

The Accuracy of Mammogram And Ultrasound in assessment of tumour size and lymph node involvement in invasive breast cancer

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ABSTRACT

Objectives: The purpose of our study is to assess the accuracy of mammogram and ultrasound in pre-operative prediction of the tumour size and lymph node involvement in patients with invasive breast carcinoma.

Methods: A retrospective study includes 200 female patients, aged 35 – 75 years diagnosed with invasive breast carcinoma at King Hussein Medical Center from October 2014 to August 2018. All patients underwent either modified radical mastectomy or breast conserving surgery with axillary dissection. Results of pre-operative mammogram and ultrasound were collected and compared with the final histopathologic findings.

Results: 84/200 patients (42%) had the same tumour size in both mammographic and histopathologic results. The mammographic tumour size was underestimated in 76 patients (38%), and overestimated in 40 patients (20%). The mean value of underestimation and overestimation of tumour size were 6.96 ± 4.70 mm and 5.30 ± 4.04 mm respectively. The difference and correlation of the mean size between mammography and histopathology were statistically significant ($t=-3.83$, $p=0.000$; $r=0.93$, $p<0.05$). Moreover mammography accurately determined the tumour size (versus pathological size) within 5 and 10mm, in 77 and 90% of cases, respectively. Sensitivity and specificity of axillary ultrasound to detect the lymph node metastasis were 87 and 67% respectively.

Conclusion: The mammography does not seem to be very accurate in detecting the tumour size. The axillary ultrasound is quite sensitive and moderately specific in the diagnosis of axillary lymph node metastasis.

Key words: Mammography, Breast ultrasound, Invasive breast carcinoma, Axillary lymph node dissection.

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Introduction

Breast cancer is the most common malignancy among women worldwide with increasing incidence rates.⁽¹⁾ It ranks second as a cause of cancer death in women (after lung cancer), with 15% estimated death in the United States in 2015.⁽²⁾ In Jordan, breast cancer is the most common cancer in females, accounting for 37.3 % of cancers in females. The crude incidence rate is 30.9 per100, 000 female population in 2011.⁽³⁾

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Both tumour size and presence of metastatic regional lymph nodes have been found to be prognostic factors.⁽⁴⁻⁷⁾ They are strong predictor of distant metastasis, disease-free and overall survival.⁽⁸⁾ The pre-operative assessment of the tumour size and status of axillary lymph nodes can affect the treatment planning, including the type of conservative surgery, the possibility for oncoplastic surgery or the need for chemotherapy.

Identifying an accurate diagnostic tool to effectively manage this disease is critical.⁽⁹⁾ Digital mammography (DM) is the preferred breast imaging technique for diagnostic and/or screening purpose.⁽¹⁰⁾ Ultrasound has been regarded as an effective complementary imaging adjunct to mammography in breast cancer screening.^(11,12) Despite it being safe and inexpensive, it has been reported to be operator-dependent with low inter-observer agreement, particularly for small malignancies⁽¹³⁾. The use of ultrasound with selective ultrasound-guided needle biopsy (UNB), based on ultrasound features of nodes, for preoperative staging of the axilla in newly diagnosed breast cancer patients has been practiced for many years.⁽¹⁴⁻¹⁶⁾

Various criteria have been used to define abnormal nodes, including morphologic features and/or node size (enlarged nodes), some of the most frequently reported morphologic features⁽¹⁷⁻²³⁾ defining suspicious nodes includes:

- Thickening of the cortex (primary studies have used various thresholds to define thickening, usually 2-3 mm, but some studies have used a wider mm threshold to define thickening). Cortical thickening may be diffuse or focal.
- Cortex shape/appearance: eccentric or irregular, asymmetric and/or lobulated.
- Absence/loss of central fatty hilum (this criterion is predictive of metastases but it is not frequently present, thus it may be insensitive).
- Rounded nodes (ratio of the longitudinal and transverse dimensions).

Methods

A retrospective study conducted at King Hussein Medical Center between October 2014 and August 2018 includes two hundred female patients. The mean age was 52 years (range: 35 to 75). Study was approved by the local ethics committee of royal medical services directorate of the Jordanian army. All patients are diagnosed with breast invasive ductal carcinoma or invasive lobular carcinoma and underwent either modified radical mastectomy (MRM) or breast conserving surgery (lumpectomy) with axillary dissection (AD). Bilateral mammogram was performed using standard cranio-caudal (CC) and Medio lateral oblique (MLO) views with 45° projections and adequate breast compression. Mammography interpretation and ultrasound were done by a senior specialist in the mammography unit (radiology department) at King Hussein Medical Center. Whereby all the results were pre-operatively classified as BIRADS 3 or more. The histopathologic reports were approved by a consultant specialized in breast pathology.

Data was reviewed from medical records including pre-operative mammography, breast and axillary ultrasound and final histopathologic reports. The pre-operative tumour size measurement in mm was correlated with results obtained from final histopathologic examination (real tumor size), always the largest tumour diameter is considered in each case, the accuracy of mammographic tumour size was measured within 2 mm of pathological size, as we considered variability between pathologists in interpreting the same tumour. The exclusion criteria includes: positive margins, neoadjuvant chemotherapy, multicentric and multifocal tumours, ductal carcinoma in situ and occult cancers.

