Effect of mammography screening on long-term survival of breast cancer patients: Results from the National Cancer Screening Program in Korea

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Abstract

Background

Breast cancer (BC) is the most commonly diagnosed cancer type globally with the geo-ethnic differences in BC epidemiology. Therefore, many countries have adopted national cancer screening programs to reduce the burden of BC. Currently, the Korean National Cancer Screening Program provides biannual mammography screening for women aged ≥40 years. However, there were limited Asian studies investigating the effect of mammography screening, especially study with the long-term follow-up. Our study investigated the effect of mammography on the long-term survival of BC patients aged 40 years or older according to the screening history and duration since screening.

Methods

The study cohort was organized from three nationwide databases of the Korean National Cancer Screening Program, the Korean Central Cancer Registry, and death certificates. We included 24,387 women diagnosed with invasive cancer or ductal carcinoma in situ in 2008 and 2009 and followed up until December 31, 2019. The Kaplan–Meier analysis and the log-rank test were used to compare the survival of the subgroups. Cox proportional-hazards regression was used to investigate the effect of BC screening on mortality.

Results

Overall, 20,916/24,387 patients (85.8%) were alive at the end of the follow-up period (median: 10.5 years). The long-term survival rate was significantly lower in the never-screened group (80.3%) than in the screened group (88.9%) (P<0.001). The survival rate ranged from only 22.4% in patients with distant stage to 96.4% in DCIS patients. A 35% BC mortality reduction (hazard ratio [HR]=0.65, 95% confidence interval [CI]=0.60–0.70) from screening was observed. Subgroup analysis based on cancer stage showed reductions of 62%, 36%, and 24% for subgroups of localized stage, regional stage, and distant stage, respectively. Women aged 40–49 years received the least benefit from BC screening (HR=0.71, 95% CI=0.62–0.81).

Conclusions

Mammography screening was effective in reducing the risk of BC-specific death in Asian women across all cancer stages. However, this effect was relatively small among women in their 40s, suggesting that more detailed and specialized screening strategies are needed.

Background

Breast cancer (BC) is the most commonly diagnosed cancer type globally based on the number of new cases and the age-standardized incidence. In 2020, BC contributed to 11.7% of new cancer cases [1]. However, the distribution of BC cases is skewed; approximately more than 80% of BC cases occur in

countries with high or very high human development index. To reduce the high burden of BC, several countries have adopted national cancer screening programs [2], which mostly use mammography as the main screening modality. With the geo-ethnic differences in BC epidemiology, the challenges in implementing the mammography screening program vary across regions [3–5]. In Asia, especially, BC screening has several additional challenges including screening at the age of 40s and the accuracy of mammography among the population with relatively high prevalence of dense breast and its relationship to overdiagnosis [3, 6, 7]. Therefore, BC screening in Asia should be considered more carefully with the regional specific evidence [3, 4]. However, studies investigating the effectiveness of mammography screening programs in Asia are still limited [8–11].

In Korea, BC is one of the most common cancer types in women. In contrast with the decreasing overall cancer incidence, BC incidence is steadily increasing over time. In 2018, the age-standardized rate of BC (57.9) was almost three times higher than those of colorectal cancer (20.6) and stomach cancer (18.3) in women [12]. Regarding the age-specific incidence, the BC incidence peaked at 45–49 years before gradually declining [12]. Currently, the Korean National Cancer Screening Program (KNCSP) provides biannual mammography screening for all women aged 40 years or older based on the age-specific BC incidence in Korea [13]. A study evaluated the effect of mammography on BC mortality [14], but it was limited in assessing the patient's long-term survival and time interval since screening exposure.

Therefore, this study investigated the effect of mammography on the long-term survival of BC patients aged 40 years or older according to the screening history and duration since screening using the KNCSP database. We also assessed the association between mammography screening and survival for in situ cases.

