

Effect of Age on Performance Parameters of Screening and Diagnostic Mammography Examinations

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ABSTRACT

Objective: To assess the effect of age specific on performance parameters among screening and diagnostic mammography examinations.

Methods: During 1 January 2006 to 31 December 2007, 22,278 screening mammography examinations (MG <mammography with/ without breast ultrasound > and 13,435 diagnostic MG < mammography alone and/or breast ultrasound >, were retrospectively reviewed. Patients with breast cancer were either confirmed by histopathology report, Siriraj cancer registry or follow-up post treatment up to 12 months, while the negative breast cancer were followed up for at least 12 months. Cancer detection rate (CDR), sensitivity, specificity, and positive predictive value (PPV) were analysed according to age group distribution.

Results: Of the total 22,278 screening examinations, 43.1% and 56.9% were below and above 50 years old, respectively. Among 13,435 diagnostic examinations, 66.9% and 33.1% were below and above 50 years, respectively. The mean age was 50.8 for screening and 53.3 for diagnostic (S.D.=8.1,9.0, respectively). The CDR of screening and diagnostic was 4.6 and 49.6 per 1,000 examinations, respectively. The CDR, PPV and specificity of screening and diagnostic mammography examination increased with higher age with statistical significance ($p<0.005$). The sensitivity of the diagnostic MG also increased with age ($p<0.05$), but not in the screening group.

Conclusion: Age is one of the most important risk factors of breast cancer and also in outcome of key parameters on mammography performance. The study showed that the CDR, PPV and specificity increase with age both in the screening and diagnostic group as in the literatures except for the sensitivity in screening was not related to increased age Our study also supported that MG screening among women 40-49 years is suitable as there were high cancer rate in both screening and diagnosis in 40-49 years with high sensitivity and specificity.

Keywords: Effect of age, screening mammography, diagnostic mammography, performance parameters, cancer detection rate

Siriraj Med J 2016;68:6-16

E-journal: <http://www.sirirajmedj.com/ojs>

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Received 8 July 2015
Revised 24 August 2015
Accepted 2 September 2015

INTRODUCTION

The incidence rates of breast cancer vary from 19.3 per 100,000 women in Eastern African countries to 89.7 per 100,000 women in Western Europe while the incidence rate of breast cancer among Thai women was 38 per 100,000 women in 2008.¹ Breast cancer has become the most common female cancer since 2004 and recently account for 37.5% of all Thai female cancer in 2011;² resulting in large economic loss.

Breast cancers are characterized by early-onset and late-onset tumor types where two peaks (modes) were observed, one peak close to 50 years old and the other around 70 years³ which is the same finding as a 2004-2006 report from the National Cancer Institute of Thailand.² This has implication to the performance of mammography.

In most breast imaging centers, mammography (MG) services were provided to patients with two purposes: screening (asymptomatic) or diagnostic (with clinical breast symptoms). Additional ultrasound (US) study was also provided in some cases where indicated. Recognizing that these two groups of breast imaging service have different interpretation approaches and statistical outcomes, our center has classified and recorded MG studies into screening and diagnostic since 1995, similar to practice in the USA. There are reports of distinct benchmarks for screening⁴ and diagnostic MG.⁵ Records of MG studies into two groups facilitate the assessment of mammography performance and statistical analysis.

Age is one of the most important risk factors,⁶ of breast cancer prevalence⁷ and one of the main factors of policy decisions on screening mammogram. Although there are reports on breast cancer by age distribution from several national cancer centers but limited reports assessed the effect of ages on mammography performance parameters, especially there has been no report from South East Asia.

This study examined the effect of age on mammography performance and breast cancer detection in screening and diagnostic examinations at Thanyarak Breast Center (TBC), Siriraj Hospital, Mahidol University during 2006 and 2007.