Axillary ultrasound results were also correlated with lymph nodes status in final histopathologic report. In this study the sonographic criteria of positivity for axillary lymph node metastasis are increase node size (enlarged node), thickening of the cortex and loss of central fatty hilum. We calculated the diagnostic accuracy of mammography and ultrasonography in predicting the tumour size and axillary lymph nodes involvement. Data analysis was done using the IBM SPSS statistics 20. A paired t-test was used to assess the difference in tumour size. Data were presented in term of mean \pm standard deviation, and p-value < 0.05 was considered statistically significant.

Results

A total of 200 patients were included in this study. The mean age was 52 years (range: 35-75). All patients underwent either MRM or breast conserving surgery with AD. The majority of patients, 184 (92%) had invasive ductal carcinoma, and 16 patients (8%) had invasive lobular carcinoma. The T1, T2 and T3 status distribution was 17.5, 68.5 and 14% respectively. None of our cases were T4 stage.

Eighty-four out of two hundred patients (42%) had the same tumour size (± 2 mm) in both mammographic and histopathologic results. In 116/200 patients there was difference in size. Furthermore, the tumour size was underestimated in 76 (38%) patients, overestimated in 40 (20%) patients (Fig. 1).

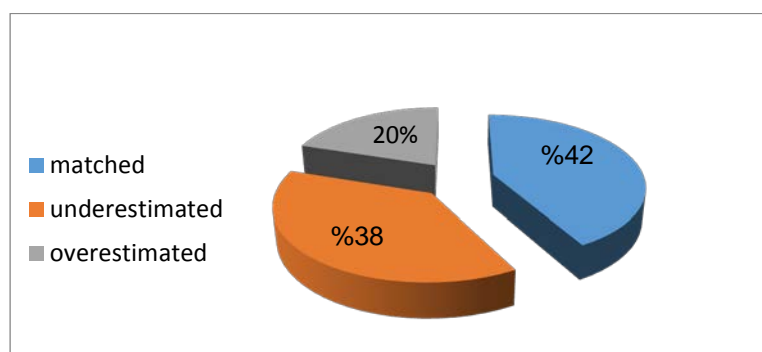


Figure. 1: Percentage of mammographic accuracy within 2 mm.

The mean tumour size measured by mammography and histopathology was 32.36 ± 14.64 and 33.87 ± 15.11 mm respectively. The mean value of underestimation and overestimation of tumour size were 6.96 ± 4.70 and 5.3 ± 4.04 mm, respectively. Lastly, the difference and correlation of the mean size between mammography and histopathology were statistically significant $t = -3.83$, $p = 0.000$; ($r = 0.93$, $p < 0.05$). The mammography accurately determined the tumour size (versus pathologic size) within 5 and 10mm, in 77 and 90% of cases, respectively (Table I).

Table I: Distribution of actual accuracy to detect tumor Size.

Mammogram Vs histopathology within 2, 5 and 10 mm.

Tumor size	Accuracy within 2 mm		Accuracy within 5 mm		Accuracy within 10 mm	
	No. of patients (n=200)	%	No. of patients (n=200)	%	No. of patients(n=200)	%
Matched	84	42	154	77	180	90
Overestimated	76	38	12	6	4	2
Underestimated	40	20	34	17	16	8

The mean number of dissected axillary lymph node was 20 (ranges: 10 – 43). Forty eight patients (24%) had no lymph node metastasis, while 152 patients (76%) had lymph node metastasis. The N0, N1, N2 and N3 status distribution was 24, 31, 25 and 20%, respectively. In axillary ultrasound, using the lymph node morphology as a criteria for positivity (increase size, thick cortex and loss of fatty hilum), sensitivity and specificity were found to be 87 and 67%, respectively. The positive predictive value (PPV) and the negative predictive value (NPV) were 88 and 66% respectively. (Table II)

Table II: Axillary ultrasound (US) results.

Findings	No. of patients (n=200)	%
True positive	127	63.5
True negative	37	18.5
False positive	17	8.5
False negative	19	9.5

Discussion

In breast carcinoma, tumour size and lymph node number are the two important prognostic factors. ⁽²⁴⁾ In a study with 20-year follow-up, Rosen et al. reported a recurrence-free survival rate of 88% for <1.0 cm tumor, 72% for 1.1 to 3.0 cm tumours, and 59% for 3.1 to 5.0 cm tumours. ⁽²⁵⁾ In a study by Hieken et al, mammography underestimated the tumour size in 60% of the patients,

the mean underestimation of the breast tumor size was 3.5 ± 0.9 mm, for mammographically determined size (versus pathologic size) correlation, r , was 0.4, the mammogram accurately determined the tumor size within 2, 5, and 10 mm in 32, 65 and 85% of cases, respectively.⁽²⁶⁾

In the present study 84/200 patients (42%) had the same tumor size (within 2 mm) in both mammography and histopathologic results. In 116/200 patient there was a difference in size. The mean value of difference estimated by mammography and histopathology was 1.51 ± 5.57 mm, while the minimum and maximum difference ranges from 1-20 mm. The tumour size was underestimated in 76 patients (38%), and it was overestimated in 40 patients (20%). Furthermore the mean value of underestimation and overestimation of tumour size were 6.96 ± 4.7 and 5.3 ± 4.04 mm, respectively. The mammography accurately determined the tumor size (versus pathologic size) within 5 and 10mm, in 77 and 90% of cases, respectively.

