RESEARCH ARTICLE

Breast Cancer Detection Rate, Incidence, Prevalence and Interval Cancer-related Mammography Screening Times among Thai Women

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Abstract

Background: A recent guideline by the American Cancer Society recommended that mammography (MMG) should be done for women starting in their mid-40s. In Thailand, information on opportunistic mammography screening is limited and data on the total incidence of breast cancer are also lacking. The purpose of this study was to estimate the breast cancer detection, incident and prevalence rates among Thai women. Materials and Methods: We retrospectively reviewed the opportunistic mammography screening of normal women between 30 and 80 years who underwent the procedure between 2001 and 2010. All cases were followed until 2012. The detection rate was calculated for the whole period of observation using 'number of women with positive findings' divided by 'total number of women screened'. The incidence rate was calculated only at the first MMG while the subsequence rate was calculated based on all new cases detected at each subsequent MMG. Results: Among the 47,430 women, there were 152,091 MMGs or approximately 3.2 occasions per person (range, 1-10). The average duration of the interval between each subsequence visit was 1.8 years. Overall, breast cancer was detected in 543 women, with a detection rate of 10.3 per 1,000 persons. The prevalence rate of breast cancer at the first visit was 5.78 per 1,000 persons. The incidence or new cases detected at any follow-up visit was 10.4 per 1,000 persons. The overall interval cancer was 0.91 per 1,000 women, mainly detected before their second and third MMG, with a rate of 0.0.47 and 0.76 per 1,000 women. Conclusions: Opportunistic mammography screening in Thailand detected 10 case of breast cancer from each 1,000 women. This paper indicated a high rate of cancer detection during a two year interval, hence, a screening mammogram should be performed more often.

Keywords: Breast cancer-opportunistic screening- detection rate- subsequent rate- interval cancer- mammography

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Introduction

Breast cancer is the most common cancer in women worldwide, including in Thailand (Jung et al., 2011; Khunaprema et al., 2013; Howlander et al., 2015; Torre et al., 2015). It is a common cause of disease-related death and morbidity in developed countries (Leong et al., 2010). The respective incidence of new cases of, and deaths from, breast cancer in the United States in 2014 *vs*. 2015 was 232,670 and 40,000 *vs*. 231,840 and 40,290 (Siegel et al., 2014; Siegel R, et al., 2015).

In Thailand, breast cancer is the most common female cancer, representing about 21.8% of all types of cancer in women, followed by cervical cancer and liver and bile duct cancer at 11.1% and 9.9%, respectively. The incidence rate for breast cancer was 28.5 per 100,000 women (Imsamran et al., 2015). Breast cancer is also the third leading cause of death of cancer after liver cancer and lung cancer. The mortality rate increased each year from 2003 to 2014 by 9.9 and 10.5 per 100,000 women respectively (Public outreach and civil society division of the ASEAN secretariat, 2015).

The age at onset of breast cancer in outside Western countries is younger than in Western countries. In Thailand, the burden of age at first diagnosis is similar to other countries in Asia; the first and second peak being at 45 and 60 years of age (Imsamran et al., 2015).

Although the mammogram campaign is well established for breast cancer screening worldwide, several age targets and duration time schedules have been reported (Lee, 2006; Chang et al., 2007; Wu et al., 2012). It is not possible to provide a screening mammogram

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for all women in Thailand because: (a) the cost of a screening mammogram is prohibitive, so most screening mammograms are voluntary; (b) there are inadequate mammography machines; and, (c) there are a few trained radiologists and technicians in this field. Currently, screening mammogram facilities are available only in large and/or well-funded hospitals (i.e., medical schools, regional hospitals, cancer hospitals, and large private hospitals). Annual mammographic screening in women starts at 45 (Oeffinger et al. 2015), and the schedule for interval screening is based on Breast Imaging Reporting and Database System (BIRADS).

Even though there is good compliance of women complying with the MMG schedule, the proportion of women who underwent breast imaging has increased over time. This may be because women are advised to do a screening mammogram annually; however, there is research that suggests annually screening is unnecessary.

In Thailand, information on opportunistic mammography screening is limited; the incidence of breast cancer is also lacking. The aims of the current study were to estimate: (a) the breast cancer detection rate by MMG; (b) the prevalence at first MMG; (c) the incidence at each subsequent follow-up MMG; and, (d) the incidence of interval cancer among Thai women. The results of the study will be used to predict the appropriate interval for mammography screening and the proper age for first mammography among Thai women.

