

Breast Cancer Detection of Screening Automated Breast US in Korean Women Aged 40-49 Years: Comparison with Screening Mammography using a Multi-center Cohort Study

Sung Hun Kim¹, Bong Joo Kang¹, Woo Jung Choi², Hee Jung Shin², Myung-su Ko², Minseo Bang³,
Kyoungkyg Bae³, Hak Hee Kim²

¹Department of Radiology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

²Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea

³Department of Radiology, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea

Purpose: To compare the diagnostic performance of mammography screening and automated breast ultrasound (ABUS) screening for asymptomatic Korean women aged 40-49 years.

Materials and Methods: This study comprised of a retrospective Cohort study for mammography screening and a prospective study for ABUS screening from 3 academic institutions. A total of 2055 and 959 women finally enrolled in each group. We analyzed cancer detection rate (CDR), recall rate, positive predictive value (PPV), sensitivity, specificity. Outcomes measures were compared according to the screening modality and participant's demographic characteristics.

Results: All screening outcomes showed no significant difference between mammography and ABUS screening. CDR per 1000 screens was 5.2 for ABUS, higher than that of 2.9 for mammography ($P=0.342$). Recall rate was 9.3% for mammography and 9.8% for ABUS ($P=0.720$). A body mass index (BMI) $< 25 \text{ kg/m}^2$ was correlated with higher recall rate of both screenings compared with women with BMI $\geq 25 \text{ kg/m}^2$ (10.0% vs. 6.0% for mammography screening, 10.7% vs. 5.6% for ABUS screening, $P<0.05$ respectively). Dense breast and heterogeneous echotexture were correlated with higher recall rate and lower specificity compared with non dense breast and homogeneous echotexture ($P<0.05$).

Conclusion: All diagnostic performances of ABUS screening were comparable to those of mammography screening for women aged 40-49 years. BMI and parenchymal pattern affected the outcomes.

Index words: Early Detection of Cancer; Mass Screening; Mammography; Ultrasonography, Mammary; Korea

통신저자: Hak Hee Kim, MD, PhD

Department of Radiology and Research Institute of Radiology, Asan Medical Center, University of Ulsan College of Medicine 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea

Tel. (02) 3010-5983 Fax. (02) 476-0090

E-mail: hhkim@amc.seoul.kr

Introduction

Breast cancer has become the major health problem in South Korea. Breast cancer incidence has been continuously increasing since 1999 (1) and 25,452 new breast cancers were expected to occur in 2020 (2), being the most common cancer in Korean women (1). The age-specific incidence rate of breast cancer increases with age, peaks at the age of 45-49 and decreases thereafter (1, 2). Moreover, breast cancer is the major cause of death among Korean women 40-49 years old (3).

For women aged 40-49 years, Western guidelines have been revised in the direction of either not recommending screening (4, 5) or delaying the starting age to 45 years (6), reflecting that the benefits-to-harms ratio in this age group was less favorable (4-7). However, recent randomized controlled trials supported the benefits of annual screening mammography in women aged 40-49 years showing the significant mortality reduction to 25 - 29% (8-10).

South Korea has adopted the Korean National Cancer Screening Program of breast cancer screening with biennial mammography for all women 40 years and older since 2002 (11) and for all women aged 40 to 69 years since 2015 (12). Compared with the Western guideline, the Korean guideline shows a big difference in that it includes the 40s age group, reflecting the unique epidemiology different from Western countries with peak age at 60-70 years (13). However, combined ultrasound screening has been widely used for Korean women in their 40s due to high prevalence of dense breast to 77-85% (14, 15).

East Asia widely uses breast ultrasound as the primary screening modality for young women, because of accessibility and low costs (16-18). Chinese guideline recommends ultrasound alone for women aged 40-44 years (19). Hand held US (HHUS) alone showed overall pooled sensitivity of 89.2% and specificity of 99.1% in low- and middle-income country, demonstrating potential

effectiveness in low-resource settings where mammography was not available (17).

We have conducted a multicenter prospective study to screen the breast cancer for Korean women aged 40-49 years and showed good diagnostic performance of automated breast ultrasound (ABUS) as primary screening modality (20). ABUS showed several advantages as screening tool over HHUS (21). It can meet the increasing demands for screening ultrasound even with limited human resources and overcome the operator dependency and lack of reproducibility of HHUS.

To our knowledge, there was no comparative study on which method was effective between mammography screening and ultrasound screening as primary screening modality for women in their 40s. Therefore, this study aimed to compare the diagnostic performance of both mammography screening alone and ABUS screening alone using a multicenter retrospective Cohort study and a multicenter prospective study for asymptomatic Korean women aged 40-49 years.

