Role of the Triple Test in the Evaluation of Breast Mass

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الخلاصة

أجريت هذه الدراسة المستقبلية على ٢١٠ من المرضى الإناث واللواتي كان لديهن عقدة في الثدي, في ردهة الجراحة, في مستشفى الديوانية التعليمي خلال مدة سنتين وذلك من شهر كانون الثاني ٢٠١٣ الى شهر كانون الاول ٢٠١٤. ولقد تم في هذه الدراسة تقييم حالة كل مريضة من خلال إجراء الفحص الثلاثي والذي يشمل الفحص السريري, فحوصات السونار والأشعة , والفحص الخلوي , ومن ثم تمت مقارنة نتيجة كل فحص من هذه الفحوصات مع التشخيص النهائي والذي تم الحصول عليه من خلال الفحص النسيجي. كانت عقدة الثدي أكثر شيوعا في العقد الرابع من العمر بنسبة ٤٠,٤٧٪ من المرضى, وكان ألم الثدي أكثر الأعراض المصاحبة لعقدة الثدي بنسبة ٣٠,٩٥٪ من المرضى. كان الورم الليفي هو أكثر العقد الحميدة شيوعا (٤١,٩ ٪) وكان سرطان الثدي القنوي هو أكثر العقد الخبيثة شيوعا (٢٧,١٤ ٪). كان أكثر عناصر الفحص الثلاثي دقة هو الفحص الخلوي بمعدل تطابق بلغ ٠,٨٩ بينما كان الفحص السريري هو أقلها دقة بمعدل تطابق بلغ ٠,٦٢. كان معدل التطابق للفحص الثلاثي بالمقارنة مع الفحص النسيجي ٠,٩٤ (والذي يعني تطابق كامل تقريبا) وهو أعلى من معدلات التطابق لعناصر الفحص الثلاثي منفردة. كانت درجة الحساسية للفحص الثلاثي ٩٣,٨٥٪, درجة الدقة ٩٩,٣١٪, قيمة التكهن الايجابية ٩٨,٣٨٪,قيمة التكهن السلبية ٩٧,٣٪,درجة الدقة الكلية ٩٧,٦٢٪,وهذه المؤشرات هي أعلى من مؤشرات عناصر الفحص الثلاثي منفردة. ولذلك يمكن استخدام الفحص الثلاثي كفحص دقيق وأمين لغرض التعامل مع المريضات اللواتي لديهن عقدة في الثدي وكذلك لغرض تشخيص سرطان الثدي.

Abstract

This prospective study was carried out on 210 female patients with a diagnosis of breast mass admitted to the surgical unit of Al-Diwaniya Teaching Hospital over a period of 2 years from January 2013 to December 2014. Each patient was assessed by the triple test which includes physical examination, imaging studies , and fine needle aspiration cytology (FNAC). The results of each modality of the triple test were classified as benign, suspicious or malignant and then compared with the final diagnosis obtained by the histopathological examination. Breast mass was more common in the fourth decade of life (40.47 %), and the most common associated clinical feature was pain in 30.95 % of cases. Fibroadenoma was the most common benign breast mass (41.9 %), while invasive ductal carcinoma was the most common malignant breast mass (27.14 %). The most accurate element of the triple test was FNAC with

a concordance rate of 0.89 (almost perfect agreement),while physical examination was the least accurate element with a concordance rate of 0.62(substantial agreement). The concordance rate of the triple test was 0.94 (almost perfect agreement) and it was higher than that of any modality used in the triple test. The sensitivity of the triple test was 93.85 % , specificity 99.31 % , positive predictive value (PPV) 98.39 %, negative predictive value (NPV) 97.30 % , and accuracy 97.62 % , and again these figures were higher than those of the elements of the triple test.So that the triple test can be safely used as an accurate and least invasive diagnostic test in the evaluation of patients with breast mass and to detect patients with breast cancer .