The total number of involved nodes gives a prognostic marker which is directly related to the recurrence rate and indirectly related to overall survival. In a study of 1,741 cases, the 10- year survival of patients with N0, N1, N2, and N3 was 75%, 62%, 42%, and 20% respectively.⁽²⁷⁾

In a study done by Alvarez et al, on sonography of axilla without palpable nodes, if the size of the node (> 5 mm) or its visibility was used as a criterion for positivity, the sensitivity and specificity varied from 48.8 to 87.1% and from 55.6 to 97.3, respectively. On the other hand, if the

morphology of the node was used as the criterion for positivity, sensitivity and specificity varied from 26.4 to 75.9% and from 88.4 to 98.1%, respectively. If palpable and non-palpable nodes are included and if the size (> 5 mm) or visibility on sonography of the node was used as the criterion for positivity, sensitivity ranged from 66.1 to 72.7%, while specificity ranged from 44.1 to 97.9%.⁽²⁸⁾ Table III shows the sensitivity and the specificity of axillary ultrasonography in the detection of lymph node metastasis in ten international studies that used the lymph node size and the node morphology as criteria for positivity.

Table III: Diagnostic accuracy of axillary sonography in patients with breast carcinoma.

Study	Date	TP	TN	FP	FN	Sensitivity (%)	<i>p</i>	Specificity (%)	<i>p</i>
Size criterion									
Bruneton et al. (29)	1986	16	37	1	6	72.7 (49.8–89.3)		97.4 (86.2–99.9)	
Tate et al. (30)	1989	39	61	20	20	66.1 (52.6–77.9)		75.3 (64.5–84.2)	
Mustonen et al. (31)	1990	12	46	1	6	66.7 (40.9–86.6)		97.9 (88.7–99.9)	
Vaidya et al. (32)	1996	78	78	9	35	69.0 (59.6–77.4)		89.7 (81.3–95.2)	
Damera et al. (33)	2003	46	45	57	18	71.8 (59.2–82.4)		44.1 (34.3–54.3)	
Summary ^b						68.4 (61.7–74.6)		87.7 (83.1–91.5)	
Heterogeneity ^{b,c}						0.38	0.94	20.86	0.000

Summary						69.2 (63.4–74.6)		75.2 (70.4–79.6)	
Heterogeneity ^c						0.67	0.95	90.27	0.000
Morphologic criterion ^d									
Lam et al. (34)	1996	8	19	1	3	72.7 (39.0–94.0)		95.0 (75.1–99.8)	
Yang et al. (35)	1996	35	68	2	9	79.5 (64.7–90.2)		97.1 (90.0–99.6)	
Verbanck et al. (15)	1997	24	20	1	2	92.3 (74.9–99.1)		95.2 (76.2–99.9)	
Yang et al. (36)	1998	31	40	2	8	79.5 (63.5–90.7)		95.2 (83.8–99.4)	
Sapino et al. (37)	2003	60	144	35	28	68.2 (57.4–77.7)		80.4 (73.9–86.2)	
Damera et al. (33)	2003	35	83	19	29	54.7 (41.7–67.2)		81.4 (72.4–88.4)	
Summary ^b						81.7 (73.6–88.1)		96.1 (91.7–98.5)	
Heterogeneity ^{b,c}						3.18	0.36	0.4	0.94
Summary ^e						71.0 (65.2–76.3)		86.2 (82.6–89.3)	
Heterogeneity ^{c,e}						18.38	0.003	23.53	0.000

Note—Numbers in parentheses are 95% confidence intervals. TP = true-positive, TN = true-negative. FP = false-positive, FN = false-negative.

^aStudies in which criterion for classifying axillary node as positive was size

^bIncludes only studies in which gold standard was axillary lymph node dissection

^cChi-square test, we used

^dStudies in which criterion for classifying axillary node as positive was morphologic or structural

^eIncludes studies in which gold standard was axillary lymph node dissection or sentinel node biopsy

In our study we used the node size, thickening of the cortex and loss of fatty hilum as a criterion for positivity. Therein, sensitivity and specificity were 87 and 67%, respectively.

Based on the results of the current study we believe that the inaccurate sizing of mammography can lead to unnecessary mastectomies and increase the incidence of positive margin tumours, but even this could happen, it will not affect the overall survival, and this actually needs more data.

Conclusion

This study demonstrates that the mammography does not seem to be very accurate in detecting the tumor size. Moreover, the axillary ultrasound is quite sensitive and moderately specific in the diagnosis of axillary lymph node metastasis.

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