

The role of combined ultrasonography and mammography in the diagnosis of breast cancer in Eritrean women with palpable abnormalities of the breast

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Abstract

Objective: The objective of our study was to determine the value of combined ultrasonography and mammography in the diagnosis of breast cancer in Eritrean women with palpable abnormalities of the breast.

Methodology: In a 30 month observational study, 235 consecutive patients with palpable abnormalities of the breast underwent combined sonographic and mammographic evaluations. Review of pathologic examination records was done for the palpable abnormalities for which histopathologic and/or cytologic evaluations were done. Pathologic examination results were compared with those of combined mammographic and sonographic tests.

Results: The mean age of patients' presented with palpable breast abnormalities was 36.7 years (range 16-79 years). The breast composition based on mammographic tissue density was dense in 37.4%, heterogeneously dense in 28.9%, predominantly fatty in 17.4%, and scattered fibroglandular tissue in 16.2%. Less than two thirds (63.8%) had a benign result with 20.4% mammographically occult cases identified only at sonographic evaluation. Imaging evaluation resulted in finding of 10.6% suspicious cases. All lesions categorized as suspicious underwent biopsy with 6.4% histologically and cytologically proven to be carcinoma. One quarter of the sample had negative imaging assessment findings. One patient had lobular carcinoma which resulted in false negative findings both on sonographic and mammographic evaluation. The sensitivity and the negative predictive value for a combined sonographic and mammographic assessment were 93.8% and 99.4%, respectively. The specificity and the positive predictive values were 60% and 94.3%, respectively.

Conclusion: Cancer was diagnosed in 6.8% of the 235 women who underwent combined imaging for palpable abnormalities of the breast. Combined mammographic and sonographic assessment was shown to be very helpful in identifying benign as well as malignant lesions causing palpable abnormalities of the breast.

Introduction

Breast cancer is the most common cancer among women in the world¹. It was responsible for the deaths of more than 41,000 women and about 400 men deaths (a third of all women deaths due to cancer) in the USA in 2004^{2,3}. The cancer is more common among postmenopausal women. Some of the risk factors for developing the disease include: female gender, getting older, early menarche and late menopause, family history of breast cancer, having changes in the breast cancer-related genes BRCA1 or BRCA2, excess estrogen exposure including hormone and hormone replacement therapy.

The most common breast problems for which women consult physician are breast pain, nipple discharge and a palpable mass. Most women with these complaints have benign breast diseases. Work up of the patient with palpable breast problems includes clinical examination by the physician, imaging studies, including mammography, sonography and magnetic resonance mammography, and cytologic and histopathologic confirmations. In spite of technological advancement in developed countries, the outcome of breast cancer management is still poor. One of the reasons is the presence of micrometastasis at the time of presentation of what might appear to be a local disease. Early diagnosis and treatment of cases

is life saving.

Regardless of the type of breast problem, the goal of imaging studies is to rule out cancer and address the patient's symptoms. Breast imaging is valuable in the investigation of symptomatic breast diseases. In our country we have all the diagnostic modalities mentioned above with the exception of MR mammography.

The large number of biopsies performed for benign breast abnormalities has long been recognized as a serious problem. Excessive biopsies for benign lesions have adverse effects on the women who undergo them by increasing the cost of screening projects, causing different degrees of morbidities, and moreover, adding its effect to the barriers that keep women from using a potentially life saving procedures such as these biopsies⁵. Many women with palpable breast abnormalities undergo biopsies each year in the United States, but have benign results. As many as 89-92 % of women with breast lumps and normal mammograms who present to breast surgery practices in the United States did not have breast cancer^{6,7}. The probability of cancer based on a positive screening physical examination in the primary care environment may even be lower^{8,9}. The accuracy of clinical evaluation of palpable abnormality of the breast is limited; signs of breast cancer are not distinctive⁹, moreover, cysts

can not be reliably distinguished from solid masses on physical examination¹¹. The primary reason for performing mammography in a woman with a palpable mass is to screen the ipsilateral and contralateral breast for occult cancer. Ultrasound is most valuable for determining whether the palpable abnormality is cystic or solid¹².

In Eritrea, though, so far there is no active breast cancer screening program the proportion of breast cancer accounts for about 12.4% of all the malignancies diagnosed in 2005 from the surgical biopsy specimens (of both male & female populations) sent to the Central Health Laboratory (CHL) of the Ministry of Health⁴.

