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The Role of Elastography in Predicting the Grade of Mammary Ductal Carcinoma

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Abstract

Background Elastography is an imaging technique which has been used in the last decades and its role in breast masses characterization is well established. However, its value for predicting breast cancer grading is yet to be studied.

Objective To determine the role of strain elastography in the prediction of the grade of mammary ductal carcinoma.

Methods A cross sectional study enrolled 44 female patients with Breast Imaging Reporting and Data System (BI-RADS) Category 5 breast mass. Complete B-mode and elastographic ultrasound examination of the breast was performed with evaluation of the elastoscore and strain ratio. Correlation with the detailed histopathological report was done for cases that were proved to be ductal type breast carcinoma.

Results Significant correlation was found between the speculated outline of the tumor and grade III tumor (p=0.03). Breast tumors with higher Elastography/B mode size ratio (>1) and with high elasticity score (score 5) were significantly associated with grade III (p=0.02). The mean strain ratio of masses was significantly higher among grade III breast tumors (p<0.001).

Conclusion Elastography is a helpful non-invasive tool that has the potential for predicting breast ductal carcinoma grade and by such predicting the prognosis.

Keywords Breast ductal carcinoma, strain elastography, ductal carcinoma grades

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List of abbreviations: BI-RADS = Breast imaging reporting and data system, ER = Estrogen receptor, ROI = Region of interest, SR = strain ration, SWE = Shear wave elastography

Introduction

Breast cancer is the most commonly diagnosed cancer and is the leading cause of cancer death among women, it represents 23% of the all cases of cancer and about 14% of the cancer related deaths, particularly in low- and middle-income countries, as a results of a combination of a late stage of presentation, diagnosis and limited access to proper treatment [(1,2)].

Owing to the lack of proper recording system in the Iraqi hospitals, there is no accurate reporting regarding tumor size, nodal state, hormonal receptor status, stage distribution at the time of initial diagnosis, proportion of patients with distant metastasis and of those treated with radical mastectomy or breast conservation surgery [(3,4)]. However, some previous recent studies had reported that invasive ductal carcinoma represents 88% of

breast cancer cases in Iraq with the tendency to occur at early age with moderately progressive grade and stage at time of presentation [5].

Elasticity is "the characteristic of a tissue or substance that makes it to be deformed when it is exposed to an external power and return to its original figure or size when the force is removed"[6]. The technique, which is now most widely used in clinical settings is real-time elastography, produce “strain imaging” by compression. Electrography can be performed using conventional ultrasound (US) device with dedicated software, by this examination we evaluate the relative elasticity of the tissues in a specific region of interest making an elastogram that is superimposed to the US image [7,8].

This study aimed to determine if quantitative and qualitative strain elastography have a role in the prediction of the grade of mammary ductal carcinoma.

Methods

Study design

The present study is a cross-sectional study conducted in Breast Clinic at Al-Imamein Al-Kadhimein Medical City for the period from October 2016 to August 2017.

Study population

The study enrolled 44 female patients who were discovered to have Breast Imaging Reporting and Data System (BI-RADS) Category 5 breast mass for whom complete B-mode and elastographic ultrasound examination of the breast was performed, and a detailed histopathological report was obtained after excisional biopsy or mastectomy that proved the presence of ductal type breast carcinoma.

Exclusion criteria

1. Previous surgical intervention and/or palliative therapy.
2. Histopathology finding of non-ductal carcinoma.
3. Women with previous breast or chest wall irradiation.
4. Women with breast masses with other BI-RADS Categories.

Methods

Data collection

After full history and clinical examination, the eligible women were referred to B-mode US and elastography. The data were collected and filling a prepared questionnaire designed by the supervisor.

US examination

Machine: GE Voluson E6 ultrasound equipped with elastography software using high frequency linear array transducer (11L-D).

Procedure: B-mode US and elastography were performed at the same session. The patient lied in supine position with arm raised and palm placed beneath the head. The breast under assessment was exposed. Initially B-mode US was conducted, the mass was first localized and its maximum dimension measured, it was assessed for the presence of the following suspicious US features (microlobulation, spiculation, posterior acoustic shadowing, echogenic halo. After which, the elastographic examination was performed and the patient was instructed to maintain shallow respiration to prevent the counter strain caused by significant motion of the anterior chest wall. The field of view (FOV) box was set to include all the borders of the breast mass under examination as well as a portion of adjacent subcutaneous fat and some surrounding normal breast tissue. This procedure is the standard procedure applied in this setting according to BI-RADS [9].

