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ORIGINAL ARTICLE

Comparison of Breast Cancer Screening Results in Korean Middle-Aged Women: A Hospital-based Prospective Cohort Study

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Abstract

Objectives: The aim of this hospital-based prospective study was to evaluate the diagnostic ability of breast cancer screening in Korean middle-aged women using age, ultrasonography, mammography, and magnification mammography, which are commonly used in most hospitals.

Methods: A total of 21 patents were examined using ultrasonography, mammography, and magnification mammography, and their data were prospectively analyzed from August 2011 to March 2013. All patients were divided into benign and malignant groups and the screening results were classified using the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS). The final pathology report was used as the reference standard and the sensitivity and specificity of ultrasonography, mammography, and magnification mammography were evaluated using receiver-operating characteristics (ROC) analysis.

Results: The analysis included 21 patients who underwent biopsy. Among them, three (14.3%) were positive and 18 (85.7%) negative for breast cancer. The average age was 50.5 years (range = 38—61 years). The sensitivity was the same for ultrasonography and magnification mammography and the specificity of magnification mammography was higher than that of ultrasonography. The highest area under the ROC curve (AUC) was observed in the combination of age and magnification mammography (1.000) and the decreasing order of AUC in others was magnification mammography (0.833), ultrasonography (0.787), mammography (0.667), and age (0.648).

Conclusions: In Korean women, the diagnostic accuracy of magnification mammography was better than that of ultrasonography and mammography. The combination of age and magnification mammography increased the sensitivity and diagnostic accuracy.

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1. Introduction

Breast cancer is one of the most frequent malignancies in Korean women, and its incidence is increasing at a rapid rate. Breast cancer upstaging is associated with lesions that are large, palpable or high grade [1]. Also, attention should be paid to prevent unnecessary mammotome procedures. Heterogeneity in the density and size of calcifications is a reliable criterion for clinical decision-making [2].

There are some important points relating to breast cancer screening. Immediate feedback of consensus Breast Imaging Reporting and Data System (BI-RADS), ultrasound features, and histopathologic results improved performance in ultrasound interpretation across all experience variables [3]. Automated whole-breast ultrasound to mammography improved callback rates, accuracy of breast cancer detection, and confidence in callbacks for women with dense breasts [4].Otherwise, there are various methods of breast cancer screening. Sonographic detection of microcalcifications in stereotactic biopsies correlates well with digital mammography [5]. Adding shear-wave elastographic features to BI-RADS analysis improved the specificity of breast ultrasonography mass assessment, without loss of sensitivity [6]. Strain ratio contributes to the standardization of sonoelastography with high sensitivity and allows significant differentiation between benign and malignant breast lesions [7].

Furthermore, breast density imaging is also important for cancer screening. Bilateral mammographic density asymmetry could be a greater risk factor for breast cancer than a woman's age and assessed mean mammographic density [8]. Analysis of contrast-enhanced ultrasound pixel intensity strengthened the monitoring of breast tumor vasculature, with the potential to improve the prediction of docetaxel efficacy [9]. Contrast-enhanced MRI of the breast is a reliable method for quantification of the response to neoadjuvant chemotherapy [10].

Hemodynamic contrast-enhanced ultrasound assessment can be used to distinguish between benign and malignant breast lesions [11]. Also, a parametric imaging method for characterization of breast lesions, using the high contrast to tissue signal provided by subharmonic imaging, has been developed [12]. A previous study suggests the possible diagnostic role of visual and quantitative analyses of double-phase scintimammography, for differentiating malignant breast lesions [13]. Similarly, the computer-aided diagnostic algorithm, that used a cell-based contour grouping segmentation method to measure boundaries, achieved a high differentiation performance [14]. In the context of computer-aided diagnosis (CAD), the information derived from multiple images of the same patient can be used to improve diagnostic performance [15].

For screening of breast cancer, the use of the logistic regression and artificial neural networks showed a similar performance to that of radiologists in the differentiation of benign and malignant breast masses [16]. Statistically significant differences in the average AUC values were found in many instances between training with and without unlabeled data, based on the sample set distributions [17]. Also, naive analysis gave an area under the receiver-operating characteristics (ROC) curve for the ultrasound read with mammography on view, that was higher than without mammography on view [18].