Early detection of cases depends on the presentation of women with breast symptoms and/or eliciting signs by the physician. Given the above investigation modalities and the cultural barriers that keep patients from seeking health care for palpable breast abnormalities, it is advisable to set a scientifically accurate and culturally acceptable work up plan to diagnose breast cancer earlier. Mammography or ultrasonography individually can not help exclude cancer, so we sought to determine the accuracy of combined sonography and mammography assessment in the diagnosis of breast cancer in our setting.

The objective of our study was to determine the value of combined ultrasonography and mammography in the diagnosis of breast cancer in Eritrean women with palpable abnormalities of the breast.

Materials and Methods

The study was conducted at Halibet and Orotta Hospitals and Selam Polyclinic, Asmara, Eritrea from 1st July 2004 to 31st of December, 2006. A total of 480 mammograms and 630 breast sonographic examinations were performed during a 30-month period 202 patients with 235 palpable abnormalities of the breast on mammography and/ or sonographic evaluation were included in the study. In all the patients studied, the palpable abnormalities were of sufficient clinical concern to be referred for imaging evaluation and were present at the time of the imaging evaluation. We included patients of all ages for whom the clinician was concerned enough about the palpable abnormalities.

The following information was documented at the time of initial visit on 'Mammography Patient Information Sheet': age, date of birth, address, date of initial visit, educational status, family history of cancer, use of herbs, breast self examination, site and duration of palpable abnormality, individuals reporting the palpable abnormality, physical finding descriptor of the palpable abnormality, and specialty of physician referring the patient.

Mammographic examinations were performed with Senographe 500T (SENIX H'F) and Mamodiagnost, (Philips medical system, Germany).

The mammographic examination consisted of at least the conventional two- view medio-lateral oblique and craniocaudal projections of each breast. In addition a spot compression tangential view of the area of concern as indicated by the patient was obtained. Each film was evaluated by the author (MG) for presence of

mass lesion and for tissue density of glandular tissue. On every mass lesions detected by mammography, further assessment was done, for its outline, presence of calcification, nipple or skin retraction.

Mammograms were examined before the sonographic examination was done, in those patients who underwent mammography before sonographic evaluation. The mammogram was considered to be negative if there was no evidence of dominant mass, suspicious clusters of micro-calcifications, or architectural distortion in the area of clinical concern.

The ultrasonographic examination was performed usually within three days of reviewing the mammogram. We used a 7-MHz or 8-MHz Linear array transducer: SSD 2000 (Aloka co. Ltd. Sony medical system, Tokyo, Japan), ASU-3000 (Ultrasound Scanner, May 1999, China), and Sono Line Omnia Imaging System, Siemens Issaquah, and WA Ultrasound Imaging System.

Routine, focused ultrasonographic examination that was targeted to the area of clinical concern was carried out by the same radiologist (MG) who interpreted the mammogram, in every patient with palpable lump, swelling or thickening by clinical examination and/ or mammography at presentation. All sonographic examinations were performed with the patient in the supine position, with her ipsilateral arm raised above her head. The breast tissue were flattened and thinned by shifting the patient into the appropriate oblique position with the help of angled mattress placed beneath the patient. The sonogram was considered to be negative if there was no evidence of a cyst, mass, focal area of hypo- or hyper echogenicity, or architectural distortion.

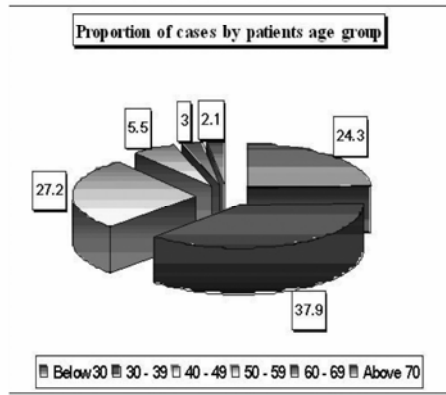
The pathologic examination records of the patients for whom excisional biopsy or cytologic evaluations were done for the palpable abnormalities of the breast which were detected on combined mammographic and /or sonographic examinations were obtained from the Central Health Laboratory of the Ministry of Health during the study period. Test characteristics of combined mammography and sonography examinations were compared with that of pathology results.

Data was entered in Excel where it is exported into statistical package for social science software (SPSS) version 12.0.

Results

There were 202 patients with 235 palpable abnormalities of the breast who underwent combined mammographic and sonographic evaluations. Palpable abnormalities were reported in the right breast in 120 cases and in the left breast in 115 cases. The mean age of the patients at presentation was 36.7 years with the range between 16-79 years (pie chart).