Materials and Methods

This study comprises of a retrospective design of mammography screening alone and a prospective design of ABUS screening alone and was approved by Institutional Review Boards of three participating centers (Seoul St. Mary's Hospital, Asan Medical Center and Ulsan University Hospital). A written informed consent was waived for mammography screening due to the retrospective design and it was obtained from all patients for ABUS screening.

Study Population

From January 2014 to December 2015, 3199 asymptomatic women aged 40-49 years underwent mammography screening alone in health screening and promotion center of three participating centers. 1,144 women (35.7%) were excluded because of

follow-up less than 12 months or more than 24 months in non-recall cases (n=1028), no further evaluation in recall cases (n=93) and history of surgery due to breast cancer or augmentation (n=23). A total of 2055 women were finally included.

From February 2017 to October 2019, 994 asymptomatic women aged 40–49 years underwent ABUS screening alone in three participating centers. 35 women (3.5%) were excluded because of follow-up loss (n=32) or poor image quality (n=3). A total 959 women were finally included. 959 women for ABUS screening overlaps with previous study evaluating the diagnostic performance of screening ABUS for Korean women in their 40's (20) (Fig. 1).

Data of age, body mass index and family history of breast cancer were collected via medical records for mammography screening and via a structured questionnaire-guided interview at enrollment for ABUS screening. Biopsy pathology and surgical pathology were reviewed with medical records.

Screening mammography

Mammography was performed with one of three digital mammography units (Mammomat Inspiration, Siemens, Germany; Lorad Selenia, Hologic, USA; Senograph DS, GE healthcare, Milwaukee) to obtain the standard craniocaudal and mediolateral oblique views.

Screening ABUS

ABUS was performed using the ACUSON S2000 Automated Breast Volume Scanner (Siemens Medical Solutions, Mountain View, CA, USA) with a 5–14 MHz wide-frequency bandwidth transducer. ABUS scan was performed by a single trained technologist in each hospital. The US image data were obtained from a $15 \times 17 \times 5$ cm volume of breast parenchyma. Three standard views of anteroposterior, medial, and lateral view were routinely obtained and superior or inferior view were additionally obtained in case of large breasts.

Image analysis

Mammographic parenchymal composition and final assessments were reviewed using medical records. Mammography was interpreted by one of 9 radiologists in three health examination centers and 3 radiologists received fellowship training for breast imaging. Parenchymal composition was classified by the radiologist into four categories (<25% glandular of “almost entirely fatty”, 25%–50% glandular of “scattered fibroglandular densities”, 51–75% dense of “heterogeneously dense”, and >75% dense of “extremely dense”) according to BI-RADS. “Almost entirely fatty” and “scattered fibroglandular densities” are assigned to non-dense breast and “heterogeneously dense” and “extremely dense”

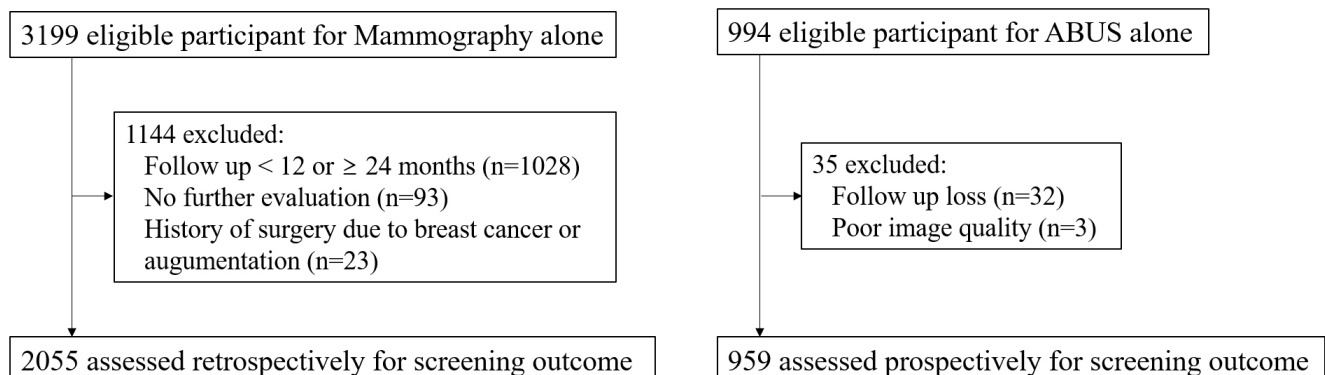


Fig. 1. Study diagram

to dense breast. Radiologist classified the final assessment according to BI-RADS as category 0 (incomplete), 1 (negative), 2 (benign), 4 (suspicious) and 5 (highly suggestive of malignancy). Cases with category 1 and 2 were recommended with annual or biennial screening and cases with category 0, 4 and 5 were recalled for further evaluation.

