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Effectiveness of the Triple Test and Its Alternatives for Breast Mass Evaluation

Meme Kitlelerini Değerlendirmede Üçlü Test ve Alternatiflerinin Etkinliği

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ABSTRACT

Objective: The aim of this study was to investigate the specificity and sensitivity of the conventional test combination used for the evaluation of the breast masses that included physical examination (PE), mammography (MG) and fine needle aspiration biopsy (FNAB) in evaluating the malignant or benign characteristics of the masses with respect to the data in our hospital, and to determine the specificity and sensitivity of alternative test combinations in order to compare the efficacy of these combinations.

Materials and Methods: The ages and PE, ultrasonography (US), MG and FNAB findings of 636 women who were detected to have a mass breast mass in the examinations performed in the Cancer Screening Early Detection and Education Center (KETEM) between 2004 and 2009, were retrospectively investigated. Those who underwent excisional operation and follow-up were also evaluated. The specificity and sensitivity of each test or test combination were individually measured.

Results: The median age of the participants was 58. All the patients were investigated with PE, USG, MG and FNAB. Excisional biopsy was performed in 448 patients and the mean follow-up period of all patients was 3 years. The sensitivity (Sn) and specificity (Sp) of the conventional triple test (PE+MG+FNAB) were 100% and 92.1% respectively, which seemed very high. It was observed that MG+US+FNAB triple test had the most successful diagnostic feature among all combinations, with a 100% Sn and 100% Sp.

Conclusion: Although physical examination is essential for the evaluation of the possible masses within the breast, it is insufficient in evaluating the malignancy of the mass. Screening tests should definitely be performed in the presence of a mass. In women older than 40 years of age, US or MG alone may not be sufficient for the evaluation of the malignancy. We believe that performing these tests in conjunction, and supporting them by FNAB, can make the treatment of the mass be possible without the need for a more invasive procedure.

Key words: Breast mass, triple test, effectiveness

ÖZET

Amaç: Bu çalışmanın amacı, meme kitlelerini değerlendirmede klasik üçlü test olan fizik muayene (FM), mamografi (MG), ince iğne aspirasyon biyopsisi (İİAB) kombinasyonunun kitlenin benign ya da malign olup olmadığını değerlendirmedeki duyarlılık ve özgüllüğünü hastanemiz verileri doğrultusunda incelemek ve buna alternatif olabilecek farklı test kombinasyonlarının duyarlılık ve özgüllüğünü de hesaplayarak etkinliklerini karşılaştırmaktır.

Yöntem ve Gereçler: Kanser erken teşhis, tarama ve eğitim merkezinde (KETEM) 2004-2009 yılları arasında meme muayenesi yapılmış olan ve memesinde kitle saptanan 636 kadın hastanın yaş, FM, ultrasonografi (US), MG, İİAB bulguları retrospektif olarak incelendi. Eksizyon yapılan ve takibe alınan hastalar da değerlendirildi. Her bir test için ve de test kombinasyonları için ayrı ayrı olmak üzere özgüllük ve duyarlılık hesaplandı.

Bulgular: Hastaların ortanca yaşı 58 idi. Tüm hastalara FM, US, MG, İİAB yapılmıştı. Eksizyonel biyopsi 448 hastaya yapılmış olup tüm hastaların ortalama takip süresi 3 yıldı. Klasik üçlü test (FM+MG+İİAB) ile değerlendirmede duyarlılık (Sn): %100, özgüllük (Sp): %92,1 olup oldukça yüksek görülmektedir. Bu üçlü testler içinde Sn ve Sp %100 olduğu izlenen FM+MG+İİAB üçlü testinin doğru tanı koydurucu özelliğinin en yüksek olduğu görüldü.

Sonuç: Meme kitlesinin varlığını değerlendirmede fizik muayene gerekli olsa da maligniteyi değerlendirmede yetersiz kalmaktadır. Kitle varlığında mutlaka görüntüleme yöntemlerine başvurulmalıdır. Kırk yaş üstü kadınlarda tek başına US ya da MG maligniteyi değerlendirmede yeterli olmayabilir. Bu görüntüleme yöntemlerinin birlikte kullanılması ve İİAB ile desteklenmesiyle daha invaziv bir işleme gerek kalmadan kitlenin tedavisi mümkün olabileceğini düşünmekteyiz.