Materials and Methods

Study population

Figure 1 show the data flow chart of this study. We retrospectively followed 47,430 normal women between 30 and 80 years of age who had undergone opportunistic mammography screening at the Thanyarak Breast Center-a breast imaging center in a tertiary hospital in Thailand-between January 2001 and December 2010. The mammography (mammography with or without ultrasound) was based on opportunistic screening. All women had a follow-up MMG and the data were collected until December 2012. The maximum number of follow-up MMGs was 12. A normal woman means a woman with no breast symptoms or a woman who has a proven benign breast lesion. Clinically undetectable but screening detectable cancer means a lesion with no symptoms but detectable by mammography or ultrasound or other investigation (e.g. micro-calcification, non-palpable mass, focal asymmetry, architectural distortion).

Outcomes measurement

The primary outcome of this research was to find the breast cancer detection rate, incidence rate and prevalence rate among Thai women from date of last breast imaging done to date of next or following breast imaging event. Analysis of a outcome of interest were based on the patient diagnosed with breast cancer-

and registered in the Thanyarak Breast Center, Siriraj Cancer Registry, Mahidol University and National Cancer Institute, Thailand-or free of cancer on follow up. This study included all types of breast cancer such as ductal carcinoma, ductal carcinoma in situ (DCIS), lobular carcinoma, mucinous adenocarcinoma, and other types of breast cancer carcinoma. In addition, the interval cancer was defined as women diagnosed for breast cancer during scheduled screening. The diagnosis of breast cancer was ascertained according to the International Classification of Diseases for Oncology: Third Edition. (Fritz et al., 2000). Interval cancer means a woman with a negative result in the last screening episode but a breast cancer diagnosed in the interval before the next scheduled screening.

Statistical analysis

In this study, the detection rate was calculated for the whole period of observation using the number of women with positive findings divided by the total number of women screened. The prevalence was calculated only at first MMG while the subsequence rate was calculated based on all new cases detected at each subsequent MMG. All data analyses were performed using STATA version 13.0 (StataCorp, College Station, TX, USA) All data analyses were performed using STATA version 13.0 (StataCorp, College Station, TX, USA)

The Ethics Consideration

This study was approved by the Khon Kaen University Ethics Committee in Human research (reference number HE 572239).

Results

We retrospectively followed 47,429 women between 30 and 80 years of age who had undergone opportunistic mammography screening at a breast imaging center in a tertiary hospital in Thailand between January 2001 and December 2010. Thirty-seven women were diagnosed with breast cancer before the first screening with mammography: the total number of women for follow-up was 47,392. At the end of the study, 534 women (1.1%) were diagnosed with breast cancer and 46,858 (98.9%) were still normal.

Baseline characteristics, breast cancer detection rate, incidence rate and subsequence rate among Thai women are summarized in Table 1. There were 534 women

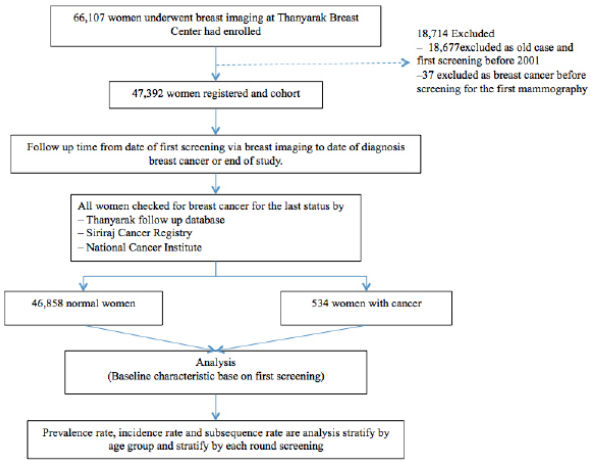

Figure 1. Study flow chart

Table 1. Data for Estimating the Incidence, prevalence and Estimation Results

Number round screening	Round screening										Overall
	1	2	3	4	5	6	7	8	9	10	
Total women attended the screening	47,392	32,335	22,430	16,725	12,180	8,378	5,564	3,570	2,229	1,288	47,392
Loss to follow-up, n		15,057	9,905	5,705	4,545	3,802	2,814	1,994	1,341	941	
Loss to follow-up, (%)		31.8	30.6	25.4	27.2	31.2	33.6	35.8	37.6	42.2	
Mean±SD duration between each round of the screening (years)	-	2.49	1.67	1.21	0.99	1.1	1.06	1.2	-	-	1.78
Total number of cancer	274	106	57	37	19	16	14	9	2	0	534
Screen-detected cases	274	91	40	34	16	15	12	9	0	0	491
Interval cancer		15	17	3	3	1	2	0	2		43
Rate per 1000 women (95% CI)											
Incident rate of all cases	5.8 (5.1-6.5)	3.3 (2.7-3.9)	2.5 (1.9-3.3)	2.2 (1.6-3.1)	1.6 (0.9-2.4)	1.9 (1.1-3.1)	2.5 (1.3-4.5)	2.5 (1.2-4.8)	0.9 (0.2-3.2)	-	11.3 (10.3-12.3)
Subsequent rate detected by the screening		2.8 (2.3-3.5)	1.8 (1.2-2.4)	2 (1.4-2.8)	1.3 (0.7-1.2)	1.8 (1.0-2.9)	2.2 (1.1-3.7)	2.5 (1.2-4.8)	-	-	10.4 (9.5-11.3)
Interval cancer rate		0.5 (0.3-0.7)	0.8 (0.4-1.2)	0.2 (0.1-0.5)	0.3 (0.1-0.7)	0.1 (*)	0.4 (0.1-1.3)	-	0.9 (0.2-3.2)	-	0.9 (0.6-1.2)

