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Role of ultrasonography to detect axillary node involvement in operable breast cancer

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Prompted by the concern about unnecessary axillary dissections, we prospectively studied the accuracy of clinical examination (CE) and conventional ultrasonography (USG, 7.5 MHz), to diagnose pre-operatively metastatic axillary lymph nodes in 200 operable breast cancer patients. USG had higher specificity (90% vs 77%, $P=0.025$) and higher positive predictive value (ppv = 90% vs 76%, $P=0.02$) than CE. Together, CE + USG had higher sensitivity (82% vs 58%, $P=0.00005$) and higher negative predictive value (npv = 76% vs 58%, $P=0.008$) than CE alone. In women <45 years, CE + USG had higher sensitivity (91% vs 76%, $P=0.037$) and npv (89% vs 67%, $P=0.018$) than in older women. The sensitivity and npv of CE + USG to detect >1 positive node were 97% (for both) in women <45 years compared to 81% and 79% in older women. The high sensitivity of CE + USG (82% for the whole group) is probably due to the higher proportion of young women (median age = 45) in our population. It suggests that using CE + USG to avoid axillary dissection in some patients is feasible.

Key words: **ultrasonography; breast cancer; axillary nodes.**

Introduction

It is estimated that if 100 patients with T1 lesions underwent axillary dissection, about 80% would have uninvolved nodes[1,2] and would therefore have had an unnecessary procedure. With T2 lesions the gain is larger but 65% of axillary dissections are still unnecessary.[2] The proportion of T1 and T2 patients is increasing and a test which can pre-operatively predict axillary lymph node involvement and help in selecting patients for axillary dissection would be welcome. Hence the search for better imaging modalities for the axillary nodal status.

Ultrasonographic (USG) examination of the axilla has been under evaluation for some time. Although better technology has resulted in higher specificity, the sensitivity of USG has not significantly improved. The specificity is 89% with a 3.5 MHz probe[3] and 97.9% with a 7.5 mHz linear-array transducer[4] but their sensitivity is only 68%.[3,4] Although the specificity of colour doppler has been reported to be 98%[5] and 100%,[6] its sensitivity is still low viz., 70%[5] and 75%.[6] The high specificity may not be relevant in clinical practice in the absence of high sensitivity. Although CT scan has been found to be more sensitive than USG (82% vs 72%),[6] it still missed 18% of node-positive patients.

We prospectively analysed the accuracy of clinical examination and ultrasonography in the detection axillary nodal metastases.

Patients and methods

Two hundred consecutive adult female patients diagnosed as operable breast cancer (clinical stages Tx, T1, T2 and T3 and N0 or N1) who were scheduled to undergo modified radical mastectomy or lumpectomy and axillary clearance at the Tata Memorial Hospital, were entered in a prospective study. There was a gap of 5 months after 121 patients were entered, due to the long absence of a radiologist.

Each patient underwent clinical examination (CE) of the axilla which recorded the number of palpable nodes, followed by axillary ultrasonography (USG) with a 7.5 MHz linear array probe which reported the number and the largest size of axillary lymph nodes. CE was considered positive if any node was palpated and USG was considered positive if any node above 0.5 cm was detected. The examinations were carried out by the authors, CE by the surgeons and USG by the radiologists.

Each patient underwent complete axillary dissection of all three levels, accompanied by a total mastectomy or a lumpectomy according to the merits of the case. The histopathology was noted and correlated with the clinical and ultrasonographic assessment of the axilla. Adjuvant treatment was routinely administered to the patients with

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Table 1. Correlation of pathology with clinical examination and ultrasonography

	All ages			<45 years			≥45 years		
	Pathologically negative	Pathologically positive	Total	Pathologically negative	Pathologically positive	Total	Pathologically negative	Pathologically positive	Total
CE negative	67	48	115	33	16	49	34	32	66
CE positive	20	65	85	7	30	37	13	35	48
USG negative	78	35	113	38	11	49	40	24	64
USG positive	9	78	87	2	35	37	7	43	50
CE + USG negative	64	20	84	32	4	36	32	16	48
CE or USG positive	23	93	116	8	42	50	15	51	66
CE +ve and USG −ve	14	15	29						
CE −ve and USG +ve	3	28	31						
CE +ve and USG +ve	6	50	56						
Total	87	113	200	40	46	86	47	67	114

involved nodes. However, if the tumour size was > 2cm, adjuvant treatment was advised even if the nodes were negative.

