

Role of fine needle aspiration in diagnosing breast lesions

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ABSTRACT

Objective: To determine the diagnostic efficacy of breast fine needle aspiration (FNA), using 72 cases that were having both FNA cytology and follow-up histology diagnosis. The study results were compared with results of 27 other studies in the literature. A review of literature regarding the additional benefits of performing "Triple Test" in increasing the cumulative diagnostic accuracy of FNA is also included.

Methods: Our study group consisted of 72 FNA cytologies of female breasts performed at our institution and followed by a histological diagnosis. The following parameters: Sensitivity, specificity, accuracy, predictive values, false positive and negative fraction rates were determined to establish the diagnostic efficacy of the breast FNA.

Results: The sensitivity of FNA procedure was 98.4% and specificity 60%, with the predictive value for positive

diagnosis 93.9% and for negative diagnosis 85.7%. The overall diagnostic accuracy was 93%. The false positive fraction was 6% and the false negative fraction was 14.2%. The false positive and false negative cases were recorded as having a minimal effect on patient management, as all the false positive and negative diagnosis' were picked up at intra operative frozen sections, and hence no over or under treatment was given to the patients due to these FNA results.

Conclusion: Fine needle aspiration breast biopsy is an efficient tool and yields a definitive diagnosis, and its use for routine diagnosis must be encouraged since it has high positive (93.9%) and negative (85.7%) predictive values.

Keywords: Breast lesions, breast neoplasm, aspiration biopsy.

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Fine needle aspiration (FNA) of palpable breast lesion is a fast and cost effective method that can be carried out as an office procedure, requires little special equipment, causes minimal morbidity and has excellent patient acceptance.¹⁻¹⁹ Many investigations have reported there results using FNA to diagnose breast masses;²⁰⁻²⁹ this is an accepted diagnostic method.^{22,30,31} However, many of these studies originated in effective diagnostic expert laboratories with experienced cytopathologists^{22-24,26,30-35} in Europe, and no report has been locally reported in this region. This study evaluated the sensitivity, specificity, positive predictive value, negative predictive value, false positive fraction (FPF) and false negative

fraction (FNF) of 72 FNAs of breast lesions with a subsequent excisional biopsy diagnosis. In order to compare our study with the literature, we are also including the information from 27^{2-6,8,9,11,13,14,16,17,19,25-29,35-44} other reports using the same statistical criterion.

Methods. Seventy-two cases having both cyto-histological diagnoses were studied. These cases were performed as a preoperative screening and diagnostic test at King Abdul-Aziz University Hospital, Jeddah, Kingdom of Saudi Arabia. All the smears for these cases, stained with geimsa stain, hematoxiline and eosin staining and papanicolaous

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stain were reviewed. The cytological examination made by light microscope classified the cases as positive, suspicious, negative or unsatisfactory. The criteria for positive classification were the presence of many isolated and loose aggregates of atypical cells with large nuclei having prominent nucleoli and high nuclear/cytoplasmic ratio and fulfilling the malignant criteria. Suspicious cases were those in which the cells had morphologic features of malignancy but there was an inadequate number of cells to evaluate or if the cells were atypical, or both, but had insufficient cytological abnormalities to allow a final diagnosis. The criterion for negative cases was the presence of only normal appearing cells. Unsatisfactory aspirates were those not representative in regard to sampling, cellularity, and quality of the smear or staining, or both. The results for various diagnostic outcomes were calculated on the basis of following criterion: 1. The suspicious and positive cytological findings were considered as true positives when subsequent histological examination revealed a carcinoma; 2. Tumors with negative cytological findings were considered true negatives when subsequent histological examination revealed a benign lesion; and 3. Unsatisfactory diagnostic cases were excluded from the analysis. Results of cytological finding were compared with the histological diagnosis of each lesion. The relationship of results was analyzed to determine the utility or relative desirability of aspiration cytology. The following values concerning the diagnostic accuracy were calculated in our study and compared with 27 other studies in literature.^{2-6,8,9,11,13,14,16,17,19}