Table 2. Number of Women Getting a Mammography and the Number of Cancers Detected by Age Group

Detection mode	Age (years)			
	<40	40-49	50-59	60-79
Overall screen				
Total screening round	24,533	67,208	42,747	12,435
Any screening round	8,056	20,238	13,879	4,688
Total number of cancer	34	215	198	87
Screen-detected cases	33	201	179	78
Interval cancer	1	13	18	8
Rate per 1000 women (95% CI)				
Incident rate	1.4 (0.9-1.9)	3.2 (2.8-3.6)	4.6 (4.0-5.3)	6.9 (5.6-8.6)
Subsequence rate	1.3 (0.9-1.9)	2.9 (2.6-3.4)	4.2 (3.6-4.8)	6.2 (4.9-7.8)

Table 3. Interval Duration for Cases of Interval Cancer

Age group	Total number of women	Number of interval cancer cases			Overall	Interval cancer rate/ 100,000 women
		≤12 months Number (%)	12-24 month Number (%)	>24 months Number (%)		
<40 year	8,094	0	0	1 (100)	1 (100)	12.4
40-49	20,238	4 (30.8)	4 (30.8)	5 (38.5)	13 (100)	64.2
50-59	14,046	6 (33.3)	4 (22.2)	8 (44.4)	18 (100)	128.2
60-69	3,884	0	4 (80.0)	1 (20.0)	5 (100)	128.7
70-79	900	2 (66.7)	0	1 (33.3)	3 (100)	333.3
Overall	47,162	12 (30.0)	12 (30.0)	16 (40.0)	40 (100)	84.8

diagnosed with breast cancer during the study. The rank of cancer in each age group was 40–49, 50–59, 60–69, under 40, and over 70 years (40.2%, 37.0%, 13.3%, 6.0 %, and 3.0 %, respectively).

The overall cancer detection rate for the whole period of observation of 10 years was 10.36 per 1,000 women (95%CI: 9.46 to 11.31). The rank of cancer detection rate in each screening round was the first, second, eighth, and seventh round (5.78 (95%CI: 5.11 to 6.50), 2.81 (95%CI: 2.26 to 3.45), 2.52 (95%CI: 1.15 to 4.78), and 2.16 (95%CI: 1.11 to 3.76) per 1,000 women. The overall mean duration from screening to cancer detection was 1.8 years. The overall interval cancer was 0.91 (95%CI: 0.65-1.22) per 1,000 women; the interval cancer rate was high between the 1st and 2nd round and between the 2nd and 3rd round (i.e., 0.46 (95%CI: 0.25 to 0.76) and 0.76 (95%CI: 0.44 to 1.21) per 1,000 women, respectively). The mean interval duration for interval cancer was 2.2 years. The longest mean duration was between the 1st and 2nd round and the shortest between the 3rd and 4th round (i.e., 2.7 years and 0.5 years, respectively).

Table 2 shows the cancer detection mode per age group. According to age at first screening, we divided age at first screening into 4 groups: under 40, 40 to 49, 50 to 59 and 60 to 79. For each screening round, the following data were collected and analyzed: (a) the total screening round; (b) the total number of cancer detected by screening examinations; (c) total number of interval cancer observed after each visit and before the next visit; (d) the cancer detection rate with 95% CI; and, (e) the total number of women attending each round.

In this study, those between 40 and 49 years and 50 and 59 years comprised the majority (42.6% and 29.6%) while those between 60 and 79 were least common (9.8%). The rank of subsequence detection rate in each age group was the 60 to 79, 50 to 59, 40 to 49, and under 40 (6.27 (95%CI: 4.96 to 7.82), 4.18 (95%CI: 3.59 to 4.84), 2.99 (95%CI: 2.59 to 3.43), and 1.34 (95%CI: 0.92 to 1.88) per 1,000 women).

