Original Research Article

Accuracy of triple assessment as a clinical tool in detection of carcinoma breast

Akshdeep, Amritpal Singh Bhatia*, Manjit Singh Uppal

Department of Surgery, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India

*Correspondence:
Dr. Amritpal Singh Bhatia,
E-mail: as3136204@gmail.com

ABSTRACT

Background: One of the commonest clinical presentation of breast diseases is a lump. A definite diagnosis of any breast lump is very important to decide the course of treatment. The study evaluated that how effectively "triple assessment" helps in diagnosing carcinoma breast.

Methods: The present study is a diagnostic study which was conducted on 50 patients. Each patient underwent a detailed history, CBE, mammography and FNAC. In this study the results of each examination were divided into three groups: benign, suspicious and malignant. The final result was compared with the HPE findings and diagnostic accuracy of triple assessment was assessed.

Results: Total 86% of cases were found to be malignant on triple assessment and 14% cases were found out to be malignant later on histopathology. Among the malignant lesions, infiltrating ductal carcinoma had the lead 96%, followed by lobular carcinoma 1 case. Sensitivity, specificity, PPV, NPV for clinical breast examination was 97%, 100%, 66%, 100%. Sensitivity, specificity, PPV and NPV for imaging was 88.89%, 100%, 100%, 88.46%. Sensitivity, specificity, PPV for FNAC was found to be 87.76%, 100%, 100%.

Conclusions: The TT was concordant in 43 cases (86%). Sensitivity of triple assessment was 95%, specificity was 100% and negative predictive value to be 100%. The TT was concordant in 43 cases (86%). In rest of the 7 lesion which were non-concordant 6 were suspicious of malignancy and 1 was probably benign entity which were later on proven to be malignant lesions by histopathology. Sensitivity of triple assessment was 95%, specificity was 100% and negative predictive value to be 100%.

Keywords: Breast lump, Triple assessment, FNAC, Mammography

INTRODUCTION

Breast cancer accounts for one in four women considering all types of cancer. It is most common reason for cancer death among women and most commonly diagnosed cancer worldwide. In India the age standard incidence rate of breast malignancies varies 9-32 per one lakh women.[1] A suspicion of malignant mass needs that care must be integrated among clinicians in several specialties. A cumulative approach with proper breast imaging, pathologists and breast surgeons can reduce

unnecessary tissue biopsies and can help diagnose breast cancer quickly and efficiently.

Currently clubbing of three tests i.e. clinical examination, radiological imaging (mammography, ultrasonography) and pathology are together called as triple assessment test is used to diagnose all breast lumps. It is simple, less traumatic and cost effective. When the three assessments are performed adequately and produce concordant results, diagnostic accuracy can reach even 100%. It is better to image the breast before tissue sampling as changes due to

the tissue sampling may confuse, change, obscure the imaging results. Ultrasonography can help differentiate between solid and cystic masses of breast. Ultrasonography is considered superior to mammography when it comes to image the dense breasts.[2]

The triple assessment has been adopted as method usually practiced in the developed world since its earliest evaluation. Clinical diagnosis of carcinoma breast has high diagnostic error when not combined with other diagnostic modalities.

Triple assessment as the name indicates, includes three components, physical examination, imaging (mammography or ultrasound), and biopsy (FNAC and core biopsy). These different methods of investigation when used separately give less reliable results, but when combined accuracy and chances of correct diagnosis increases. A triple assessment cumulative approach or clinics are a great example for a multistep or multidisciplinary approach as it involves surgeons/physicians to whom first patient presents, clinical pathologists and radiologists or sonographers as core team. In such a setting where all three investigations are available under one roof inter-professional communication must be promoted and practiced to reach the most likely diagnosis.[3]

The triple test score (TTS) was developed to help physicians interpret equivocal or inconclusive triple test results. A three-point scale is used to score each component of the triple test (1=benign, 2=suspicious, 3=malignant). A TTS of 3 or 4 indicates a benign lesion; a TTS of 6 or more raises the chances of malignant lesion that may require surgical intervention. Tissue diagnosis is advised in patients with a TTS of 5 to reach a final diagnosis. Discordant results or results that cannot be evaluated require excisional biopsy for proper diagnosis.[4]

At present triple assessment has become a gold standard approach to any patient with breast mass. Timely examination of breast with lump by a surgeon or physician can prevent further delay in reaching the diagnosis. Any kind of breast disorder or lesion is psychologically disturbing as mostly patients are cancer phobic and breast related diseases also alter the woman's self-image of body thus adding on to more psychological trauma.[5] So timely counseling and examination can decrease the trauma and undergoing triple assessment in case of any suspicious lump and timely treatment.

