Biomedical Research 2016; 27 (4): 1038-1044 *ISSN 0970-938X*
www.biomedres.info

Diagnostic accuracy of clinical examination, mammogram, ultrasonogram to detect size of tumor and lymph node in carcinoma of breast.

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Abstract

Background: In this study, we are aiming in determine diagnostic accuracy of clinical examination (CE), ultrasonography (USG) and mammography (MG) in pretreatment evaluation of breast cancer.
Materials and methods: This present prospective clinical study was conducted during sept-2009 to May-2014 includes 540 patients of breast cancer. All these patients were underwent CE,USG and MG. After these entire test patient underwent Surgery. The exact tumor size, lymph nodes number and size were analyzed from the surgical specimen.
Results: The diameter of the tumor determined with CE, MG, USG and final histopathological examination(HPE) were 6.58 ± 2.24 cm, 5.20 ± 1.68 cm, 4.63 ± 2.03 and 4.7 ± 1.88 cm respectively. The total number and size of the Lymph node were 2.187 ± 1.22 and 1.87 ± 1.22 cm by CE, 2.53 ± 2.6 and 1.37 ± 0.96 cm by USG, 2.1 ± 3.6 and 1.67 ± 0.796 cm by final HPE, respectively. The mean actual difference in tumor Size-Histopathological Vs CE Vs MG Vs USG was 1.208 ± 0.629 cm. 0.559 ± 0.084 cm, and 1.19 ± 1.06 cms, respectively. The mean actual difference in lymph nodes Size-HPE Vs CE Vs. USG were 0.573 ± 0.517 cm. 0.758 ± 0.573 cm respectively. The correlation between HPE of tumor size with CE, MMG and USG were N=440, t=-5.2, r=0.886 (P<0.05) Vs t=2.06, r=0.902 (p<0.05) Vs t=-3.93, r=0.601(p<0.05), respectively. For the Lymph node by clinically and sonographically were N=440, t=4.19, r=0.687 (P<0.05) Vs t=6.7, r=0.648(p<0.05), respectively.
Conclusion: MG is seems to be the better modality than CE and USG in detecting the tumor size and CE is better modality in detecting lymph nodes than USG.

Keywords: Tumor size, Lymph node, Carcinoma breast, Mammogram, Clinical examination, Ultrasonogram.

Accepted on March 23, 2016

Introduction

In patients with breast cancer, the tumor size and lymph nodes status are important prognostic factors. The accurate estimation of tumor size or staging is important for the initial decision-making [1]. The exact staging of the disease can be achieved by clinical examination, mammography or ultrasonography, MRI and PET etc. Even though MRI and PET have good sensitivity in diagnosing breast cancer, affordability in weaker economic patients and unavailability in all centre is major issue [2]. The non invasive nature of mammography and ultrasonography procedure can be an advantage [3].

Combined mammography, clinical examination, and ultrasonography have been found to be more sensitive than any other individual test in the diagnosis and staging of breast cancer [4]. Because of high correlation among themselves, individually they can used as equivalent technique in determining exact tumor size pre-surgically. Due to specific Pros and cons of each technique, they should be used together as complimentary to each other in accurate staging of breast cancer.

The present study has been taken up in patients of breast cancer to determine diagnostic ability of clinical examination, ultrasonography and mammography in pre treatment evaluation of breast cancer. As the breast cancer is the most prevalent cancer among women in the worldwide [5], any decision making issues involved in these cancer is making global impact.

Methods and Materials

The present prospective clinical study was conducted during sept- 2009 to May 2014 includes 540 patients of breast cancer. All these patients were underwent Clinical examination, ultrasonography and mammography. Clinical examination of breasts and axillas was done by experience single oncologist. The diameter of breast lump was measured along two perpendicular diameters using Vernier calipers, the mean diameter and Volume (clinical volume (Vc)= π /6xd3, where d=mean diameter in centimeters) were calculated. For the lymph node maximum size and number were recorded.

Ultrasonograpgy examination of the tumor and regional lymph node regions were done by using a high frequency (11 MHz)

linear electronic array probe. USG was performed by a single radiologist and they were blinded to clinical examination and mammographic findings. The USG was done in multiple planes in whole breast, bilateral axilla, bilateral supraclavicular region & internal mammary region. The margin was defined by the both normal and B-mode images. The maximum diameter, perpendicular to maximum diameter and thickness was recorded by using electronic calipers. The sonographic tumor volume (Vs) was calculated by the formula (volume of the ellipsoid):

$Vs = \pi /6 \times d1 \times d2 \times D;$

Where d1, d2 are maximum diameter, perpendicular to maximum diameters of the tumor in centimeters and D is depth/thickness of the tumor in centimeters. The total number and the maximum dimension of the lymph nodes were recorded.