Methods

Study participants

The baseline population comprised 24,454 patients aged 40–79 years who were diagnosed with BC or ductal carcinoma in situ (DCIS) between January 1, 2008, and December 31, 2009, and registered in the Korea Central Cancer Registry (KCCR), which covered more than 95% of cancer cases in South Korea [12]. Subsequently, we excluded 67 breast cancer patients identified from only death certificates without diagnostic information. Finally, a total of 24,387 women were included in our final analysis.

Using the resident's unique 13-digit registration number, we linked our baseline BC patients identified from the KCCR and the KNCSP database for information on the history of mammographic screening between 2002 and 2009. We followed them up from the date of BC diagnosis till the end of 2019, allowing us to determine the long-term survival of the entire study population for at least 10 years. The date and cause of death were ascertained from the death certificates provided by Statistics Korea.

The current retrospective study was approved by the Institutional Review Board of the National Cancer Center, Korea (No. NCCNCS08129). We used de-identified data for a relatively large population from the

National Health Insurance Service (NHIS) database, and the requirement for informed consent for this study was waived.

Measurement

Information on the date of the primary diagnosis and tumor characteristics were ascertained from the KCCR database [12]. We used the International Classification of Diseases, 10th revision (ICD-10), codes [15], and the BC cases were defined as those with the ICD-10 codes of C50 and D05. The anatomic sites were grouped into the inner part, the outer part, central portion, and others (nipple and axillary tail of breast) using the topographical code of the international classification of diseases for oncology – 3rd edition (ICD-O-3) [16]. For the histological subtype, we divided the patients into 4 main groups based on the ICD-O-3 morphology codes, as suggested by previous studies: DICS, ductal carcinoma, lobular carcinoma, and others [17, 18]. The stage at diagnosis was presented as DCIS, localized stage, regional stage, or distant stage according to the summary stage classification in the Surveillance, Epidemiology, and End Results (SEER) Cancer Statistics Review of the National Cancer Institute [19].

The mammography screening history and the basic sociodemographic information were extracted from the KNCSP database. The mammography screening exposure of BC patients was assessed using screening records from 2002 to 2009 when KNCSP for BC was introduced[13]. The socioeconomic statuses were categorized into three according to the health insurance type: medical aids program (MAP) recipients (people who live under the poverty line and receive livelihood assistance from the Government), NHI beneficiaries with a premium of 50% or lower, and NHI beneficiaries with a premium above 50%.

Study outcome

The primary outcome of the study was the long-term survival of BC patients according to their mammography screening history. To ascertain death, all BC patients were followed for at least 10 years or more. The primary outcome of this study was BC-specific mortality. All-cause deaths, including and excluding those from BC as secondary outcomes, were also assessed to adjust for methodological bias, such as misclassification bias and competing risks. Besides, the person-year of all BC patients was measured from the date of BC diagnosis to the date of death or the end of follow-up, whichever occurred first, corresponding to the end of the observation period, which was December 31, 2019.

Statistical analysis

The baseline characteristics including, sociodemographic information and tumor characteristics, of the screened and never-screened patients were compared using the chi-squared test. The Kaplan–Meier analysis and the log-rank test were used to compare the survival of the subgroups according to screening history.

We conducted Cox proportional-hazards regression analysis to estimate the hazard ratios (HRs) with 95% confidence intervals (CIs) for investigating the effect of BC screening on BC mortality. We assessed the HRs for all-cause death, except from BC, to adjust for methodological bias, such as competing risks. All the models were adjusted for age, socioeconomic status, and tumor characteristics such as cancer stage,

anatomic site, and histological subtype. Additionally, the models were run on several subpopulations stratified by age and cancer stage to investigate the variation of the BC screening effects in the different groups.

The net benefit of mammography screening was estimated to address the risk of self-selection bias in a cohort study using a formula suggested by the previous study: net benefit = (HR^b-HR^a)/HR^bX100, where HR^b represents the HR for total mortality except BC, and HR^a represents the HR for BC-specific mortality [20]. SAS version 9.4 (SAS Institute, Cary, NC) was used for all the statistical analyses, and *P*-values of < 0.05 denoted statistical significance.