1. Sensitivity, the probability of a positive FNA result given that the patient has carcinoma;
2. Specificity, the probability of negative FNA result given that the patient has benign lesion;
3. Positive predictive value, the probability of having carcinoma when the results of FNA are positive;
4. Negative predictive value, the probability that a tumor is benign when the results of FNA are negative;
5. False positive fraction, the fraction of all benign lesion reported as positive by FNA;
6. Fine negative fraction, the fraction of all carcinomas reported as negative on FNA; and
7. Accuracy, the proportion of true results (namely true positive + true negative) among all results.

Results. A total of 72 FNAs of the breast were evaluated. Fifty-two specimens were classified as positive, 7 as negative, 13 as suspicious and 3 as unsatisfactory (not included in total numbers). Out of 52 positive cases, 4 were proved negative on histology (namely false positive = 4), and of 7 lesions diagnosed on FNA as negative, 6 were confirmed as benign, and one as malignant on excisional biopsy (false negative=one). Thirteen of the 13 suspicious specimens taken at FNA proved to be malignant on

Table 1 - Statistical analysis of fine needle aspiration diagnosis.

Diagnosis	n (%)
True positive	61 (84.7)
False positive	4 (5.5)
False negative	1 (1.3)
True negative	6 (8.3)
Total	72 (99.8)
n - number	

Table 2 - Performance and predictive values of fine needle aspiration diagnosis.

Values	%
Sensitivity	98.4
Specificity	60
Positive predictive value	93.9
Negative predictive value	85.7
False positive fraction	6.1
False negative fraction	14.2
Unsatisfactory rate	4
Global efficiency	93

histology, so they were considered as true positives (true positive =13+48=61) (**Table 1**).

Thus FNA detected cancer with sensitivity of 98.4%, specificity of 60%, Positive predictive value of 93.9%, negative predictive value of 85.7%, FPF of 6.1%, FNF of 14.2% and overall accuracy of the test was 93% (**Table 2**). **Table 3** shows the comparison of the data published in the literature and the results obtained in this study.

Discussion. Fine needle aspiration biopsy is an efficient tool for diagnosing breast lesions. The sensitivity and specificity data for breast FNA diagnosis of malignancy in the literature shows a broad range of sensitivity from 66-100% with specificity of 82-99% (**Table 3**). The results of the present study allow a reliable evaluation of the accuracy of FNA in the diagnosis of breast lesions. The comparison between 27 studies of the literature using the same criterion to calculate accuracy values insures a real evaluation of FNA of the breast as a diagnostic tool.

In our study FPF was 6.1% much closer to the means in the series analyzed in **Table 3** (7.1%). It seems that as with literature fibroadenoma is one of the most frequent causes of pitfall in our study.^{1-5,7,18,19} Among the 4 false positive cases there were 2 fibroadenoma cases, one case of fibrocystic change and one of sclerosis. Our FNF was 14.2%, somewhat higher than the mean rate in the literature (9.5%). We had only one false negative case and the cause of this false negative diagnosis was due to hypocellular smear with some interpretive error by the pathologist. In our standardized analysis of the literature (**Table 3**), that value varied from 0-32.6%. The major causes of a false negative diagnosis discussed in the literature are the lack of experience in either aspiration or interpretation of smears, geographic miss by the needle, small tumor size, deep location, well differentiated carcinomas, fibroses and association with a fluid or benign specimen.^{5,17-19} The specificity we calculated in our study (60%) was lower than the mean analyzed in **Table 3** (93.6%). We could not find any constructive explanation for our low specificity value, but it could be due to a small study size or the FPF.