The sensitivity, negative predictive value (npv), specificity and positive predictive value (ppv) were calculated for CE alone and USG alone. Sensitivity and npv were also calculated for CE + USG together.

To evaluate the effect of age, we compared the sensitivity and npv of two physiologically different groups viz., the pre-menopausal group of women less than 45 years, and the peri- and post-menopausal group of women ⩾ 45 years.

The statistical analyses for sensitivity, npv, specificity and ppv were carried out using the chi-squared test for differences between two proportions.

Results

Histopathology revealed that an average of 15 nodes (range: 8 to 28) were dissected from each axilla and 57% of patients had positive nodes, of which 3/4 had more than one positive node. The average number of positive nodes was five (range: 1 to 24). There were no major post-operative complications. The overall higher node positivity rate in this series is a reflection of the fact that stage for stage, Indian patients have larger tumours than Western counterparts; a matter of awareness.

The raw data are given in Table 1 and the parameters of accuracy in Table 2. The findings of USG were in concordance with CE, with negativity in 84 and positivity in 56 cases, the findings disagreed in 60 cases. There was no significant inter-operator difference in either CE or USG.

When analysed individually, USG had a higher positive predictive value and specificity than CE. However, USG was not better than CE in terms of either sensitivity or negative predictive value. However, when either CE or USG was positive, (CE + ve or USG + ve), 82% of the axillary metastases were detected, which was significantly higher than with CE alone (58%, $P = 0.00005$). Similarly, negative predictive value of CE-ve and USG-ve was higher than CE alone. Thus, the combined use of both modalities had a false-positive rate of 1 in 5 and false-negative rate of 1 in 4.

Table 2. Accuracy of clinical examination and ultrasonography

Test		(chi-squared) and P value as compared to CE alone
n	200	
pathologically positive %	57	
Positive predictive value % CE	76	
Positive predictive value % USG	**90**	**(5.33) 0.02**
Specificity % CE	77	
Specificity % USG	**90**	**(5.01) 0.025**
Negative predictive value % CE	58	
Negative predictive value % USG	69	(2.8) 0.19 NS
Negative predictive value % (CE − ve and USG − ve)	**76**	**(6.94) 0.008**
Sensitivity % CE	58	
Sensitivity % USG	69	(3.3) 0.07 NS
Sensitivity % (CE +ve or USG +ve)	**82**	**(16.5) 0.00005**

Effect of age on sensitivity and negative predictive value of CE and USG

In each of the two age groups studied, (<45 years and ⩾45 years), sensitivity of CE + USG was significantly higher than CE alone ($P = 0.002$ and $P = 0.004$). We found that the sensitivity of CE + USG among women <45 years was significantly higher than in women ⩾45 years (91% vs 76%, chi-squared 4.32, $P = 0.037$). Thus among women <45 years, the false-positive rate of CE + USG was 1 in 6 and false-negative rate was 1 in 9. This is much higher than these rates in older women (1 in 4 and 1 in 3, respectively).

Of the four (9%) cases in which nodes were missed by both USG and CE (<45 years), three patients had single positive nodes and one patient had four positive nodes. CE + USG could detect 97% (30/31) of patients with more than one positive node, compared with 81% (43/53) among older women ($P = 0.048$) or compared with 65% (20/31) by CE alone ($p = 0.001$).

The negative predictive value of CE + USG together also was higher among women <45 years of age compared with women 45 years and older (89% vs 67%, chi-squared = 5.6, $P = 0.018$) or compared with CE alone (vs 67%, chi-squared = 3.35, $P = 0.02$). For detection of more than one positive node, CE + USG had a negative predictive value of 97% (35/36) which was higher compared with older women (79% (38/48), $P = 0.023$) or compared with CE alone (78% (38/49), $P = 0.01$).