Mammogram

Bilateral mammogram was performed with dedicated mammographic using standard cranio-caudal (CC) and medio-lateral oblique (MLO) with 30º projections with adequate breast compression. Mammogram were performed by technicians under the supervision of experienced radiologist. Depending on breast texture, adjustments were made between 20-35 kV and 30-180 mAs. Mammograms were analysed by an experienced radiologist and the largest tumor dimension, tumor volume were recorded.

After these tests, patients underwent either lumpectomy with axillay dissection or modified radical mastectomy. The exact size of the tumor, lymph nodes number and size were assessed from the surgical samples which are considered as a gold standard.

Statistical analysis

Relevant statistical tests such as Karl Pearson's Correlation Co-efficient and paired t-tests were used by using statistical software package SPSS version 16.

Results

A total of 540 patients were enrolled in which two patients were male, the detailed patients characteristics were recorded in Table 1. Majority of the patients i.e. 38.8%, presented with T3 disease and 24.1% of patients had T4b disease. About nodes majority of the patients i.e. 78/108 (72.2%), presented with N1 lymph node status followed by N0 and N2 (13% each). The largest size and the volume of the tumor assessed by clinical examination, mammogram and ultrasonogram were recorded in Table 2.

Out of 540 patients 100 patients were excluded as no histopathology reports were available. The diameter of the tumor determined with Clinical examination, Mammogram, sonogram and final histopathological examination were 6.58 ± 2.24, 5.20 ± 1.68, 4.63 ± 2.03 and 4.7 ± 1.88 respectively.

Table1. Showing patients characteristics.

Characteristics	Total no. of patients (540)
Age (years)	Mean -53.20 ± 11.31
Menopausal status	160 (30.18)
Pre Menopausal	70(13.2)
Peri menopausal	300 (56.6)
Menopausal	10(1.9)
Male patients	
Laterality	300 (55.6)
Right	220 (40.7)
Left	20(3.7)
Bilateral	
Duration (mean in months)	12.30 ± 10.76
Quadrant	304 (56.3)
Upper outer	98 (18.1)
Upper inner	42 (7.7)
Lower outer	0
Lower inner	102 (18.8)
Central	
Parous (n=106)	10(1.8)
Nulliparous	80(7.5)
1	100(18.8)
2	120(22.6)
3	260(49.05)
>3	
T status	110 (20.4)
T2	210(38.8)
T3	20(3.7)
T4a	130(24.1)
T4b	70 (13)
T4c	
N status	70 (13)
N0	390 (72.2)
N1	70 (13)
N2	10 (1.9)
N3	

The total number and size of the Lymph node were 2.187 ± 1.22 and 1.87 ± 1.22 by clinical examination, 2.53 ± 2.6 and 1.37 ± 0.96 by sonogram, 2.1 ± 3.6 and 1.67 ± 0.796 by final histopathological examination, respectively. The actual difference between mammographic size when compared with histopathological size shows 16% cases were shows no differences and 50% patients were within 0.5 cm and 20 % patients were in the range of 0.51- 1 cm. While in sonogram

36% patient and 16% patients clinical examination shows no differences as shows in Table 3.

Table 2. Table showing tumor and lymph node measurements by different methods.

Characteristics (N=540)	Clinical examination: in cm range(mean ± SD)	Mammogram: in cm range(mean ± SD)	Ultra sonography: in cm range(mean ± SD)	Histopathology: in cms
Tumor	3.5-15 (6.58±2.24)	32.4-9.6 (5.20 ± 1.68)	1.7-13.7 (4.63 ± 2.03)	2-9 (4.97 ± 1.92)
Largest diameter(cms)	14.12-1765	4.84-381.26	2.37-666.05	2.7-235.8
Volume (cc)	(213.15 ± 322)	(74.7 ± 77.49)	(60.99 ± 103.19)	(43.10 ± 47.09)
Lymph nodes	1-5 (2.187 ± 1.22)	-	2-8(2.53 ± 2.6)	2-15(2.1 ± 3.6)
Total number	1-4(1.87 ± 1.22)	-	0.8-4.1 (1.37 ± 0.96)	0.6-3.8(1.67 ± 0.796)
Largest diameter(cms)		-		

Table 3. Distribution of actual difference in tumor Size-Histopathological Vs Mammogarm Vs Sonogram and clinical Examination.

