COMPARATIVE ACCURACY OF MAMMOGRAPHY AND ULTRASOUND IN WOMEN WITH BREAST SYMPTOMS ACCORDING TO AGE AND BREAST DENSITY

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Abstract

Breast cancer is the most common cancer and the second most common cause of death from cancer in women.The aim of this studywas to determine which is more accurate imaging test mammography or ultrasound for diagnosis of breast cancer based on the women's age and breast density. We examined 546 patients with breast symptoms, by clinical breast examination, mammography and ultrasound. A total of 546 breast lesions were examined by histopathology analyses. Histopathology results revealed the presence of 259 invasive cancers, and 287 benign lesions. Sensitivity varied significantly with age and breast density. In the 259 women who had both tests, ultrasound had a higher sensitivity than mammography in women younger than 45 years, whereas mammography had a higher sensitivity than ultrasound in women older than 60 years. The sensitivity according to age was 52,1% for mammography and 72,6% for ultrasound. The specificity according to age was 88, 5% for ultrasound and 73, 9% for mammography. Comparing the sensitivity of mammography and ultrasound according to the breast density indicates that mammographic sensitivity was 82,2% among women with predominantly fatty breast, but 23.7% in women with heterogeneous dense breasts, with the increase of fibro glandular density the level of sensitivity with mammography decreases, while ultrasonographic sensitivity was 71,1% among women with predominantly fatty breast and 57,0% for heterogeneous dense breasts. Our data indicate that sensitivity and specificity of ultrasound was statistically significantly greater than mammography in patients with breast symptoms for the detection of breast cancer and benign lesions particularly in dense breast and in young women.

KEY WORDS: breast lesions, diagnostic methods, mammography, ultrasound

Introduction

Excluding cancers of the skin, breast cancer is the most common type of cancer in women today, accounting for 1 of every 3 cancers diagnosed. A woman's chance of developing invasive breast cancer at some time in her life is approximately 1 in 8 (12%). It is one of the leading causes of cancer mortality among women (1). Breast cancer is a heterogeneous disease with no single characterized cause. Epidemiological studies have identified many risk factors that increase the chance for a woman to develop breast cancer. Important risk factors for female breast cancer include early age at onset of menarche, late age at onset of menopause, a first full-term pregnancy after the age of 30 years, a history of premenopausal breast cancer for a mother and a sister, and a personal history of breast cancer or benign proliferative breast disease. Obesity, nulliparity, and urban residence have also been associated with an increased risk of breast cancer. Mammography plays a major role in early detection of breast cancers, detecting about 75% of cancers at least a year before they can be felt. There are 2 types of mammography examinations: screening and diagnostic. Screening mammography is done in asymptomatic women. Early detection of small breast cancers by screening mammography greatly improves a woman's chances for successful treatment. Screening mammography is recommended every 1-2 years for women once they reach 40 years of age and every year once they reach 50 years of age. In some instances, physicians may recommend beginning screening mammography before age 40 if the woman has a strong family history of breast cancer. Studies have shown that regular mammograms may decrease the risk of late-stage breast cancer in women 80 years of age and older (2,3). Diagnostic mammography is performed in symptomatic women, when a breast lump or nipple discharge is found during self-examination or an abnormality is found during screening mammography. Diagnostic mammography is more involved and time-consuming than screening mammography and is used to determine exact size and location of breast abnormalities and to image the surrounding tissue and lymph nodes. Mammography is known to a have a certain false-negative rates. According to data from the Breast Cancer Detection Demonstration Project, the false-negative rate of mammography is approximately 8-10%. Approximately 1-3% of women with a clinically suspicious abnormality, a negative mammogram, and a negative sonogram may still have breast cancer. Possible causes for missed breast cancers include dense parenchyma obscuring a lesion, poor positioning or technique, perception error, incorrect interpretation of a suspect finding, subtle features of malignancy, and slow growth of a lesion.(4). Ultrasonography has been playing an increasingly important role in the evaluation of breast cancer. Breast ultrasound is the preferable method in the case of a symptomatic patient, after clinical examination. In the case of a patient without symptoms, breast ultrasound is ascribed a higher sensitivity for detecting breast cancer in women with dense breast tissue, women under the age of 50 and high-risk women. Many specific indications for breast US have been enumerated, including:evaluation of a palpable mass incompletely evaluated at mammography;differentiation of a cyst from a solid nodule; evaluation of palpable lesions with associated mammographic asymmetry, no mammographic findings, the presence of implants, or a history of lumpectomy or segmentectomy. Mammographically occult cancers can be detected by ultrasound in 10 to 40 % of the cases depending on the patient's breast density and age (5,6,7).The aim of this studywas to determine which is more accurate imaging test mammography or ultrasound for diagnosis of breast cancer based on the women's age and breast density.