Generally, a meaningful determination of the sensitivity and specificity from the probability of malignancy estimates requires the use of user-dependent thresholds [19]. However, the lack of influence of patient age and tumor size on the test results might be advantageous in terms of early diagnosis in young women [20]. For this problem, there are fusion methods which are used for breast cancer screening. The combination of mammography and sonography increased the sensitivity and diagnostic accuracy [21]. Also, with regards to the treatment decisions, the best predictive value was seen for the complementary use of mammography, ultrasound, and clinical examination [22]. The incidence of breast cancer in Korean women was highest in patients aged between 40 and 49 years [23]. Therefore, age is a significant risk factor for breast cancer in Korean women. Thus, the aim of this prospective study was to evaluate the diagnostic ability of breast cancer screening using age, ultrasonography, mammography, and magnification mammography, which are commonly used in most hospitals.

2. Materials and Methods

2.1. Study design and patient population

This hospital-based prospective study was approved by the institutional review board at Seoul National University Bundang Hospital, and written informed consent was obtained from all patients. The study evaluated women with breast complaints who were referred to the department of radiology of Seoul National University Bundang Hospital, between 2011 and 2013.

The exclusion criteria were incomplete diagnostic reports, impossibility of pathology evaluation of the specimen, lack of follow up, pediatric patients, and women who were planning to become pregnant.

A total of 21 patients were examined using ultrasonography, mammography, and magnification mammography, and their data were prospectively analyzed from August 2011 to March 2013. Patients were divided into benign and malignant groups and the screening results were classified using the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS). The final pathology report was used as a reference standard and the sensitivity and specificity of ultrasonography, mammography, and magnification mammography were evaluated using ROC analysis.

Ultrasonography was performed in the supine position, by a radiologist. Mammography and magnification mammography were performed in two mediolateral and craniocaudal views for these cases, as an incidental evaluation. A mammography-guided stereotactic biopsy was also performed for calcified lesions in patients.

2.2. Statistical analysis

All reported p values are two sided; $p < 0.05$ was set as the threshold for significance. All confidence intervals are reported at the 95% level.

Breast cancer screening results by BI-RADS of the benign patients and malignant patients were compared using the Mann-Whitney U test, Pearson's Chi-square test and Fisher's exact test. A BI-RADS assessment of four or over was considered malignant for the mammographic or ultrasonographic imaging examination. Results based on pathological diagnosis were analyzed separately. Empirical and model based ROC curves were estimated from the degree of BI-RADS.

We analyzed the effectiveness of the combination of all variables, such as age, ultrasonography, mammography, and magnification mammography diagnosis for breast cancer, by fitting subject level multivariable logistic regression models to evaluate the breast cancer detectability. To verify the logistic regression model, an ROC curve was conducted and the AUC was obtained. The IBM SPSS Statistics 20 statistical software (Armonk, NY, U.S.) was used for the analysis.

3. Results

3.1. Characteristics of participants

The characteristics of the participants are described in Table 1.

The mean age of the patients was 50.5 years and the mean biopsy procedure time was 55.1 minutes. The location of the lesion in 11 patients was the left breast (52.4%) and the location in 10 patients was the right breast (47.6%).

In the ultrasonography BI-RADS results, one malignant patient was assigned to category C2, and two malignant patients were assigned to category C4a. In the mammography BI-RADS results, two malignant patients were assigned to category C4a, and one malignant patient was assigned to category C4b. In the magnification mammography BI-RADS results, one malignant patient was assigned to category C4a, and two malignant patients were assigned to category C4b.

Only in the magnification mammography results was the different between benign and malignant patients ($p < 0.05$).

3.2. Multivariate analysis of breast cancer diagnosis

Table 2 shows the relevant variables that were included in the analysis of breast cancer detectability.