Anahtar sözcükler: Meme kitlesi, üçlü test, etkinlik

Introduction

Breast cancer continues to be the leading cause of cancer-related morbidity and mortality among women today. Early diagnosis and treatment, besides being life-saving, reduces morbidity (1). Various examinations, interventions or their combinations are used for early diagnosis. While an accurate and adequate examination, according to the characteristics of the lesion and the patient's age, increases the cancer detection rate, it also minimizes unnecessary tests and interventions (2).

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A solid mass detected on physical examination (PE) of a woman, over the age of 40 years, should be considered a potential cancer unless proven otherwise, and tests should be planned in order to exclude this possibility. In these circumstances, the first procedure should be mammography (MG) followed by fine needle aspiration biopsy (FNAB) (3). On the other hand, MG is not useful in women under the age of 40 due to the more dense breast pattern and these patients should be evaluated with ultrasonography. PE may be repeated at 2-4 month intervals if the mass cannot be identified with ultrasonography (US) (4). In addition, MG may be useful for women between the ages 35-40 if US reveals normal or suspicious findings. In the presence of a mass having benign properties on PE, the decision for excision or PE follow up can be made with the patients' and surgeon's shared judgment. FNAB and US should be performed in order to verify that masses, which are planned to be followed clinically, are benign (5). The Triple test (TT), which has been widely used over the past 30 years in women over 40 who have a mass on PE, is accepted as the best combination to detect the characteristics of a mass. This test is based on the correlation of these three parameters: physical examination, mammography and fine needle aspiration biopsy (5, 6). The diagnostic accuracy of the TT reaches 100% if all three tests indicate benign or malignant findings in a palpable mass (7-9). In some studies, similar accuracy rates have also been obtained in non-palpable masses (10).

In this study, the correlation of the standard TT, composed of PE, MG and FNAB, and different triple test groupings were evaluated, calculations of sensitivity and specificity were made and the effectiveness of different TTs in the assessment of breast masses were investigated.

Materials and Methods

Of the 6243 women who were admitted to the Cancer Early Diagnosis, Screening and Education Center for breast cancer screening between January 2004 and December 2009, the data of 636 patients who were detected to have a breast mass were retrospectively analysed. The history, physical examination and mammography and ultrasonography findings of the patients were evaluated. All patients had physical examinations, imaging methods and FNAB, and 448 cases who had suspicious masses and consented had excisional biopsies. Mammographic and ultrasongraphic evaluation was performed by two radiologists according to the BI-RADS criteria (11). FNAB were performed under US guidance and excisional biopsies were carried out in the General Surgery Clinic and evaluated by a pathologist. The accuracy of the triple tests was verified pathologically in the 448 patients who had excisional biopsies and with a 3-year follow up in the remainder of the patients.

Patients were evaluated with the standard TT, PE+MG+FNAB and additionally with the alternative TT combinations of PE+US+FNAB, PE+MG+US and MG+US+FNAB. The standards in the literature were used for assessment (12).

Statistical analysis

Sensitivity, specificity, positive predictive and negative predictive values were calculated from the obtained data and comparatively evaluated.

Results

The median age of the 636 women was 55 years (38-76). The individual values found for each analysis method and triple test are presented in Table 1-8.

First of all, every patient was evaluated with each diagnostic test. Then the final diagnosis with excisional biopsy and long term follow up was compared and the values of true positive (TP), false positive (FP), false negative (FN), true negative (TN), sensitivity (Sn), specificity (Sp), positive predictive (PP) and negative predictive (NP) were calculated. Cases defined as 'intermediate' in the table were the suspicious cases where the determination of benign or malignant could not be made. These cases were not included in the calculations. As none of the cases that were detected to have a mass on physical examination were considered to be definitely benign, all cases except those thought to be malignant were included in the suspicious (main) group (Table 1). Evaluations with mammography, ultrasonography and FNAB decreased the number of patients in the intermediate group but were observed to not be enough individually (Table 2-4).

Sn was 100% and Sp was 92.1% with the classical triple test (PE+MG+FNAB) and these ratios were observed to be quite high (Table 5).