The motive of making a patient of breast lump to undergo triple assessment is to not miss the most dreaded cause that is breast cancer. So proper approach to any case of breast lump or any other breast complain which indicates towards possibility of breast cancer is necessary. The clinician should correlate the pathological results with the clinical and imaging findings of the patient. Most women show no signs of cancer on these tests, but those who show a positive result for one or more tests should be advised to undergo further investigations. Usually, it is recommended to take complete responsibility of triple assessment results evaluation by a single treating surgeon. It helps to establish a better correlation from the results and symptoms.

To understand and interpret the results of triple assessment a clinician must be thorough with the type of symptoms with which a carcinomatous lesion might present and correct interpreting of mammography comes with a good understanding of various anatomical features of normal architecture of breast and specific distortions caused by various breast lesions.

Objectives

Objectives were to 1) find the sensitivity and specificity of triple assessment in diagnosing carcinoma breast 2) to study the efficacy of triple assessment with that of HPE (gross specimen) in diagnosing carcinoma breast 3) to find limitations of triple assessment (CBE+ Mammography+ FNAC).

METHODS

The present study is a prospective study conducted on patients over 35years of age having a palpable undiagnosed breast lump presenting in outpatient department of general surgery, SGRDIMS, Amritsar from Dec 2018 to Jan 2020. The cases were consecutively taken without any selection bias provided they satisfy the selection criteria. Then each patient will be subjected to a detailed history, clinical breast examination, diagnostic mammography and FNAC. The sample size of the study is 50 cases. Sample size was calculated using G-Power software.

The eligibility criteria of patients under study was as follows:

Inclusion criteria

Inclusion criteria were 1) age 35 years and above 2) palpable breast lumps of variable duration

Exclusion criteria

Exclusion criteria were 1) patients having breast abscess 2) patients having fungating growth, breast lump with skin ulceration and necrosis 3) pregnant females 4) open biopsy and HPE performed prior to presentation to our hospital

Method of evaluation –Patients were subjected to following investigations 1) clinical examination of breasts 2) mammography of both breasts 3) FNAC 4) Histopathological examination [excision biopsy/lumpectomy/BCS/MRM]

Clinical examination

It was done under following heads 1) patient position were examined in sitting position with hands by sides and hands above head, supine position, recumbent position and leaning forward position 2) the three middle fingers with metacarpophalangeal joint slightly flexed were used and the pads of these fingers were used for palpation.

Mammography (x-ray/USG)

It was done on patients before FNAC. The results were categorized according to BIRADS (Breast Imaging Reporting and Data System) score. Both craniocaudal and mediolateral views were taken.

FNAC (fine needle aspiration cytology)

The following equipments were used 1) 10ml disposable plastic syringe with locking tip 2) 22gauge disposable needles 3) 95% ethanol 4) spirit swabs 5) glass slides

Technique

Techniques used were 1) cleaning of skin (sterilization) 2) application of surface anesthetic (optional) 3) introduction of the needle 4) needle maneuver under negative pressure 5) withdrawal of the needle 6) immediate slide preparation and fixation 7) repetition of the procedure as indicated

Data analysis

In this study, the results of each modality were divided in three groups: benign, suspicious and malignant. The tests which showed suspicious result were taken as malignant. The test results were analyzed separately in concordant and non-concordant cases. With collection of data and after calculation of "Kappa statistic" for each test in triple test against gold standard (HPE) and its statistical significance was taken up by calculating 'p'. The sensitivity, specificity, positive predictive value, negative predictive value of each test was calculated individually and as combined.

Source of data

The study was conducted in the department of General Surgery at SGRDIMS, Amritsar on 50 patients who presented to OPD with an undiagnosed breast lump. All the patients were subjected to triple assessment, and further results were compared with final histopathological diagnosis.

Apart from clinical examination, routine blood and urine examination, including biochemical analysis was carried out. Subjects were covered under this study only after obtaining informed consent.

