Araştırma Makalesi
Research Article

Relationship Of Shear-wave Elastography Findings With Breast Cancer Molecular Subtypes And Comparison With Other Radiological Imaging Techniques

SHEAR-WAVE ELASTOGRAFİ BULGULARININ MEME KANSERİ MOLEKÜLER ALT TİPLERİ İLE İLİŞKİSİ VE DİĞER RADYOLOJİK GÖRÜNTÜLEME TEKNİKLERİ İLE KARŞILAŞTIRILMASI

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ABSTRACT

Purpose: We aimed to evaluate the shear-wave elastography (SWE) findings of breast cancer and to compare their differences with other imaging techniques and to determine the relationship between molecular subtypes.

Methods: Radiological findings and histopathology results of patients who underwent biopsy due to breast mass and diagnosed as malignant were evaluated retrospectively. SWE findings, ultrasonography (US), mammography and magnetic resonance imaging (MRI) findings were evaluated. The histopathology results of the tru-cut biopsy performed under the guidance of US-SWE were analyzed. The findings of SWE and other radiological techniques were compared statistically and relationship with molecular subtypes was evaluated.

Results: We had 51 patients with a median age of 58 years. In SWE, the mean tumor size was 20 mm, and the tumor elasticity was 105 kPa. Statistically significant correlation was found between the tumor size differences measured by B mode US-SWE and the tumor elasticity value. No correlation was found between SWE findings and molecular subtypes. SWE had significantly high positive correlation with mamography and MRI in terms of lesion size, with US very high positive correlation and with estrogen receptor (ER) positivity weak negative correlation.

Conclusion: In addition to conventional radiological imaging techniques the use of SWE provides useful insight to evaluation of breast cancer.

Keywords: Shear-wave elastography; breast cancer; molecular subtype.

ÖZ

Çalışmanın özeti Euroson School 2022 İstanbul toplantısında, 01.10.2022' de sözlü bildiri olarak sunulmuştur.

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DEU Tıp Derg 2023;37(1): 37-46
J DEU Med 2023;37(1):37-46
doi: 10.18614/deutip.1214423

Gönderim tarihi / Submitted: 11.12.2022
Kabul tarihi / Accepted: 07.02.2023

Amaç: Meme kanserinin shear-wave elastografi (SWE) bulgularını değerlendirerek, diğer görüntüleme teknikleri ile farklılıklarını karşılaştırmayı ve moleküler alt tipler ile arasındaki ilişkiyi belirlemeyi amaçladık.

Yöntem: Meme kitlesi nedeniyle biyopsi yapılan ve malign tanı alan hastaların radyolojik bulguları ve histopatoloji sonuçları retrospektif olarak değerlendirildi. SWE bulguları, ultrasonografi (US), mamografi ve manyetik rezonans görüntüleme (MRG) bulguları değerlendirildi. US-SWE rehberliğinde yapılan tru-cut biyopsinin histopatoloji sonuçları incelendi. SWE ve diğer radyolojik tekniklerin bulguları istatistiksel olarak karşılaştırıldı ve moleküler alt tipler ile ilişkisi değerlendirildi.

Bulgular: 51 hastanın median yaş değeri 58′ di. SWE' de ortalama tümör boyutu 20 mm ve tümör elastisite değeri 105 kPa idi. B mod US-SWE ile ölçülen tümör boyutu farklılıkları ile tümör elastisite değeri arasında istatistiksel olarak anlamlı korelasyon bulundu. SWE bulguları ile moleküler alt tipler arasında anlamlı ilişki saptanmadı. SWE, lezyon boyutu açısından mamografi ve MRG ile anlamlı derecede yüksek pozitif korelasyona, US ile çok yüksek pozitif korelasyona ve ER pozitifliği ile zayıf negatif korelasyona sahipti.

Sonuç: Konvansiyonel radyolojik görüntüleme tekniklerine ek olarak, SWE' nin kullanımı meme kanserinin değerlendirilmesinde yararlı bilgiler sağlamaktadır.

Anahtar Kelimeler: Shear-wave elastografi; meme kanseri, moleküler alt tip.

