

TRIPLE ASSESSMENT IN THE DIAGNOSIS OF BREAST NEOPLASMS- WHAT HAPPENS IN NON-CONCORDANT CASES?

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ABSTRACT: INTRODUCTION: Triple assessment and its components are widely used for the evaluation of breast neoplasms. The efficacy of these modalities varies in different studies. While its usefulness is usually studied for the concordant cases, analysis of the non-concordant cases is all the more important. **OBJECTIVES:** To assess the diagnostic value of triple assessment and its components for the evaluation of palpable breast neoplasms with an emphasis on non-concordant cases. **METHODS:** The study included 105 cases of breast neoplasms over 18 months. Mammograms were reported using BI-RADS and cytology smears using the five scale reporting system. The clinical, mammographic and cytologic diagnoses were compared with histopathologic diagnosis. **RESULTS:** Clinical examination (CE) showed the highest sensitivity (86%) and negative predictive value (88.33%) while FNAC (Fine Needle Aspiration Cytology) was highly specific (100%). By using various combinations of the individual modalities, sensitivity was found to be highest (97.06%) when CE and mammography were concordant and specificity was maximal (100%) when FNAC concurred with either CE or mammography. The triple assessment was concordant in 73.33% of cases with 100% accuracy. Among the non-concordant cases, when at least one method diagnosed malignancy, 84% of them were confirmed on biopsy. Also, CE had the highest chance of detecting malignancy either singly or in combination with either of the other two modalities in non-concordant cases. **CONCLUSIONS:** Multidisciplinary approach enhances the accuracy of diagnosing breast neoplasms and when one of the diagnostic methods is indicative of malignancy, further investigations must be performed to rule out the same.

KEYWORDS: Breast neoplasms, Efficacy, Non-concordance, Triple assessment.

INTRODUCTION: Fine needle aspiration cytology (FNAC) and mammography along with clinical examination (CE) have become an integral part the evaluation of breast lumps. The main purpose of the investigations is to pre-operatively confirm malignancy and to avoid unnecessary surgery in benign conditions. de Ferietas et al. found the sensitivity and specificity of breast FNAC to range between 87% and 99%.^[1] A metaanalysis study showed sensitivity and specificity of FNAC to range between 78-100% and 76-100% respectively.^[2] Similarly, mammography has been shown to have a sensitivity of about 78% and a specificity range of 80 to 97%.^[3-4]

By combining CE, mammography and FNAC, triple test helps reduce the error in diagnosis. By scoring the various components of triple assessment (TA), Arden Morris et al.^[5] showed that patients can be triaged for proper management, thereby reducing the rate of open biopsies. Though various studies have looked into the concordance rates of TA, what exactly happens in the non-concordant cases is seldom mentioned.

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As mammography was recently started in our institute and data on the efficacy of TA was not available from this part of the country, we undertook this study to assess its usefulness in our setting. We also tried to look into the non-concordant cases in detail.

AIMS AND OBJECTIVES: This study was undertaken with the following objectives:

1. To evaluate the efficacy of triple assessment and its individual components (clinical examination (CE), FNAC and mammography) in the diagnosis of palpable breast neoplasms
2. With a special emphasis on the study of non-concordant cases.

METHODS AND METHODOLOGY: The study was approved by institutional ethical committee. This study was conducted over a period of 18 months and included patients who presented with palpable breast lump to the surgery outpatient department. A total of 105 cases presenting with palpable breast neoplasm during the period and who willingly gave the consent were included in the study. After obtaining consent all of them were evaluated sequentially with CE, mammography and FNAC. Mammograms were reported by the radiologists as per Breast Imaging Reporting and Data System (BI-RADS).^[6] For statistical analysis, categories 2 and 3 were considered benign and categories 4 and 5 were considered malignant. Category 6 was excluded from the study. Cytology smears were reported using the 5-scale reporting system of the UK Royal College of Pathologists.^[7] C2 and C3 were considered benign and C4 and C5 were considered malignant for statistical analysis. Histopathologic diagnosis was considered gold standard and only neoplastic lesions were included.

