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Correlation Between Imaging and Pathologic Measurement of Breast Cancer Tumor Size

Afsaneh Alikhassi*[a], Ramesh Omranipour[b], Shahriyar Shahriyaran[a], Maryam Hadji[c], Afshin Abdi[d], Zahra Alikhassy[e]

[a] *Department of Radiology, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*
[b] *Division of Surgical Oncology, Department of Surgery, Tehran University of Medical Sciences, Tehran, Iran*
[c] *Cancer Research Center, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*
[d] *Department of Pathology, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*
[e] *Department of Emergency, Isfahan University of Medical Sciences, Isfahan, Iran*

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ABSTRACT

Background: Our study aims to determine the correlation between breast cancer tumor size according to imaging (ultrasonography and mammography) with final pathologic report as a gold standard.

Methods: We included 132 women with pathologically proven invasive breast cancer between April 2011 and December 2013. Study variables included tumor size according to pathology (as a gold standard), ultrasonography and mammography. Pearson correlation coefficient was used to show correlations.

Results: A total of 132 patients were included in the final analysis. The correlation coefficient between tumor size in mammography and pathology was 0.74 ($P < 0.001$) and between ultrasonography and pathology was 0.67 ($P < 0.001$). Age had a modifying effect on the correlation between mammography and pathology; the correlation coefficient in women who aged 40 years or above was 0.92 ($P < 0.001$) and in women younger than 40 years was 0.74 ($P < 0.001$). Similarly, regarding the association between ultrasonography and pathologic tumor size, higher correlation coefficient was observed for women aging 40 years or above compared with their younger counterparts (0.74 versus 0.62, respectively).

Conclusions: measuring tumor size in mammography whenever possible would be recommended considering the higher and significant observed correlation with the pathologic tumor size compared to ultrasonography. Both associations were stronger in women aging 40 years and above.

Address for correspondence:
Afsaneh Alikhassi, M.D.
Address: Radiology Department, Cancer Institute, Imam Khomeini Hospital, Keshavarz Blvd., Tehran, 33141-14197, Iran
Phone: +982161192849
Fax: +9821 66581626
Email: afsanehalikhassi@yahoo.co.uk

Introduction

The breast cancer tumor size is an important independent prognostic factor for short-term and long-term survival.[1-4] It is not only a main component of TNM classification system; but, also has an important role in predicting lymph node metastases.[1,3] In addition, indication of neoadjuvant chemotherapy depends on staging which is depended upon breast

cancer size.[5] The measurement of tumor size should be accurate as possible as and even small discrepancies among the estimated tumor size according to various imaging modalities can affect staging and treatment strategy.[6]

Despite the introduction of new diagnostic modalities such as vacuum biopsy, in some circumstances determining definitive pathologic size of tumors is not readily available and the surgeon is obligated to rely on clinical and imaging tumor size. This also adds to the importance of assessment and improvement of the currently available imaging modalities. Previous studies provide conflicting results about the accuracy of ultrasonography and mammography in tumor size measurement and most of them did not determine if the shape of the tumor, peritumoral hyperechogenicity in ultrasonography and spiculation in mammography should be included in the measurement.[7-9] Our study aims to determine the correlation of breast cancer tumor size according to imaging (ultrasono-graphy and mammography) with final pathologic report as a gold standard.

Methods

A total of 132 patients with pathologically proven breast cancer attending the breast clinic of the Cancer Institute affiliated to Tehran University of Medical Sciences, Tehran, Iran, from April 2011 to December 2013 were included for this cross-sectional study. Patients without a definite diagnosis of breast cancer, and those with inflammatory carcinoma were excluded. An informed consent form was signed by patients. The study was approved by the ethics committee of Tehran University of Medical Sciences.

Using the patients' profile, the tumor size which was estimated through ultrasonography, mammography and final pathology were retrieved and compared.

Mammography was performed using standard craniocaudal and mediolateral oblique projections (Full digital Hologic mammography). The attending radiologist, specialized in mammography, measured the largest dimension of any mammographic lesion in true size mammography. Spiculated lesions were measured according to the whole part of spicules and the central region of mass. When a tumor was associated with microcalcifications that extended beyond the tumor, the size of the main tumor without the external microcalcification was considered as the tumor size measurement. For a lesion consisting only of microcalcifications, the length between the two most distant calcifications was used to define the largest tumor size. Asymmetry of the mass was considered when focal asymmetry or distortion was visible in both CC and MLO views.