Breast cancer is a heterogeneous and complex disease with different morphological, biological and molecular features (1). Factors such as age, tumor type, molecular subtype, stage and axillary lymph node metastasis have an important place in the prognosis of breast cancer. (2-3). Molecular subtype is one of the important parameters in determining the treatment protocol today. Molecular subtypes are classified as Luminal A, Luminal B, Her-2-positive, Triple negative breast cancer (TNBC). Molecular subtypes are determined by immunohistochemical studies according to the percentage of estrogen receptor (ER), progesterone receptor (PR), proliferating cell nuclear antigen (Ki-67) and the presence of human epidermal growth factor receptor-2 (HER-2) in the tumor (3-4).

Radiological imaging methods can provide insight into the molecular subtype prediction of breast cancer (5). Ultrasonography (US) and mammography (MG) are used in daily practice in the evaluation of breast cancer. Breast magnetic resonance imaging (MRI) is applied when clinically necessary. Elastography is an additional US method based on the evaluation of the stiffness properties of tissues. Shear wave elastography is an elastography technique in which tissue elasticity is expressed with quantitative data (6-7). It has been shown in the literature that SWE achieves high sensitivity and specificity in distinguishing benign and malignant lesions (7-8-9).

The World federation of Ultrasound in Medicine and Biology (WFUMB) guidelines have shown that 80 kPa (5.2 m/s) can be used to differentiate between BIRADS3 and 4A lesions and in the biopsy decision (10). As a unit of elasticity, it is measured in shear wave velocity (m/s) or Young's modulus-elasticity (kPa). Quantitative data obtained are expressed in meters per second (m/s) or kilopascals (kPa). The SWE color scale ranges from 0 kPa (blue) to 180 kPa (red) (6). High elasticity values support the diagnosis of malignant lesion.

SWE increases the specificity and sensitivity in the diagnosis of breast cancer (11). The 'stiff rim' feature around the mass and tumor elasticity measurement (kPa) are used to measure tumor diameter with SWE. Compared with US, the lesion size may be higher in breast cancer in SWE (7). In SWE, the high degree of stiffness in the stroma around the tumor compared to the stiffness within the tumor is a defining feature in invasive cancers. (7-12).

Due to the presence of different molecular subtypes, differences can be seen in SWE as well as in breast cancer radiological findings. In this study, we aimed to evaluate the shear-wave elastography (SWE) findings of breast cancer and to compare their differences with other imaging techniques and to determine the relationship between molecular subtypes and histological grade.

MATERIALS AND METHODS

Ethics committee approval was obtained from our instution (Approval number: 22-9T/16). Written informed consent form was obtained from all patients. Radiologic imaging findings (US, SWE, MG, MRI) and histopathology results of patients who underwent biopsy due to breast mass and diagnosed as malignant between November 2021 and July 2022 were evaluated retrospectively. Breast cancer was diagnosed in 79 of 138 patients who underwent tru-cut biopsy under US-SWE guidance. Those patients who had deficiencies in other imaging tests (such as MG or MRI) were excluded from the study (n:28). 51 patients whose radiological images and biopsy histopathology results could be accessed were included in the study. US and SWE images were obtained with 9L14 probe (Siemens Acuson S2000 model US machine). Mammography images were obtained via Selenia Dimensions model, Hologic and dynamic contrast breast MRIs were done with Magnetom Amira model, Siemens 1.5 Tesla MR. B-mode US and SWE images were taken before the tru-cut biopsy, in the same session, by a 10-year radiologist with 4 years of breast radiology experience. All lesions were imaged in 2 orthogonal planes for US and SWE (Fig.1).

Figure1.

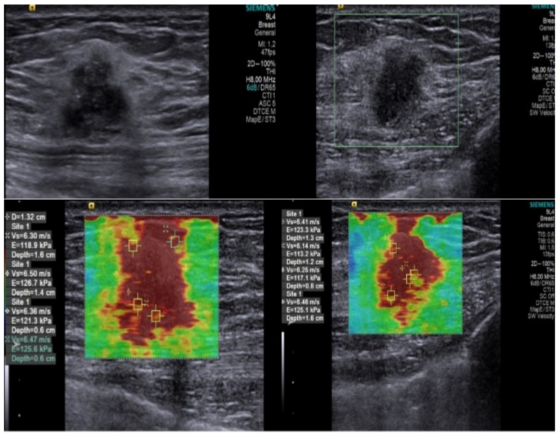

Figure 1. B-mode US and SWE images of 50 years old woman; Invasive ductal carcinoma diagnosis, Luminal A disease, tumor grade (MBRG: Modified Bloom-Richardson Grade) 2.

