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ORIGINAL ARTICLE

The Role of Doppler Sonography in Distinguishing Malignant from Benign Breast Lesions

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Background: The use of color Doppler ultrasound (CDUS) for characterizing breast lesions has increased in recent years. The aim of this study was to assess the value of CDUS and resistance index (RI), in evaluating solid breast masses.
Methods: In total, 38 cases with one or more solid breast masses were enrolled. CDUS was performed for each participant, evaluating RI, and all of them underwent a tissue biopsy. The results were categorized and compared with pathology results.
Results: Malignant breast lesions were more vascular than the benign lesions. Blood vessels were detected in 97.4% of the malignant group and only 35% of the benign group. The mean values of RI in benign lesions and malignant lesions were 0.65 ± 0.065 (range, 0.52—0.89) and 0.71 ± 0.093 (range, 0.57—0.75), respectively. The difference was just short of statistical significance ($p = 0.061$).
Conclusion: Hypervascularity of a breast mass is the most reliable sign in Doppler ultrasound to predict its possibility of malignancy. However, it appears that the use of RI alone has little value in differentiating between malignant and benign breast lesions. Pathological findings are still the gold standard for diagnosing the type of breast nodules.

Conflicts of interest: All contributing authors declare no conflicts of interest.

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Introduction

Breast cancer, the most frequently diagnosed cancer and the leading cause of cancer death among women accounts for 23% of all cancer cases and 14% of cancer deaths globally [1,2]. In Iran, the age specific rate for breast cancer, the fifth cause of cancer death, is 27.15 in 100,000 people [3].

Mammography is considered the primary screening tool for breast cancer [4,5]. However, the sensitivity of mammography declines with increased density of breast tissue and it is estimated that in women with dense breasts, the sensitivity of mammography decreases to 30–48% [6,7]. Although, there is no recommendation for routine ultrasound imaging currently, it has been revealed that supplemental ultrasound can detect small breast cancers not detected by mammography [8–12]. A study has shown that using ultrasound in addition to mammography increases the sensitivity to 77.5% compared to that of mammography alone (50%) in women with dense breasts and increased risk of breast cancer [13].

The use of color Doppler ultrasonography (CDUS) for characterizing breast lesions has increased in recent years. The presence and distribution of blood vessels associated with malignant lesions is visualized by CDUS. Doppler criteria such as resistive index (RI), pulsatility index, and flow velocity are used to distinguish benign from malignant lesions. Most of the studies are based on RI comparison between malignant and benign lesions. However, different sensitivities, specificities, and positive and negative predictive values have been reported. [14].

The aim of this study is to assess the value of CDUS and RI, in evaluating solid breast masses, to compare it with pathology results, and to evaluate its potential role in differentiating benign from malignant breast lesions.

Materials and methods

In a period of 1 year, a total of 38 patients with one or more solid breast mass who were candidates for breast biopsy were enrolled in this prospective cohort study. Age of the patients ranged from 28 years to 66 years. The study was approved by the Mashhad University of Medical Sciences Ethics Committee (Mashhad, Iran) and informed written consent was obtained from all patients. Clinical examination, ultrasound examination, and CDUS were performed for each participant. All of the examinations were performed by one qualified radiologist using an LN5-12 linear transducer with a SonoAce X8 machine (Samsung Medison, Seoul, South Korea). Doppler criteria including the size of the lesion, presence or absence of blood vessel, degree of vascularity compared with the surrounding normal tissue and RI of the vessels in the lesion were evaluated. All the participants underwent a tissue biopsy and the samples were reviewed twice by a consultant pathologist who was not aware of the Doppler sonographic data.

Chi-square test, Fisher's exact test, Student *t* test, Mann–Whitney *U* test, Pearson correlation test and analysis of variance were used for statistical analysis. A p value of < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 14.0 (SPSS, Chicago, IL, USA).