ABUS images were prospectively interpreted with double reading by two specialist breast radiologists. If there was a discrepancy between the readers, they reviewed the images together and reached to consensus. New interpretation criteria modified from BI-RADS and Japanese Association of Breast and Thyroid Sonology guidelines was used (21). Background echotexture is divided into homogeneous or heterogeneous echotexture. Screening BI-RADS assessments were categorized as follows: category 0 (incomplete), 1 (negative), 2 (benign), 3 (probably benign), 4 (suspicious) and 5 (highly suggestive of malignancy). Cases with category 1 and 2 were recommended with 1 year follow up with imaging or clinical interview and cases with category 0 or ≥ 3 were recalled for further evaluation (details have been published (20)).

Reference Standard

All women with incomplete assessment and suspicious findings were recalled. Lesions with incomplete assessment underwent magnification view or HHUS and then were finally classified. The lesions with suspicious findings underwent stereotactic or US guided biopsy. Reference standard information for mammography screening included a combination of biopsy or surgical results and imaging follow up between 1 and 2 years. For ABUS screening, biopsy or surgical results and clinical follow-up at 1 year were considered as reference standard. Surgical excision was performed in case with high-risk lesion on biopsy. Histopathology results revealing breast cancer, including ductal carcinoma in situ, were considered

disease positive.

Statistical Analysis

Outcomes were cancer detection rate (CDR), recall rate, positive predictive value 1 (PPV1), positive predictive value 3 (PPV3), sensitivity and specificity with 95% confidence intervals (CIs). These outcomes were calculated according to BI-RADS. Interval cancer was defined as that diagnosed because of a clinical abnormality occurring shorter than the recommended screening interval after the screening (less than 1-2 year for mammography screening and less than 1 year for ABUS screening). Outcome measures were compared according to the characteristics by using the chi-square test or Fisher's exact test in each group. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 21 (IBM Corp., Armonk, NY, USA) and SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA). Statistical tests resulting in P values < 0.05 were considered statistically significant.

Results

Patient and demographic characteristics of women are summarized in Table 1. All 2,055 women for mammography screening and all 959 women for ABUS screening were included. The median age of women for mammography screening was 44.4 years, older than 43.9 years for ABUS screening (P value < 0.0001). The proportion of women with family history of breast cancer was 3.8% for mammography screening, lower than 9.6% women for ABUS screening (P value < 0.0001). The proportion of body mass index was not different between two groups (P value = 0.304).

Total 6 breast cancers with 2 ductal carcinoma in situ (DCIS) and 4 invasive cancers were detected by mammography screening. The median size was 13.5 mm (interquartile range [IQR], 9.75-19.5 mm) and

there was no axillary LN metastasis or no interval cancer.

Table 1. Patient and Demographic Characteristics According to Screening Modality in Women Aged 40-49 Years (n=3,014)

Characteristics	Mammography	ABUS	P value
Number	2055	959	
Age (y), mean $\pm$ SD	44.4 $\pm$ 2.6	43.9 $\pm$ 3.1	<.0001
BMI (kg/m ²), median (IQR)			0.304
< 25	316 (15.3)	165 (17.2)	
$\geq$ 25	1733 (84.3)	794 (82.8)	
Unknown	6 (0.2)		
Family history of breast cancer			<.0001
Yes	79 (3.8)	92 (9.6)	
No	1976 (96.1)	858 (89.5)	
Unknown		9 (0.9)	

Note - Data are the number of enrolled participants with percentages in parentheses.

y, year; SD, standard deviation; BMI, body mass index; IQR, interquartile range.

Total 5 breast cancers with 1 DCIS and 4 invasive cancers. The median size was 15 mm (interquartile range [IQR], 12–17 mm) and there were 2 invasive cancers with axillary nodal metastases. One interval cancer was detected as palpable lump (35 mm, invasive ductal carcinoma) (Table 2).

Diagnostic performance of MMG screening and ABUS screening

CDR was 5.2 per 1000 exams (95% CI, –0.6 to 11.0) for ABUS screening, higher than that of 2.9 per 1000 exams (95% CI, 0.5 to 5.2) for mammography screening, but was not statistically different (P=0.342). PPV3 for mammography screening were 42.8% (95% CI, 16.9 to 68.7), higher than that of 20% (95% CI, 4.3 to 35.6) for ABUS screening, but there was no significant difference. Recall rate was 9.3% (95% CI, 8.1 to 10.6) for mammography screening and 9.8% (95% CI, 7.9 to

Table 2. Characteristics of Screening Detected Cancer and Interval Cancer According to Screening Modality

