morphological features, enhancement patterns and hemodynamics of lesions, and helps to determine the relationship between lesions and their nearby tissues, blood vessels and lymph nodes [24]. Previous studies have shown that the boundaries of some masses in BC patients are clear in color Doppler ultrasound images,

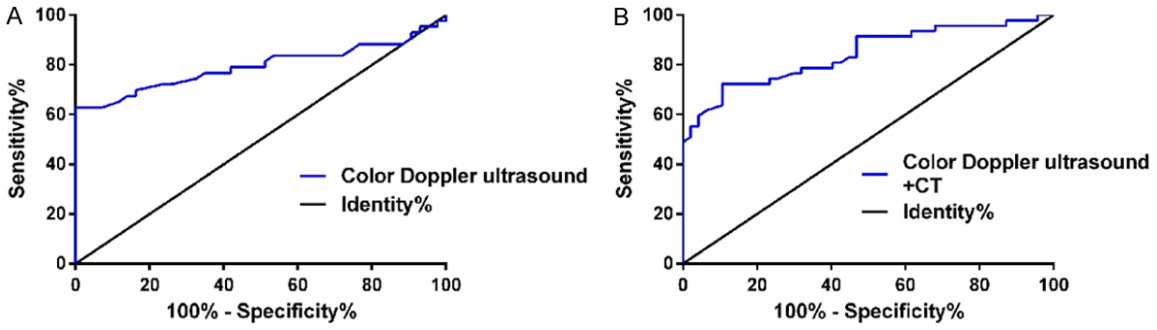

Figure 1. ROC curve. A: ROC curve for assessing diagnostic value of CDU; B: ROC curve for assessing diagnostic value of CDU combined with CT.

Table 3. Diagnostic value of CDU and CT

	AUC	S.E	95% CI	Sensitivity (%)	Specificity (%)
CDU	0.7939	0.053	0.6904-0.8974	60.93	77.42
CDU + CT	0.8431	0.041	0.7626-0.9237	75.76	83.62

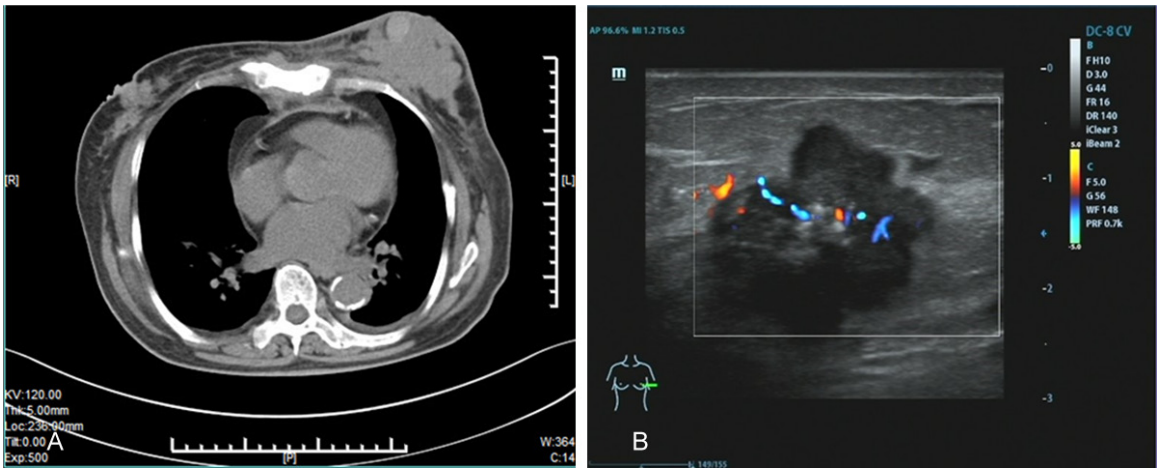

Figure 2. CT scan and Color Doppler ultrasound results. A: CT scan; B: Color Doppler ultrasound.