RESULTS

Distribution of all patients accoding to the age group

In present study female patients presenting with palpable breast masses which are suspicious on examination in the surgery department were studied. Maximum number of cases i.e. 17 (34%) were found to occur in 51-60 years of age group, followed by 16 cases (32%) in 41-50 years of age group. Only one case was found in more than 70years of age group (Table 1).

Table 1: Age-group distribution.

Age group (years)	No. of cases	%age
30-40	7	14.0
41-50	16	32.0
51-60	17	34.0
61-70	9	18.0
>70	1	2.0
Total	50	100.0

Distribution of patients in relation to the histopathology of various suspicious breast masses

In the present study histopathology evidence gained from breast tissue sample after MRM the 96% cases were found out to be infiltrating ductal carcinoma and 2% were found out to be lobular carcinoma and 2% were found to be micro-invasive ductal carcinoma (Table 2).

Table 2: Results of breast lesions on HPE.

Conclusion on HPE	No. of cases	%age
Lobular Carcinoma	1	2.0
Infiltrating Ductal Carcinoma	48	96.0
Micro-invasive Ductal Carcinoma	1	2.0
Total	50	100.0

Distribution of patients on basis of clinical breast examination

On the basis of clinical breast examination 94% of patients breast lump were suspicious, only 4% of patients breast lump felt benign on breast examination and 2% were malignant with features of fixity and skin dimpling (Table 3).

Table 3: Grading of breast lesions on CBE.

CBE Grade	No. of cases	%age
Benign	2	4.0
Suspicious	47	94.0
Malignant	1	2.0
Total	50	100.0

Distribution of patient on basis of imaging [mammography]

On basis of mammographic findings 48% of patients were having malignant lumps and 46% of patients had suspicious lumps and only 2% were probably benign on mammography (Table 4).

Table 4: Grading of breast lesions on imaging.

Imaging grade	No. of cases	%age
Benign	3	6.0
Suspicious	23	46.0
Malignant	24	48.0
Total	50	100.0

Distribution of patient on basis of FNAC

On the basis of FNAC findings 86% of cases were found out to be having carcinoma breast and 12% were found to have atypical cells and were needed to be investigated further and only 2% were having benign cystic disease (Table 5).

Table 5: Results of breast lesins on FNAC.

FNAC	No. of cases	%age
Atypical cells	6	12.0
Benign cystic disease	1	2.0
Carcinoma breast	43	86.0
Total	50	100.0

Distribution of patients on all the four modalities [CBE+mammography+FNAC and histopathology]

On the basis of the results of each investigational modality total number of 50 patients were subdivided into three categories for each as follows: benign, suspicious and malignant. FNAC was out to give more similar results as compared to histopathology whereas clinical breast examination tends to vary in results as compared to histopathology when considered alone.

Table 6: Distribution of type of lesions on CBE, imaging, FNAC and HPE.

Category	CBE	Imaging	FNAC	HPE
Benign	2	3	1	0
Suspicious	47	23	6	1
Malignant	1	24	43	49

On CBE, the one case was labelled as malignant as patient had fixed lump along with fixed axillary lymph nodes which were indicative of malignancy. Similarly, on imaging cases were divided into these categories on basis of BIRADS scoring. On FNAC 1 benign case was cystic breast entity and 6 cases have atypical cells and 43 were confirmative. On HPE 49 cases were confirmative of malignancy whereas the case labelled as cystic lesion on

FNAC came out to be cystic breast disease along with few hyperchromatic cells on HPE and repeat biopsy was advised. Excision biopsy was performed in that case which later on came out to be microinvasive ductal carcinoma. Thus 1 case was considered suspicious on histopathology.

Grading of clinical breast examination versus histopathology report

In clinical breast examination, 47 patients were found out to be suspicious or highly suggestive of malignancy, which was confirmed on histopathology. However, 2 cases were graded as benign which were found out to be malignant on histopathology. 1 case was graded as malignant on clinical breast examination as patient had axillary fixed, immobile nodes with fixed breast lump. So, in the present study sensitivity, specificity, positive predictive value for clinical examination is found out to be 97%, 100%, 100% (Table 7).