Case No.	Screening	Age, years	Family history	BMI, kg/m ²	Parenchymal pattern#	Final histology	Tumor size, mm	Axillary nodes	Estrogen receptor	Progesterone receptor	HER2
1	Mammography	46	No	21.8	Dense	DCIS	9	Negative	Positive	Positive	Negative
2	Mammography	47	No	22.0	Dense	DCIS	21	Negative	Positive	Positive	Negative
3	Mammography	45	No	21.2	Dense	IDC	12	Negative	Positive	Positive	Negative
4	Mammography	45	No	20.7	Dense	IDC	9	Negative	Positive	Positive	Negative
5	Mammography	45	No	23.7	Dense	IDC	15	Negative	Positive	Positive	Negative
6	Mammography	46	No	23.6	Non dense	IDC	21	Negative	Positive	Positive	Positive
7	ABUS	44	Yes	24.8	Heterogeneous	Mixed invasive ductal and mucinous ca.	15	Negative	Positive	Positive	Negative
8	ABUS	40	Yes	20.4	Homogeneous	IDC	12	Negative	Positive	Positive	Negative
9	ABUS	40	No	21.7	Heterogeneous	DCIS	3	Negative	Positive	Positive	Negative
10†	ABUS	40	No	24.6	Homogeneous	IDC	65	Positive	Negative	Negative	Negative
11	ABUS	44	No	25.5	Heterogeneous	IDC	17	Positive	Positive	Positive	Positive
12‡	ABUS	42	Yes	27.9	Homogeneous	IDC	35	Positive	Positive	Positive	Negative

Note-ABUS, automated breast US; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; HER2, human epidermal growth factor receptor 2

Parenchymal pattern was classified based on parenchymal composition on mammography and background echotexture on ABUS

† This patient underwent neoadjuvant chemotherapy and showed pathologic complete response. The tumor size and axillary status are based on pretreatment imaging.

‡ One interval cancer was detected after 6 months of follow-up.

11.6) for ABUS screening. Sensitivity and specificity were 100% and 90.8% (95% CI, 89.6 to 92.1) for mammography screening and 83.3% (95% CI, 53.5 to 100) and 90.6% (95% CI, 88.8 to 92.5) for ABUS screening, respectively. All outcome measures between mammography screening and ABUS screening were not significantly different (Table 3).

Demographic characteristics and Outcomes of MMG screening and ABUS screening

A BMI < 25 kg/m² was correlated with higher recall rate of both screenings compared with women with BMI ≥ 25 kg/m² (10.0% [95% CI, 8.6 to 11.4] vs. 6.0% [95% CI, 3.3 to 8.6] for mammography screening, 10.7% [95% CI, 8.5 to 12.8] vs. 5.6% [95% CI, 2.0 to 9.1] for ABUS screening, P<0.05 respectively). A BMI <25 kg/m² was associated with lower specificity of mammography screening (92.5% [95% CI, 91.3 to 93.8] vs. 93.9% [95% CI, 91.3 to 96.6], P=0.035). Dense breast was correlated with higher recall rate and lower specificity compared with women with non dense breast (9.9% [95% CI, 8.5 to 11.2], 90.3% [95% CI, 88.9 to 91.6] vs. 4.5% [95% CI, 1.6 to 7.4], 95.9% [95% CI, 93.1 to 98.7], P<0.05 respectively). Heterogeneous echotexture was correlated with higher recall rate and lower specificity compared with women with homogeneous echotexture (13.8% [95% CI, 9.7 to 17.8], 87.6% [95% CI, 83.6 to 91.5] vs. 8.2% [95% CI, 6.1 to 10.3], 91.9% [95% CI, 89.9 to 94.0], P<0.05

respectively) (Table 4). Family history was not correlated with screening outcomes (Supplementary Table).

Discussion

The purpose of this study was to compare the diagnostic performance of mammography screening alone and ABUS screening alone to screen Korean women aged 40–49 years. In our study, CDR was 2.9 per 1,000 exams in mammography screening and 5.2 per 1000 exams in ABUS screening. The outcomes of mammography screening were comparable with ABUS screening, demonstrating that both were effective as a primary screening modality for women aged 40–49 years. The Japan Strategic Anti-cancer Randomized Trial (J-START) to screen Japanese women aged 40–49 years showed CDR, 3.2 per 1,000 exams in mammography screening and 5.0 per 1000 exams in combined mammography and handheld US screening. Our result of mammography screening was similar to that in J-START trial and the result of ABUS screening was comparable to that of combined screening in J-START trial. American College of Radiology Imaging Network (ACRIN) 6,666 trial to screen asymptomatic women with dense breast and risk factor for breast cancer showed higher CDR, 7.5 per 1000 exams for mammography screening and 9.0 per 1,000 exams for handheld US screening (22), which was thought to be due to inclusion of high