Breast ultrasonography was performed using an ultrasonography scanner Esoate MyLab with a 12-15 MHz linear array transducer. The largest dimension of the tumor was measured during real-time scanning with calipers. A different radiologist, from the one who interpreted the mammograms, performed the ultrasound measurement and she was not informed regarding the mammo-graphic results. A mass which had peritumoral echogenicity was measured with and without peripheral echogenicity.

The patients with malignant biopsy results underwent either breast conserving surgery or mastectomy. Excised masses were sent to pathology lab in formalin and were fixed for 24 hours. Then, the largest diameter of the invasive carcinoma was measured by a pathologist. In masses with both *insitu* and invasive components, just invasive component was included in measurement.

Statistical Analysis

In this study, we assumed the pathologic size of the tumor as the gold standard method and ultrasonography and mammography as the test methods. Pearson correlation coefficient was used to compare the tumor size according to mammography and ultrasonography with the pathologic size. In order to adjust the effect of the potential confounding factors, we estimated partial correlation coefficient and the related P value. The comparative analyses of the measurements by mammography and ultrasound modalities were performed.

Stepwise linear regression analysis was performed considering tumor shape and size in ultrasonography and tumor shape, size and mammographic breast density in mammography. Furthermore, T classifications of TNM staging based on mammo-graphic and ultrasonographic tumor size versus pathologic size were compared with each other. P value less than 0.05 was considered as statistically significant.

Results

We recruited 132 breast cancer patients in this study. Their mean age was 47.8±8.8. A total of 92.1% of them were married and 88.5% of them were housewives.

Only 117 out of 132 tumors could be measured in mammography. Spiculated lesions were found in 43 cases, 24 lesions were described as irregular border masses, 20 lobulated, 18 with focal asymmetry or distortion and 12 as microcalcifications only. The correlation coefficient between tumor size in mammography and pathology was 0.74 ($P < 0.001$) and between ultrasonography and pathology was 0.67 ($P < 0.001$).

A total of 125 lesions out of 132 could be defined and measured by ultrasound. Thirty one of these tumors had peritumoral echogenic halo. The highest correlation between tumor size in ultrasonography and pathology was seen for T2 lesions ($r = 0.43$ and $p < 0.001$).

Age had a modifying effect on the correlation

Table 1. Correlation coefficient between mammography and pathology in different age groups

	All	T1	T2
All			
Correlation coefficient	0.72	0.35	0.6
P-Value	< 0.001	0.1	< 0.001
Age ⩾ 40			
Correlation coefficient	0.92	0.44	0.64
P-Value	< 0.001	0.3	< 0.001
Age < 40			
Correlation coefficient	0.7	0.34	0.93
P-Value	< 0.001	0.02	0.06

between mammography and pathology; the correlation coefficient in women who aged 40 years or above was 0.92 ($P < 0.001$) and in women younger than 40 years was 0.74 ($P < 0.001$) (Table 1).

Similarly, regarding the association between tumor size in ultrasonography and pathology, higher correlation coefficient was observed for women aging 40 years or above compared with their younger counterparts (0.74 versus 0.62, respectively) (Table 2).

In tumors which had peritumoral hyperechogenicity, including peritumoral echogenicity in measurement increased ultrasonographic measurement correlation ($r = 0.94$, $p < 0.001$).

Table 2. Correlation coefficient between ultrasonography and pathology in different age groups

	All	T1	T2
All			
Correlation coefficient	0.62	0.4	0.5
P-Value	< 0.001	< 0.001	0.002
Age ⩾ 40			
Correlation coefficient	0.74	0.6	0.53
P-Value	0.5	0.7	0.6
Age < 40			
Correlation coefficient	0.62	0.4	0.5
P-Value	< 0.001	< 0.001	0.004