MATERIALS AND METHODS

The study was approved by the Siriraj Institutional Review Board (Si No.351/2011). A total of 46,660 consecutive MG examinations with or without US performed in our center during 1 January 2006 to 31 December 2007 were retrospectively reviewed. The exclusion criterias were (1) cases with personal history of previous breast cancer (2) cases with undetermined cancer status or no follow up history at least 12 months after the examination date. (3) those with breast ultrasound only or male sex in the screening group. There was no age limitation for both screening and diagnosis MG examinations. By using these exclusion criterias, 22 % and 1.4% were excluded from screening and diagnostic examination, respectively. Only 22,278 of screening (mammogram with/without ultrasound), and 13,435 of diagnostic MG examinations (mammogram and/or ultrasound) were included in this study.

Screening MG examinations in Thailand are opportunistic screenings. Our center defines screening as services provided to asymptomatic women, or to those with previous BI-RADS 2 or previous proof of benign breast disease. The MG examinations in screening group refer to MG alone or MG with US or US alone. In this study we excluded screening with US alone which is usually provided to younger age women, less than 35 years.

Diagnostic MG examination is defined as services provided to patients with breast symptoms, or those with previous BI-RADS 3 or breast augmentation. The MG examinations in diagnostic group include mammogram alone, mammogram with ultrasound, or ultrasound examination alone. The ultrasound alone in diagnostic group is provided to patients with previous BI-RADS 3 assessment and recommended to follow up with ultrasound in 6 months or provided to younger age women, less than 35 years.

In our practice, breast ultrasound is usually performed in women after MG with dense breast composition which included heterogeneous dense breast and extremely dense breast composition according to ACR BI-RADS. Breast US is also done in those with suspicious of abnormal finding noted in mammogram. Other additional special

mammographic views would be provided when abnormal mammogram findings are suspected. The combined MG and US are interpreted immediately in one visit, and there is usually no recall for further study in our service practice. In such case, we have no BIRAD 0 assessment.

Demographic data i.e.: date of birth, family history of breast cancer, previous history of breast cancer, date of previous MG examination, date of previous breast biopsy or surgery and the reason for each MG were collected real time through 'Breast Information System' (BIS) in the computer under the supervision of a technologist.

All MG and/or ultrasound examinations were performed using digital machines. For MG we used GE Full Field Digital MG with Senographic <GE healthcare USA>, and Lorad-Selenia Full Field Digital MG System <Hologic Belford, MA, USA>. For Ultrasound we used GE Logiq 7 and Logiq 9, <GE healthcare, and Milwaukee, WI, USA>. The image interpretations were done with hard copy before December 2006 and PACs (picture archived communication system) since December 2006 by radiologists with experience on breast imaging 1-10 years. MG and US Reporting were done based on American College of Radiology, Breast Imaging Reporting and Data system (ACR, BI-RADS) 4th edition. BI-RADS assessment category is as follows, BI-RADS 1 negative, BI-RADS 2 benign finding, BI-RADS 3 probably benign findings - short interval follow up suggested, BI-RADS 4 suspicious abnormality - biopsy should be considered, BI-RADS 5 - highly suggestive of malignancy- appropriate action should be taken.

Pathological results from all cases with biopsy performed and also any surgical pathological results of cases in our center were also recorded through BIS.

Breast cancer status was verified by either positive histopathology from breast surgery or at least core needle biopsy, or confirmed breast cancer with Siriraj Cancer Registry, or follow-up with record in our Breast Information System or Medical Record of Siriraj Hospital within 12 months after the date that MG was performed. Non breast cancer status means no breast cancer after follow up for at least 12 months.

A positive mammogram (BI-RADS 4-5) result and a proven breast cancer status was defined as a true positive; or false positive if not a proven cancer status. A negative mammogram (BI-RADS 1-3) result and a proven non-breast cancer was defined as a true negative; or false negative if there was a proven cancer status.