Fine needle aspiration of the breast has some unavoidable limitations, mainly due to poor sampling; poor cellular yield of mammary tumors with fibrotic stroma, poor preservation and difficulty in cytologic differentiation of atypical benign lesions and well-differentiated malignant neoplasms. Because the sensitivity and specificity rates of FNA are not always 100%, the technique should be used with this limitation in mind.^{2-6,8,9,11,13,14,16,17,19} These unavoidable limitations of FNA can be further reduced if we take into account the clinical and radiological findings as well as making it a triple test. The "triple test" for palpable breast lesions consists of physical examination, mammography, and fine-needle aspiration. There are many studies in literature that have shown that the triple test was 100% accurate in the diagnosis of palpable breast lesions when all 3 elements were concordant.⁴⁵⁻⁵¹ However, FNA is the most reliable element of the triple test in cases where the elements of the test were nonconcordant.⁴⁶

The incidence of unsatisfactory reports in other series ranges from 0-57.2% with a mean of 13.4% (**Table 3**). Poor cellularity is the main reason for inadequate smears, and it is mostly due to the aspiration of small or desmoplastic carcinomas and ill-defined fibrocystic or inflammatory lesion. Unfortunately lack of experience and persistence on the part of the aspirator are some other causes of unsatisfactory material for analysis.³ There were 3 cases of unsatisfactory aspirates (4%) in the present study and the reasons of the unsatisfactory cases in our study were mainly hypocellular smears.

Additionally, implementing the triple test which consists of physical examination, mammography, and

FNA will further increase the cumulative sensitivity and specificity of the final diagnosis. The triple test can be coordinated by any of the patient's physicians either, the cytopathologist, the clinician coordinating the patient's case or the collaboration of both physicians. If there is a discrepancy between any of these results, then it is recommended to have a surgical biopsy and clinical follow-up. Fine needle aspiration performed by well-trained, highly experienced physicians and in combination with the triple test will achieve the most accurate results in the diagnosis of palpable breast lesions. A lot of studies have discussed the high accuracy and cost effectiveness of the FNA with triple test in management of breast lesions.⁴⁵⁻⁵¹ In one paper by Vetto et al⁵⁰ showed that the triple test was 100% accurate in the diagnosis of palpable breast lesions when all three elements were concordant. Cost analysis revealed that elimination of confirmatory open biopsy in such cases and also in cases in which the FNA and one other element of the test had a suspicious or malignant result, could yield an average per-case cost savings of up to \$1,412 compared to triple test followed by routine confirmatory open biopsy.⁵⁰ Triple test scoring can also help in evaluating suspicious cases, according to Morris et al⁴⁶ masses that score 6 points or higher are malignant and should undergo definitive therapy; masses that score 4 points or lower are benign and may be clinically followed up. Only those masses that score 5 points require open biopsy.⁴⁶

In another large study by Schuhmann et al⁴⁹ who analyzed 608 malignant and 224 benign cases by triple test to find out whether the triple diagnostic test can replace surgical biopsy and thereby reduce the number of unnecessary biopsies. In his study all lesions triple-diagnosed as malignant were histologically proved to be malignant, namely there were no false positive results. The rate of false negative results was found to be within the range reported for false negative results in fresh frozen sections. Based on these results he stated that the dogmatic statement "every palpable mass in the breast must be excised" should be replaced by the recommendation "every palpable mass must be assessed and clarified". A great number of retrospectively unnecessary biopsies can be avoided by a systematic use of the triple diagnosis. The diagnostic safety of this method is close to that of open biopsy. In all cases where positive or negative concordant triplets are found, histological confirmation by biopsy can be avoided. Patients with benign lesions can be thoroughly followed up by repeated physical and radiological examinations. Patients with triple diagnostic malignant results can be adequately treated. Lesions for which triple diagnosis yields neither benign nor malignant, must be biopsied: This is also necessary in all cases with suspicious findings in mammography without a

Efficacy of breast fine needle aspiration ... *Mansoor & Jamal*

Table 3 - Analytical comparison of sensitivity, specificity, positive predictive value, negative predictive value, false positive fraction, false negative fraction and unsatisfactory rate in 27 studies from the literature.