Results

The baseline characteristics of the BC patients are presented in Table 1. Of the 24,387 BC patients, 8,823 (36.2%) were never screened and 15,564 (63.8%) were screened for BC. There were significant differences in the sociodemographic and tumor characteristics between the never-screened and screened patients. BC involving the inner and outer parts of the breast, DCIS, and localized BC were significantly more prevalent among the screened patients than among the never-screened patients (P < 0.001). Of the screened patients, 54.6% underwent screening only once, and 68.5% underwent screening within a year on the date of cancer diagnosis. Overall, 3,471 patients died (14.2%); 2,614 died from BC during the median follow-up duration of 10.5 years (interquartile range: 10.3–11.5 years).

Table 1
Baseline characteristics of breast cancer patients diagnosed from 2008 to 2009

Variables	Total	Never-Screened	Screened	*P*-value
	N = 24387	N = 8823	N = 15564	
Age at diagnosis (years), n (%)				
40–49	10387 (42.6)	4176 (47.3)	6211 (39.9)	< 0.001
50–59	8409 (34.5)	2739 (31.0)	5670 (36.4)	
60–69	3909 (16.0)	1171 (13.3)	2738 (17.6)	
70–79	1682 (6.9)	737 (8.4)	945 (6.1)	
Socioeconomic status, n (%)				
NHI premium, upper 50%	12361 (50.7)	4539 (51.4)	7822 (50.3)	< 0.001
NHI premium, lower 50%	11033 (45.2)	3917 (44.4)	7116 (45.7)	
MAP	993 (4.1)	367 (4.2)	626 (4)	
Anatomical site, n (%)				
Inner part	3833 (15.7)	1330 (15.1)	2503 (16.1)	< 0.001
Outer part	9295 (38.1)	3175 (36.0)	6120 (39.3)	
Central portion	1127 (4.6)	421 (4.8)	706 (4.5)	
Others	10132 (41.5)	3897 (44.2)	6235 (40.1)	
Stage at diagnosis, n (%)				
DCIS	3046 (12.5)	883 (10.0)	2163 (13.9)	< 0.001
Localized	11374 (46.6)	3829 (43.4)	7545 (48.5)	
Regional	7232 (29.7)	2846 (32.3)	4386 (28.2)	
Distant	1034 (4.2)	612 (6.9)	422 (2.7)	
Unknown	1701 (7.0)	653 (7.4)	1048 (6.7)	
Histological subtype, n (%)				
DICS	3046 (12.5)	883 (10.0)	2163 (13.9)	< 0.001
Ductal carcinoma	18432 (75.6)	6789 (76.9)	11643 (74.8)	
Lobular carcinoma	1158 (4.7)	431 (4.9)	727 (4.7)	
Others	1751 (7.2)	720 (8.2)	1031 (6.6)	
Screening frequency, n (%)				

Variables	Total	Never-Screened	Screened	*P*-value
Never	8823 (36.2)	8823 (100)	-	NA
1 time	8505 (34.9)	-	8505 (54.6)	
2 times	4490 (18.4)	-	4490 (28.8)	
3 times or more	2569 (10.5)	-	2569 (16.5)	
Time interval since screening, n (%)				
Never	8823 (36.2)	8823 (100)	-	NA
> 3 year	1231 (5.0)	-	1231 (7.9)	
2–3 years	1120 (4.6)	-	1120 (7.2)	
1–2 years	2548 (10.4)	-	2548 (16.4)	
< 1 year	10665 (43.7)	-	10665 (68.5)	
Survival status, n (%)				
Alive	20916 (85.8)	7081 (80.3)	13835 (88.9)	< 0.001
BC death	2614 (10.7)	1371 (15.5)	1243 (8.0)	
All-cause mortality except BC	857 (3.5)	371 (4.2)	486 (3.1)	
NHI, National Health Insurance; MAP, Medical Aid Program; DCIS, Ductal carcinoma in situ; BC, Breast Cancer.				