Cancer detection rate (CDR) is defined as the number of true-positive results among 1,000 examinations. Positive predictive value (PPV) is defined as number of true positive results divided by total positive examinations. False positive rate (FPR) is defined as positive finding with no known breast cancer within 12 months or number of false positives divided by total non-cancer status. False negative rate (FNR) is defined as negative finding, but had proven breast cancer within 12 months or number of false negatives divided by total cancer cases. False positive rate is also equal to 1-specificity while false negative rate is equal to 1-sensitivity.

Statistical analyses were performed using PASW v 18.0. Key performance parameters i.e.; the CDR, PPV, sensitivity, specificity, FPR and FNR were calculated with 95% confidence interval (CI). Chi-square test was used to test the difference in CDR, PPV, sensitivity and specificity among different age groups in both screening and diagnostic group. A p-value of less than 0.05 was considered statistical significant.

RESULTS

There were 22,278 screening examinations and 13,435 diagnostic examinations included in this study. The mean ages among the screening and diagnostic groups were 50.8 and 53.3 years (S.D.=8.1,9.0). The mean ages of breast cancer detection were 53.5 and 52.2 years (S.D.=9.0,11.3) for the two groups, respectively, with age range 34.2-88.6 years for screening, and 26.6-87.6 years for diagnostic group.

1. Screening Group

Table 1 showed that CDR consistently increased with age for both first and subsequent screenings with statistical significance, $p=0.002$. For example, among the first screening, the CDR

TABLE 1. Mammography performance by age distribution among screening, 2006-2007.

Screening	TP	FP	FN	TN	Total	CDR Per 1,000 (95% CI)	PPV % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	FPR %	FNR %
First screening											
<40	1	40	0	765	806	1.2 (0.03, 6.9)	2.4 (0.1, 12.9)	100.0 (2.5, 100)	95.0 (93.3, 96.4)	5.0	0.0
40-49	26	137	2	2328	2493	10.4 (6.8, 15.2)	16.0 (10.7, 22.5)	92.9 (76.5, 99.1)	94.4 (93.5, 95.3)	5.6	7.1
50-59	13	69	2	1467	1551	8.4 (4.5, 14.3)	15.9 (8.7, 25.6)	86.7 (59.5, 98.3)	95.5 (94.4, 96.5)	4.5	13.3
60-69	7	14	1	369	391	17.9 (7.2, 36.5)	33.3 (14.6, 57.0)	87.5 (47.4, 99.7)	96.3 (93.9, 98)	3.7	12.5
≥70	3	2	0	59	64	46.9 (9.8, 130.9)	60.0 (14.7, 94.7)	100.0 (29.2, 100)	96.7 (88.7, 99.6)	3.3	0.0
Total	50	262	5	4988	5305	9.4	16.0	90.9	95.0	5.0	9.1
<i>p value</i>						0.002	<0.001	0.820	0.125		
Subsequent screening											
<40	1	29	0	847	877	1.1 (0, 6.3)	3.3 (0.1, 17.2)	100.0 (2.5, 100)	96.7 (95.3, 97.8)	3.3	0.0
40-49	16	141	11	6574	6742	2.4 (1.4, 3.9)	10.2 (5.9, 16)	59.3 (38.8, 77.6)	97.9 (97.5, 98.2)	2.1	40.7
50-59	24	87	15	6889	7015	3.4 (2.2, 5.1)	21.6 (14.4, 30.4)	61.5 (46.6, 76.6)	98.8 (98.5, 99)	1.2	38.5
60-69	9	20	4	1882	1915	4.7 (2.2, 8.9)	31.0 (15.3, 50.8)	69.2 (38.5, 90.9)	98.9 (98.4, 99.4)	1.0	30.8
≥70	2	4	2	416	424	4.7 (0.6, 16.9)	33.3 (4.3, 77.7)	50.0 (6.8, 93.2)	99.0 (97.6, 99.7)	0.9	50.0
Total	52	281	32	16608	16973	3.1	15.6	61.9	98.3	1.7	38.1
<i>p value</i>						0.037	<0.001	0.990	<0.001		
All screening											
<40	2	69	0	1612	1683	1.2 (0.1, 4.3)	2.8 (0.3, 9.8)	100.0 (15.8, 100)	95.9 (94.8, 96.8)	4.1	0.0
40-49	42	278	13	8902	9235	4.5 (3.3, 6.1)	13.1 (9.6, 13.7)	76.4 (63, 86.8)	97.0 (96.6, 97.3)	3.0	23.6
50-59	37	156	17	8356	8566	4.3 (3.0, 5.9)	19.2 (13.9, 25.4)	68.5 (54.5, 80.5)	98.2 (97.9, 98.4)	1.8	31.5
60-69	16	34	5	2251	2306	6.9 (4.0, 11.2)	32.0 (19.5, 46.7)	76.2 (52.8, 91.8)	98.5 (97.9, 99)	1.5	23.8
≥70	5	6	2	475	488	10.2 (3.3, 23.8)	45.5 (6.8, 76.6)	71.4 (29, 96.3)	98.8 (97.3, 99.5)	1.2	28.6
Total	102	543	37	21596	22278	4.6	15.8	73.4	97.5	2.5	26.6
<i>p value</i>						0.009	<0.001	0.604	<0.001		