Table 4. Diagnostic rate for TNM stages

		Pathologically confirmed patients (n)	Diagnosis rate	χ^2/t	P
T stage	Control group (n=25)	19	76.0%	4.8081	0.0283
	Research group (n=28)	27	96.4%		
N stage	Control group (n=11)	6	54.5%	4.9571	0.0260
	Research group (n=14)	13	92.8%		
M stage	Control group (n=7)	3	42.8%	4.2861	0.0384
	Research group (n=5)	5	100%		

but the specificity of smaller ones is weaker, resulting in a higher rate of misdiagnosis and missed diagnosis [25]. Therefore, CDU combined with CT greatly increases the diagnostic accuracy. It supports our findings that the diagnostic accuracy for both T, N and M stages and ALNM in CDU + CT group was higher than that in CDU group ($P<0.05$). High-grade lesions are characterized by high invasiveness, enrichment of tumor vessels and lymph node involvement [26]. The morphology, structure and blood flow of lymph nodes are the main indicators of ultrasound identification

Table 5. Diagnostic rate for ALNM

	Pathologically diagnosed patients (n)	Confirmed	Misdiagnosed	Diagnosis rate
Control group	17	9	2	52.9%
Research group	15	13	0	86.7%
χ^2/t				4.2191
P				0.0400

of lymph node metastasis, but these are greatly influenced by the location of lymph nodes: those with deeper location are poorly imaged and have lower diagnostic stability. CT post-processing reconstructions can analyze the shape, diameter and margin of lesions from various angles. Thus, the combination of CDU and CT achieves a higher diagnosis rate for ALNM in BC. There are still some limitations: For one thing, the sample size is not large. For another, in addition to color Doppler ultrasound and CT, there are other ways that can be combined in diagnosis. Further study will expand the sample size and diagnostic methods in order to obtain a higher rate.

To sum up, CDU combined with CT is highly accurate in the early diagnosis of BC, and provides practical and reliable basis for follow-up treatment, thus improves the overall diagnosis.

Disclosure of conflict of interest

None.

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References

[1] Waks AG and Winer EP. Breast cancer treatment: a review. JAMA 2019; 321: 288-300.

[2] Gucalp A, Traina TA, Eisner JR, Parker JS, Selitsky SR, Park BH, Elias AD, Baskin-Bey ES and Cardoso F. Male breast cancer: a disease distinct from female breast cancer. Breast Cancer Res Treat 2019; 173: 37-48.

[3] DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Goding Sauer A, Jemal A and Siegel RL. Breast cancer statistics, 2019. CA Cancer J Clin 2019; 69: 438-451.

[4] Li YL, Qin YC, Tang LY, Liao YH, Zhang W, Xie XM, Liu Q, Lin Y and Ren ZF. Patient and care delays of breast cancer in China. Cancer Res Treat 2019; 51: 1098-1106.

[5] Sitt JC, Lui CY, Sinn LH and Fong JC. Understanding breast cancer screening--past, present, and future. Hong Kong Med J 2018; 24: 166-174.

[6] Filetti S, Durante C, Hartl D, Leboulleux S, Locati LD, Newbold K, Papotti MG and Berruti A; ESMO Guidelines Committee. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-updagger. Ann Oncol 2019; 30: 1194-1220.

[7] Moustafa AF, Cary TW, Sultan LR, Schultz SM, Conant EF, Venkatesh SS and Sehgal CM. Color doppler ultrasound improves machine learning diagnosis of breast cancer. Diagnostics (Basel) 2020; 10: 631.

[8] Simanek M and Koranda P. SPECT/CT imaging in breast cancer - current status and challenges. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2016; 160: 474-483.

[9] Partovi S, Sin D, Lu Z, Sieck L, Marshall H, Pham R and Plecha D. Fast MRI breast cancer screening - Ready for prime time. Clin Imaging 2020; 60: 160-168.