Table 7: CBE vs HPE

HPE	CBE			
	M	S	B	Total
Malignant	1	47	2	50
Suspicious	0	0	0	0
Total	1	47	2	50

Sensitivity: 97.90, Specificity: 100.00, Negative predictive value: 66.66, Positive predictive value: 100.00

Grading of imaging versus histopathology reports

24 cases of malignancy and 3 cases of benign pathology were reported on imaging. However, 23 cases were graded as suspicious, which were reported as malignant on histopathology. Grading on imaging was on basis of BIRADS and results were compared with histopathology. So, in case of imaging, sensitivity was 88.9% and specificity was 100%, positive predictive value was 88.5% and negative predictive value is 100% (Table 8).

Table 8: Imaging Vs HPE.

HPE	IMAGING			
	M	S	B	Total
M	24	23	3	50
S	0	0	0	0
Total	24	23	3	50

Sensitivity: 88.89, Specificity: 100.00, Negative predictive value: 100.00, Positive predictive value: 88.46

Grading of FNAC versus histopathology reports

As per the results of FNAC 43 cases were found to be malignant, 6 were found to be suspicious and 1 was found to be benign. Whereas as per histopathology report the 6 cases suspicious (atypical cells) on FNAC were found out to be malignant on histopathology and 1case found benign on FNAC was found out to be micro-

invasive. So, sensitivity of FNAC was found to be 87.76% and specificity was 100% (Table 9).

Table 9: FNAV Vs HPE.

HPE	FNAC			
	M	**S**	**B**	**Total**
M	43	6	1	50
S	0	0	0	0
Total	43	6	1	50

Sensitivity: 87.76, Specificity: 100.00, Negative predictive value: 14.29, Positive predictive value: 100.00

Results of triple test for 50 palpable breast lumps in diagnosing carcinoma breast as comparative to histopathology

The TT was concordant in 43 cases. 6 cases on TT were found out to be suspicious which were later proven to be malignant on histopathology. 1 case found benign on triple test came out to be micro-invasive on histopathology. Therefore, TT was found out be non-concordant in total of 7 cases out of 50. However, in all 6 suspicious cases out of various elements of triple test, FNAC was considered most accurate. The detailed description of grading, triple test score and final diagnosis on histopathology of all concordant and non-concordant cases is given (Table 10).

Table 10: Triple test vs HPE results.

TT results	No. of lesions		HPE results	
			Suspicious	**Malignant**
Concordant	Malignant	43	0	49
	Benign	1	0	0
Non concordant	Suspicious	6	1	0

Sensitivity: 95.90, Specificity: 100.00, Negative predictive value: 100.00, Positive predictive value: 33.33

DISCUSSION

Breast cancer is most common cancer in India both in rural and urban setup. The number of patients presenting with breast lump had increased considerably during the recent years due to increased health awareness and medical facilities. Most of the patients were themselves able to discover the lesion of breast and visit the doctor for assessment with potential fear of breast cancer. The main objective of the present study was to analyze the accuracy of diagnosing breast cancer on basis of clinical breast examination, imaging technology and fine needle aspiration cytology. This study gives a view about how effectively breast cancer can be diagnosed by triple test.

A total of 50 female patients presenting to the surgery department with breast lump of suspicious nature were studied by all the three components of triple test. All the

cases underwent lumpectomy/quadrantectomy/BCS/ Modified radical mastectomy with axillary lymph node dissection for histopathological confirmation of diagnosis. The TT components [clinical breast examination, imaging technology, fine needle aspiration cytology] were categorized as benign, suspicious and malignant. Each component is designated as benign, suspicious and malignant and rated as 1, 2 and 3 respectively. TTS is the sum of these scores with a minimum score of 3 [3-4 is concordant benign] and a maximum score of 9 [6-7 is concordant malignant], 5 is having intermediate risk needing further evaluation before any definitive treatment.

TT was considered concordant when all three elements indicated benign or all three elements indicated malignant. The findings were correlated as triple assessment and compared with histopathology reports. The youngest patient in the study was 35 years and oldest was 82 years.

Distribution of all patients according to age group

In the present study female patients presenting with palpable breast masses in surgery department were studied. Maximum number of cases i.e. 17 (34%) were found to occur in 51-60 years of age group, followed by 16 cases (32%) in 41-50 years of age group. Only one case was seen in more than 70 years of age group.