Difference in Size (cm)	Mammogram (%)	Sonogram (%)	Clinical Examination (%)
0	15.9	00.0	15.9
≤0.5	50.0	36.3	22.7
0.51-1	20.4	4.54	29.5
1.1-1.5	4.50	18.1	15.9
>1.51	9.10	40.9	15.9
Mean ± SD	0.559 ± 0.084	1.19 ± 1.06	1.208 ± 0.629
Max	2.20	3.83	3.00
Min	0.00	0.08	0.20
Overestimation (%)	43.2	22.7	83.7
Under estimation (%)	56.7	77.2	16.3

On calculating the size of the Lymph nodes 34% Vs 4.5% no differences, 27% Vs 34 % by <0.5 cm, 30 % Vs 38% by 0.51-1 cm and 7 % Vs 18 % by 1.1-1.5 cm by clinical examination and sonogram respectively as shown in Table 4.

The mammogram was overestimate the tumor in 43.2 % cases and underestimates in 56.7% patients. The sonogram was underestimate in 77.2 % patient and overestimate in 22.7 patients.

By clinical examination 83.6 % patients were overestimated and 16.3% cases were underestimated.

The mean difference between tumor size by mammogram, sonogram and clinically when compared with histopathologically were 0.254, -1.1 and -0.745 respectively ($p<0.05$) as shown in Table 5.

Table 4. Distribution of actual difference in Lymph node Size-Histopathological Vs Sonogram VS clinical examination in axillary lymph node.

Difference in Size (cm)	Clinical Examination (%)	Sonogram (%)
0	34.0	4.50
≤0.5	27.2	34.1
0.51-1	29.5	38.6
1.1-1.5	6.80	18.1
>1.51	2.20	4.50
Mean ± SD (cms)	0.573 ± 0.517,	0.758 ± 0.573
Max	2	3

Min	0	0

Table 5. To test the clinical examination with histopathological examination for estimation of breast tumor size.

Patients	Mean ± SD (cm)	Histopathological size (mean ± SD) (cm)	Mean difference cms	t value (p)	r (p)
Mammogram	4.45 ± 1.61	4.77 ± 1.80	0.254	2.061(0.045)	0.902(0.000)
Sonogram	3.67 ± 2.00	4.77 ± 1.80	-1.100	-3.93 (0.000)	0.601(0.000)
Clinical Examination	5.45 ± 2.03	4.77 ± 1.80	-0.745	-5.20 (0.000)	0.886(0.000)

For the lymph nodes size the mean difference between largest node size by sonogram and clinically when compared with histopathologically were 0.413 and 0.677 respectively ($p<0.05$) as shown in Table 6.

Table 6. To test the Clinical examination with histopathological examination for estimation of axillary lymph node size

Patients	Size (Me an ± SD) (cm)	Histopathological size (mean ± SD) (cm)	Mean difference cms	t (p) (N=88)	r (p) (N=88)
Clinical Examination	1.26 ± 0.852	1.67 ± 0.796	0.413	4.19(0.000)	0.687(0.000)
Sonogram	0.998 ± 0.799	1.67 ± 0.796	0.677	6.7(0.000)	0.648(0.000)

Discussion

In breast carcinoma, tumor size and Lymph node number are the important prognostic factors [6]. In a study with 20-year follow-up, Rosen et al. reported a recurrence-free survival rate of 88% for <1 cm tumor, 72% for 1.1 to 3.0 cm tumors, and 59% for 3.1 to 5.0 cm tumors. In a study of 826 node-negative breast cancer patients treated by mastectomy. With a median follow-up of 13.5 years, 20-year disease-free survival of <2 cm tumor was 79%, compared to 64% with tumors >2 cm [7].

Kumar A et al. in their study found that the mean diameter of the breast mass by clinical examination was 8.4 cms (range 6.7-14.6 cms). In the present study, mean of the largest diameter and mean volume of the breast lump determined by clinical examination, sonogram, mammogram were 6.58 ± 2.24 cms and 213.15 ± 322 cc; 4.63 ± 2.03 cms and 60.99±103.19 cc; 5.20 ± 1.68 cms and 43.10 ± 47.09 cc, respectively (2).

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. [8] In this study, the number of axillary lymph nodes determined at presentation by CE is 33.33% patients had 2 lymph nodes and 25.92% patients had one lymph node and remaining 45.7% patients had no lymph nodes. The number of axillary lymph nodes determined at presentation by sonography were: 43.39% patients had 0-3 lymph node, 24.1% patients had 7-9 lymph nodes and remaining 32.51% had 3-6 lymph nodes. The mean number of lymph node was 2.18 ± 1.2 and 2.53 ± 2.6 by clinical examination and sonogram respectively.