Material and Methods

In Department of Radiology in University of Prishtina, between January 2003 and September 2007, we examined 546 women with breast symptoms.The mean age of the patient was 56 years, standard deviation (SD), 12, 9 (age range 30 to 77 years). Breast lesions were detected by clinical breast examination, mammography and ultrasound. A total of 546 breast lesions were examined by histological methodology. Histopathology results revealed the presence of 259 invasive cancers, and 287 benign lesions.

Anamnesis:

To each patient, detailed history was taken including: Age at first childbearing, age at menarche, age at menopause, history of breastfeeding, number of children,history of hormone therapy, a history of premenopausal breast cancer for a mother and a sister, a personal history of breast cancer or benign proliferative breast disease, radiation, chemical exposure and smoking.

Analysis in detail:

The protocol ofdiagnosis consisted of clinical breast examination, ultrasound, mammography and histopathological examination.

Physical examination

Clinical breast examination of the whole breasts and axillary's regions was performed with the patient in the

sitting position with arms both lowered and raised. In an upright position, we visually inspects the breasts, noting asymmetry, nipple discharge, obvious masses, and skin changes, such as dimpling, inflammation, rashes, and unilateral nipple retraction or inversion. With the patient supine and one arm raised, we thoroughly palpates breast tissue, axillary's region and supraclavicular area, assessing the size, texture, and location of any masses. After the patient history is obtained and the clinical breast examination is performed, the next diagnostic step was mammography, ultrasound and biopsy.

Mammography

Conventional film-screen mammography was performed with at least two views per breast, medio-lateral oblique and cranio-caudal views. Additional views or spot compression views were obtained where appropriate. Mammograms were obtained with dedicated mammography units (Alpha RT Imaging, General Electric Medical Systems, Milwaukee). Patient younger than 30 years were excluded because mammography was not performed in this age group. Mammograms were interpreted according to the Breast Imaging Reporting and Data system (BI-RADS)diagnostic categories on a five-point scale, with BI-RADS 1 (negative), 2 (benign finding), 3 (probably benign), 4 (suspicious abnormality), and 5 (highly suggestive of malignancy). Breast density grades were also determined according to the BI-RADS on a scale of 1–4, with 4 corresponding to a dense breast, 3 to a heterogeneous breast, 2 to scattered fibro glandular densities and 1 to an almost entirely fat breast (8).In this series, of 546 women, examinations were performed in 87 women (mean age: 74,1 years; SD, 3,5) with fatty breasts, in 203 women (mean age: 60,4 years; SD: 7,9) with scattered fibro glandular dense breast, in 197 women (mean age: 49,5 years, SD: 7,6) with heterogeneously dense breast and in 59 women with dense breast (mean age: 36,1 years, SD: 4,7).

Breast Ultrasound

The radiologist who had performed the physical examination and who had interpreted the mammograms of that patient performed breast ultrasound. Ultrasound examinations were performed using a high-resolution unit (Aloka SSD 620; Tokyo, Japanand Mindray DP1100 Plus) with a linear array probe centred at 7, 5 MHz. All ultrasound examinations were performed with the patient in a supine position for the medial parts of the breast and in a contra lateral posterior oblique position with arms raised for the lateral parts of the breast. The whole breasts were scanned. Diagnoses were scored on a five-point scale identical to the mammographic BI-RADS categories (8).