CDR Cancer Detection Rate = TP/all examinations *1,000

PPV Positive Predictive Value% = TP/TP+FP

FPR False Positive Rate% = FP/FP+TN

FNR False Negative Rate% = FN/FN+TP

increased from 1.2 per 1,000 examinations in women <40 years to 46.9 per 1,000 examinations in women age above 70 years. We also found that CDR among the first screening was three folds higher than in subsequent screenings i.e.; 9.4 per 1,000 in first screening versus 3.1 per 1,000 in the subsequent screening.

PPV also consistently increased with age, among the first and subsequent screenings; from 2.4% among the youngest (<40 years) to 60% in the oldest (>70 years) in the first screening, $p<0.001$. There was no difference in the PPV between the first and subsequent screenings.

In our study, the sensitivity among screening examinations did not increase with age. Sensitivity in the subsequent screening was very low 61.9%, which was lower than the first screening, 90.9%. The average sensitivity of screening was 73.4%. Our center had achieved high specificity, up to 95% in the first screening and 98.3% in the subsequent screening.

The false positive rate was higher, 5% in the first screening and was lower, 1.7% among subsequent screenings, and there was no clear pattern in association with age group distribution.

The false negative rate was not associated with increased age. False negative rate was higher, 38.1% in subsequent screening, while it was 9.1% in the first screening. Two peaks of false negative rate was among 50-59 and 60-69 years age groups in the first screenings. The peak of false negative rate shifted to the younger women of 40-49 years in subsequent screening.

2. Diagnostic Group

Similar to the screening group, Table 2 showed that CDR in the diagnostic group also consistently increased with age for both first ($p<0.001$) and subsequent examinations ($p=0.001$). For example, among the first examinations, the CDR increased from 32.8 per 1,000 examinations in women <40 years to 355.7 per 1,000 examinations among women aged above 70 years old. However, CDR among the first examination was eight folds higher than the CDR in subsequent examinations. CDR was 89.0 per 1,000 in the first examination compared with 11.3 per 1,000 in the subsequent examinations.

PPV also consistently increased with age both in the first ($p<0.001$) and subsequent examinations ($p<0.001$). For example, PPV increased from 21.1% among the youngest (<40 years) to 81.5% in the oldest (>70 years) among the first examination. PPV in the first examination (44%) was higher than subsequent examination (17.8%). In our study, the sensitivity in the diagnostic group increased with age ($p<0.001$). The sensitivity among the diagnostic group in our center was high, 95.3% in the first examination and 79.4% in the subsequent examinations. Our center had achieved high specificity, 94.7% in the subsequent examinations though slightly lower, 87.5% in the first examination.