Pie chart: Age distribution of patients with palpable



About two thirds were reported by the patient and surgeon with the rest of the cases referred by physicians of different specialties.

Physical finding descriptors (terms used by the referring physician to describe the palpable abnormalities) were mass in 36.2 %, lump in 34.5 %, swelling in 18.3%, and nodule in 3.0%. Pain was an associated but not primary complaint in most cases.

Just over one third of the patients had a dense pattern on mammography, 28.9% a heterogeneously dense pattern, 17.4% a predominantly fat- replaced pattern, and 16.2% scattered fibro glandular density on mammographic evaluation (Table 1).

Frequency	Percent	
Predominantly fatty	41	17.4
Scattered fibro glandular density	38	16.2
Dense	88	37.4
Heterogeneous dense	68	28.9
total	235	100.0

Mammographic evaluations of the palpable abnormalities showed that a third of the patients with palpable masses were having fibro-adenoma or cysts, whereas one fifth had normal findings, with the remaining one fifth occult (Table 2).

Mammographic finding	Frequency	Percent
Occult	48	20.4
Normal Breast	54	23.0
Cyst or fibro adenoma	79	33.6
Cyst plus fibro- adenoma or radio opaque density	16	6.8
Poorly defined low density mass	19	8.1
Intra-mammary LN	6	2.6
Fibro adenoma cyst lipoma	4	1.7
Big mass cyst sarcoma phylliodes	4	1.7
Asymmetric in density	2	.9
Calcification	2	.9
Hematoma	1	.4
Total	235	100.0

The ultrasonographic studies indicated that, out of the 235 palpable abnormalities 107(45.5%) to be fibro-adenoma, 57(24.3%) normal findings, and 2(.9%) occult, (Table 3).

Sonographic finding	Frequency	Percent
Occult	2	0.9
Normal Breast	57	24.3
Fibro-adenoma	107	45.5
Cyst	38	16.2
Malignant lesion /ill defined mass	24	10.2
Others	7	5.9
Total	235	100.0

The findings from combined sonographic and mammographic studies showed that 63.8% of the all the abnormalities were benign changes with one quarter of the cases negative, and ten percent suspicious of cancer (Table 4).

Age group	Total	Benign	Negative	Suspicious				
#	Age group	#	%	#	%	#	%	
Below 30	57	Below 30	42	73.7	15	26.3	0	0.0
30 - 39	89	30 - 39	53	59.6	29	32.6	7	7.9
40 - 49	64	40 - 49	43	67.2	10	15.6	11	17.2
50 - 59	13	50 - 59	8	61.5	4	30.8	1	7.7
60 - 69	7	60 - 69	2	28.6	1	14.3	4	57.1
Above 70	5	Above 70	2	40.0	1	20.0	2	40.0
Total	235	Total	150	63.8	60	25.5	25	10.6

Of the 150 palpable benign abnormalities, 44 (29.3%) were mammographically occult and identified only at sonographic evaluation, conversely only two palpable benign abnormalities were sonographically occult, but mammographically visible, and the cases were lipoma. Four patients with cancer were mammographically occult and identified on sonography.

Eighteen patients with suspicious findings were in the age range of 30-49 years. No patient in the age range of less than 30 had suspicious findings. There were only few patients with suspicious findings in the older age group (>70 years). 73.7% of the benign findings were in the younger age group, below 30 years of age.

Of the total 235 lesions identified by a combination of mammographic and sonographic features, biopsy was done on 191(81.2%) of the patients. Thirty seven (19.4%) had excisional biopsy, 145 (75.9%) fine needle aspiration cytology, and 9 (4.7%) both fine needle aspiration cytology and excisional biopsy. The pathologic investigation results of 175 (91.6%) of the lesions were found to be benign, and 16 (8.4%) of them to be carcinoma. Benign causes of palpable abnormalities included fibro adenoma 63 (26.8%), fibrocystic disease (cysts) 29 (12.3%), benign mastopathies 38 (16.2%), and lipoma 4(0.02%). Most of the patients with cancer of the breast are in the age group of 30-49 years.

Of the 25 palpable lesions that had a suspicious appearance on combined imaging who underwent biopsy, 15 (60%) had pathologic diagnosis of cancer. Seven of them (46.6%) being ductal carcinoma, 3(20.0%) infiltrative ductal carcinoma, 3(20.0%) invasive ductal carcinoma with metastases to bones, blood vessels and lungs, one colloid type of carcinoma, and one lobular carcinoma (Table 4).