Table 1. Results of physical examination

Definite diagnosis	Result			TP	FP	FN	TN	Sn (%)	Sp (%)	Pp (%)	Np (%)	A (%)
	Benign	Intermediate	Malignant									
Benign	0	567	41	567	41	0	0	100	93.10	51.85	H	H
Malignant	0	28	567									

TP: True positive, FP: False positive, FN: False negative, TN: True negative, Sn: Sensitivity, Sp: Specificity, Pp: Positive predictive, Np: Negative predictive, A: Accuracy, H: Mathematical calculation cannot be made

Table 2. Results of mammography

Definite diagnosis	Result			TP	FP	FN	TN	Sn (%)	Sp (%)	Pp (%)	Np (%)	A (%)
	Benign	Intermediate	Malignant									
Benign	503	88	3	18	3	6	503	75.00	99.41	85.71	98.82	81.92
Malignant	6	18	18									

TP: True positive, FP: False positive, FN: False negative, TN: True negative, Sn: Sensitivity, Sp: Specificity, Pp: Positive predictive, Np: Negative predictive, A: Accuracy

Table 3. Ultrasonography results

Definite diagnosis	Result			TP	FP	FN	TN	Sn (%)	Sp (%)	Pp (%)	Np (%)	A (%)
	Benign	Intermediate	Malignant									
Benign	521	65	8	33	8	0	521	100	98.49	80.49	100	87.11
Malignant	0	9	33									

TP: True positive, FP: False positive, FN: False negative, TN: True negative, Sn: Sensitivity, Sp: Specificity, Pp: Positive predictive, Np: Negative predictive, A: Accuracy

Table 4. Fine needle aspiration biopsy results

Definite diagnosis	Result			TP	FP	FN	TN	Sn (%)	Sp (%)	Pp (%)	Np (%)	A (%)
	Benign	Intermediate	Malignant									
Benign	504	90	0	31	0	0	504	100	100	100	100	84.12
Malignant	0	11	31									

TP: True positive, FP: False positive, FN: False negative, TN: True negative, Sn: Sensitivity, Sp: Specificity, Pp: Positive predictive, Np: Negative predictive, A: Accuracy

Table 5. Results of the triple test including physical examination-mammography-fine needle aspiration biopsy

Definite diagnosis	Score			TP	FP	FN	TN	Sn (%)	Sp (%)	Pp (%)	Np (%)	A (%)
	Benign	Intermediate	Malignant									
Benign	416	139	39	42	39	0	416	100	91.43	51.85	100	72.01
Malignant	0	0	42									

TP: True positive, FP: False positive, FN: False negative, TN: True negative, Sn: Sensitivity, Sp: Specificity, Pp: Positive predictive, Np: Negative predictive, A: Accuracy

Table 6. Results of the triple test including physical examination-ultrasonography-fine needle aspiration biopsy

Definite diagnosis	Score			TP	FP	FN	TN	Sn (%)	Sp (%)	Pp (%)	Np (%)	A (%)
	Benign	Intermediate	Malignant									
Benign	426	131	37	42	37	0	426	100	92.01	53.16	100	73.58
Malignant	0	0	42									

TP: True positive, FP: False positive, FN: False negative, TN: True negative, Sn: Sensitivity, Sp: Specificity, Pp: Positive predictive, Np: Negative predictive, A: Accuracy

On the other hand, the Sn and Sp for our newly described triple test, PE+MG+US and MG + US + FNAB were 100% and 91.8%, respectively (Table 6).

Of these triple tests, MG+US+FNAB was found to have the highest diagnostic accuracy with a Sn and Sp of 100% (Table 7).

Discussion and Conclusions

The examination including PE, MG and FNAB, which is known as the triple test, was first described in 1975 and in recent years is the most preferred and widely used for diagnosis of palpable masses in women over the age of 40 years (5, 6, 13, 14). Reports are available stating that the diagnostic accuracy of TT is 100% when the three parameters are benign or malignant (8, 9, 14). The same accuracy rates were also obtained with the TT in non-palpable breast masses (10). With the TT, the possibility of a mass with benign characteristics being malignant is about 0.6-0.7% and studies have shown that these masses may be followed safely without performing more invasive procedures when all three parameters are benign (6, 14-18). In the review presented by Irwig et al. (19), the sensitivity of PE, MG and FNAB were found to be 85%, 90% and 91% respectively and specificity was found to be 80%, 73% and 93%, respectively for 735 cancer cases and 1128 non-cancer cases (19). In a large series published by Ciatto et al. (20), the sensitivity of the TT was reported as being 99.7%. In the study of Steinberg et al. (14), the components of the TT were studied both individually and in combination and compared with open biopsy. Sensitivity was found to be 95.5%, specificity 100%, positive predictive value 100% and negative predictive value 98.3% in the combined TT (12). Morris et al. (4) developed TT and formed a TT score for each parameter called 1, 2 and 3 according to the mass being benign, suspicious or malignant (12). A total score of 3-4 was defined as being benign (benign triple), 5 as being benign or malignant lesions (mixed triple) and 6-9 as being malignant (malignant triple). The aim of this scoring system was to reduce the ratio of cases that would have open biopsy. 169 out of 484 patients