TA and various combinations of the three modalities were studied for their combined diagnostic efficacy. For this purpose, the tests were said to be concordant only if all the modalities under study were either benign or malignant for one particular case.

For statistical analysis, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated.

RESULTS: Over the study period, there were 105 patients with palpable breast neoplasm who were evaluated by TA. The age ranged from 15 to 72 years (mean age of 38.02 years). The maximum number of lesions were in the age group of 21-30 years (28.57%) and the least in >60 years of age (4.77%). Majority were females (98.10%) with only 2 male patients. Right breast was more commonly involved than the left (55.24% vs 42.86%) and 2 cases showed bilateral involvement.

The upper outer quadrant was most commonly involved (49.07%). There were 3 patients with involvement of multiple quadrants and 6 with involvement of all the quadrants of breast. The 6 cases included two cases each of male breast carcinoma and benign phyllodes tumour and one case each of malignant phyllodes tumour and invasive lobular carcinoma.

Histopathologically, there were 55 (52.38%) benign and 50 (47.62%) malignant neoplasms. Among the benign neoplasms, fibroadenoma was the most common while infiltrating ductal carcinoma—not otherwise specified (IDC-NOS) was the most common malignancy. (Table 1).

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On mammography, five cases were reported normal (i.e. category1) which included 2 cases each of fibroadenoma and DCIS ((Ductal Carcinoma in Situ) and 1 case of IDC-NOS.

In cytology, the aspirates of only 2 cases were inadequate (i.e. C1) giving an inadequacy rate of 1.90%. Of these cases, one was of Benign Phylloides Tumor (BPT) where aspirates yielded only fluid and the other were IDC-NOS where FNAC yielded necrotic material with few scattered tumour cells.

EFFICACY OF VARIOUS MODALITIES IN THE EVALUATION OF BREAST NEOPLASMS

(TABLE 2): In the present study, CE had sensitivity of 86% and specificity of 96.36%. The sensitivity and specificity for mammography were observed to be 76% and 90.91% respectively and the same for FNAC were 81.63% and 100% respectively.

The various combinations of the components of TA were evaluated for their combined diagnostic accuracy. The sensitivity and PPV were 97.06% and specificity and NPV were 98% for CE+mammography. The sensitivity, specificity, PPV and NPV for CE+FNAC were 92.31%, 100%, 100% and 94.64% respectively and the same for mammography+FNAC were 96.87%, 100%, 100% and 98.04%.

TRIPLE ASSESSMENT IN THE EVALUATION OF BREAST NEOPLASMS: Of the 105 cases, 77 cases (73.33%) were concordant and 28 cases (26.67%) were non-concordant for TA. Out of the 77 concordant cases, 49 were benign and 28 were malignant. When components of TA were concordant, there were no false positive or false negative cases.

NON CONCORDANT CASES IN TA (TABLE 3): The non-concordant cases included 22 malignant and 6 benign neoplasms.

Among the benign cases, there were 4 fibroadenomas, one each of BPT and central duct papilloma. The cytology was benign in all the cases except for BPT, where it was inadequate. Two of the fibroadenomas had BIRADS category 1 on mammography.

All the DCIS were non-concordant and the malignant non-concordant cases included 16 IDC-NOS and one case each of mucinous carcinoma, malignant phylloides tumor and invasive papillary carcinoma. One IDC-NOS had inadequate aspirate while one IDC-NOS and two DCIS were category 1 on mammography.

There were five malignant non-concordant cases which had only one malignant parameter, where CE and mammography had the highest chance of detecting it (40% each). When two parameters were malignant, CE and FNAC could pick up 50% of cases followed by CE+mammography and mammography+FNAC. 21 of the malignant non concordant cases had at least one of the modalities as malignant. Only one case of DCIS had category1 on mammography with clinical impression was of papilloma and C3 (probable benign) cytology.