DISCUSSION

Age is one of the most important risk factors of human malignancies, including breast cancer. Breast cancer incidence increases with age,^{8,9} therefore cancer detection rate also increases with age.

1. Screening group

Our study showed that the CDR, had consistently increased with age in both first ($p=0.002$) and subsequent screenings ($p=0.037$) which was the same finding as compared to the previous studies of the University of California San Francisco (UCSF)¹⁰ Breast Cancer Surveillance Consortium (BCSC) 2009,¹¹ J&J Keen⁷ and Baker⁹ (Table 3). It should be noted that only UCSF had detail of the CDR of the first and subsequent screening as our study. This study showed that the CDR among the first screening (9.1/1,000) was three folds that of subsequent screening (3.1/1,000) which was similar to that was reported by Nass.¹²

We further classified age of screening into two broad groups: 40-49 years and 50-69 years; the CDR among older women (50-69) was 10.3, 3.7 and 4.9 in the first, subsequent and all screening examinations, respectively, compared with CDR of younger women (40-49 years) which was 10.4, 2.4 and 4.5, respectively. Our study showed no difference in CDR in the first screening between the two broad age groups. We did not compute the CDR among women age <40 and ≥ 70

TABLE 2. Mammography performance by age distribution among Diagnostic group, 2006-2007.

Diagnostic	TP	FP	FN	TN	Total	CDR Per 1,000 (95% CI)	PPV % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	FPR %	FNR %
First diagnostic											
<40	78	292	7	1999	2376	32.8 (26, 40.8)	21.1 (17, 25.6)	91.8 (83.8, 96.6)	87.3 (85.8, 88.6)	12.7	8.2
40-49	196	290	13	1995	2494	78.6 (68.3,89.9)	40.3 (35.9 44.8)	93.8 (89.6, 96.7)	87.3 (85.9, 88.7)	12.7	6.2
50-59	178	121	7	923	1229	144.8 (125.6,165.8)	59.5 (53.7, 65.1)	96.2 (92.4, 98.5)	88.4 (86.3, 90.3)	11.6	3.8
60-69	85	35	2	259	381	223.1 (182.3,268.3)	70.8 (61.8, 78.8)	97.7 (91.9, 99.7)	88.1 (83.8, 91.6)	11.9	2.3
≥70	53	12	0	84	149	355.7 (279.1,438.2)	81.5 (70, 90.1)	100.0 (93.3,100)	87.5 (79.2,93.4)	12.5	0.0
Total	590	750	29	5260	6629	89.0	44.0	95.3	87.5	12.5	4.7
<i>p value</i>						<0.001	<0.001	0.006	0.439		
Subsequent diagnostic											
<40	7	73	1	970	1051	6.7 (2.7,13.7)	8.75 (3.6,17.2)	87.5 (47.5,99.7)	93.0 (91.3,94.5)	7.0	12.5
40-49	30	172	10	2852	3064	9.8 (6.6, 14)	14.9 (10.3,20.5)	75.0 (58.7,87.3)	94.3 (93.4,95.1)	5.7	25.0
50-59	25	85	7	2002	2119	11.8 (7.6,17.2)	22.7 (15.3,31.7)	78.1 (60,90.7)	95.9 (95,96.7)	4.1	21.9
60-69	10	19	2	424	455	22 (10.6,40.4)	34.5 (17.9,54.3)	83.3 (51.1,97.9)	95.7 (93.4,97.4)	4.3	16.7
≥70	5	7	0	105	117	42.7 (14,96.9)	41.7 (15.2,72.3)	100.0 (47.8,100)	93.8 (87.6,97.5)	6.3	0.0
Total	77	356	20	6353	6806	11.3	17.8	79.4	94.7	5.3	20.6
<i>p value</i>						0.001	<0.001	0.444	0.002		
All diagnostic											
<40	85	365	8	2969	3427	24.8 (19.9,30.6)	18.9 (15.4,22.8)	91.4 (83.8,96.2)	89.1 (87.9,90.1)	10.9	8.6
40-49	226	462	23	4847	5558	40.7 (35.6,46.2)	32.8 (29.4,36.5)	90.8 (86.5,94.1)	91.3 (90.5,92)	8.7	9.2
50-59	203	206	14	2925	3348	60.6 (52.8,69.3)	49.6 (44.7,54.6)	93.5 (89.4,96.8)	93.4 (92.5,94.3)	6.6	6.5
60-69	95	54	4	683	836	113.6 (92.9,137.1)	63.8 (55.5,71.5)	96.0 (90,98.9)	92.7 (90.6,99.5)	7.3	4.0
≥70	58	19	0	189	266	218.0 (169.9,272.6)	75.3 (64.2,84.4)	100.0 (93.8,100)	90.9 (86.1,94.4)	9.1	0.0
total	667	1106	49	11613	13435	49.6	37.6	93.2	91.3	8.7	6.8
<i>p value</i>						<0.001	<0.001	0.008	<0.0001		