Table 3. Diagnostic Performance According to Screening Modality

Characteristics	Mammography		ABUS		P value
	n/total	Rate (95% CI), %	n/total	Rate (95% CI), %	
Cancer detection rate (per 1000)	6/2055	2.9 (0.5, 5.2)	5/959	5.2 (-0.6, 11.0)	0.342
Recall rate	193/2055	9.3 (8.1, 10.6)	94/959	9.8 (7.9, 11.6)	0.720
PPV1	6/193	3.1 (0.6, 5.5)	5/94	5.3 (0.7, 9.8)	0.348
PPV3	6/14	42.8 (16.9, 68.7)	5/25	20 (4.3, 35.6)	0.155
sensitivity	6/6	100 (100, 100)	5/6	83.3 (53.5, 100)	>.999
specificity	1862/2049	90.8 (89.6, 92.1)	864/953	90.6 (88.8, 92.5)	0.851

Note-ABUS, automated breast US; n, number; 95% CI, 95% confidence interval; PPV, positive predictive value

Table 4. Diagnostic Performance According to Body Mass Index and Parenchymal Pattern

	Body mass index (kg/m ²)				Parenchymal pattern			
	Mammography		ABUS		Mammography		ABUS	
	< 25	≥ 25	< 25	≥ 25	non dense	dense	Homo-geneous	Hetero-geneous
Cancer detection rate per 1000 screen								
n/total	6/1733	0/316	4/797	1/162	1/198	5/1857	2/683	3/276
rate	3.5	0.0	0.5	0.6	5.1	2.7	0.3	1.1
95% CI	0.7, 6.2	0.0, 0.0	0.0, 1.0	-0.6, 1.8	-4.8, 14.9	0.3, 5.0	-0.1, 0.7	-0.1, 2.3
p value	0.598		> 0.999		0.455		0.147	
Recall rate								
n/total	174/1733	19/316	85/797	9/162	9/198	184/1857	56/683	38/276
rate	10	6	10.7	5.6	4.5	9.9	8.2	13.8
95% CI	8.6, 11.4	3.3, 8.6	8.5, 12.8	2.0, 9.1	1.6, 7.4	8.5, 11.2	6.1, 10.3	9.7, 17.8
p value	0.024		0.046		0.013		0.013	
PPV1								
n/total	6/174	0/19	4/84	1/10	1/9	5/184	2/57	3/37
rate	3.4	0.0	4.8	10	11.1	2.7	3.5	7.7
95% CI	0.7, 6.1	0.0, 0.0	0.2, 9.3	-8.6, 28.6	-9.4, 31.6	0.3, 5.0	-1.3, 8.3	-0.7, 16.9
p value	>.999		0.438		0.252		0.379	
PPV3								
n/total	6/14	0/14	4/24	1/1	1/1	5/13	2/17	3/8
rate	42.8	0.0	16.7	100	100	38.4	12.5	12.5
95% CI	16.9, 68.7	0.0, 0.0	1.8, 31.6	100, 100	100, 100	12.0, 64.9	-3.2, 28.2	-10.4, 35.4
p value	N/A		0.200		0.428		0.283	
Sensitivity								
n/total	6/6	0/0	4/4	1/2	1/1	5/5	2/3	3/3
rate	100	0.0	100	50	100	100	66.7	100
95% CI	100, 100	0.0, 0.0	100, 100	0, 100	100, 100	100, 100	13.3, 100	100, 100
p value	N/A		0.333		N/A		> .999	
Specificity								
n/total	1559/1727	297/316	713/793	151/160	189/197	1673/1852	625/680	239/273
rate	92.5	93.9	89.9	94.4	95.9	90.3	91.9	87.6
95% CI	91.3, 93.8	91.3, 96.6	87.8, 92.0	90.8, 98.0	93.1, 98.7	88.9, 91.6	89.9, 94.0	83.6, 91.5
p value	0.035		0.077		0.009		0.036	

Note, ABUS, automated breast ultrasound; n, number; 95% CI, 95% confidence interval; PPV, positive predictive value, NA-not applicable

risk group. However, CDR between two groups was not statistically different as in our study.

Recall rate in our study was 9.3% for mammography screening and 9.8% for ABUS screening, which reached 10%, the desirable mammography screening goal suggested by the ACR-BIRADS. Our recall rate of mammography screening was favorable in comparison with those of 8.8% in J-START trial

and 11.5% in ACRIN study (22, 23). Our recall rate of ABUS screening was much lower than that of year 1, 20.9% in ACRIN 6,666 study, which decreased to 10.7% on the year 2 and 3 rounds (22). Our reasonable recall rate for ABUS screening was probably due to adoption of new interpretation criteria for ABUS screening and double reading by experts in breast imaging.