In the SWE color map, hard tissues are shown in red and soft tissues are shown in blue. Measurements were made from the mass centralized without manual pressure, with a ROI of 2 mm in diameter, and the minimum, maximum, mean stiffness values, and the ratio between the mean stiffness in the mass and the fatty tissue (Fig1,2). The mean stiffness value was determined with 4 measurements made from different areas of the mass. In B mode US and SWE, the largest diameters of the lesions were measured from the same axis (Fig.2).

Figure 2.

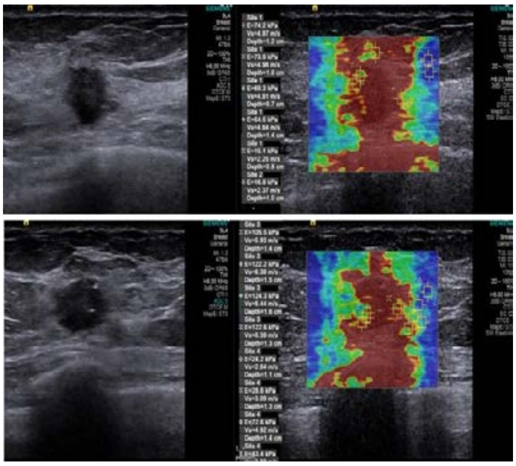

Figure 2. B-mode US images and SWE measurements of 44 years of women with a invasive ductal carcinoma diagnosis. Triple negative breast cancer, tumor grade (MBRG: Modified Bloom-Richardson Grade) was 2.carcinoma diagnosis.

The largest diameter of the lesion was measured on mammography (Fig.3). In MRI, evaluation was made for the presence of edema around the lesion in T2W sequences. The largest diameter of the lesion was measured from dynamic contrast subtraction images (Fig.3). The histopathology results (molecular subtype, hormone receptors, Ki67 index, tumor grade [MBRG: Modified Bloom-Richardson Grade]) of the tru-cut biopsy performed under the guidance of US-SWE were analyzed.

Figure 3.

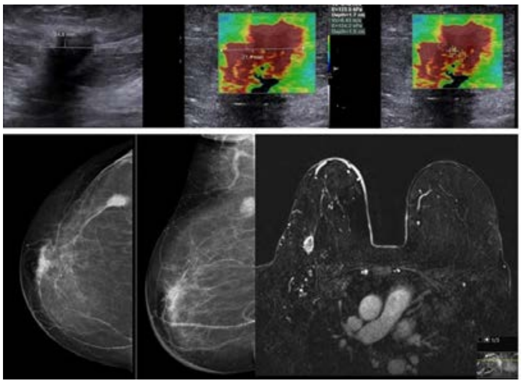

Figure 3. 65 years old patient with invasive ductal carcinoma, luminal B disease. US, SWE, Mammography and MR images.

Statistical Analysis

Analyzes were made with the SPSS V28 package program. Whether the data were suitable for normal distribution was examined with the Shapiro-Wilk test. Due to the non-normal distribution of the data, the comparisons between the groups were examined with the Mann Whitney U test and Kruskal Wallis test, and the relations between the variables were examined with the Spearman correlation coefficient. Since the data were not normally distributed, nonparametric tests were performed, so descriptive statistics were expressed as median (minimum-maximum) and categorical data as frequency and percentage. The significance level was taken as α=0.05. The findings of SWE and other radiological imaging techniques were compared statistically and relationship with molecular subtypes was evaluated.

RESULTS

Our study was carried out with 51 patients with a median age of 58 years (range, 36-91 years)
(Table 1).

Table 1. Age and lesion measurements

		Median value (min-max.)
Age (years)		58 (36-91)
Lesion size (mm)	B-mode US	18 (5-66)
	SWE	20 (8-65)
	MG	23 (0-70)
	MRI	24 (10-73)
Lesion elasticity value in SWE (kPa)		105 (35-150)

***US**: Ultrasonography **SWE**: Shear wave ultrasonography **MG:** Mammography **MRI:** Magnetic resonance imaging **kPa**: Kilopascal

The most common breast pattern was type C, with a rate of 59% (Table 2). The quadrant with the highest number of masses was the upper outer quadrant with a rate of 58% (n:30), followed by the upper inner quadrant with 22% (Table 2).