Author	n	Sensitivity	Specificity	PPV	NPV	FPF	FNF	Unsatisfactory
Beltrani et al ⁶	44	72.7	100	100	70	0	30	18.1
Norton et al ²⁵	49	82.3	78.5	82.3	78.5	17.7	21.5	36.7
Ibrahim et al ^{**}	72	98.4	60	93.9	85.7	6.1	14.2	4
Rangwala et al ³⁷	78	77.7	100	100	95.9	0	4.1	15.7
Zuk et al ⁴⁴	87	80.7	93.3	84	89.3	16	10.7	10.2
Atamdede and Isaacs ³	100	97	95.4	94.2	97.6	5.8	2.4	22
Lannin et al ³⁸	100	92.8	100	100	96.9	0	3.1	9
Gelabert et al ¹¹	107	96.7	100	100	80	0	20	1.8
Bulter et al ⁸	113	98	93.4	92.7	98.2	7.3	1.8*	-
Pisa et al ³⁹	129	85.2	85.2	67.4	94.1	32.6	5.9*	-
Kern ¹⁷	161	79.5	88.2	90.2	75.9	9.8	24.1*	-
Vetrani et al ⁴⁰	265	96.5	93.9	95.1	95.5	4.9	4.5	5.2
Collaco et al ³⁵	276	92.1	98.6	99.4	82.1	0.6	17.9	6.2
Alvarez et al ²	280	97.7	93.1	87.1	98.8	12.9	1.2	12.8
Wollenberg et al ²⁸	321	61	100	100	89.3	0	10.7	4.3
Griffith et al ¹³	335	87.3	86.3	88	85.5	12	14.5*	-
Watson et al ⁴¹	350	77.9	99.5	97.8	93.8	2.2	6.2	25.7
Dominguez et al ³⁶	450	93.5	95.7	93.5	95.7	*	*	*
Guimaraes et al ¹⁴	496	87.6	99.3	98.8	92.5	1.2	7.5	57.2
Ciatto et al ⁹	534	97.4	99.3	98.6	98.7	1.4	1.3	11.4
Palombini et al ⁴²	674	96.9	89.8	96.5	90.9	3.5	9.1	2.5
Bell et al ⁵	1145	77.6	97.1	90.2	93.3	9.8	6.7	13.6
Barrows et al ⁴	1283	82.2	86	91	87.5	8.9	12.5	21.2
Martelli et al ⁴³	1708	83	96.1	95.5	84.8	4.5	15.2	23.8
Horgan et al ¹⁶	2000	85.3	99.2	95.2	97.4	4.8	2.6	12.9
Sheikh et al ²⁶	2623	100	98.2	87.9	100	12.1	0	0
Zajdela et al ²⁹	2772	96.1	95.3	97.2	93.5	2.8	6.5	5.5
Kline ¹⁹	3545	90.1	98.1	84.5	98.8	15.5	1.2	0.1
Mean	-	88.3	93.6	92.9	90.7	7.1	9.5	13.4

n - number, PPV - positive predictive value, NPV - negative predictive value, FPF - false positive fraction, FNF - false negative fraction
* - some studies do not mention unsatisfactory rates

palpable mass, if the equipment for stereotactic or ultrasound- guided biopsies is not available.⁴⁸

Now a new modification in this test has been introduced called "Modified Triple Test" (MTT: physical examination, ultrasonography instead of mammography, and FNA) that has appeared to be

more effective and accurate in young breast lesions.⁴⁷ It is now highly recommended to utilize the 3 diagnostic parameters of cytology, clinical findings and radiology together as the "triple test", to achieve the best diagnostic accuracy in breast FNAs and patient management.^{1-9,45-51}

In conclusion, this study described the experience of FNA breast at our institute. The results were compared favorably with those reported in literature. We have also included the review of literature regarding the additional benefit of performing "Triple test" in increasing the cumulative sensitivity and specificity of FNA in final diagnosis. We conclude that FNA biopsy especially if combined with triple test is an efficient tool for screening and diagnosing breast lesions when performed properly. We desire to encourage wider and more confident use of FNA in routine practice of diagnosing breast lesions.

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