In non-concordant neoplasms, when two methods were malignant, 94.12% were confirmed by histopathology and when only one was malignant, 62.50% were confirmed. (Table 4)

DISCUSSION: The demographic profile of our study population was similar to that observed by others.^[8-10] In our study, benign neoplasms were more common than malignant and their

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distribution was similar to other studies.^[11,12] However, Mande et al.^[8] had 67% malignant cases while Char-Hong Ng et al.^[13] reported only 8.2% malignancies.

According to the guidelines laid down by the Royal College of Pathologists, the inadequacy rate for FNAC for the diagnosis of breast lumps should be less than 15%.^[14] Yoo Duk Choi, et al.^[15] found 7.4% of the smears unsatisfactory for diagnosis, 64.3% of which were malignant on histopathology. In the present study, the inadequacy rate of FNAC was 1.90% which is very low as compared to other studies.^[9,16,17] This could be due to the fact that our patients usually present late in the disease course, when the lump is easily palpable or when there are secondary skin changes, or associated pain. In such situations, the chance of aspirating diagnostic material obviously becomes high. Out of the two cases, one turned out to be malignant.

We observed that CE showed the highest sensitivity (86%) and NPV (88.33%) while FNAC was highly specific (100%) with maximum PPV (100%). All the parameters were lowest with mammography. While this result concurred with some studies,^[8] yet others got differing results. Some studies found FNAC to be the most sensitive and specific^[11,17,18] while mammography was found highly effective by others.^[19,20] These varied results probably reflect the availability of expertise in an institute as cytological and radiological interpretations are dependent on training and experience. In our institute, mammography was started recently, which could be the reason for the reduced sensitivity and specificity of the same.

By using various combinations of the diagnostic modalities, the present study showed that the diagnostic accuracy improved significantly. Sensitivity was found to be highest (97.06%) when CE and mammography were considered together and specificity was maximal (100%) when FNAC was combined either with CE or mammography. Similar observations was made by Abdulrahman Saleh Al-Mulhim et al.^[18]

In the present study, 73.33% of cases were concordant for TA. The concordance rate for TA varied from about 50 to 99% in other studies.^[12,18,21] When the triple test was concordant, there was no discrepancy with the histopathological report which was also observed by many others.^[12,18,19] But Philip J Drew et al. found the sensitivity to be 99.2% with a marked reduction in the specificity and PPV (59.1% and 67.4% respectively).^[20] Similar decrease in specificity (75%) was also observed by Kaufman Z et al.¹¹

78.57% of our non-concordant cases were malignant. For malignant non-concordant lesions, CE stood out as the best modality to detect malignancy and when two parameters were used, CE and FNAC could pick up 50% of cases. For benign non concordant lesions, FNAC was the most efficient. Ahmed I et al.^[12] found FNAC as the single most important investigation for benign and malignant lesions, either by itself or in combination while we found CE the most helpful.

Also seen in this study was the fact that when at least one of the three diagnostic methods was malignant, 84% of such cases were confirmed by histopathology. Overall, for non-concordant cases, clinical examination turned out to be the best modality to predict the nature of lesion.

CONCLUSION: With this study we conclude that when combinations of tests are used for assessment of breast neoplasms, the diagnostic efficacy increases and TA highly accurate.

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However, when the tests do not agree with each other, CE and cytology can predict the nature of lesion better. Also when one of them is malignant, the patient should be further evaluated.