Supplement Table. Diagnostic Performance According to Family History of Breast Cancer

	Family history of breast cancer				
	Mammography		ABUS		
	Yes	No	Yes	No	Unknown
Cancer detection rate per 1000 screen					
n/total	6/1976	0/79	3/858	2/92	0/9
rate	3	0.0	0.4	2.2	0.0
95% CI	0.6, 5.5	0.0, 0.0	-0.1, 0.7	-0.8, 5.2	0.0, 0.0
p value	>.999		0.119		
Recall rate					
n/total	186/1976	7/79	81/858	12/92	1/9
rate	9.4	8.8	9.4	13	11.1
95% CI	8.1, 10.7	2.5, 15.1	7.5, 11.4	6.2, 19.9	-9.4, 31.6
p value	0.869		0.539		
PPV1					
n/total	6/186	0/7	3/81	2/12	0/1
rate	3.2	0.0	3.7	16.7	0.0
95% CI	0.6, 5.7	0.0, 0.0	-0.4, 7.8	-4.4, 37.8	0.0, 0.0
p value	>.999		0.170		
PPV3					
n/total	6/14	0/14	3/17	2/7	0/1
rate	42.8	0.0	17.7	28.6	0.0
95% CI	16.9, 68.7	0.0, 0.0	-0.5, 35.8	-4.9, 62.0	0.0, 0.0
p value	N/A		0.686		
Sensitivity					
n/total	6/6	0/0	3/3	2/3	0/0
rate	100	0.0	100	66.7	0.0
95% CI	100, 100	0.0, 0.0	100, 100	13.3, 100	0.0, 0.0
p value	N/A		>.999		
Specificity					
n/total	1790/1970	72/79	777/855	79/89	8/9
rate	90.8	91.1	90.9	88.8	88.9
95% CI	89.5, 92.1	84.8, 97.4	89.0, 92.8	82.2, 95.3	68.4, 109.4
p value	0.933		0.795		

Note, ABUS, automated breast ultrasound; n, number; 95% CI, 95% confidence interval; PPV, positive predictive value, NA-not applicable

Sensitivity, specificity and PPV of both screenings in our study were similar to or superior to those reported in previous studies (17, 18, 22, 23). In the results of the Korean national cancer screening program including 343,747 women aged 40–49 years, sensitivity, specificity and PPV1 for digital mammography screening were 65.8%, 83.2% and 1.2% in the age 40–44 years and 67.8%, 83.8%

and 1.8% in the age 45–49 years (24). Our results showed higher sensitivity of 100%, specificity of 90.8% and PPV1 of 3.1%.

Two recent meta-analyses showed contradictory results about US screening alone (17, 18). In one study using Asian population, pooled sensitivity of ultrasound was 65%, significantly lower than 81% of mammography and pooled specificity of

ultrasound was 98%, not different with 99% of mammography (18). This study concluded that there was no indication for US screening to replace mammography screening in Asian women. On the other hand, the other study concluded that US would be effective primary screening tool and beneficial in low-resource settings without available mammography device, demonstrating pooled sensitivity of 80.1% and specificity of 88.4% (17). Our results of ABUS screening alone showed higher or similar sensitivity and specificity.

Diagnostic performance was associated with subgroup of body mass index and parenchymal composition in our study. Low BMI was correlated with higher recall rate, 10.0% of mammography screening and 10.7% of ABUS screening compared with 6.0% of mammography screening and 5.6% of ABUS screening in women with high BMI. In addition, low BMI was associated with lower specificity of mammography screening. Dense breast was correlated with higher recall rate, 9.9% and lower specificity, 90.3% compared with recall rate, 4.5% and specificity, 95.9% in women with non dense breast. Like dense breast, heterogeneous echotexture was correlated with higher recall rate, 13.8% and lower specificity, 87.6% compared with recall rate, 8.2% and specificity, 91.9% in women with homogeneous echotexture. BMI was known to be risk factor for breast cancer and was inversely related with mammographic percent density and interfere with each other's effects (25). Heterogeneous echotexture was analogous to mammographic density and positively correlated with mammographic density (26). Higher mammographic density generally decreased performance of screening due to higher recall rate and lower sensitivity (27). Our study also demonstrated that lower BMI, dense breast and heterogeneous echotexture were correlated with higher recall rate. Further researches are needed for the interaction among breast cancer risk factors and parenchymal patterns and their effects on screening

performance.