Distribution of patients in relation to the histopathology of breast masses

In the present study on basis of triple assessment 43 cases [86%] were found malignant, 6 [12%] cases were suspicious and 1 [2%] case was benign.

Similar results were found in the study of Steinberg JL4 in which following triple assessment 79% cases revealed breast carcinoma. Though number of suspicious lesions are less as compared to our study.

The higher rate of malignant lesion in our study due to a smaller number of specialized hospitals and most of the patients with suspicious breast lumps are referred to specialized surgery department like ours.

Incidence of various lesions in relation to the histopathology reports

In the present study, malignant breast disorders diagnosed on histopathology 48 cases [96%] were found out to be infiltrating ductal carcinoma, 1 case [2%] was lobular carcinoma and 1 case [2%] was of microinvasive ductal carcinoma.

These findings are similar to the study of Khokher et al in which infilterating ductal carcinoma was found in 91% of total malignant cases followed by lobular carcinoma and then by mucinous carcinoma.[6]

Age wise distribution of various lesions

The majority of cases, that is 48 out of 50 patients of carcinoma breast diagnosed on histopathology were infiltrating ductal carcinoma [96%] mainly found in age group of 51-60 years and lobular carcinoma was found only in 2% of cases [1 case] only in 82 years old female patient and micro-invasive ductal carcinoma was also found in only 1 case of age 48 years.

Similar results were seen in the study of Sulhyan et al in which maximum number of malignant cases were in females more than 50 years of age.[7]

Clinical breast examination versus histopathology reports

In present study sensitivity, specificity, positive predictive value for clinical examination is found to be 88.89%, 100%, 88.46%. On clinical breast examination out of 50 examined cases majority 47 cases [94%] were categorized as suspicious of malignancy.

However, a very slight variation is seen in the study of Ravi et al in which the sensitivity and specificity for clinical breast examination as 94.5%, 87.7% respectively.[8]

Imaging versus histopathology reports

In case of imaging, sensitivity was 88.89% and specificity was 100%. Positive predictive value was 88.46% and negative predictive value was 100%. On mammographic examination 23 cases were categorized as suspicious and 24 cases were categorized as malignant on basis of BIRADS scoring.

Our results were in close proximity with other studies. Shetty et al. in which sensitivity for combined mammographic and sonographic assessment were 100% and specificity was 80.1%.[9]

FNAC versus histopathology reports

Sensitivity, specificity, positive predictive value and negative predictive value was found to be 95.9%, 100%, 100% and negative predictive value of 33.3% respectively. 6 cases [12%] on FNAC were categorized as suspicious because of presence of atypical cells and 43 cases [86%] were categorized as malignancy of breast.

Similar results were seen in study of Ariga et al in which it was found that FNAC had a sensitivity of 99%, positive predictive value of 99%, specificity of 99% respectively.[10]

Results of triple test for 50 palpable breast lumps and histopathology confirmation

The TT was concordant in 43 cases [86%]. In rest of the 7 lesion which were non-concordant 6 were suspicious of malignancy and 1 was considered as probably benign entity which were later on proven to be malignant lesion by histopathology on repeat biopsy. In the all non-concordant cases, where at least one of the elements was considered benign, FNAC was most accurate with 0 false positive and just 1 false negative case.

Overall sensitivity of triple assessment was 95%, specificity was 100% and negative predictive value to be 100%. More or less similar results were seen in the study of Jan et al in which the concordance for the triple assessment was 99.3%, positive predictive value was 93.3%, negative predictive value was 100%, sensitivity was 100% and specificity was 99.3%.[11]

Limitations

The study shows that when TT is concordant, final treatment may be ensued without open biopsy but in non-concordant cases, FNAC stands as single most important investigation. However due to its false negative results, other components of triple test need to be employed to enhance its efficacy and diagnostic yield in diagnosing carcinoma breast.

CONCLUSION

Thus, we conclude from this present study that triple assessment in the patients whom all the elements were malignant or suspicious, the diagnosis was certain enough to proceed with definite treatment without delay. The TT was concordant in 43 cases [86%]. In rest of the 7 lesion which were non-concordant 6 were suspicious of malignancy and 1 was probably benign entity which were later on proven to be malignant lesions by histopathology. Sensitivity of triple assessment was 95%, specificity was 100% and negative predictive value to be 100%.

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