Results

All 38 enrolled patients completed the course of the study. Patients were divided into two groups based on pathology results, benign (20 cases) and malignant (18 cases). The mean age of the patients was 43.68 ± 10.61. There was no statistical difference between the mean age of the two groups diagnosed as benign and malignant ($p = 0.85$). Likewise, there was no statistical association between the malignancy and site ($p = 0.329$) or side of the mass ($p = 0.745$).

The mean size of the tumor (height $\times$ width) was 156.59 ± 72.7 mm^2 in the benign group and 266.75 ± 153.29 mm^2 in the malignant group. This difference in the size of the lesions was statistically significant ($p = 0.012$).

When all the benign and malignant lesions were pooled, the r value (correlation coefficient) was 0.399 ($p = 0.066$). When we analyzed malignant and benign lesions separately the correlation between the size and RI for the benign lesions was 0.133 ($p = 0.777$) and that of malignant lesions was 0.319 ($p = 0.246$).

Doppler characteristics of the lesions were compared between the two groups. Among the 18 malignant lesions, 17 (94%) showed vascularity and all were hypervascularized when compared with the normal surrounding tissue.

In the benign group, vascularization was detected only in seven lesions (35%): three with hypervascularity, two with hypovascularity, and one showed no difference between vascularity of the lesion and the normal surrounding tissue. Mann–Whitney was used to analyze the difference of vascularity between the two groups. The difference was statistically significant ($p < 0.05$). Fisher exact test was also used between the groups for the degree of vascularity, which was also statistically significant, as shown in Table 1.

The positive and negative predictive values of vascularity for detecting malignancy were 70% and 92%, respectively.

The mean values of RI in benign lesions and malignant lesions were 0.65 ± 0.065 (range, 0.52–0.89) and 0.71 ± 0.093 (range, 0.57–0.75), respectively. Receiver operating characteristic analysis was used to calculate RI. The difference was just short of statistical significance ($p = 0.061$; Table 1). A threshold RI value of 0.625 was obtained from this analysis. Based on this value, sensitivity and specificity of RI values were 88% and 57%, respectively, to predict malignancy.

Histological examinations revealed that 70% of the benign lesions, were fibroadenoma and 83.3% of the malignant lesions were invasive ductal carcinoma.

Blood vessels were detected in 93% of the cases of invasive ductal carcinoma and all were associated with increased vascularity. In 36% of fibroadenomas, blood vessels were also detected, 60% of which showed increased vascularity.

Discussion

Malignant neoplasms, including those of breasts, need angiogenesis for further growth and metastasis. Thus, a technique such as Doppler sonography with the ability to

Table 1 The difference between the two groups based on the presence of blood vessel, vascularity, and resistive index (RI).

		Benign	Malignant	*p*
		Frequency (%)	Frequency (%)	
Blood vessel	No	13 (65)	1 (5.6)	<0.001
	Yes	7 (35)	17 (94.4)	
Degree of vascularity	Increased	3 (15)	17 (94.4)	0.003
	Normal	1 (5)	0 (0)	
	Decreased	3 (15)	0 (0)	
RI, mean ± SD (range)		0.650 ± 0.065 (0.57–0.75)	0.716 ± 0.093 (0.52–0.89)	0.061

SD = standard deviation.

visualize the blood vessels might be useful for differentiating benign and malignant breast lesions. This study was designed to determine the value of Doppler sonography and RI in distinguishing benign from malignant breast lesions.

The main finding of this study was that malignant breast lesions are more vascular than the benign lesions, in corroboration with previous studies [11–16]. In this study, blood vessels were detected in 97.4% of the malignant group and only 35% of the benign group. This difference was statistically significant.

Another finding of our study was that there was no statistically significant difference between the mean age of patients (44 years) in the two benign and malignant groups, which is in line with Ozdemir et al's [13] report. However, some other researchers have reported significantly older age among the malignant breast lesions compared with the benign group [11–13]. This difference might be due to different screening programs in different countries [14]. The importance of age emerged when Giuseppetti et al [14] reported a correlation between the patient's age and Doppler findings in benign lesions, with younger women being more likely to have hypervascular fibroadenomas and that degenerative features of benign lesions in older women are responsible for avascular fibroadenomas. This indicates that the vascularity of breast lesions might be affected by a patients' age. The lack of significant difference between the age of malignant and benign groups in our study allowed us to give a more realistic interpretation of the results. That is, the occurrence of greater vascularity in malignant lesions observed in our study could not be attributed to the age of patients. Collectively, our results indicate that malignant breast lesions are more likely to show increased vascularity as opposed to benign lesions. Also it appears that this increased vascularity is independent of patient age.