[10] Zhang C, Li J, Jiang H and Li M. Use of fiberoductoscopy for the management of pathological nipple discharge: ten years follow up of a single center in China. Gland Surg 2020; 9: 2035-2043.

[11] Boers J, de Vries EFJ, Glaudemans A, Hospers GAP and Schroder CP. Application of PET tracers in molecular imaging for breast cancer. Curr Oncol Rep 2020; 22: 85.

[12] Buonanno F, Sarno A, De Lucia PA, Di Lillo F, Masi M, Di Franco F, Mettivier G and Russo P. Rotational radiotherapy of breast cancer with polyenergetic kilovoltage X-ray beams: an experimental and Monte Carlo phantom study. Phys Med 2019; 62: 63-72.

[13] Yeo SH, Kim GR, Lee SH and Moon WK. Comparison of ultrasound elastography and color doppler ultrasonography for distinguishing small triple-negative breast cancer from fibroadenoma. J Ultrasound Med 2018; 37: 2135-2146.

[14] Paydary K, Seraj SM, Zadeh MZ, Emamzadehfard S, Shamchi SP, Gholami S, Werner TJ and Alavi A. The evolving role of FDG-PET/CT in the diagnosis, staging, and treatment of breast cancer. Mol Imaging Biol 2019; 21: 1-10.

[15] Naredo E and Monteagudo I. Doppler techniques. Clin Exp Rheumatol 2014; 32: S12-19.
[16] Gannon AW, Langer JE, Bellah R, Ratcliffe S, Pizza J, Mostoufi-Moab S, Cappola AR and Bauer AJ. Diagnostic accuracy of ultrasound with color flow doppler in children with thyroid nodules. J Clin Endocrinol Metab 2018; 103: 1958-1965.
[17] Arnold MJ, Jonas CE and Carter RE. Point-of-care ultrasonography. Am Fam Physician 2020; 101: 275-285.
[18] Milosevic M, Jankovic D, Milenkovic A and Stojanov D. Early diagnosis and detection of breast cancer. Technol Health Care 2018; 26: 729-759.
[19] Black E and Richmond R. Improving early detection of breast cancer in sub-Saharan Africa: why mammography may not be the way forward. Global Health 2019; 15: 3.
[20] Coughlin SS. Social determinants of breast cancer risk, stage, and survival. Breast Cancer Res Treat 2019; 177: 537-548.
[21] Masuda S. Pathological examination of breast cancer biomarkers: current status in Japan. Breast Cancer 2016; 23: 546-551.
[22] Shen ZY, Hu B and Wu MF. Correlation between blood flow signal of color flow imaging and nottingham prognostic index in patients with breast carcinoma. Breast Care (Basel) 2012; 7: 126-130.
[23] Jayachandran S and Sachdeva SK. Diagnostic accuracy of color doppler ultrasonography in evaluation of cervical lymph nodes in oral cancer patients. Indian J Dent Res 2012; 23: 557-558.
[24] Gentileschi S, Albanese R, Pino V, Stefanizzi G, Fragomeni S, Zagaria L, Ieria FP, Salgarello M, Scambia G and Garganese G. SPECT/CT and fusion ultrasound to target the efferent groin lymph node for lymphatic surgery. Microsurgery 2019; 39: 605-612.
[25] Della Pepa GM, Sabatino G, Sturiale CL, Marchese E, Puca A, Olivi A and Albanese A. Integration of real-time intraoperative contrast-enhanced ultrasound and color doppler ultrasound in the surgical treatment of spinal cord dural arteriovenous fistulas. World Neurosurg 2018; 112: 138-142.
[26] Zhou J, Zhang B, Dong Y, Yu L, Gao T and Wang Z. Value on the diagnosis of axillary lymph node metastasis in breast cancer by color Doppler ultrasound combined with computed tomography. J BUON 2020; 25: 1784-1791.