Surgery Section

Triple Test in Carcinoma Breast

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ABSTRACT

Introduction: The commonest clinical presentation in majority of breast pathology is a lump. A definite diagnosis of breast lump is very important for the surgeon to decide on the final course of treatment and also saves the patient from unnecessary physical, emotional and psychological trauma if there is a definite preoperative diagnosis of benign lesion. The present study was done to evaluate the effectiveness and relevance of "TRIPLE TEST" in diagnosis of carcinoma breast in rural labour class population.

Materials and Methods: The present study was a prospective study conducted on patients over 35 years of age having palpable breast lumps presenting in the out patient department of general surgery, ESI Hospital Basaidarapur New Delhi, India. The duration of study was from May 2007 to June 2009 and a total of 100 cases were studied. Each patient was subjected to a detailed history, clinical breast examination ,diagnostic mammography and FNAC. In this study, the results of each modality was divided in three groups: benign, suspicious and malignant. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of each test was calculated individually and as combined.

Result: Out of 100 patients enrolled in this study, 60 cases were benign and 40 cases were of malignant breast disease. The age of patients with carcinoma breast in the series varied from 35 years to 70 years. The highest incidence of malignancy noted was 30% in 41-50 years age group (4th decade) followed by 27.5% in 51-60 years age group (5th decade). The sensitivity of clinical examination was found to be 75%, specificity was 83.3%, positive predictive value (PPV) of 75% and diagnostic accuracy of 80%. The sensitivity, specificity, positive predictive value and diagnostic accuracy of mammography was calculated and was found to be 94.9% , 90% , 86% and 92% respectively. The sensitivity, specificity, positive predictive value and diagnostic accuracy of FNAC was 94.7%, 98.3%, 97.3% and 96.6% respectively. Out of 100 cases triple test was concordant (all three test either benign or malignant) in 80 cases, all the benign cases detected by triple test were benign on final biopsy i.e. 100% specificity and 100% negative predictive value.

Conclusion: TTS is an accurate and least invasive diagnostic test based on which definitive treatment can be initiated.

INTRODUCTION

The commonest clinical presentation in majority of breast pathology is a lump. A breast lump may be either benign or malignant. A definite diagnosis of breast lump is very important for the surgeon to decide on the final course of treatment. It also saves the patient from unnecessary physical, emotional and psychological trauma if there is a definite preoperative diagnosis of benign lesion. The nature of breast lump cannot be diagnosed accurately only on clinical examination. The accuracy of diagnosis of breast cancer on physical examination is only 70% even in the most experienced hands [1]. To come to a definite diagnosis, clinical judgment needs to be supported by specialized investigations. The two techniques currently available that have excellent patient tolerability are mammography and FNAC [2,3]. However, if employed alone, the accuracy of mammography and FNAC is only around 82% and 78% respectively [4]. There are numerous reports which emphasize that if clinical examination, mammography and FNAC are combined which is known as "Triple Test", the accuracy of diagnosis reaches 100% [5].

The present study was done to evaluate the effectiveness and relevance of "TRIPLE TEST" in diagnosis of carcinoma breast in rural labor class population. The study was conducted in ESI hospital Delhi which exclusively caters to rural labor class insured under ESI act of government of India. ESI act provides medical and social insurance to the laborers working in factories and is a social security system for the factory workers.

MATERIALS AND METHODS

The present study was a prospective study conducted on patients over 35 years of age having palpable breast lumps presenting in the outpatient department of general surgery, ESI Hospital Basaidarapur New Delhi. The duration of study was from May 2007 to June 2009 and a total of 100 cases were studied. The cases were taken consecutively without any selection bias provided they satisfied the eligibility criteria. Each patient was subjected to a detailed history, clinical breast examination, diagnostic mammography and FNAC.

The eligibility criteria of patients under study were:

Inclusion criteria
1. Age 35 years and above
2. Palpable breast lump of variable duration.

Exclusion criteria
1. Patients having breast abscess
2. Patients having fungating growth, breast lumps with skin ulceration or necrosis
3. Pregnant females.

Data Analysis
In this study, the results of each modality was divided in three groups: benign, suspicious and malignant. The tests which showed result as suspicious were taken as malignant. The test results were analyzed separately in concordant and non concordant cases.