The survival rate was significantly higher among the screened patients (88.9%) than among the never-screened patients (80.3%) (*p*-value < 0.001). Similar trend of survival was also observed in each cancer stage group excepting DCIS group (Fig. 1, p-value-0.28). The long-term survival was significantly different for women with different sociodemographic characteristics and screening histories (Supplement Table S1). The risk of BC-specific death (hazard ratio) increased significantly with age, lower socioeconomic status, and advanced stage at diagnosis.

The hazard ratios for total mortality, BC-specific mortality, and non-BC mortality according to the screening history are shown in Table 2. For model 1, after adjusting for age and economic status, mammography screening was associated with an approximately 53% lower risk of death from BC (HR = 0.47, 95% CI = 0.44–0.51). This figure was 35% for model 2 with additional adjustment of tumor characteristics (HR = 0.65, 95% CI = 0.60–70) and the fully adjusted model 3 with invasive cancer only (HR = 0.65, 95% CI = 0.60–0.70). A similar decrease was observed for overall mortality and mortality from conditions other than BC, with fully adjusted HRs (including invasive cancer only) of 0.68 (95% CI = 0.63–0.72) and 0.74 (95% CI, 0.64–0.86), respectively.

Table 2
Hazard ratios for total mortality, breast cancer-specific mortality, and non-breast cancer mortality according to the screening history

				Hazard ratio			
	Death	**Person-year**	**Death rate per 1000**	Crude	Model 1[1]	Model 2[2]	Model 3[3]
				HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Total mortality							
Never screened	1742	84910.2	20.5	1.00	1.00	1.00	1.00
Screened	1729	158590.1	10.9	0.53 (0.5–0.57)	0.52 (0.48–0.55)	0.67 (0.62–0.71)	0.68 (0.63–0.72)
BC-specific mortality							
Never screened	1371	84910.2	16.1	1.00	1.00	1.00	1.00
Screened	1243	158590.1	7.8	0.49 (0.45–0.53)	0.47 (0.44–0.51)	0.65 (0.60–0.70)	0.65 (0.60–0.70)
Non-BC mortality							
Never screened	371	84910.2	4.4	1.00	1.00	1.00	1.00
Screened	486	158590.1	3.1	0.70 (0.61–0.80)	0.67 (0.59–0.77)	0.69 (0.60–0.79)	0.74 (0.64–0.86)

BC, Breast cancer; HR, hazard ratio; 95% CI, 95% confident interval.

[1] Adjusted for age and socioeconomic status.

[2] Adjusted for age, socioeconomic status, stage, histological subtype, and anatomic site.

[3] Adjusted for age, socioeconomic status, stage, anatomic site, and histological subtype (invasive cancer only N = 21,341)

The effect of screening on BC mortality varied with age and the stage of BC at diagnosis (Table 3). The risk reduction for BC-specific death was the highest for patients older than 70 years (HR = 0.50, 95% CI = 0.40–0.63) who had been screened and the lowest for those in their 40s (HR = 0.71, 95% CI = 0.62–0.81).

The largest risk reduction for BC-specific death was observed in patients with localized BC who had been screened (HR = 0.58; 95% CI = 0.49–0.70). For cases of distant-stage cancer, the risk of death was significantly reduced by approximately 24% (HR = 0.76; 95% CI = 0.66–0.89). However, there was no significant difference between the BC-specific survival among patients diagnosed with DCIS (HR = 0.62, 95%CI = 0.26–1.43, p-value = 0.280). Overall, the mammography screening was significantly associated with 42%, 36%, and 24% mortality reductions in the localized stage, regional stage, and distant stage subgroups, respectively (Table 3). Given the similar results for all-cause mortality, BC-specific mortality, and other causes of mortality except BC, further subgroup analyses were conducted (Supplementary Table S2).