There were some limitations. First, our study had modest sample size. Korean women from only three academic institutions were included. These may not be representative of diverse population and clinical environment. Second, this study had heterogeneity of study design and exclusion. A prospective study for ABUS screening determined the sample size by considering the crude rate and prevalence of breast cancer, but for the retrospective study for mammography screening, we collected the cohorts for 2 years. 3.5% out of eligible participants were excluded from the ABUS study, but 35.7% were excluded from the mammography cohort study. ABUS was interpreted via double reading, but mammography was read by one radiologist. Thus comparison of diagnostic performance was limited and our results may not be generalizable to Asian population. Third, 1–2 years for mammography screening and 1 year for ABUS screening was followed to evaluate the interval cancer rate. Different and relatively short follow up period could not exclude screen detected breast cancers or interval cancers that developed later. Finally, although ABUS screening showed potential role as primary screening modality, cost-effectiveness and practical workflow associated with acquisition time, reading time and computer-aided detection were not evaluated and were not compared with those for mammography screening. Further studies with randomized controlled study, large sample size, longer-term follow up including diagnostic performance and mortality reduction rate were needed to validate the efficacy of screening

In conclusion, CDR by ABUS screening alone was higher than that by mammography screening alone, but all the outcomes of CDR, recall rate, PPV, sensitivity and specificity were not statistically different. Our study results support that ABUS screening as well as mammography screening could be also effective primary screening modality to screen Asian women aged 40–49 years. Thus, given

a more aggressive course and higher mortality of breast cancer in this age group, these results suggest that ABUS screening may be an effective alternative to mammography screening and both screenings may be used interchangeably among Asian women aged 40-49 years.

Funding

This study was supported by grant from the Korean Society of Breast Imaging and Korean Society for Breast Screening (No. KSBI & KSFB-2015-01). The funder had no role in study design, data collection, and analysis, decision to publish, or preparation of the manuscript

References

1. Hong S, Won YJ, Park YR, Jung KW, Kong HJ, Lee ES. Cancer Statistics in Korea: Incidence, Mortality, Survival, and Prevalence in 2017. *Cancer Res Treat* 2020;52:335-350.
2. Jung KW, Won YJ, Hong S, Kong HJ, Lee ES. Prediction of Cancer Incidence and Mortality in Korea, 2020. *Cancer Res Treat* 2020;52:351-358.
3. Causes of death statistics in 2019 by Korean Statistical Information Service 2020; <http://kostat.go.kr/portal/eng/index.action> Accessed January 26, 2021.
4. Siu AL. Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med* 2016;164:279-296.
5. Schünemann HJ, Lerda D, Quinn C, et al. Breast Cancer Screening and Diagnosis: A Synopsis of the European Breast Guidelines. *Ann Intern Med* 2020;172:46-56.
6. Oeffinger KC, Fontham ET, Etzioni R, et al. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. *Jama* 2015;314:1599-1614.
7. van den Ende C, Oordt-Speets AM, Vroiling H, van Agt HME. Benefits and harms of breast cancer screening with mammography in women aged 40-49 years: A systematic review. *Int J Cancer* 2017;141:1295-1306.
8. Ray KM, Joe BN, Freimanis RI, Sickles EA, Hendrick RE. Screening Mammography in Women 40-49 Years Old: Current Evidence. *AJR Am J Roentgenol* 2018;210:264-270.
9. Mao Z, Nyström L, Jonsson H. Breast cancer screening with mammography in women aged 40-49 years: Impact of length of screening interval on effectiveness of the program. *J Med Screen* 2020;969141320918283.
10. Duffy S, Vulkan D, Cuckle H, et al. Annual mammographic screening to reduce breast cancer mortality in women from age 40 years: long-term follow-up of the UK Age RCT. *Health Technol Assess* 2020;24:1-24.
11. Suh M, Choi KS, Park B, et al. Trends in Cancer Screening Rates among Korean Men and Women: Results of the Korean National Cancer Screening Survey, 2004-2013. *Cancer Res Treat* 2016;48:1-10.
12. Eun Hye Lee BP, Nam-Soon Kim, Hyun-Ju Seo, Kyoung Lan Ko, Jun Won Min, Myung-Hee Shin, et al. The Korean guideline for breast cancer screening. *J Korean Med Assoc* 2015;58:408-419.
13. Yap YS, Lu YS, Tamura K, et al. Insights Into Breast Cancer in the East vs the West: A Review. *JAMA Oncol* 2019;
14. Jo HM, Lee EH, Ko K, et al. Prevalence of Women with Dense Breasts in Korea: Results from a Nationwide Cross-sectional Study. *Cancer Res Treat* 2019;51:1295-1301.
15. Kim YJ, Lee EH, Jun JK, et al. Analysis of Participant Factors That Affect the Diagnostic Performance of Screening Mammography: A Report of the Alliance for Breast Cancer Screening in Korea. *Korean J Radiol* 2017;18:624-631.
16. Huang Y, Dai H, Song F, et al. Preliminary effectiveness of breast cancer screening among 1.22 million Chinese females and different cancer patterns between urban and rural women. *Sci Rep* 2016;6:39459.
17. Sood R, Rositch AF, Shakoob D, et al. Ultrasound for Breast Cancer Detection Globally: A Systematic Review and Meta-Analysis. *J Glob Oncol* 2019;5:1-17.
18. Wang J, Zheng S, Ding L, et al. Is Ultrasound an Accurate Alternative for Mammography in Breast Cancer Screening in an Asian Population? A Meta-Analysis. *Diagnostics (Basel)* 2020;10:
19. Huang Y, Tong Z, Chen K, et al. Interpretation of breast cancer screening guideline for Chinese women. *Cancer Biol Med* 2019;16:825-835.