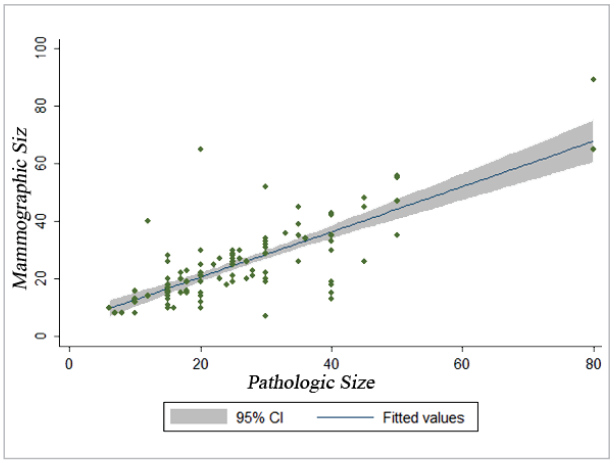

Figure 1. Pathologic tumor size and mammography size

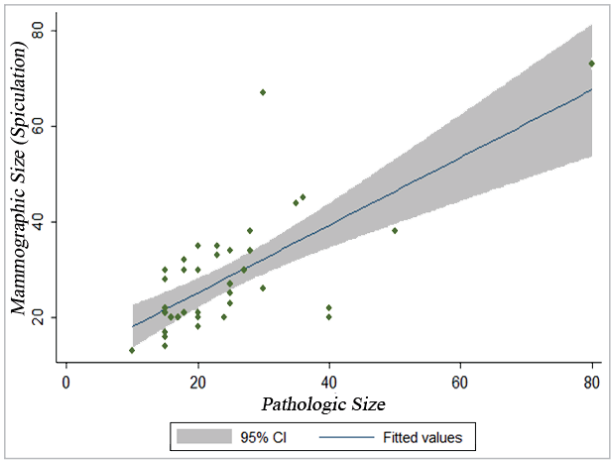

Figure 2. Pathologic tumor size and mammographic tumor size based on size including spicules

Figure 1 showed the regression line corresponding to the equation including "Mammo-graphic tumor size (mm) = 0.8 * pathologic size (mm) + 4.9 (mm)". Furthermore, the residual ranged from (-22.4 to 45.3) and the standard deviation was ±9.02 (mm).

In addition, including the spicules size measurement, the equation was "mammography size (mm) = 0.7 * pathologic size (mm) + 11 (mm)" and the residual range and standard deviation were (-18.4, 35.7) and ±9.2, respectively (Figure 2).

In terms of equation, ultrasonographic tumor size (in mm) was equal to "0.6 * pathologic size (mm) + 6.8 (mm)". The residual range and the standard deviation were (-3.9, 6.03) and ±2.6, respectively (Figure 3). Moreover, this equation based on the halo size (considering halo in tumor size measurement) was as follows: "ultrasonographic tumor size (in mm) = 0.9 * pathologic size (mm) +2.1 (mm)". Furthermore, the residual range was (-37.2, 24.8) and the standard deviation was ± 8.2 (Figure 4).

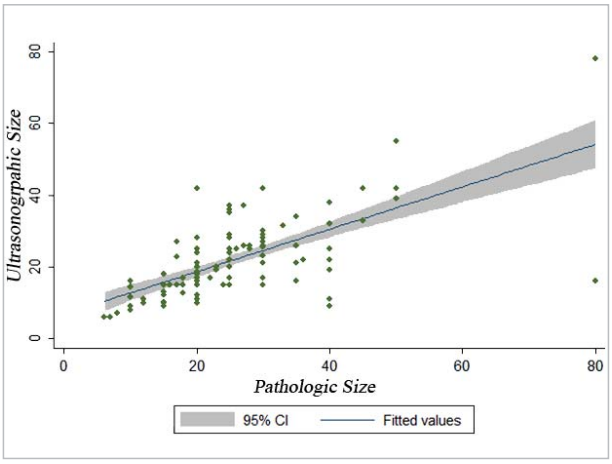

Figure 3. Pathologic tumor size and ultrasonic tumor size

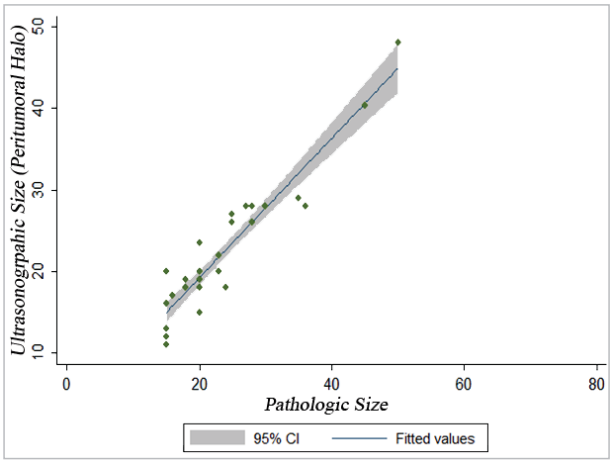

Figure 4. Pathologic tumor size and ultrasonographic tumor size including the peritumoral halo