Table: 5 Pathological test results by age group

Age group	Total	Benign		Cancer	
#		#	%	#	%
Below 30	46	46	100.0	0	0.0
30 - 39	70	64	91.4	6	8.6
40 - 49	57	52	91.2	5	8.8
50 - 59	7	6	85.7	1	14.3
60 - 69	7	4	57.1	3	42.9
Above 70	4	3	75.0	1	25.0
Total	191	175	91.6	16	8.4

The sensitivity (15/ 16) and the negative predictive value (15/25) of the combined mammographic and sonographic assessment, taking the pathologic investigation as the gold standard, were consistently high. Test characteristics for combined mammographic and sonographic evaluation in 191 patients with palpable abnormalities of the breast were very high (Table 6).

Table 6: Test characteristics for combined mammographic and sonographic evaluation in 191 patients with palpable abnormalities of the breast

Test characteristics	Value%
Sensitivity	93.8
Specificity	60
Positive predictive Value	94.3
Negative Predictive Value	99.4

Discussion

In this study, 10.6% of breast lumps were suspected to be breast cancer based on combined mammographic and sonographic evaluations with 6.8% confirmed by pathologic evaluation. Reports from studies on breast screening programs have detected breast cancer rates of 3.4% and 4 %^{13,14,15}. The higher breast cancer proportion in our study can be explained by that in our case it was not a screening program, rather patients with breast lumps were referred for identification of the nature of their breast disease.

The peak age group of breast cancer from our study was much lower than those reported in developed countries where the incidence peaked in predominantly postmenopausal women and older. This factor was not investigated in our study but one can speculate that the relatively low life expectancy of the population and the cultural barrier of the older segment of the population that prefers to go to traditional healers and avoid visits to health facilities where there is the "knife and the needle", could have contributed to this observation.

A palpable breast lump may be detected on self breast examination or clinical breast examination and has the potential of being a malignant mass. However, the positive result rate for breast cancer biopsy of palpable breast lumps is low even when the palpable lump is detected during a surgeon-performed clinical breast evaluation^{16,17}. More than three quarters of palpable abnormalities undergoing excisional biopsy were histologically benign, a finding which confirms that from the study by Meyer and Kopans which reported that 70-80% of all biopsies to be benign^{7,18}.

The sensitivity of the combined mammography and ultrasonography in detecting breast cancer in our study was about 94%, which is comparable to other studies done elsewhere^{19,20}. This together with high level of negative predictive value (99.4%) provides evidence to support the interpretation that the two tests combined can reliably identify a case and rules out one that is not. Therefore, clinicians can depend on combined test results of mammography and sonography to proceed on further investigation in cases of positive results; or may follow the patient clinically, sonographically and/or mammographically in case of benign or negative test results- minimizing invasive procedures.

In societies like ours where there is misconception about breast cancer or any cancer for that matter,

invasive procedures like biopsies or needle aspiration cytologic evaluations are thought to hasten the disease process and spread. This may keep patients from seeking health care for any palpable breast abnormality for fear of the 'knife or the needle' exposure. Therefore, restricting this otherwise life saving procedure to clearly indicated cases will help decrease the cultural barrier of health seeking behavior.

The sensitivity, specificity and positive and negative predictive values of mammography depend on several factors, the most important of which are the composition of the study population and the prevalence of breast cancer in the population. In addition, the number of symptomatic patients, the age distribution, and the tumor stage, in combination with the percentage of intraductal carcinoma, the duration of follow-up, and the definition of the true- negative mammogram, play a role²¹.

Mammographic sensitivity is lower in younger women due to the fact that younger women have dense breasts more often²², in which it is harder to find smaller tumors in the background of fibro glandular tissue^{23,24,25,26}. In this study there was no case of breast cancer found under the age of 30 years. Mammography is less sensitive than sonography in dense breasts, and sonography is superior to mammography in differentiating between, and characterizing solid and cystic tumors. Therefore, one can use sonography for the younger age group and for the abnormalities that are cystic, and mammography at a later age group. Combining these modalities will result in a higher sensitivity for detecting cancer.

Imaging has an important role in the managements of palpable abnormalities of the breast. Combined use of mammography and sonography is appropriate to characterize palpable lesions and to minimize unnecessary interventions in those cases in which imaging findings are unequivocally benign. Negative findings on combined mammographic and sonographic imaging have very high specificity and are reassuring to the patient. A national multi institutional study that involves clinicians, surgeons, radiologists and pathologists is important to establish the prevalence of breast cancer in Eritrea as a baseline study for screening mammography program and justification for the establishment of a Breast care Foundation Center in Eritrea.

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