Introduction

The female patients present with a variety of complaints in the breast like mastalgia , nipple discharge , cystic leasions , and more commonly a lump[1] . One-fourth of women suffer from breast disease in their life time[2,3].Palpable breast masses are common and usually benign , but efficient evaluation and prompt diagnosis are necessary to rule out malignancy[4] . Breast masses have a variety of aetiologies, benign and malignant. Fibroadenoma is the most common benign breast mass, while invasive ductal carcinoma is the most common malignancy[5]. Breast cancer is the most common cancer and the second leading cause of cancer deaths in women[6]. There are various modalities for the diagnosis of a breast lump such as mammography, ultrasonography ,fine needle aspiration cytology but none of them are without impunity. Delay can lead to deprivement of curative treatment where as aggressive management can expose the patient to unwarrented surgeries and hence psychological and social trauma to the patient[7]. The general approach for the evaluation of breast mass or other symptoms suspicious of malignancy has become formalized as triple assessment which involves a combination of clinical assessment (history and examination),imaging studies (usually ultrasound and or mammography) and tissue sampling taken for either cytological or histopathological analysis[8]. When the triple assessment is performed adequately and produces concordant results (all benign or all malignant) , the diagnostic accuracy approaches 100%. However 40% of cases are non-concordant and require open biopsy[9,10].

Aim of Study

To evaluate the role of the triple test (a combination of clinical assessment , imaging studies , and fine needle aspiration cytology) in the diagnosis of breast mass.

Patients and Methods

This prospective study was conducted at Al-Diwaniya Teaching Hospital, Department of Surgery from January 2013 to December 2014. A total number of 210 female patients who have presented with a breast lump were included in this study. Each patient was assessed by the triple test which includes: physical examination (PE), mammography (MG) and /or ultrasonography (US), and FNAC (fine needle aspiration cytology). The results of each modality of the triple test were reported as either benign, suspicious or malignant, and then compared with the final diagnosis which was the histopathological results of tissue specimens obtained from open biopsy , lumpectomy or mastectomy. All cases were examined carefully looking for clinical features of malignancy, and afterwards referred to a sonographist for ultrasonography of both breasts and axillae. Mammographic examination was done for all patients aged 35 years and more with two standard views(craniocaudal and mediolateral oblique) for the affected breast and craniocaudal view for the opposite breast. FNAC of breast mass was done by means of a number 21 gauge needle attached to 5 ml syringe. Statistical analysis was carried out using the kappa test to find the concordance rate for each test in comparison with the histopathological examination[11] . The results of the triple test and its components were statistically analyzed using the following measures:sensitivity,specificity,positive predictive value (PPV), negative predictive value (NPV), and accuracy.

Results

Breast mass was more common in the fourth decade of life (40.47%) as shown in table (1). The age range was from 15 to 75 years, and the mean of age was 36.19 years.

Table (1): Age distribution of patients.

Age (years)	No.	%
11.20	13	6.19
21-30	51	24.28
31-40	85	40.47
41-50	35	16.66
51-60	14	6.66
61-70	9	4.28
>70	3	1.42
Total	210	100

Table (2) : Associated clinical features with the breast mass.

Associated feature	No.	%
Pain	65	30.95
Skin tethering	50	23.80
Nipple retraction	32	15.23
Nipple discharge	55	26.19
Redness of skin	23	10.95
Peau d'orange	45	21.42
Pukering with nodules	15	7.14
Palpable axillary lymph nodes	28	13.33

Table (3) : Ultrasonic findings of breast mass.

Finding	No.	%
Fibroadenoma	95	45.23
Fibrocystic disease	35	16.66
Inflammatory conditions(mastitis, breast absces	18	8.57
Duct ectasia	2	0.95
Solid mass	16	7.61
Solid mass with irregular margins	25	11.90
Loss of normal architecture	15	7.14
Cyst	4	1.90
Total	210	100

Mammographic examination was done only for patients aged 35 years and more, and the total number was 122 patients.