In a review article, in sonography of axilla without palpable nodes, and using lymph node size as the criterion for positivity, sensitivity and specificity were 48.8% -87.1% and 55.6%-97.3%, respectively. When lymph node morphology was used for the criterion for positivity, sensitivity and specificity ranged from 26.4% to 75.9% and 88.4% to 98.1%, respectively [9]. In an another systemic review, when lymph node size is >5 mm was taken size as the criterion for positivity, sensibility and specificity of USG varied from 66.1- 87.1% ($p > 0.05$) and from 44.1-97.9% ($p < 0.05$) respectively. When lymph node morphology was the criterion for positivity, sensibility and specificity were 40.5-92.3% ($p < 0.05$) and 55.6-95.2%, respectively ($p < 0.05$) [10].

Out of 540 patients 100 patients were excluded as no histopathology reports were available. On 70/440(15.9%) patients, there was no difference in the size of the breast tumor detected by clinical and histopathological examination. A difference in size was seen in 370/440(84.1%) patients. The mean value of the difference in size in 370 patients estimated by histopathological and clinical examination in breast tumor was 1.208 ± 0.629 cms, and minimum and maximum differences were 0.2 cms and 3.0 cms respectively. The size measurement in 83.78% of the patients was overestimated and in 16.21% patients it was underestimated by clinical examination compared to histopathological examination. The mean overestimation and underestimation were 1.219±0.636 cms and 0.833 ± 0.4 cm respectively.

In the study by Herrada et al. in primary tumor, on comparing the 3 noninvasive tests, clinical examination was best in prediction of residual pathological tumor size (P= 0.0003), followed by ultrasonography (P = 0.0005) then mammography (P = 0.0132) [11]. The mean difference in largest diameter of tumor size of 440 patients between clinical examination and histopathological examination was 0.745 cms, where clinical examination was overestimated the breast tumor size. The difference and correlation of the mean size between the tests is statistically highly significant (t=-5.20, p=0.000 ; r=0.886; p<.

01).). In another study, the mean difference in largest diameter of tumor size of 440 patients between clinical examination and histopathological examination was - 0.01 cm, and with sonological examination was 1.10 cm. Clinical examination seems to be overestimated the tumor size (t=.064, p=0.949). However, sonological examination seems to be underestimated the tumor size (t=-3.93, p=<0.001) [12]. Forouhi et al. found there was a moderate correlation between size of the tumor by clinical examination and pathological examination (N=51, r=0.680, *P*<0.0001), while with mammogram and ultrasonogram there will be close correlation with pathological tumor size (n=45, r=0.84, *P*<0.0001) and (n=52, r=0.89, *P*<0.0001) [13].

In another study, USG examination underestimated both tumor size and axillary lymph node size in most of patients and there was a strong correlation (r =0.719; p=<0.001) between clinical and pathological tumor size, however for axillary lymph nodes the correlation was moderate (r=0.536; p=0.001). A moderate correlation (r=0.601; p=<0.001) was observed between ultrasonographic and pathological tumor size, while strong correlation (r=0.652; p<0.001) was found for axillary lymph nodes [14].

In present study, in none of the patients the size of the breast tumor detected by sonological and histopathological examination was found to be similar. In 101/440 (22.73%) of the patients the tumor size was overestimated and in 339/440 (77.2%) patients the size was underestimated by sonological examination compared to histopathological examination. The mean of overestimation and underestimation by sonological examination were 0.84 ± 1.22 and 1.32 ± 0.97 cms, respectively.

In a study of 189 cases by Chagpar et al, an accuracy of ± 1 cm in 66% of patients by clinical examination, 75% by sonography and 70% by mammogram was obtained by comparison to pathological tumor size. In locally advanced breast cancer where patient was kept on neoadjuvant chemotherapy clinical examination was better correlated with residual breast lesion compared to sonogram and mammogram [15-17].

In the present study, the difference between mean sonological and histopathological size of breast tumor among all patients is 1.10 cm and in 339/440 (77.2%) patient's sonological examination underestimated the breast tumor size by considering the pathological examination as gold standard. The difference of the mean size between the two is statistically highly significant (t=3.93, p=.000), Thus, in this study sonological examination was found to be a poor method for breast tumor size estimation compared to histopathological examination. There was a significant linear correlation between the size of the breast tumor determined by sonological and histopathological examination among all patients r=0.601: p<. 001). The minimum and maximum value of over estimation by sonological examination was 0.1cm and 3.8 respectively. The actual difference in the size of the tumor between histopathological and sonological estimation was >1.51 cms in 36/88(40.9%) patients and in 160/440 (36.36%) patients was <0.5 cm. In the study by Heiken et al, sonograpgy underestimated the breast tumor size by 1 mm in 63% of cases. The mean underestimation of tumor size by sonogram was 3.8 (median 1.7 mm) [18].