There was no difference between the node-positive rates in the two age groups of women (56% and 59%, $P = 0.45$).

Discussion

In our study, ultrasonography has a higher specificity and positive predictive value than clinical examination. However, this may not be clinically significant since we are interested in deciding which axilla not to dissect. We should have a test which does not miss positive axillary nodes.

The sensitivity and negative predictive value of USG was not higher than CE. However, CE and USG, when taken together, yielded a high sensitivity (82%) which means that when either CE or USG were positive, 82% of the pathologically positive nodes were detected. Thus, conventional USG added significantly to the sensitivity of CE. Even so, 18% of nodes were missed, which reduces the significance of this finding. However, among women less than 45 years, mainly consisting of the pre-menopausal group, the sensitivity and negative predictive value of CE + USG taken together were high viz., 91% and 89%, and they were significantly higher than of CE alone ($P = 0.002$ and $P = 0.002$). The sensitivity and negative predictive value in this group of women were also significantly higher than in women $\geqslant 45$ years of age ($P = 0.037$ and $P = 0.018$).

It is noteworthy that if a woman < 45 years had two or more involved nodes, CE + USG together had a 97% chance of detecting them pre-operatively.

Correlation between weight and age

Why was CE + USG so sensitive in women <45 years? We investigated whether body weights of women differ in the two age groups. We recorded the weights of 164 subsequent patients of breast cancer. In this group of patients, whose age distribution was similar to the original study group, we compared the weights of women <45 years with older women. The median body weight was 55 kg; 64% of women <45 years were found to be less than 55 kg compared with 35% of older women (OR = 3.32, $P = 0.00002$). The median weight of women $\geqslant 45$ years (57 kg) was 14% higher than the median weight of women <45 years (50 kg) and the difference between the mean weights of the two groups (51.4 kg and 57.3 kg), when analysed by the Student's t-test, was statistically significant ($P = 0.0004$). The lower body weight could, in part, explain the higher sensitivity of CE + USG in the younger group. The other explanation could be the differing distribution of body fat in these two physiologically distinct groups.

Indian women with breast cancer are young (median age = 45 years) and lean (median weight = 55 kg, a median height = 155 cm, median body mass index = 22.9). Lower overall prevalence of obesity and a higher proportion of younger women who are less obese, may have contributed to the high overall sensitivity (82%) of the USG and CE in our study. Western studies have not achieved similar results, probably because a smaller proportion of their breast cancer patients are young and lean. In the studies which have found higher sensitivity of USG compared to clinical examination (CE),[7-9] the sensitivity of CE was low (33%, 42% and 32%, respectively) and the higher sensitivity of USG (60%, 66% and 72%, respectively), was still too low to make it clinically significant.

It is important to note that these results have been achieved using the conventional USG which is economical and freely available. In India, women less than 45 years form 40 to 45% of the breast cancer patients. The low false-negative rate (1 in 9) and high sensitivity (91%) of CE + USG in this group may be useful to select patients for observation without axillary dissection. In a randomized trial (NSABP-B04)[10] axillary recurrences (all of which were resectable) occurred in only 18% of patients in the total mastectomy arm despite the fact that 40% of patients in the radical mastectomy arm had positive nodes; furthermore, survival was not compromised by not dissecting the axilla. As indicated by our study, in women <45 years, 9% of 'positive' nodes would be expected to be missed by both CE and USG; leaving these patients without treatment would result in clinical axillary recurrence in less than 4% of patients, while treating them all would mean unnecessary dissection in 96%. Although disabling lymphoedema does not usually occur after axillary dissection, the tingling and numbness of upper arm and stiffness of shoulder is a frequent cause of discomfort. In young and thin patients, negative CE and USG could allow axilla-sparing surgery with little risk of local recurrence.

Conclusions

Conventional ultrasonography with a 7.5 MHz probe adds significantly to clinical examination in pre-operatively detecting metastatic axillary lymph nodes in operable breast cancer (sensitivity: CE + USG: 82% vs CE: 58%). The sensitivity was even higher in younger women (<45 years), in whom, using USG and CE together, 91% of pathologically positive axillary nodes could be detected pre-operatively.

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