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Histopathological diagnosis	Number of cases	Percentage (%)
Fibroadenoma	48	45.72
Benign phyllodes tumor	6	5.71
Central duct papilloma	1	0.95
DCIS (Ductal Carcinoma in Situ)	3	2.86
IDC-NOS	43	40.96
Invasive lobular carcinoma	1	0.95
Mucinous carcinoma	1	0.95
Invasive papillary carcinoma	1	0.95
Malignant phyllodes tumor	1	0.95
Total	105	100

Table 1: Distribution of cases based on histopathology

Parameters			Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Clinical diagnosis	HP diagnosis		43/50	53/55	43/45	53/60	(53+43)/105
	B	M					

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B	53	7	60					
M	2	43	45					
T	55	50	105	86	96.36	95.56	88.33	91.43
Mammography	HP diagnosis		T	38/(47+3) *	50/(53+2) *	38/41	50/59	(50+38)/105
	B	M						
B	50	9	59					
M	3	38	41					
T	53	47	100					
FNAC⁺	HP diagnosis		T	40/49	54/54	40/40	54/63	(54+40)/103
	B	M						
B	54	9	63					
M	0	40	40					
T	54	49	103					
Clinical diagnosis + mammography	HP diagnosis		T	33/34	49/50	33/34	49/50	(49+33)/84
	B	M						
B	49	1	50					
M	1	33	34					
T	50	34	84					
Clinical diagnosis + FNAC	HP diagnosis		T	36/39	53/53	36/36	53/56	(53+36)/92
	B	M						
B	53	3	56					
M	0	36	36					
T	53	39	92					
Mammography + FNAC	HP diagnosis		T	31/32	50/50	31/31	50/51	(50+31)/82
	B	M						
B	50	1	51					
M	0	31	31					
T	50	32	82					
	HP		T	28/28	49/49	28/28	49/49	(49+28)/77

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Triple assessment	diagnosis							
	B	M						
B	49	0	49	100	100	100	100	100
M	0	28	28					
T	49	28	77					

Table 2: Evaluation of various diagnostic modalities for breast neoplasms

*Five cases were mammographically normal; out of these, 3 cases were proven malignant and 2 were benign on histopathology. All these cases are included for statistical analysis.

†Aspirates from 2 cases were inadequate in FNAC and are excluded for statistical analysis.

B – Benign; HP- Histopathologic; M – Malignant; T – Total

Number of methods with Malignant diagnosis	Number of cases		Percentage of malignancy confirmed (%)
	Suspected	Confirmed	
2	17	16	94.12
1	8	5	62.50
At least 1	25	21	84

Table 3: Distribution of malignant neoplasms in non-concordant cases

Diagnosis on			Histopathology diagnosis
Clinical examination	Mammography (BIRADS category)	FNAC	
Fibroadenoma	5	C3	IDC-NOS
Fibroadenoma	5	C5	IDC-NOS
Carcinoma	3	C5	IDC-NOS
Papilloma	1	C3	DCIS
Fibroadenoma	1	C2	Fibroadenoma
Fibroadenoma	1	C2	Fibroadenoma
Carcinoma	4	C1	Benign phyllodes tumor
Carcinoma	5	C2	IDC-NOS
Papilloma	4	C2	Central duct papilloma
Carcinoma	5	C3	IDC-NOS
Carcinoma	2	C3	IDC-NOS
Carcinoma	5	C3	IDC-NOS
Carcinoma	3	C5	IDC-NOS
Carcinoma	5	C3	IDC-NOS
Carcinoma	3	C5	IDC-NOS

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Carcinoma	3	C5	IDC-NOS
Carcinoma	2	C2	Fibroadenoma
Fibrocystic disease	3	C5	IDC-NOS
Fibroadenoma	4	C3	IDC-NOS
Carcinoma	5	C3	DCIS
Carcinoma	2	C1	IDC-NOS
Fibroadenoma	4	C2	Fibroadenoma
Carcinoma	1	C5	DCIS
Carcinoma	2	C5	Mucinous carcinoma
Carcinoma	3	C5	Malignant phyllodes tumor
Fibrocystic disease	5	C4	Invasive papillary carcinoma
Carcinoma	1	C5	IDC-NOS
Fibroadenoma	4	C4	IDC-NOS

Table 4: Non concordant cases on triple assessment

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