

Original Article

Ultrasonographic findings of triple-negative breast cancer

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Abstract: *Objective:* Our aim was to determine whether triple-negative breast cancer (TNBC) has distinguishing sonographic features compared to non-TNBC. *Methods:* Data from 145 consecutive breast cancer patients were collected. The images were reevaluated by two dedicated breast imaging experts according to the Breast Imaging Reporting and Data System. The sonographic features of 45 TNBC patients were compared with those of 100 non-TNBC patients. *Results:* TNBC showed a high histological tumor grade. On ultrasound, TNBC was more frequently to present as oval or round mass shape (48.9%, 17.8%; respectively), more likely to have circumscribed margins (82.2%), and less likely to show posterior attenuating (8.9%). Additionally, compared with non-TNBC, TNBC was less likely to have calcification (35.6%). *Conclusion:* TNBC has distinguishing imaging features on breast ultrasound, and more likely to be associated with benign masses. Knowledge of the distinct sonographic features would be useful in diagnosing TNBC.

Keywords: Triple-negative breast cancer, sonographic features, ultrasound

Introduction

Breast cancer is a heterogeneous disease including a variety of entities, which are morphologically and clinically distinct. Triple-negative breast cancer (TNBC) is a distinctive subtype of breast cancer that do not express estrogen receptor (ER), progesterone receptor (PR) or overexpress human epidermal growth factor receptor-2 (HER-2) [1]. TNBC constitutes about 10-20% of breast cancer patients with poor overall prognosis [1, 2]. Patients with TNBC have an increased likelihood of early recurrence and distant metastasis to brain and lungs compared to other breast cancer subtypes [1, 3, 4]. Chemotherapy is the only systemic therapy currently available for TNBC. Recently, TNBC has become a focus of breast cancer research because of its unique clinical and pathologic characteristics [5]. And early detection of this particularly aggressive subtype of breast cancer is vital.

Breast ultrasonography, alone or as an adjunct to mammography, is an indispensable tool for

diagnosis of breast masses with high sensitivity and specificity [6, 7]. The ability to predict the presence of this subtype based on ultrasound would lead to accelerate diagnosis and treatment and improve outcomes, however, there are few comprehensive imaging reports. In this paper, we aimed to identify and describe the imaging characteristics of TNBC using information obtained from ultrasound, and compare these features to those of non-TNBC diagnosed over the same period.

Materials and methods

Patients

Data from 45 consecutive TNBC were collected from our hospital between May 2013 and July 2014. All patients were women between the ages of 31 and 71 years (mean age 49 years). As control patient groups, 100 consecutive patients (age range 29-85 years, mean 54 years) with non-TNBC identified in the same period were recruited for the study. All cases were confirmed by postoperative pathology.

Ultrasonography in triple-negative breast cancer

Table 1. Characteristics data for the triple-negative and non-triple-negative breast cancer patients

	TNBC (n=45)	non-TNBC (n=100)	P
Characteristics			
Age, y	49 (31-71)	54 (29-85)	>0.05
Tumor size, mm	21±4.9	20±5.0	>0.05
Grade, %			
1	3.2	15.0	
2	16.8	63.1	
3	80.0	21.9	<0.05
Tumor type, %			
Invasive ductal carcinoma	82.6	78.6	
Non-Invasive ductal carcinoma	17.4	21.4	>0.05

Table 2. Ultrasound features for the triple-negative and non-triple-negative breast cancer patients

Ultrasound features	TNBC (n=45)	non-TNBC (n=100)	P
Mass shape, %			
Oval	48.9	18.0	
Round	17.8	55.7	
Irregular	33.3	77.0	<0.05
Margin, %			
Circumscribed	82.2	52.0	
Not-circumscribed	17.8	43.0	<0.05
Orientation, n			
Parallel	4	11	
Not-parallel	41	89	>0.05
Lesion boundary, n			
Abrupt interface	25	46	
Echogenichalo	20	54	>0.05
Posterior features, %			
Enhancement	20.0	8.0	<0.05
No change	71.1	72.0	>0.05
Attenuating	8.9	20.0	<0.05
Calcification, %			
Yes	35.6	69.0	
No	64.4	31.0	<0.05
Vascularity, n			
Avascular	11	20	
Spotty	6	23	
Hypovascular	10	23	
Hypervascular	18	34	>0.05

Routine examinations of patients by ultrasound were conducted before operation and any other therapy.