CDR Cancer Detection Rate = TP/all examinations *1,000
 PPV Positive Predictive Value% = TP/TP+FP
 FPR False Positive Rate% = FP/FP+TN
 FNR False Negative Rate% = FN/FN+TP

TABLE 3. CDR by age distribution among screening, various series comparison.

Sources	Screening	≤40	40-49	50-59	60-69	≥70	All age group
UCSF* ^{10,13}	First	1.3	2.7	6.0	13.1	14.2	
	Subsequent	1.4	1.3	2.9	1.3	3.0	
	All screening	1.9	3.4	5.4	7.5	9.5	
Anusinha et al [#]	First	1.2	10.4	8.4	17.9	46.9	9.4
	Subsequent	1.1	2.4	3.4	4.7	4.7	3.1
	All screening	1.2	4.5	4.3	6.9	10.2	4.6
BCSC [§] 2009 ¹¹	All screening		2.3	3.5	4.8	6.1	3.9
J & J Keen ⁷	All screening		1.9	7.2	15.1		
Baker et al ⁹	All screening		1.8	3.2	5.1		

UCSF* University of California San Francisco

Anusinha et al[#] ≥ This study

BCSC[§] Breast Cancer Surveillance Consortium

years due to the smaller number of examinations which may hamper the validity of result.

Kerlikowske K, et al¹³ reported that the first-screening mammographic examinations among women 50 years or older was five times higher than women less than 50 years. Kerlikowske's report supported screening MG should be introduced at age ≥50 years, and also for women 40-49 years with family history of breast cancer. Since our study reported the CDR among the first screening examinations among women 50-59 years which was 10.3 per 1,000 and equal to those age 40-49 years, 10.4 per 1,000 examinations (Table 1), it therefore supported that MG screening among women 40-49 years among Thai women is suitable. Our study showed that 43.1% (44/102) of screening breast cancer (TP) occurred below age 50 years which was close to Kwong A, et al¹⁴ who reported that 47.4% of breast cancer in Hong Kong was age 49 years and younger, while the remaining 52% in women were 50 year or over. However Richelia et al¹⁵ provided different findings from Singapore, higher CDR among older women; 3.3 per 1,000 in 40-49 years and 5.8 per 1,000 in ≥50 years. However, the average CDR of Breast Screening Singapore (BSS) between 2002-2007 was 4.6 which was the same as our study.

Our study detected carcinoma in situ at 32.4% while Chuwa EW¹⁶ from Singapore detected it among their screening at 31%. Our study showed crudely the ratio of carcinoma in situ

and invasive carcinoma was 1:2 especially among age groups 40-49 and 50-59 years. For 60 years of age or older, we detected carcinoma in situ nearly the same as invasive carcinoma (Table 4).