Histopathological examination

A total of 546 breast lesions were examined by histological methodology. Final histologic diagnosis was obtained for all patients who underwent surgical biopsy, and all cases were verified by reviewing the histopathology report. Histopathology results revealed the presence of 259 invasive cancers and 287 benign lesions.

Therapy

Treatment of patient with breast cancer was based on a multimodality approach combining surgery, radiation therapy hormonal therapy and/or chemotherapy. Treatment is tailored for an individual patient based on tumor size, axillary lymph node involvement, estrogens and progesterone status, histologic tumour type, standardized pathologic grade, and menopausal status. Lumpectomy or wide local excision was performed for patient with benign tumour.

Statistical analysis

χ^2 test, and student t-test were used for statistical data processing. The significance of differences observed was assessed using Pearson's chi-square test, with $p<0,01$ considering to be statistically significant.

RESULTS

The study included 546 patients with breast symptoms, who had all undergone both mammography and ultrasound and then underwent breast surgery. A total of 546 breast lesions were examined by histological method, revealing the presence of 259 invasive cancers, and 287 benign lesions. The mean age of the patient was 56 years, ranging from 30 to 77

		No of subjects with lesions				Total	
		Benign		Malign			
Age group		Nº	%	Nº	%	Nº	%
30-39		35	12,2	26	10,0	61	11,2
40-49		65	22,6	57	22,0	122	22,3
50-59		73	25,4	66	25,5	139	25,5
60-69		63	22,0	61	23,6	124	22,7
70-79		51	17,8	49	18,9	100	18,3
Total	Nº	287	100,0	259	100,0	546	100,0
	%	52,6	-	47,4	-	100,0	-
Average age	XB	55,5	-	56,6	-	56,0	-
Standard deviation	SD	13,1	-	12,6	-	12,9	-
		P>0,05					

TABLE 1. Number of subjects according to age and kind of lesions

years (Table 1). The histological types of cancer in 259 patients were: invasive ductal (60, 6%), invasive lobular (9, 7%), mixed (ductal/lobular) 22%, tubular (2, 7%), medullary (2,3%), mucinous (2,7%) (Table 2)

Histopathology diagnosis	No of subjects		Average age	Standard deviation
	Nº	%	Years	SD
Ductal carcinoma	157	60,6	55,03	13,59
Lobular carcinoma	25	9,7	58,20	10,07
Mixed ductal/lobular carcinoma	57	22,0	57,46	11,40
Mucinous carcinoma	7	2,7	62,14	7,63
Medullary carcinoma	6	2,3	65,17	6,74
Tubular carcinoma	7	2,7	64,71	6,42
Total	259	100,0	56,56	12,60

TABLE 2. The histological types of cancer in 259 patients

The sensitivity of ultrasound was significantly higher than of mammography (P<0, 01) (Table 3.).

		Mammography		Ultrasound	
Age group	Nº of subjects	Nº	%	Nº	%
30-39	26	4	15,4	18	69,2
40-49	57	22	38,6	42	73,7
50-59	66	34	51,5	48	72,7
60-69	61	39	63,9	48	78,7
70-79	49	36	73,5	32	65,3
Total	259	135	52,1	188	72,6
Mean age (XB)		60,8		56,5	
Standard deviation (SD)		11,3		12,4	
T- test		T = 3,21			P<0,01

TABLE 3. Comparative sensitivity of ultrasound and mammography in all subjects in different age groups

The specificity of ultrasound was significantly higher than mammography (P<0, 05)(Table 4.).

Age group (yr)	Nº of subjects	Mammography		Ultrasound	
		Nº	%	Nº	%
30-39	35	12	34,3	29	82,9
40-49	65	41	63,1	57	87,7
50-59	73	54	74,0	65	89,0
60-69	63	55	87,3	57	90,5
70-79	51	50	98,0	46	90,2
Total	287	212	73,9	254	88,5
Average age (XB)		58,9		55,9	
Standard deviation (SD)		12,4		13,0	
T-test		T=2,50			P<0,05

TABLE 4. Comparative specificity of mammography and ultrasound in all subjects in different age groups

Mammography was false negative in 124 (47, 9%) out of 259 invasive cancers;ultrasound was false negative in 71 out of 259 cancers(Table 5.).