Using the pathology results, we categorized the patients into benign and malignant patients. Next, we defined the dependent variable as the breast cancer, and the independent variables were age, lesion location, ultrasonography, mammography, and magnification mammography.

The variables included in the logistic regression model were tested by the significance of score statistics, and excluded variables in the logistic regression model tested the probability of likelihood-ratio statistics, using maximum partial likelihood estimates. Two significant variables in the final logistic regression model remained after all of the variables were tested; these two variables were age and magnification mammography. Therefore, we induced a breast cancer detectability of a combination of age and magnification

Table 1. Characteristics of participants

Variables [mean ± SD, n (%)]		Benign (n = 18)	Malignant (n = 3)	p
Age (y)		50.0 ± 5.8	53.3 ± 12.5	0.471
Lesion	Left	10 (47.6%)	1 (4.8%)	0.476
	Right	8 (38.1%)	2 (9.5%)	
Biopsy procedure time (min)		55.5 ± 19.9	55.0 ± 7.1	1.000
Ultrasonography	C0	6 (28.6%)	0	0.093
	C1	2 (9.5%)	0	
	C2	3 (14.3%)	1 (4.8%)	
	C3	5 (23.8%)	0	
	C4a	1 (4.8%)	2 (9.5%)	
	C6	1 (4.8%)	0	
Mammography	C0	18 (85.7%)	2 (9.5%)	0.143
	C4a	0	1 (4.8%)	
Magnification mammography	C4a	18 (85.7%)	1 (4.8%)	0.014
	C4b	0	2 (9.5%)	

Table 2. Breast cancer detectability

Variables [*n* (%)]	Age	Ultrasonography	Mammography	Magnification mammography	Age + magnification mammography
Cut-off point	59.0	3.5	1.5	3.5	0.5
Youden's index	0.61	0.56	0.33	0.67	1.00
Sensitivity (%)	66.7	66.7	33.3	66.7	100.0
Specificity (%)	94.4	88.9	100.0	100.0	100.0
AUC (95% CI)	0.648 (0.127−1.000)	0.787 (0.534−1.000)	0.667 (0.272−1.000)	0.833 (0.499−1.000)	1.000 (1.000−1.000)
Standard error	0.266	0.129	0.201	0.171	0.000
p	0.421	0.119	0.366	0.070	0.007

AUC = Area Under Curve.

mammography, and this method was analyzed with other variables.

3.3. ROC analysis

Using the above methods for breast cancer screening, ROC analysis was conducted as shown in Figure 1.

The sensitivity was the same for ultrasonography and magnification mammography and the specificity of magnification for mammography was higher than that for ultrasonography. The highest AUC was observed in the combination of age and magnification mammography (1.000) and the decreasing order of AUC in others was magnification mammography (0.833), ultrasonography (0.787), mammography (0.667) and age (0.648).

4. Discussion

The objective of the present study was to compare the relative accuracy of ultrasonography, mammography, and magnification mammography in screening patients for breast cancer.

Recently, some methods have been developed for breast cancer screening. Quantitative elastosonography is a promising ultrasound technique in the detection of breast cancer, but large prospective trials are necessary