The descriptive statistic of different study variable was presented in terms of frequency (%) for categorical variables and minimum, maximum and mean for quantitative variables such as age, duration of lump. The measurement of agreement "Kappa statistic was calculated for each test (CBE , FNAC) against gold standard (HPE) and its statistical significance by chi square test .The level of

Parameter			Sensitivity	Specificity	PPV	NPV	Accuracy	Kappa Statistic.	p-value
Histology		T	TP / TP+FN	TN / TN+FP	TP / TP+FP	TN / TN+FN			
B	M								
Benign 51	9	60							
Malignant 10	30	40	76.9%	83.6%	75%	85%	81%	0.603	p< .001
Total 60	40	100							

Symmetric Measures

		Value	Asymp. Std. Error	Approx. T	Approx. Sig.
Measure of Agreement	Kappa	0.603	.084	5.644	.000
N of Valid Cases		100			

[Table/Fig-1]: Sensitivity, specificity positive predictive value, negative predictive value and accuracy of clinical breast examination
The sensitivity, specificity and diagnostic accuracy of CBE in this series was 76.9%, 83.6% and 81% respectively. The measurement of agreement "Kappa Statistic was calculated and found to be 0.603. p-value was less than .001 which is highly significant

Parameter			Sensitivity	Specificity	PPV	NPV	Accuracy	Kappa Statistic.	p-value
Histology		T	TP / TP+FN	TN / TN+FP	TP / TP+FP	TN / TN+FN			
B	M								
Benign 55	2	57							
Malignant 6	37	43	94.9%	90.2%	86%	96.5%	92%	0.835	p< .001
Total 60	40	100							

Symmetric Measures

		Value	Asymp. Std. Error	Approx. T	Approx. Sig.
Measure of Agreement	Kappa	0.835	.061	7.955	.000
N of Valid Cases		100			

[Table/Fig-2]: Sensitivity, specificity positive predictive value, negative predictive value and accuracy of Diagnostic mammography

Parameter			Sensitivity	Specificity	PPV	NPV	Accuracy
Histology		T	TP / TP+FN	TN / TN+FP	TP / TP+FP	TN / TN+FN	
B	M						
Benign 58	2	60					
Malignant 1	36	37	94.7%	98.3%	97.3%	96.6%	96%
Total 59	38	97					

[Table/Fig-3]: Sensitivity, specificity positive predictive value and accuracy of fine needle aspiration cytology
Out of 100, in 3 patients cytological grading came as C1 and therefore those 3 cases were not included in computation of results of FNAC. Out of 3 C1 category 2 were found to be benign on histopathology and 1 was malignant

Parameter			Sensitivity	Specificity	PPV	NPV	Accuracy
Histology		T	TP / TP+FN	TN / TN+FP	TP / TP+FP	TN / TN+FN	
B	M						
Benign 51	0	51					
Malignant 0	29	29	100%	100%	100%	100%	100%
Total 51	29	80					

[Table/Fig-4]: Sensitivity, specificity positive predictive value, negative predictive value and accuracy of concordant triple test
It is clear from this table that when all elements (CBE, DM, FNAC) of triple test are in concordance with each other, the test is 100% accurate

age group (4th decade) followed by 27.5% in 51-60 years age group (5th decade).

Evaluation of clinical diagnosis
The results of clinical breast examination were compared with that of histopathological diagnosis and sensitivity and specificity, positive predictive value and diagnostic accuracy was calculated and tabulated [Table/Fig-1].

Evaluation of Diagnostic Mammography
The results of diagnostic mammography were given as per BI –RADS grading. For the computation of Triple Test B3 and B4 were grouped together as suspicious.

The sensitivity, specificity, positive predictive value and diagnostic accuracy of mammography was calculated and was found to be 94.9% , 90.2% , 86% and 92% respectively [Table/Fig-2].

Evaluation of FNAC
The results of FNAC were grouped into 5 categories in accordance with NHS BSP guidelines. In this study the suspicious results were considered as malignant for the purpose of calculating the statistical value.

In our series, there were 3 cases which yielded inadequate material for cytological evaluation inspite of repeated aspirations and were grouped as C1. All 3 cases were subjected to open biopsy to reach to a definite diagnosis. Of the three, one subsequently proved to be malignant (intra lobular carcinoma) and 2 other turned out to benign (fibroadenosis with extensive fibrosis and fibroadenosis with hyaline change. The rate of C1 or unsatisfactory aspirates in this series was 3%.The sensitivity, specificity, positive predictive value and diagnostic accuracy of FNAC was 94.7%,98.3%,97.3%,96.6% respectively [Table/Fig-3].

Evaluation of Triple Assessment
Out of 100 cases, triple test was concordant (all three test either benign or malignant) in 80 cases.When triple test was concordant,it had100% sensitivity and 100% positive predictive value ,100% specificity and 100% negative predictive value [Table/Fig-4].Triple test was non concordant in 20 cases. Out of 20 non concordant cases 9 were found benign and 11 were malignant on histopathological analysis. It was seen that in non concordant cases FNAC was most accurate (2 false negative and 0 false positive).