Table 2. Distrubition of breast parenchyma and quadrant of lesion

	n (%)
Breast parenchyma pattern	
A	2 (3.92)
B	12 (23.53)
C	30 (58.82)
D	7 (13.73)
Quadrant of lesion	
Upper outer	30(58.82)
Upper inner	11 (21.57)
Central	3 (5.88)
Lower outer	3 (5.88)
Lower inner	4 (7.84)

There was more than one mass in 3 of the patients and measurement was made from the largest lesion, while the other patients (n:48) had a single solid mass. In B-mode US, 37.3% (n:19) had a slightly irregularly circumscribed solid mass, 62.7% (n:32) had an irregularly circumscribed mass morphology accompanied by parenchymal distortion and posterior acoustic shadowing. In B mode US, the mean mass size was 18 mm, the masses were irregularly circumscribed and solid. In SWE, the mean tumor size was 20 mm, and the tumor elasticity was 105 ± 36 (standard deviation) kPa (Table 1). Mean lesion size measurements were 22 mm in MG and 24 mm in MRI. 73% (n:37) of the patients, there was edema around the mass on MRI. The most common type of breast cancer in biopsy results was ductal carcinoma in situ accompanying invasive ductal carcinoma with 63%, followed by invasive lobular carcinoma with 12%. The most common molecular subtype was Luminal disease (60.8%) (Table 3).

Table 3. Breast cancer features

	n (%)
Pathological subtype	
IDC+DCIS	32 (62.75)
Invasive lobular carcinoma	6 (11.76)
Metaplastic breast carcinoma	2 (3.92)
Glycogen-rich breast carcinoma with neuroendocrine differentiation	4 (7.84)
Mucinous carcinoma	4 (7.84)
DCIS	3 (5.88)
Molecular subtype	
Luminal A	25 (49.02)
Luminal B	6 (11.77)
Her-2 positive	13 (25.49)
Triple negative	7 (13.72)
MBRG	
1	5 (9.8)
2	38 (74.51)
3	8 (15.69)

IDC: Invasive ductal carcinoma **DCIS:** Ductal carcinoma in situ **MBRG:** Modified Bloom-Richardson Grade

Ki67 index mean value was 20%. The mean values of ER and PR receptor positivity (%) were 100 and 20, respectively. Axillary lymph node metastases were present in 39% (n:20) of the patients. Modified Bloom Richardson grade was 2 in 75% of breast cancers. According to the lesion diameter, a high level of statistically significant correlation was found between B mode US and mammography and MRI measurements. Statistically significant correlation was found between the tumor size differences measured by B mode US-SWE and the tumor elasticity value (kPa) (Table 4).

Table 4. Statistical analysis results - I

	Lesion size differences between US & SWE		Lesion size SWE (mm)		Lesion size US (mm)	
	r	p	r	p	r	p
Lesion size in MG (mm)	0.062	0.664	0.751	<0.001	0.704	<0.001
Lesion size in MRI (mm)	-0.014	0.920	0.721	<0.001	0.705	<0.001

***US:** Ultrasonography **SWE:** Shear wave ultrasonography **MG:** Mammography MRI: Magnetic resonance imaging
kPa: Kilopascal

SWE had statistically significantly high positive correlation with mamography and MRI in terms of lesion diameter (p<0.001), with B mode US very high positive correlation (p<0.001) and with ER positivity (%) weak negative correlation (p=0,008) (Table 4,5).

Table 5. Statistical analysis results - II

	Lesion size difference between US & SWE		Lesion size SWE (mm)		SWE kPa value	
	r	p	r	p	r	p
Ki67 index (%)	-0.195	0.170	0.158	0.269	-0.085	0,553
ER positivity (%)	0.112	0.434	-0.367	0.008	-0.050	0.727
PR positivity (%)			-0.185	0.194	0.169	0.235

***ER:** Estrogen receptor **PR:** Progesterone receptor **US:** Ultrasonography **SWE:** Shear wave ultrasonography
kPa: Kilopascal

No statistically significant correlation was found between SWE findings and molecular subtypes, edema findings in MRI, axillary lymph node metastasis, tumor grade (Table 6).