The elastographic examination was performed by very gentle initial pressure with the transducer perpendicular to the skin surface. After obtaining adequate images according to green task bar, the largest lesion size was estimated, the elasticity score of the mass was estimated and the strain ration (SR) was obtained. For the size and SR, three measurements were taken and the average value reported. The SR was measured through

placing two small region of interest (ROI) circles of approximately comparable sizes: The first circle (Ref) placed within the fatty tissue at the same depth as the tumor if possible or placed within the adjacent subcutaneous fat if no fatty tissue was present at the same depth of the mass in the elastography FOV and the second circle (ROI) was put over the stiffest portion of the lesion as determined by color encoding. The SR from those two ROI circles was calculated automatically and displayed at the left lower corner of the monitor.

Follow up

After performing the B-mode US and elastography, the patients were followed up to receive their histopathology reports to correlate the sonographic and elastographic findings with the tumor grade the presence of the in-situ component and the lymphovascular invasion (LVI).

Ethical considerations

1. Approval was obtained from the Institutional Review Board, College of Medicine, Al- Nahrain University provided to the Journal Committee.
2. Verbal consent was taken from the patients to participate in the study.

Statistical analysis

The data of patients were analyzed by application of Microsoft excel program and Statistical Package for Social Sciences (SPSS) version 23. Outcomes of analysis were arranged in scales variables (means and standard deviation) and in categorical variables. Fishers' exact test was used for comparison between categorical data. One way ANOVA analysis was used to compare between more than two means. The level of significance (p value) was set as ≤ 0.05.

Results

This study included 44 women with ductal breast carcinoma. Histopathology revealed that 6.8% (N=3) of women had grade I, 81.8% (N=36) of women had grade II and 11.4% (N=5) of women had grade III breast carcinoma. Mean age of studied women was 49.6±13.4 years, 6.8% (N=3) of them were <30 years age, and 20.5% (N=9) of them were above 60 years as shown in table 1.

Table 1. Age groups and breast cancer grades in the study population

Variable		No.	%
Age groups	<30 years	3	6.8
	30-59 years	32	72.5
	≥60 years	9	20.5
Grades of tumor	Grade I	3	6.8
	Grade II	36	81.8
	Grade III	5	11.4
Total		44	100.0

The breast tumor size of women with ductal breast carcinoma as measured by B-mode US was 25.3±8.9 mm; ranged between 8-52 mm. All the tumors exhibited a hypoechoic texture. The other most common gray scale US findings were irregular outlines 90.9% (N=40) followed by speculated margins (84.1%, N=37), post shadowing (70.5%, N=31), microlobulated (50%, N=22) and echogenic halo (34.1%, N=15). 2.3% (N=1) of women had size ratio of less than 1, 25% (N=11) had size ratio 1 and 72.7% (N=32) of them had size ratio of more than 1. The mean elasticity SR of women with breast carcinoma was 5.5±2.2; ranged between 3.5-

16.5. The elasticity SR mean±SD (5.5±2.2) and range (3.5-16.5), elasticity score of women with ductal breast carcinoma was score 3 among 2.3% (N=1) of women, score 4 among 25% (N=11) of them and score 5 among 72.7% (N=32) of women (Tables 2 and 3).

Table 2. Elastography characteristics of breast tumor

Elasticity characteristics	No.	%
<1	1	2.3
1	11	25.0
>1	32	72.7
Total	44	100.0

Table 3. Elastography score of breast tumor

Elasticity score	No.	%
3	1	2.3
4	11	25.0
5	32	72.7
Total	44	100.0

A significant association was observed between increased elasticity score and breast tumor grade III (p=0.02). No significant relationships were observed between each of LVI variable. Significantly higher mean of elastography SR was found among women with breast tumor grade III (p<0.001) (Table 4).