Discussion

The aim of this research was to assess the correlation of ultrasonographic and mammographic breast tumor size with pathologic tumor size as the gold standard. We observed a higher correlation coefficient between mammographic and pathologic tumor size.

According to literature, correlation coefficients between clinical and pathological tumor sizes have been reported to range from 0.68 to 0.79 for physical examination, 0.48 for mammography, and from 0.47 to 0.92 for ultrasound.[9-11]

A larger tumor has a higher chance for lymph node metastasis. In large tumors, the chance of false negative sentinel lymph node biopsy results outweighs the advantages of sparing the unnecessary axillary dissection.[6,12-14] Tumor size evaluation before and after neo-adjuvant chemotherapy is another interesting topic worth to be evaluated.

Invasive tumor size rather than *in situ* component is considered as the reference for both ultrasonography and mammography.[15] This is in concordance with the TNM staging system, which includes only invasive tumor size.

In a retrospective study of 200 patients with breast cancer, Pain *et al.* concluded that physical examination, ultrasound and mammography had a similar accuracy for predicting the pathological size.[16] The authors found that mammography underestimated large tumors, and ultrasound underestimated all tumors.

The prospective study of Madjar *et al.* showed that ultrasonographic measurements are far superior to physical examination and mammography.[8]

Forouhi and co-authors reported correlation coefficients of 0.84 and 0.89 for mammographic (n = 45) and ultrasonographic (n = 52) determinations of tumor size.[11]

Flanagan *et al.* compared mammographic and pathologic measurements of 134 cancers and reported a correlation coefficient of 0.78.[17] They said that mammographic measurements have a tendency to be slightly larger than pathologic measurements.

Yang *et al.* also noted that ultrasonographic measurements were more correlated with pathologic size (r = 0.92) in comparison with mammographic results (r = 0.84).[9]

Fornage *et al.* compared ultrasonographic measurements of tumor size to pathologic measurement in 31 cases, of which 21 also had mammographic measurements of size.[18] The correlation coefficient for ultrasonography was 0.84. In their study, mammographic size measurements were less accurate, with a correlation coefficient of 0.72.

Bosch *et al.* compared physical examination, mammography and ultrasonography for the prediction of the pathological size of the breast cancer.[7] According to their study ultrasound was the best modality.

In the study of Golshan and colleagues, the accuracy of ultrasound, mammography and core biopsy in determining tumor size was assessed in 202 patients with stages I and II breast cancer.[19] The most accurate single modality for determining clinical tumor size in this study was mammography with a correlation coefficients of 0.66, followed by ultrasonography (r = 0.48) and core biopsy (r = 0.28).

Theoretically, mammographic imaging may have magnification. A few other authors mentioned this and even fewer attempt to compensate for it.[16,17,20] The magnification factor in our study was nearly 1 and therefore, it is less probable to affect the validity of our results.

In our study, we included the shape of the mass in mammography including spiculated and lobulated masses in addition to microcalcifications only and mass with microcalcifications. Correlation of mammography in well-defined lobulated or irregular shape masses was even more (> 0.83). If we include shape of the mass, type of the mass (infiltrating ductal versus other pathology), breast density and patient age in prediction, mammography would have significant acceptable accuracy in predicting tumor size. In contrast, in subjects with dense breast, young patients, T1 tumors, pathology other than invasive ductal carcinoma and cancers with focal asymmetry and distortion

in mammography, mammography might not be accurate enough in tumor size estimation and caution should be warranted.

In conclusion, measuring tumor size in mammography whenever possible would be recommended considering the higher and significant observed correlation with the pathologic tumor size compared to ultrasonography. Both associations were stronger in women aging 40 years and above.

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