Table 6. Statistical analysis results - III

	SWE kPa value mean (min-max.)	**Lesion size (mm) difference between US & SWE mean (min-max.)**
Edema around the tumor in MRI		
Negative [n=37]	105(70-150)	2 (0-8)
Positive [n=14]	104.5 (35-125)	2 (0-6)
p value	0.512	0.511
Molecular subtype		
Luminal disease (n=31)	108 (72-150)	2 (0-8)
Her-2 positive (n=13)	105 (70-125)	2 (0-7)
Triple negative (n=7)	96 (35-123)	1 (0-3)
p value	0.155	0.305
Axillary lymph node metastasis		
Negative (n=31)	105 (38-150)	2 (0-6)
Positive (n=20)	106 (35-124)	1 (0-8)
p value	0.743	0.222
Tumor grade (MBRG)		
1 (n=5)	95 (78-120)	2 (0-5)
2 (n=38)	106 (38-150)	2 (0-8)
3 (n=8)	103 (35-116)	0.5 (0-4)
p value	0.380	0.196

***US:** Ultrasonography **SWE:** Shear wave ultrasonography **MG:** Mammography **MRI:** Magnetic resonance imaging

kPa: Kilopascal

DISCUSSION

Breast cancer is a complex, heterogeneous disease. Therefore, when breast cancer B-mode US and SWE findings are evaluated together, it gives more accurate results (11). In our study, a statistically significant relationship was found between SWE and other radiological methods (US, MG, MRI) in measuring the lesion size, similar to the literature.

The SWE elasticity cut-off value is variable. In the study by Evans et al., in which the stiffness cutoff value was selected as 50 kPa in the differentiation of benign and malignant solid lesions, it was shown that SWE gave valuable findings as B-mode US (13). BRCA1 positive and triple negative breast cancers may have benign findings on US and MG (9,14).

In our study, 3 patients with TNBC had a well-contoured solid mass, but the SWE values were high and consistent with malignancy. We suggest SWE findings can guide the diagnosis in these cases. It has been reported that high tumor diameter, high grade, lymph node invasion and vascular invasion are more common in HER-2-positive and TNBC subtypes (7). In our study, patients with these group had higher tumor size and grades, but no significant correlation was found, probably because of the low number of patients. SWE stiffness valuess can be interpreted more accurately in low-grade cancers whose B-mode US findings are uncharacteristic (7,9,15). As in the literature, invasive lobular carcinoma and invasive ductal carcinoma cases gave similarly high stiffnes values in our study (7).

There are studies showing the relationship between B mode US findings and molecular subtypes (7,16). In this study, similar to the literature, parenchymal distortion and posterior acoustic shadowing findings on B-mode US were observed more frequently in Luminal disease than in other subtypes (n:26/32). Lobule solid lesions were more numerous in patients with Her-2-positive and TNBC diagnosis (n:14/19). Although no statistical relationship was found between tumor stiffness values and molecular subtypes in our study, we think that more information can be obtained with studies with higher case numbers. In the literature, the relationship between aggressive tumor types and high stiffness values has been shown (9).

Axillary lymph node metastasis, which is important in breast cancer mortality and prognosis, is also very important in determining the treatment protocol. Although there was no significant relationship between SWE findings of a breast mass and axillary lymph node metastasis in this study, it has been reported in the literature that axillary lymph node SWE findings guide the evaluation of molecular subtypes (3). With appropriate cut-off values, studies can be conducted with axillary lymph node SWE findings in a large case group and artificial intelligence prediction models can be developed.

The stiffness values of the mass were higher in cases with a larger mass diameter in SWE than in B-mode US, but no statistically significant relationship was observed in terms of molecular subtypes. When we look at the molecular subtype distribution, this can be explained by the fact that a high percentage (60%) of the patients are Luminal subtypes. The limitations of this study are that it was planned retrospectively and the number of patients was low. Due to the significant difference in the number of molecular subtypes in the patient group, statistically sufficient results could not be obtained. There is a need for more detailed evaluations with new studies involving a larger patient groups and postoperative surgical results.

As a result, nowadays the incidence of breast cancer is increasing gradually; in addition to conventional radiological imaging techniques (US, MG, MRI), the use of SWE provides useful insight to evaluation of breast cancer.

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