The PPV is related to the cancer incidence, and cancer incidence increases with age; therefore PPV also increases with age.^{8,17,18} The standard PPV in breast MG screening was classified to PPV1 (percentage of abnormal interpretation), PPV2 (percentage of biopsy recommended), and PPV3 (percentage of positive biopsy performed or positive biopsy rate) according to ACR BI-RADS.¹⁹ In our study, PPV refers to PPV2 which increased with age in both first or subsequent screening (Table 1) as expected and similar to the previous report.^{7,20} The average PPV of the first and subsequent screening in our study were nearly the same value (16.0% and 15.6%).

For sensitivity of screening MG, there was a consistent trend, in international literature, of increased level of sensitivity with age such as Saarenmaa I,²¹ and Olivotto IA reports.²² The sensitivity of screening in our study did not increase with age (p=0.6). This could be explained by the fact that, a large majority, 70-80%, of our screening examinations were MG with US, due to dense breast composition on MG which resulted in low sensitivity. Also breast US had lower sensitivity than mammogram especially in screening.²³ The sensitivity in our first screening was 86.7-92.9% while the subsequent screening was much lower, and ranged 59.3-69.2% with the

TABLE 4. Detected breast cancer among Screening 2006-7: histopathology by age distribution.

	Age group	Breast Cancer Histopathology				Total
		Insitu	Invasive	Other*	Unknown	
First screening	<40	0	1	0	0	1
	40-49	7	15	1	2	25
	50-59	4	8	0	1	13
	60-69	4	3	0	0	7
	≥70	1	2	0	1	4
	Total	16	29	1	4	50
Subsequent SCR	<40					
	40-49	5	9	0	2	16
	50-59	8	16	0	1	25
	60-69	3	5	1	0	9
	≥70	1	1	0	0	2
	Total	17	31	1	3	52
All screening	<40	0	1	0	0	1
	40-49	12	24	1	4	41
	50-59	12	24	0	2	38
	60-69	7	8	1	0	16
	≥70	2	3	0	1	6
	Total	33	60	2	7	102

*Other ≥lymphoma, malignant phyllodes tumor

lowest in age group 40-49 years. These findings are similar to U.S. Preventive Services Task Force (USPSTF) report that the sensitivity of first MG ranged from 71-96%; while the sensitivity was substantially lower, particularly among women in their 40s than for older women.²⁴

The probability of a false-positive screening MG result was estimated at 0.9% to 6.5% in a meta-analysis of studies of sensitivity and specificity of MG published 10 years ago.²⁵ False positive rate (FPR) is higher among women 40-49 years than among women 50 years or older.²⁶ Our false positive rate of first screening (5%) was higher than subsequent screening (1.7%), which also decreased with age. Our study confirmed a previous report that the younger women had higher level of false positive mammogram results. The harm of false positive mammograms relates to the inconvenience, additional outpatient visits, invasive procedures and its related costs and anxiety among women. However, the average false positive rate in our study was low, at 2.5%

False negative finding or interval breast cancers are cancers that present clinically in a screened population in the time period between a normal screening result and the next screening invitation. Interval cancers are an inevitable part of any breast screening program. Their main importance relates to assessing the effectiveness of screening programs.²⁷ False negative rate (FNR) in our study showed higher in subsequent screening (38.1%) than first screening (9.1%) with an average FNR of 26.6%. The highest false negative rates were among age group of 40-49 and 50-59 years of subsequent screening, 40.7% and 38.5%, respectively. The US National Cancer Center had documented that mammogram would have false negative rate approximately 5% to 25% in women 40-49 years, and 10% in women 50-59 years.²⁸ Our center has classified false negative findings into 4 groups i.e.; (1) True interval cancer (refer to cancers arising between screens to people who were negative at the previous screening even though retrospectively reviewed), (2) Under

estimated lesion (detected lesion as BI-RADS 2 or 3), (3) minimal or occult cancer, and (4) missed case. Of the total false negative cases of our study, 73% (27/37) were true interval cancer and 85.2% (23/27) of these interval cancers were invasive cancer.