DISCUSSION
In present study the highest incidence of malignancy noted was 30% in 41-50 years age group (4th decade) followed by 27.5% in 51-60 years age group (5th decade). This is in accordance to other reports published from Indian subcontinent which show that ca breast in Indian population occurs a decade earlier than western group [6,7].

In our study the sensitivity of clinical examination was found to be 75%, specificity was 83.3%, positive predictive value (PPV) of 75%

statistical significance was taken as p less than or equal to .05 . The data was analyzed by using SPSS statistical software version 16.0.

The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of each test was calculated individually and as combined.

RESULTS
Out of 100 patients enrolled in this study, 60 cases were benign and 40 cases were of malignant breast disease.The age of patients with carcinoma breast in the series varied from 35 years to 70 years. Youngest patient of carcinoma in the series was of 35 years and the oldest patient of carcinoma breast in this series was 70 years. The highest incidence of malignancy noted was 30% in 41-50 years

and diagnostic accuracy of 80%. Most of the published series have shown the sensitivity of clinical breast examination as 80-90 % and specificity as 60-70% [8-10] [Table/Fig-5].

The sensitivity, specificity and diagnostic accuracy of clinical examination in diagnosis of palpable breast lump observed in this

S.No.	Studies	Sensitivity	Specificity	Positive Predictive Value	Diagnostic Accuracy
1.	ZVI Kaufmann et al., [8]	89%	60%	66%	74%
2.	Ibrar Ahmed et al., [9]	83.33%	76.4%	84.2%	
3.	Gabraiele Martelli et al., [10]	82%	63%		
4.	Our Study	75%	83.3%	75%	80%

[Table/Fig-5]: Correlation of our study with previous studies

study was found better than most of published series probably because most of our patients in this study presented with lump size of more than 2 cm. This finding also highlights the fact that in our country especially in low socio-economic class there is still a lack of awareness about breast cancer, the incidence of detection of early breast cancer is still very low with most cases being detected with T2 and above stages.This finding also shows that CBE can be used as a clinical screening tool in third world countries where cost of screening mammography can be a limiting factor.

In this study the sensitivity and specificity of diagnostic mammography was found to be 94.9% and 90% which is in accordance with the most of published series [11-14].

The rate of C1 or unsatisfactory aspirates in FNAC in our series was 3%. The incidence of unsatisfactory aspirates in literature range from 1.7% for palpable lesions to 34.5% for all breast lesions [15]. Some of the contributing factors for C1 smears are intrinsic properties of tissue mass (sclerosis, fibrosis, cell type), difference in aspirate techniques and lack of needle guidance technique for smaller lesions. The sensitivity, specificity, positive predictive value and diagnostic accuracy of FNAC was 94.7%,98.3%,97.3% and 96.6% respectively.

John Vittoet et al., [16] in their study found the sensitivity specificity and positive predictive value of FNAC as 96%, 100%, and 100% respectively.

ZVI Kaufmann et al., [8] found FNAC to be 93% sensitive, 97% specific and with a positive predictive value of 96%.Katherine T Morris et al., [14] found the sensitivity and specificity of FNAC as 92% and 96% respectively. Medina Franco et al., [17] found the positive predictive value and specificity of FNAC as 100% and sensitivity as 82.6%.

Study by Virginia K et al., [18] showed the sensitivity and specificity of FNAC as 96% and 94%. Thus the sensitivity specificity, positive predictive value and diagnostic accuracy of FNAC in diagnosis of palpable breast lump observed in this series is similar to those of published series.

In the present study, the sensitivity, specificity, positive predictive value and negative predictive value of concordant triple Test was 100 %. In non concordant it was seen that FNAC was most accurate (2

false negative and 0 false positive). Similar results were obtained by John Vitto et al., [16], Ibrar Ahmed et al., [9] and Gabriele Martille et al., [10] in cases where triple test was concordant.

Mande N et al., [19] in a study of 200 patients with breast lump found the sensitivity, the specificity and accuracy of triple test to be 100%.

Thus it is clear that when the triple test is concordant it has high diagnostic accuracy approaching 100% and can be considered as 'standard diagnostic method' to evaluate palpable breast lump. Definitive treatment can be started if the triple test is concordant for benign or malignant.

CONCLUSION

Use of triple test in this study resulted in 100% sensitivity when each element was interpreted as malignant and 100% specificity when each element was interpreted as benign proving that the triple test can safely be used for definite treatment for breast lump. When the Triple Test is nonconcordant, additional measures like biopsy will be required.The study also highlights the fact that CBE is quite effective as a screening tool for carcinoma breast and is still relevant as an investigation especially in developing countries where cost constraints can be an issue.

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