			Ultrasound		Total	
			Positive	Negative	N	%
Mammo-graphy	Positive		123	12	135	52,1
	Negative		65	59	124	47,9
	Total	Nº	188	71	259	100,0
		%	72,6	27,4	100,0	-
P<0,01						

TABLE 5. Correlation between mammography and ultrasound for malign lesions

Mammography was false negative in 75 (26, 1%) out of 287 patients without cancer;ultrasound was false negative in 33 (11, 5%) out of 287 patients without cancer (Table 6.).

			Ultrasound		Total	
			Positive	Negative	Nº	%
Mammo-graphy	Positive		206	6	212	73,9
	Negative		48	27	75	26,1
	Total	Nº	254	33	287	100,0
		%	88,5	11,5	100,0	-
P<0,01						

TABLE 6. Correlation between mammography and ultrasound for benign lesions

The sensitivity of ultrasound for dense and heterogeneously dense breast was significantly higher than mammography (P<0, 01)(Table 7.).

	Nº of subjects	Mammography		Ultrasound	
Breast density		Nº	%	Nº	%
Predominantly fatty	45	37	82,2	32	71,1
Scattered fibro glandular density	105	76	72,4	92	87,6
Heterogeneously dense	93	22	23,7	53	57,0
Extremely dense	16		0,0	11	68,8
Total	259	135	52,1	188	72,6

TABLE 7. Comparative sensitivity of mammography and ultrasound in patient with different breast density

The specificity of ultrasound for dense and heterogeneously dense breast was significantly higher than mammography (P<0, 01)(Table 8.).

	Nº of subjects	Mammography		Ultrasound	
Breast density	Nº	Nº	%	Nº	%
Predominantly fatty	42	42	100,0	42	100,0
Scattered fibro glandular density	98	97	99,0	91	92,9
Heterogeneously dense	104	66	63,5	90	86,5
Extremely dense	43	7	16,3	31	72,1
Total	287	212	73,9	254	88,5

TABLE 8. Comparative specificity of mammography and ultrasound in patient with different breast density

Table 3. shows the comparative sensitivity of the two tests in all subjects and in the different age groups.

Sensitivity of both tests in relation to age has variability. The sensitivity of mammography increases substantially after age 60, ultrasound was more sensitive than mammography in women younger than 45 years. The ultrasound sensitivity was 72, 6%, and mammography sensitivity was 52,1% (9, 10, 22, 23). The ultrasound sensitivity of 72, 6% was 20, 5% greater than the mammography sensitivity of 52, 1%. The sensitivity of ultrasound was significantly higher than of mammography (P<0, 01). Table 4. shows that ultrasound specificity of 88, 5% was 14,6% greater than the mammography sensitivity of 73,9%. The specificity of ultrasound was significantly higher than mammography (P<0,05) (11, 12, 13, 19, 20, 23, 24). Table 5. shows that, of all cancers, 25,1% were correctly identified as cancer on ultrasound but not correctly identified as cancer on mammography, and 4,6% were correctly identified on mammography but not on ultrasound. Mammography was false negative in 124 (47, 9%) out of 259 invasive cancers;ultrasound was false negative in 71 out of 259 cancers. Table 6. shows that, of all women who did not have breast cancer, about 2, 1% had false-positive findings on one test but were correctly identified as not having cancer on the other test. Mammography was false negative in 75 (26,1%) out of 287 patient without cancer, ultrasound was false-negative in 33 (11, 5%) out of 287 patients without cancer. Table 7. shows that sensitivity for mammography and subsequent ultrasound for dense breast was 0% (0 of 16) and 68, 8% (11 of 16), for heterogeneous dense breasts 23,7% (22 of 93) and 57,0% (53 of 93) for scattered fibro glandular dense breast 72, 4% (76 of 105) and 87,6% (92 of 105) for entirely fatty breast 82,2% (37 of 45) and 71,1% (32 of 45). Comparing the sensitivity of mammography and ultrasound according to the breast density, indicates that mammography is more sensitive in the dominate of fat tissue (82, 2%) and at the scattered fibro glandular density (72, 2%). With the increase of fibro glandular density the level of sensitivity with mammography decreases, while with the ultrasound the level of sensitivity increase to the higher breast density 68, 8% and heterogeneously breast density 57,0% The differences between these two diagnostic methods are significant (P<0,01). Table 8. shows that comparing the specificity of mammography and ultrasound according to the breast density,ultrasound is more sensitive in the heterogeneously dense 86, 5% and extremely dense breast 72, 1%, while with mammography the results are 63, 5% and 16, 3%. The sensitivity and the specificity of ultrasound for dense and heterogeneously dense breast was significantly higher than mammography (P<0, 01) (17, 18). Specificity for mammography and subsequent ultrasound for dense breast was 16,3% (7 of 43) and 72,1% (31 of 43), for heterogeneous dense breasts 63,5% (66 of 104) and 86, 5% (90 of 104) for scattered fibro glandular dense breast 99,0% (97 of 98) and 92,9% (91 of 98) for entirely fatty breast 100% (42 of 42) and 100% (42 of 42).Ultrasound can be used in the early detection of breast cancer, especially in women with dense breast tissue.