Ultrasound

Breast ultrasound was performed by two dedicated breast imaging experts (with at least 5 years of experience in breast sonography) using high-resolution US equipment with a 14-16 MHz linear array transducer (LOGIQ 700, GE Medical Systems, Milwaukee, WI, USA). The imaging included shape (oval, round, irregular), margin (circumscribed or not-circumscribed), orientation (parallel, not-parallel), lesion boundary (abrupt interface or echogenic halo), echo pattern (hypoechoic, complex, hyperechoic), posterior features (enhancement, no change, attenuating), calcifications (yes or no), and vascularity (avascular, spotty, hypovascular, hypervascular), based on the American College of Radiology Breast Imaging-Reporting and Data System (BI-RADS) lexicon [8].

Histopathological analysis

We used the surgical findings from excisional biopsies, breast-conserving surgery or mastectomy specimens as the reference standard. ER, PR, and HER-2 were determined by immunohistochemistry. The cutoff point for ER- and PR-positive expression was 10%. HER-2 status was graded as 0, 1+, 2+ and 3+. And 3+ was deemed to be positive, and 2+ was checked by fluorescence in situ hybridization for its positivity.

Statistical analysis

We used chi-square test or Fisher's exact test for qualitative data and the Mann-Whitney *U* test or the Student *t* test for quantitative data. Statistical analysis was carried out by using SPSS (version 13.0; Chicago, IL, USA), with $P < 0.05$ to indicate a significant difference.

Results

As shown in **Table 1**, there was no significant difference between these two groups in terms of age, tumour size or tumor type. However, patients with TNBC were more likely to have histologically intermediate or high-grade tumors, compared with patients with non-TNBC breast cancers ($P < 0.05$).

On ultrasound, there was no significant difference in the orientation, lesion boundary or vascularity ($P>0.05$) (Table 2). However, TNBC was more frequently had a oval or round mass shape (66.7% vs 23.0% for non-TNBC) and non-TNBC was more frequently had an irregular mass shape (77.0% vs 33.3% for TNBC). TNBC had circumscribed margins more often than non-TNBC (82.2% vs 52.0%, $P<0.05$). Posterior acoustic enhancement was more frequent in TNBC (20.0% vs 8.0%, $P<0.05$) and posterior acoustic attenuating was less often observed (8.9% vs 20.0%, $P<0.05$). And there were less calcification in TNBC (35.6%) than in non-TNBC (69.0%) ($P<0.05$).

Discussion

Although constituting only a relatively small proportion of breast cancers, TNBC represents an aggressive subtype with poor overall prognosis [9]. Similar to previous studies [10-13], in our study, there were more intermediate or high grade tumours in TNBC than in non-TNBC. Early detection of these tumors is important, and breast ultrasonography is considered to be an indispensable tool in breast imaging and a first-line examination for both detection and characterization of breast masses [14, 15].

In our study, we determined the radiological characteristics observed by way of ultrasound findings of TNBC. We noted that TNBC were more likely to be seen as mass lesions with oval or round shapes, and more likely to show circumscribed margins, which is in agreement with previous reports [12, 13, 16]. Reflecting an aggressive, rapidly proliferating tumor with pushing margins without any stromal reaction.

Furthermore, we found TNBC is less frequently associated with calcifications, which were regarded as the specific pictures of ductal carcinoma in situ (DCIS). This might have been because TNBC were less often accompanied by DCIS [16]. Suggesting that TNBC may lead directly to an invasive stage with no major in situ components or to a precancerous stage. In addition, we found that TNBC was less likely to show posterior attenuating, which is similar to other subtypes of high grade tumours and familial breast cancers [17]. This finding can be explained by the typical growth pattern of TNBC, indicating an internal fluid element, such as in tumor necrosis, which is a feature regu-

larly reported on pathological appraisal in TNBC [18]. In contrary to non-TNBC, TNBC was more likely to manifest with benign morphological features. Suggesting some of the mass lesions might be misinterpreted as benign on ultrasound, tissue sampling cannot be replaced. However, we did not identify the ultrasound elastography in our study, which may be a proper measure to distinguish TNBC [19]. Additionally, breast magnetic resonance imaging (MRI) could be used in patients suspected of TNBC with benign findings in ultrasound, although MRI is not a part of regular clinical examination [20, 21]. Further studies would be required.

In conclusion, our results suggest that TNBC has distinguishing sonographic features compared to non-TNBC. TNBC may mimic lesions with benign morphologies. Being familiar with this behavior would enable the examiner to improve the diagnostic accuracy in the evaluation of breast lesions and finally lead to more proper pretreatment planning.

Disclosure of conflict of interest

None.

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Ultrasonography in triple-negative breast cancer

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