2. Diagnostic group

There were few reports of CDR of diagnostic MG related to age distribution. Our study also showed that the CDR of diagnostic MG had significantly increased with age in both first and subsequent examinations, which confirmed the report of Miglioretti DL.²⁹ The CDR of diagnostic MG of women 40-49 years in the first, subsequent and all diagnostic examinations (78.6, 9.8 and 40.7) was quite high (Table 2). In diagnostic MG, 46.6% (311/667) of diagnostic breast cancer (TP) occurred in age less than 50 years (while the screening MG was 43.1% (44/102) as mentioned above). This finding also supports MG screening in age 40-49 years.

The PPV and sensitivity of our diagnostic examination also increased with age as reported.²⁹

False positive rate was higher, 12.5% in the first examination and lower, 5.3% among the subsequent examinations. False positive was much higher in the diagnostic group when compared with the screening group (Table 1, 2). There was no clear pattern of false positive rates in association with age.

For false negative diagnostic MG, there were two peaks of false negative rate at 40-49 years (25.0%) and 50-59 years (21.9%) in subsequent diagnostic examinations, similar to our screening false negative finding (Table 1, 2). Among the false negative diagnostic examinations, most of them were BI-RADS 3 assessment (77.3%). Both false positive and false negative rates in our study were not associated with age.

In summary, our study from Asia showed that the CDR, PPV, sensitivity and specificity increased with higher age in both screening and diagnostic groups similar to the previous literatures, except for the sensitivity in screening which was not related to increased age as mentioned above. However, the rather high rate of breast cancer detection in women age 40-49 years in both screen-

ing and diagnostic groups with standard high sensitivity and specificity as mentioned above, supports that MG screening in Thai women age 40-49 years is suitable.

The limitations of this study were identified. First, the mammogram with breast ultrasound examinations were not analysed separately as they were not reported independently in our practice. In this study the proportions of mammogram alone and mammogram with US in screening examinations were 20 to 80, respectively. Also the proportions of mammogram alone, mammogram with US and US alone in diagnostic examinations were 7 to 65 to 28, respectively. For these reasons, it may create bias or help in favour of a higher sensitivity of the two groups. Second, our study had no BI-RADS 0 as we tailored and offered additional special mammogram view and/or US on the same visit. Third, our definition of positive MG examinations (BI-RADS assessments 4, 5) and negative MG examination : BI-RADS assessments 1-3 were used in both screening and diagnostic mammograms. These are different from medical audit of ACR BI-RADS (4th edition) suggestion, which gives positive screening MG examinations to include BI-RADS assessment 0, 4, 5 and negative screening MG examination means BI-RADS assessments 1-2 only.

CONCLUSION

Age is one of the most important risk factors of breast cancer and also in outcome of key parameters on mammography performance. Our study is the first report of screening and diagnostic mammography examination-key parameters both first, subsequent and all examinations of Thai women related to age group distribution. The study showed that the CDR, PPV and specificity increase with age both in screening and diagnostic group as in the literatures except for the sensitivity in screening was not related to increase aged. Our study also supported that MG screening among women 40-49 years is suitable as high cancer rate in both screening and diagnosis in 40-49 years with high sensitivity and specificity and may contribute to the development of health policy in Thailand.

ACKNOWLEDGEMENT

The study used breast information systems of Thanyarak Breast Center, Siriraj Hospital, as the main database for this assessment. We recognized the support from staffs of Thanyarak Breast Center, Pathology Department & Siriraj Cancer Registry, Faculty of Medicine Siriraj Hospital, Mahidol University. The authors would like to thank you Mr. Teerawat Lerttrirat for data retrieval and data verification and Professor Shusee Visalyaputra for the support writing the manuscript.

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