The lack of association between site or side of the lesion and malignancy found in our study is in agreement with the results of McNicholas et al [11].

In our study we found a significantly larger size lesion among malignant groups as opposed to the benign group. This finding is in contrary to previous studies performed by Ozdemir et al [13] and Sehgal et al [10]. However, these differences in results should be interpreted with caution because it is logical to assume that the malignant lesions tend to grow larger at a much quicker rate than the benign lesions. The longer the period between the actual occurrence of the tumor and seeking of medical help by the patient, the greater the probability of finding larger malignant lesions as compared to benign lesions. Nevertheless, our data indicate that the relationship between the size and RI value of tumors was weak and nonsignificant.

In this study, we found a higher RI in the malignant group. The RI of 0.625 was identified as a threshold with 88% of sensitivity in diagnosing malignancy. However in spite of previous studies, this threshold was not statistically significant. Lee et al [15] reported that RI of 0.78 was a suitable threshold for distinguishing malignant from benign tumors. Choi et al observed that, in more than 80% of malignant breast nodules, the RI exceeded 0.70 with a sensitivity of 80.9% and specificity of 89.1% [12]. However, they also concluded that this threshold could not be used alone and a biopsy is the gold standard for diagnosis. Peters-Engl et al [16] have also reported that RI of 0.70 is the best cut-off value for differentiating malignant nodules, with 82% sensitivity, 81% specificity, 70% positive predictive value and 89% negative predictive value. Konishi et al [17] and Madjar et al [18] reported that a threshold of 0.75 and 0.7 was the suitable cut-off, respectively. After 1 decade, in spite of the technological development, similar results were concluded from the more recent studies. Schmillevitch et al [19] proposed RI cut-off value of 0.69 with 84.2% sensitivity and 88.9% specificity.

The difference between the cut-off points of RI and the discrepancy between sensitivity and specificity proposed in different studies and our study could be explained by the fact that the behavior of a tumor depends on its vascularity. The fact that the majority of our cases were invasive ductal carcinoma and most of the benign lesions in our study were fibroadenoma could be responsible for the disparity between the results of our study and those of the prior ones. The majority of benign lesions were fibroadenoma, and, in the malignant group, 15 out of 18 cases were invasive ductal carcinoma. There was very little other pathology in either benign or malignant groups. This made it impossible to analyze the impact of the tumor type of the RI. Nevertheless, a larger size study with a greater number of variants of malignant and benign tumors could have allowed a better insight on the effect of tumor types on RI. Another potential reason would be the difference between the age of the groups with malignant and benign breast lesions in most of the mentioned studies. As discussed earlier, the age of the patients might affect the vascularity of the breast lesion. The same could be proposed for RI of the tumoral vessels. Given the various types of carcinomas, different patterns of vascularization, different grades of differentiation, varying types of benign lesions, age and ethnicity

associated changes in breast tissue, age associated changes in blood flow, and many other possible factors, it might be practically pointless to identify an absolute value for differentiating malignant from benign lesions within different studies. Further studies with larger sample sizes and covering more factors using multivariate logistic regression are needed. We especially recommend studies on age-matched benign and malignant breast lesions to be able to have more definite results.

In conclusion, CDUS is a useful tool in predicting malignancy in breast lesions. Hypervascularity of a breast mass is the most reliable sign in Doppler ultrasound to predict its malignancy. However, it appears that the use of RI alone has little value in differentiating between malignant and benign breast lesions, and pathological findings are still the gold standard for diagnosing the type of breast nodules. Larger sized human studies are needed to elucidate further the potential benefits of CDUS in evaluating breast lesions.

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