Table 3 presented the interval cancer case per age group. The total of interval cancer was 40 cases. Rank of interval cancer cases were showed in age between 50 to

59 and 40 to 49 (18 cases (45.0%) and 13 cases (32.5%)). Only one case of interval cancer showed in women under 40 years. Anyway, the interval cancer case in women age under 40 year found without 24 months. Twenty-four cases were found within 24 months (60%). The interval cancer rate were 25.3 (12 cases) and 50.6 (24 cases) per 100,000 women for interval time to screening as 12 and 24 months, respectively.

Discussion

This study is the first longitudinal cohort for women with opportunistic mammographic screening in Thailand: 47,430 women were included. The study had some limitations and possible biases. First, not all women who came for screening returned for a follow-up screening. Second, some women were lost to follow-up for a long period but later returned to the Thanyarak Breast Center with a BIRADS assessment of 4 or 5. Third, we checked for breast cancer status at only 3 institutes (i.e., the National Cancer Center, Siriraj Cancer Registry, and the Thanyarak Breast Center), so if any of our cases were diagnosed with breast cancer and treated elsewhere, these cases were missed.

The current study showed that the incidence and subsequence rate peaks in women between 40 and 49 and again between 60 and 69; the incidence rate in those under 40 is low. The respective incidence rate was high at the first, second, and third screening. The incidence for interval cancer within 12 months was 19.7 per 100,000 women, compared to 39.4 per 100,000 within 24 months. Screening for women between 40 and 44 would be more beneficial than after menopause (Mandelblatt et al., 2009; Hubbard et al., 2011; Kerlikowske et al., 2013). Screening with breast imaging should start at aged 40 years and continue regularly for at least 3 rounds

Breast cancers are known to be common in women between 40 and 59, data from this opportunistic mammography screening study confirm that cancer detection rate were high in women age 40 to 49, 50 to 59 and 60 to 79 years. The incidence of cancer detection rate was 3.19, 4.63 and 6.99 per 1,000 women in women age 40 to 49, 50 to 59 and 60 to 79 years, respectively. Incidence rate in women age less than 40 years quit low besides other age group (1.38 per 1,000 women). Since incidence rate in this age less than 40 years are quite low when compared to screening benchmarks by American College of Radiology (4.7 *vs*. 3.7 per 1,000 women as screening mammography *vs*. screening ultrasound, respectively), screening in this age group might have to be reconsidered (D'Orsi CJ et al., 2013).

Interval cancer is an important factor for decision-making regarding the age for starting mammography screening (Wilson and Jungner., 1968), so it is important to know the age-specific subgroup of first diagnosis. In the current study, we found 40 interval cancer cases; 32.5% occurred between 40-49 years of age. Twenty-four interval cancer cases occurred within 24 months for whom the incidence rate was 50.6 per 100,000 women. By comparison, 16 cases occurred more than 2 years after the last screening for whom the incidence of interval cancer cases was 33.7 per 100,000 women. Definitions of interval cancer cases varies, depends on the judgments of physicians or policy makers. Some protocols define interval cancer as occurring within one year after the last mammogram screening, while others define it as occurring within 2 years. According to the first definition, if a case occurs after 2 years, it is not defined as interval cancer and not eligible for benefits from mammogram screening (Tabar et al., 1987). In the current study, according to the data from the Thanyarak Breast Center, interval cancer was defined as women diagnosed with breast cancer between 2 years after the last mammogram screening. According to our data, 25.3 *vs*. 50.6 per 100,000 women will NOT get early treatment if policy makers define the interval time to screening as 12 *vs*. 24 months, respectively.

There are varies recommendations for age at first mammography and the interval between each screening. The American Cancer Society recommends that women have an annual mammography between 45 and 54 years of age while the U.S. Preventive Services Task Force Mammogram Guidelines recommend women begin screening at 50 with a follow-up every two years until they are 74 (Oeffinger et al., 2015). Thailand follows the American Cancer Society Guidelines and those of the Mayo Clinic; namely, that women should undergo an annual mammography starting at age 40 (American Cancer Society, 2013; Chaiwerawattana et al., 2013).

Opportunistic mammography screening in Thailand suggests a case of breast cancer for every hundred women tested. Although breast cancer screening using breast imaging cannot be implemented as a national program in Thailand at present, the results of the current study show the duration between onset of disease and clinical phase by age group; this is good information for policy decisions on how to prevent and detect breast cancer in each age group. Moreover, both the high cost of screening mammogram and the number of rounds of screening are important factors when developing policy on screening.

A follow-on study should include a larger of number of screening and follow-up cases to estimate the sensitivity and positive predictive value. The method of estimation for multi-stage disease should include mean sojourn time, PPV, and multi-stage Markov chain mode for in women of program screening. A randomized control trial would be an appropriate methodology for the next study.

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