Table (4) : Mammographic findings of breast mass.

Finding	No	%
Well circumscribed mass with regular margins	48	39.34
Density leasion with microcalcification	34	27.86
Density leasion with irregular margins and spiculations	15	12.29
Density leasion with microcalcification,irregular marg and spiculation	25	20,99
Total	122	100

Table (5) : Results of FNAC.

FNAC	No	%
Fibroadenoma	92	43.80

Fibrocystic disease	38	18.09
Inflammatory conditions (mastitis, abscess)	18	8.57
Invasive ductal carcinoma	57	27.1
Invasive lobular carcinoma	5	2.38
Total	210	100

Table (6) : Results of histopathology.

Histopathology	No.	%
Fibroadenoma	88	41.90
Fibrocystic disease	30	14.28
Inflammatory conditions (mastitis, absces	16	7.61
Duct ectasia	2	0.95
Duct papilloma	4	1.90
Lipoma	3	1.42
Fat necrosis	2	0.95
Invasive ductal carcinoma	57	27.14
Invasive lobular carcinoma	5	2.38
Carcinoma insitu	2	0.95
Malignant phyllodes tumour	1	0.47
Total	210	100

Table (7) : Distribution of patients with breast mass in relation to the results of histopathology.

Histopathology	No.	%
Benign	145	69.04
Malignant	65	30.95
Total	210	100

Table (8) : Physical examination versus histopathology results (the suspicious cases were considered as malignant cases).

Histopathology	Physical examination			
	Benign	Suspicious	Malignant	Total
Benign	125	12	8	145
Malignant	15	30	20	65
Total	140	42	28	210

Concordance rate (kappa value) = 0.62 (substantial agreement).
The interpretation of kappa test is as follows:

Kappa value	Agreement
0.01 – 0.20	Slight agreement
0.21 – 0.40	Fair agreement
0.41 – 0.60	Moderate agreement
0.61 – 0.80	Substantial agreement
0.81 – 0.99	Almost perfect agreement

Table (9) : Ultrasound (US) versus histopathology results (the suspicious cases were considered as malignant cases).

Histopathology	Ultrasound			
	Benign	Suspicious	Malignant	Total

Benign	136	4	5	145
Malignant	13	21	31	65
Total	149	25	36	210

Concordance rate (kappa value) = 0.75 (substantial agreement).

Table (10) : Mammogram (MG) versus histopathology results (the suspicious cases were considered as malignant cases).

Histopathology	Mammogram			
	Benign	Suspicious	Malignant	Total
Benign	54	5	5	64
Malignant	8	12	38	58
Total	62	17	43	122

Concordance rate (kappa value) = 0.70 (substantial agreement).

Table (11) : FNAC versus histopathology results (the suspicious cases were considered as malignant cases).

Histopathology	FNAC			
	Benign	Suspicious	Malignant	Total
Benign	142	3	0	145
Malignant	7	10	48	65
Total	149	13	48	210

Concordance rate (kappa value) = 0.89 (almost perfect agreement).

Table (12) : Triple test (TT) versus histopathology results (the suspicious cases were considered as malignant cases).

Histopathology	TT			
	Benign	Suspicious	Malignant	Total
Benign	144	1	0	145
Malignant	4	3	58	65
Total	148	4	58	210

Concordance rate (kappa value) = 0.94 (almost perfect agreement).

Table (13) : Analysis of triple test (TT) and its components.