Table 4. Elastography strain ratio according to grading of breast tumor

Variable	Grade I Mean±SD	Grade II Mean±SD	Grade III Mean±SD	P value*
Strain ratio	3.8±0.2	5.0±0.8	10.2±4.1	<0.001

*One way ANOVA test

Discussion

During the last decade, the role of strain elastography in differentiating benign form malignant breast masses has been studied extensively, however; little has been said about its potential value in prediction of breast tumor grade [9]. In this study, the correlation of various strain elastographic parameters as well as some B-mode features with the grade of breast ductal carcinoma has been assessed.

The most frequently recorded B-mode US findings in breast ductal carcinomas in this study were spiculation, posterior acoustic shadowing, microlobulation and echogenic halo. These findings are in agreement with the results of a previous study conducted in Iraq, which stated that the main US findings of ductal breast carcinoma among a sample of women in Hilla city were irregularity, posterior acoustic shadowing and spiculated margins [10]. The spiculated margins detected by B-mode US

in the current study was significantly correlated with grade III breast carcinoma. A study done by Wojcinski et al. [11] in Germany reported that US criteria of breast tumors are dependent on biological and clinical profile of women (like presence of other risk factors, comorbidities, family history, etc.. and this might be helpful in grading breast cancer, however, they showed that grade III tumors were more likely to exhibit microlobulation and posterior acoustic enhancement. Likewise, a previous Canadian study [12] documented that grade III invasive ductal carcinomas of breast are more likely to show microlobulation and posterior acoustic enhancement, nevertheless, the findings in the current study might be attributed to the small number of grade III carcinomas (n=5).

Regarding elastography findings; a significant correlation of elasticity score and size ratio of ductal carcinoma with tumor grade (p=0.02) has been observed in this study. This finding is in agreement with results of Grajo et al. [4] study in USA, which studied the relation between tumor histological grade and E/B size ratio as an elastographic marker of tumor stiffness and found significant correlation between the two.

Current study found that the mean SR was significantly associated with the grade of ductal breast carcinoma (p<0.001). A study by Kim et al. [13] reviewed the records of 284 women found that the mean SR was significantly higher among women with positive LN status, unlike the current results, they did not report significant correlation between SR and histological grading of breast carcinoma. The larger sample size and the larger tumor size range (2-90 mm) in Kim et al. study could also have influenced the difference between the two results.

Several studies in the recent literature have evaluated the role of shear wave elastography in predicting breast tumor prognostic factors including histological grading. A study done by Evans et al. [14] in UK showed significant correlation between the mean stiffness and the histological grade of breast carcinoma.

Although the latter two studies used shear wave elastography (SWE) rather than strain elastography, the results showed that the diagnostic performance of strain elastography is not significantly different from that of SWE.

In regard to histopathological findings; the results of histopathology in this study showed that most (81.8%) of ductal breast carcinomas were grade II. This proportion of grade II ductal carcinoma is slightly higher than the results of a previous study in northern Iraq [15] in which, grade II carcinomas represented 55.5%. This difference might be attributed to the fact that in the aforementioned study all histological types of breast carcinomas were included unlike in this study which enrolled only ductal type of breast carcinoma.

Regarding LVI, several previous studies showed that it is correlated with the prognosis. A study in China by Wang et al [16] revealed that LVI among women with ER positive ductal breast carcinoma is an independent predictor for poor prognosis, and stiffness of elastography is great predictor for LVI in invasive ductal breast carcinoma. Another study in South Korea [17] revealed that lymphangiogenesis among women with ductal breast carcinoma is significantly correlated to breast tumor stiffness and histological grade.

The findings of the present study have many clinical impacts as it showed that elastography can be used not only for diagnosing breast carcinomas but also in predicting its grading and by such predicting the prognosis and biological behavior. Furthermore, implementing both elastography and B-mode US routinely for breast tumor radiological evaluation will be helpful in guiding the clinical work-up and will provide additional support in diagnosing and predicting grading of breast carcinomas preoperatively.

In conclusions, all three elastographic parameters implicated in the study have strong association with the grade of the tumor. Elastography is a helpful non-invasive tool that has the potential for predicting breast ductal carcinoma grade and by such predicting the prognosis.

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Author contribution

Dr. Said: study design and data collection. Dr. Sheet: writing and editing. Dr. Nuaman: data analysis.

Conflict of interest

None.

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