20. Choi WJ, Kim SH, Shin HJ, et al. Automated breast US as the primary screening test for breast cancer among East Asian women aged 40–49 years: a multicenter prospective study. *Eur Radiol* 2021;
21. Kim SH, Kim HH , Moon WK. Automated Breast Ultrasound Screening for Dense Breasts. *Korean J Radiol* 2020;21:15–24.
22. Berg WA, Bandos AI, Mendelson EB, Lehrer D, Jong RA , Pisano ED. Ultrasound as the Primary Screening Test for Breast Cancer: Analysis From ACRIN 6666. *J Natl Cancer Inst* 2016;108:
23. Ohuchi N, Suzuki A, Sobue T, et al. Sensitivity and specificity of mammography and adjunctive ultrasonography to screen for breast cancer in the Japan Strategic Anti-cancer Randomized Trial (J-START): a randomised controlled trial. *Lancet* 2016;387:341–348.
24. Hong S, Song SY, Park B, et al. Effect of Digital Mammography for Breast Cancer Screening: A Comparative Study of More than 8 Million Korean Women. *Radiology* 2020;294:247–255.
25. Pettersson A, Graff RE, Ursin G, et al. Mammographic density phenotypes and risk of breast cancer: a meta-analysis. *J Natl Cancer Inst* 2014;106:
26. Kim WH, Lee SH, Chang JM, Cho N , Moon WK. Background echotexture classification in breast ultrasound: inter-observer agreement study. *Acta Radiol* 2017;58:1427–1433.
27. Carney PA, Kasales CJ, Tosteson AN, et al. Likelihood of additional work-up among women undergoing routine screening mammography: the impact of age, breast density, and hormone therapy use. *Prev Med* 2004;39:48–55.

40-49세 한국 여성에서 선별 자동 유방 초음파 검사의 유방암 발견능: 다기관 코호트 연구를 이용한 선별 유방촬영술 검사와의 비교

김성현¹ · 강봉주¹ · 최우정² · 신희정² · 고명수² · 방민서³ · 배경국³ · 김학희²

¹가톨릭대학교 서울성모병원 영상의학과

²울산의과대학교 아산병원 영상의학과

³울산의과대학교 울산병원 영상의학과

목적: 40 ~ 49세의 무증상 한국 여성의 선별 유방 촬영술과 선별 자동 유방 초음파 검사의 진단성능을 비교하고자 한다.

대상 및 방법: 이 연구는 3개 대학병원의 선별 유방 촬영술에 대한 후향적 코호트 연구와 선별 자동 유방 초음파에 대한 전향적 연구로 구성되었다. 2,055명과 959명이 각 군에 최종적으로 포함되었다. 유방암 발견율, 소환율, 양성예측치, 민감도, 특이도를 분석하였다. 결과 측정값들은 선별검사방법과 참여자 특성에 따라 비교 분석하였다.

결과: 모든 선별 결과값들은 유방 촬영술과 자동 유방 초음파 사이에 유의 한 차이를 보이지 않았다. 1,000개 검사 당 유방암 발견율은 자동 유방 초음파에서는 5.2개였고, 유방 촬영술 2.9보다 높았다 ($P = 0.342$). 소환율은 유방 촬영술에서 9.3%, 자동 유방 초음파에서 9.8%였다 ($P = 0.720$). 25kg/m^2 미만의 신체질량지수를 갖는 여성은 25kg/m^2 이상인 여성에 비해 두 선별 검사에서 더 높은 소환율과 관계가 있었다 (유방 촬영 검사, 10.0% vs. 6.0%, 자동 유방 초음파 검사, 10.7% vs. 5.6%, $P < 0.05$). 치밀 유방과 불균질한 에코양상은 비치밀유방과 균질한 에코양상을 갖는 여성군에 비해 더 높은 소환율과 더 낮은 특이도와 관계가 있었다 ($P < 0.05$).

결론: 40-49세 여성에 대한 선별 자동 유방 초음파의 모든 진단 성능은 선별 유방 촬영술과 비슷했다. 신체질량지수와 유방 실질 양상이 결과에 영향을 미쳤다.

Index words: Early Detection of Cancer; Mass Screening; Mammography; Ultrasonography, Mammary; Republic of Korea

Corresponding author: Hak Hee Kim, M.D., Ph.D.