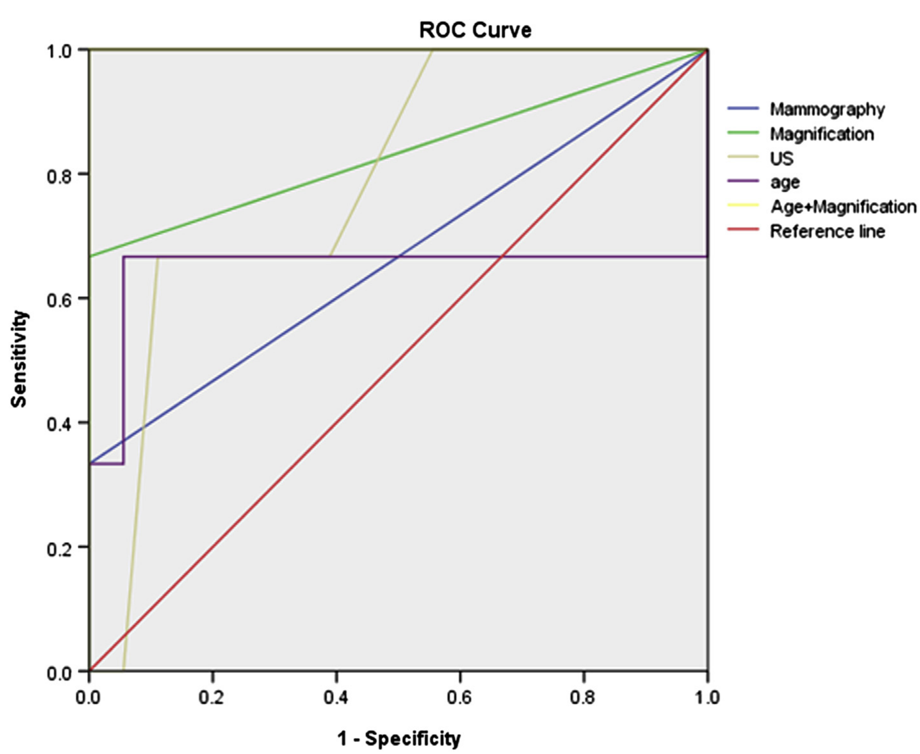

Figure 1. ROC curve and AUC for breast cancer screening. AUC = area under the ROC curve; ROC = receiver-operating characteristics; US = ultrasonography.

to determine [24]. Elastography is known for good method to improves the specificity, positive predictive value, and accuracy of ultrasound. However, significant interobserver variability exists [25]. Also, acoustic radiation force impulse imaging provides quantitative elasticity measurements, which may complement US and potentially improve the characterization of breast lesions [26]. Otherwise, computer-provided confidence levels may be helpful to radiologists who are using computer-aided diagnosis output in diagnostic image interpretation [27]. Current levels of computer performance warrant a clinical evaluation of the potential of US CAD to aid radiologists in lesion work-up recommendations [28].

However, the results of the present study suggest that a combination of age and magnification mammography is more sensitive than other methods. Other than age as a variable, magnification mammography has the highest AUC (0.833) when compared to other methods.

The strengths of the present study include analyzing the magnification mammography results. Most research considers only mammography as mammographic results, but in practice, magnification mammography is frequently used in breast cancer screening. Therefore, our analysis constitutes magnification mammography with other methods.

While the overall cancer incidence in Korea has increased rapidly, age-standardized cancer mortality rates have declined since 2002 and survival has improved [29]. The National Cancer Screening Program for breast cancer in Korea could be improved by increasing the sensitivity of breast cancer screening and by setting appropriate age limits [30].

Our study has several limitations. First, there were too few participants to evaluate the breast cancer detectability; especially there were only three malignant patients. This limit is brought in the study model as a prospective study to find the patients through mammographic guided stereotactic biopsy. However, we found the efficacy of mammography guided stereotactic biopsy as a diagnostic method to screening breast cancer. Second, the BI-RADS results of the patients have a variety of its classification by the screening methods. However, this is not a particular problem of our study and is a common phenomenon in the medical field.

The most important finding of the present study in Korean women is the association between breast cancer and the combination of age and magnification mammography. In our study, we observed an improvement of 16.7% in AUC values as a result of adding age to magnification mammography models. The increase is likely to be partially due to the good observer reliability using the BI-RADS method.

The approach used for assessing the efficiency of the combination screening method is simplistic. It assumes that women being screened are under constant surveillance and that cancer is instantaneously detectable without error. Moreover, our approach was based on further simplifying assumptions, for example, that the effects are age independent.

More refined approaches for evaluating screening strategies need to be developed and applied. It is important to incorporate breast cancer mortality, as well as incidence, and to at least partially reflect that breast cancer is a complex disease with a number of subtypes and that patient survival outlooks vary.

5. Conclusions

The diagnostic accuracy of magnification mammography was better than that of ultrasonography and mammography of Korean women. The combination of age and magnification mammography increased the sensitivity and diagnostic accuracy.

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