In our study, 70/ 440 patients showed size of breast tumor similar by both mammographic and histopathological examination. A difference in size was seen in 370 patients the mean value of the difference in size in these patients estimated by histopathological and mammogarphic examination in breast tumor was 0.559 ± 0.084 cm. The minimum and maximum difference was 0.1 cm and 2.2 cms. In 160/440 (36.36%) patients, the tumor size was overestimated and in 210/440(47.72%) patients it was underestimated by mammogram compared to histopathological examination. The mean value of overestimation and underestimation of size was 0.538 ± 0.255 cm and 0.943 ± 0.609 cm, respectively.

In the study by Londero et al, mammogram was overestimated the mean diameter of the breast tumor by 6.4 mm (P=0.398) and the correlation between mammograms and the pathologic examination was statistically significant (P=0.670, P=0.012). In a study by Heiken et al, mammography was underestimated the tumor size in 60% of the patients. The mean underestimation of the breast tumor size by mammogram was 3.5 ± 0.9 mm. In 32 % of the patients mammogram was accurately determined the tumor size within 2 mm , within 5 mm in 65% of cases and in 85% of cases by 10 mm [19]. In the present study, the difference in mean size for breast tumor estimated by mammography with respect to histopathology was 0.254 cms (p=<0.05). There is significant linear correlation among mammogram and histopathologial examination on estimation of the tumor size. (r=0.902; p=<0.00)

In the study by Carla et al, [20] measurements done by the three methods correlated with each other either before or after treatment. Tumor size evaluated by both mammography and echography showed a low correlation with the size assessed by physical examination (Spearman R 0.38 and 0.24 in tumors assessed before chemotherapy and 0.33 and 0.45 in tumors assessed afterwards, respectively, p<0.001). In the present study, it is evident that difference in size estimated for breast tumor is more by sonological examination than clinical examination than mammographic examination 1.10 cms vs 0.745cms vs 0.254 cm for all patients(n=440; r=0.601). So, it may be concluded that mammographic examination method gives better estimation of breast tumor size than clinical and sonological examination while considering histopathology as gold standard.

In the present study, in 150/440 (34.09%) patients the size of the lymph node assessed clinically were same as histopathological size [21]. Out of 290/440 patients Lymph nodes were positive, 230/290 (79.39%) had underestimated values and 60/290 (20.6%) patients had overestimated values. The mean size of the lymph nodes was 0.635 ± 0.56. The mean value of underestimation and overestimation of lymph nodes were 0.583 ± 0.204 cm and 0.943 ± 0.383 cms respectively.

The difference between mean diameter of clinical examination and histopathological size of axillary lymph nodes among all patients was 0.413 cm. This implies clinical examination underestimated the lymph node size by considering pathological examination as the gold standard. The difference of the mean size between the two is statistically highly significant (t=4.19, p= <0.000). Thus, in this study clinical examination was found to be a poor method for axillary lymph node size estimation. A significant linear correlation was found between the size of the axillary lymph node size determined by clinical and histopathological examination among all patients (n=440; r=0.687; p=0.000).

In 100 patients, size of the axillary lymph node detected by sonological and histopathological examination was found to be the same. A difference in size was seen in 420 patients. The mean value of the difference in size in 180 patients estimated by histopathological and sonological examination in axillary lymph nodes was 0.758 ± 0.573 cm and the minimum and maximum difference was nil and 3cm respectively. In 170/440 (38.63%) patients, actual difference between sonological examination and histopathological examination was 0.51-1 cm and in 150/440 (34.09%) patients it was <0.5cm.

The difference between mean sonological and histopathological size of axillary lymph nodes among all patients was 0.677 cms. Sonological examination underestimated the axillary lymph node size while considering histopathological examination as the gold standard. The difference of the mean size between the two is statistically significant (t=6.7, p=<0.00), Thus, in this study, sonological examination was found to be a poor method for axillary lymph node size estimation. Highly significant correlation was found between the size of the axillary lymph node size determined by sonological and histopathological examination among the entire group (n=440; r=0.648; p= p<0.001).

Conclusion:

In the present study, Mammogram is seems to be the better modality than clinical examination and sonogram in detecting the tumor size and Clinical examination is better modality in detecting lymph nodes than ultrasonogram.

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