Measur	PE	US	MG	FNAC	TT
Sensitivity	76.92 %	80 %	86.21 %	89.23 %	93.85 %
Specificity	86.21 %	93.79 %	84.38 %	97.93 %	99.31 %
PPV	71.43 %	85.25 %	83.33 %	95.08 %	98.39 %
NPV	89.29 %	91.28 %	87.10 %	95.30 %	97.30 %
Accuracy	83.33 %	89.52 %	85.25 %	95.24 %	97.62 %

Discussion

The breast mass was more common in the fourth decade of life (40.47 %) as shown in table (1). Malignant breast mass was mostly found above the age of 40 years. In our study, 49 patients out of 65 patients with malignant breast mass (75.38 %) were above this age, so carcinoma of breast is typically a disease of old aged patients . Contrary to that , benign breast mass was seen in younger age group. In this study, 120 patients out of 145 patients with benign breast mass (82.75 %) were found among women aged 20 – 40 years. These findings were seen in other studies [12,13] . Pain was the most common associated feature in 30.95 % of patients (Table 2) and it mainly had accompanied the inflammatory conditions (mastitis and breast abscess) and fibrocystic disease of breast , while axillary lymphadenopathy was present in 13.33 % of patients and it

was mainly associated with carcinoma. Fibroadenoma was the most common benign mass in 60.68 % of patients (88 patients out of 145 patients with benign breast mass). On the other hand, invasive ductal carcinoma was the most common malignant tumour in 87.69 % of patients (57 patients out of 65 patients with malignant breast mass), and this is in agreement with other studies [14,15,16] .

FNAC proved to be the most accurate element of the triple test with a concordance rate (Kappa value) of 0.89 which means almost perfect agreement. The sensitivity of FNAC was 89.23%, specificity 97.93 %, PPV 95.08 %, NPV 95.30 %, and accuracy 95.24 %, and these figures were higher than those of other elements of the triple test. These findings can be seen in other studies [17,18] . Ultrasound was the next most accurate element of the triple test with a concordance rate (kappa value) of 0.75 which means substantial agreement, and it was higher than that of physical examination and mammography. This can be contributed to the fact that ultrasound is an operator dependent and there is a significant overlap in the appearance of benign and malignant palpable solid breast masses. Some studies had showed the same results [19,20] . Mammography was the next accurate element of the triple test with a concordance rate (kappa value) of 0.70 (substantial agreement). Again this was connected to the overlapping features of benign and a circumscribed well defined malignant breast leasion and to the fact that dense breast tissue has been mentioned as an important obstacle in the mammographic diagnosis and a source of number of false negative results. This is in agreement with other studies [21,22] . The physical examination was the least accurate element of the triple test with a concordance rate of 0.62 (substantial agreement), and this may be due to overestimation or underestimation of malignancy.

The triple test which includes physical examination, imaging studies and FNAC had achieved the highest concordance rate (0.94) which means almost perfect agreement, the sensitivity was 93.85 %, specificity 99.31 %, PPV 98.39 %, NPV 97.30 %, and accuracy 97.62%. Again these figures were higher than those of any element alone. These findings were seen in other studies [17,19,20,21] . It is obvious that there is a great value of using the triple test to diagnose malignancy in women with breast cancer. A review of several studies showed that the triple test is consistently more sensitive than any single test alone, and it is capable of picking up 95% to 100% of cancers when at least one component is positive. When all three tests give the same result, whether positive or negative, the probability that the diagnosis is correct is about 99% [23] . The triple test is a feasible, accurate, and reliable guide with diagnostic effectiveness for the evaluation of breast mass and is equivalent and cheaper when compared to open biopsy and can be carried out in a single visit. It is obviously of great importance in reducing morbidities and expenses in breast mass evaluation by preventing unnecessary surgeries[8,10,24.25] .

Conclusions and Recommendations

The triple test can be safely used as an accurate and least invasive diagnostic test in the evaluation of patients with breast mass and to detect patients with breast cancer. Triple test is useful in diagnosing breast cancer at an earlier stage, with most of breast cancers detected at stage I or stage II. The triple test can achieve 99% or even 100% diagnosting accuracy when all elements of the test are concordant (in agreement) or when all elements of the test are either suspicious or malignant. It was found that when all elements of the test are benign, the patients can be safely observed, obviating the need for an open biopsy and the patients with suspicious masses in whom all elements of the triple test are only malignant or suspicious, the diagnosis is certain enough to proceed with definitive treatment without delay.

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