Discussion

Breast cancer, is an important health problem in the Republic of Kosovo. In the last decades there is little increasing of knowledge and development of breast cancer management, which resulted in increasing of mortality rates from breast cancer. All women are at risk for developing breast cancer. The older a women is, the greater her chances of developing breast cancer. Approximately 77% of breast cancer cases occur in women over 50 years of age. Most important factor in reducing death from breast cancer is early detection. Early detection and treatment is a key to preventing breast cancer from spreading. Mammography and ultrasound are the standard imaging techniques for detection and evaluation of breast disease (2). Women who present with breast symptoms or who have palpable findings on clinical examination are usually investigated with breast imaging, which generally consists of mammography or breast ultrasound or both. The choice of primary breast imaging in examining women with symptoms is partly based on age. However, despite the importance of age in clinical practice, little evidence exists as to the appropriate age that delineates the choice of initial diagnostic breast imaging in symptomatic women. In the absence of evidence, experts suggest that women younger than 35 years be examined with ultrasound, and women 35 years and older be examined with mammography, as the primary breast imaging modality (21). In our data we show a progressive improvement in sensitivity of mammography in women 60 years or older relative to younger women, that has been shown in other studies(9, 10, 22,23). Overall, the difference in the sensitivity of the two tests in all subjects is statistically significant. However, in women 45 years or younger, ultrasound has a significantly greater sensitivity than mammography. Our study also shows that there is difference in the specificity of the two imaging tests, ultrasound has a significantly greater spec-

ificity than mammography. This fact may explain the different findings in published studies, with some reporting a greater specificity for ultrasound than for mammography (11,12,13,19,20,23,24).Ultrasound has long been used as an effective diagnostic tool in the evaluation of palpable and mammography abnormalities (14, 15, 16). Although ultrasonography, it is more sensitive than mammography in detecting lesions in women with dense breast tissue (7,10,12,13,16,17,18). In young women and women with dense breasts, ultrasound appears superior to mammography.Dense fibro glandular tissue is the most important inherent limitation of mammography in the diagnosis of breast cancer. Bilateral whole-breast US can be an effective adjunct imaging examination in the evaluation of women with dense breast tissue at mammography.

Conclusion

Our results indicate that breast density and age are important predictors of the accuracy of mammography. Breast ultrasound is more accurate than mammography in symptomatic women 45 years or younger, mammography has progressive improvement in sensitivity in women 60 years or older. The accuracy of mammograms increased as women's breasts became fattier and less dense. In young women and women with dense breasts, ultrasound appears superior to mammography, and may be an appropriate initial imaging test in those women.

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