Table 7. Results of the TT test including physical examination-mammography-ultrasonography

Definite diagnosis	Score			GP	YP	YN	GN	Sn (%)	Sp (%)	Pk (%)	Nk (%)	A (%)
	Benign	Intermediate	Malignant									
Benign	429	123	42	42	42	0	429	100	91.08	50.00	100	74.06
Malignant	0	0	42									

TP: True positive, FP: False positive, FN: False negative, TN: True negative, Sn: Sensitivity, Sp: Specificity, Pp: Positive predictive, Np: Negative predictive, A: Accuracy

Table 8. Results of the triple test including mammography-ultrasonography-fine needle aspiration biopsy

Definite diagnosis	Score			TP	FP	FN	TN	Sn (%)	Sp (%)	Pp (%)	Np (%)	A (%)
	Benign	Intermediate	Malignant									
Benign	537	57	0	42	0	0	537	100	100	100	100	91.04
Malignant	0	0	42									

TP: True positive, FP: False positive, FN: False negative, TN: True negative, Sn: Sensitivity, Sp: Specificity, Pp: Positive predictive, Np: Negative predictive, A: Accuracy

who had a breast mass on physical examination underwent excision for histological verification and all 130 cases that had a score of 5 or above were found to be malignant. As a result of this study, the authors suggested that follow up and definite treatment may be safely planned without the need for biopsy by TT scoring in 92% of cases in the presence of a palpable mass in women over the age of 40 (12, 16). The ratio of cases having open biopsy was reduced to 8% from 40% with the standard TT scoring method (3, 12).

In our study, the sensitivity of the standard TT was found to be 51.85% and the specificity to be 91.43%. When these values were compared with the literature, the sensitivity was particularly low. This may have been due to the physicians who evaluated the patients; they may not have been especially experienced on this issue.

The most important problems with the TT are the reliability /accuracy and the applicability by different centers or clinics. Clinics that use the classical TT or the modified scoring system are recommended to evaluate the accuracy rates of each parameter of the test and interpret the TT results according to this. Clinical follow up at 6 months can be advised when all three parameters of the TT are benign (12, 16). When the mass is considered to be malignant based on PE, MG and FNAB, definite treatment (radical surgical intervention or neoadjuvant therapy with or without frozen section) may be planned. If there is any inconsistency between PE, MG, US and FNAB, in other words when a definite discrimination of benign or malignant cannot be made, definite treatment should not be planned without histopathology verification (open biopsy/intraoperative biopsy) (9, 12, 16, 21). Besides modifying the scoring of the classic TT, recently different TTs have come into question (12, 19, 22, 23). In these modified tests, US has been recommended instead of mammography in women under the age of 40 and core biopsy (classical or vacuum-assisted) has been recommended as an alternative or an addition to FNAB (12, 19).

In this study, we calculated the sensitivity and specificity of PE+US+FNAB and US+MG+FNAB combinations as possible alternatives to the classical TT. According to our findings, which are seen in detail in Table 6, 7 and 8, the combination which has the highest specificity (100%) and sensitivity (100%) is the trio of US+MG+FNAB.

According to these results, we believe that the findings of physical examinations do not provide data as reliable as those of imaging methods for the discrimination of benign or malignant masses. Certainly, physical examination is a necessary method as it is a simple, inexpensive and easily applicable method and it provides communication with the patient to detect the presence of a mass. However, its effectiveness is very low in determining whether the mass is malignant or benign. Therefore, additional imaging methods should certainly be performed in the presence of a suspicious mass on physical examination.

Imaging methods have great importance for the assessment of breast masses. US or MG may not be sufficient alone for the evaluation of malignity in women over 40. We believe that the treatment of a mass may be possible without the need for more invasive method by using imaging methods supported with FNAB findings.

Conflict of Interest
No conflict of interest was declared by the authors.

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