Table 3
Hazard ratios for breast cancer-specific mortality stratified by age group and stage at diagnosis according to the screening history

	Number of BC deaths	Person-year	Death rate per 1000	Fully adjusted hazard ratio[1] HR (95% CI)
Stage at diagnosis				
DCIS				
Never screened	9	9417.4	0.96	1.00
Screened	14	23173.5	0.60	0.62 (0.26–1.43)
Localized				
Never screened	220	39763.1	5.53	1.00
Screened	266	79090.9	3.36	0.58 (0.49–0.70)
Regional				
Never screened	529	26923.9	19.65	1.00
Screened	551	43473.4	12.67	0.64 (0.57–0.73)
Distant				
Never screened	474	2796.0	169.53	1.00
Screened	297	2318.0	128.13	0.76 (0.66–0.89)
Unknown				
Never screened	139	6009.9	23.13	1.00
Screened	115	10534.4	10.92	0.48 (0.37–0.62)
Age at diagnosis (years)				
40–49[2]				
Never screened	504	36728.3	12.11	1.00
Screened	406	53949.7	6.44	0.71 (0.62–0.81)
50–59[2]				

	Number of BC deaths	Person-year	Death rate per 1000	Fully adjusted hazard ratio[1] HR (95% CI)
Never screened	442	23675.6	16.74	1.00
Screened	454	49914.5	7.90	0.65 (0.57–0.74)
60–69[2]				
Never screened	212	9933.9	19.78	1.00
Screened	252	23777.7	9.21	0.61 (0.51–0.74)
≥ 70[2]				
Never screened	204	5155.2	36.05	1.00
Screened	117	7774.7	13.37	0.50 (0.40–0.63)

BC, Breast cancer; HR, hazard ratio; 95% CI, 95% confident interval; DCIS, Ductal carcinoma in situ.

[1] *Adjusted for age, socioeconomic status, stage, histological subtype, and anatomic site.*

[2] *Adjusted for socioeconomic status, stage, histological subtype, and anatomic site (invasive cancer only)*

Additionally, our results showed a relatively similar effect of screening on BC mortality between people who had a time interval since the last screening of less than 1 year (HR = 0.63, 95% CI = 0.57–0.69) and 1–2 years (HR = 0.65, 95% CI = 0.56–0.76) (Table 4). The 25% lower risk of death from BC was still observed among people who had their last screening more than two years earlier (2–3 years: HR = 0.75, 95%CI = 0.62–0.91; >3 years: HR = 0.75, 95%CI = 0.62–0.91). Further, women who underwent mammography screening more than three times before BC diagnosis had a statistically significant 48% reduction of the risk of death from BC.

Table 4
Hazard ratios for breast cancer-specific mortality according to time interval since the last screening and screening frequency

	Number of BC deaths	Person-year	Death rate per 1000	Fully adjusted hazard ratio[1] HR (95% CI)
Screening frequency				
Never screened	1362	75492.9	18.04	1.00
1 time	739	74426.1	9.93	0.70 (0.64–0.77)
2 times	333	38938.3	8.55	0.62 (0.55–0.70)
3 times or more	157	22052.3	7.12	0.52 (0.44–0.62)
P-value for trend				< 0.001
Time interval since screening				
Never screened	1362	75492.9	18.04	1.00
≥ 36 months	108	10498.5	10.29	0.75 (0.62–0.92)
24–35 months	111	9694.3	11.45	0.75 (0.62–0.91)
12–23 months	206	22208.6	9.28	0.65 (0.56–0.75)
≤ 11 months	804	93015.3	8.64	0.63 (0.57–0.69)
P-value for trend				< 0.001

BC, Breast cancer; HR, hazard ratio; 95% CI, 95% confident interval;

[1] Adjusted for age, socioeconomic status, stage, histological subtype, and anatomic site.

Discussion

Long-term follow-up studies for estimating the screening effects of BC patients in Asian women are very limited. The current study reported that the rate of BC-specific deaths decreased by 35% among screened BC patients relative to their never-screened counterparts (HR = 0.65, 95% CI = 0.60–0.70) based on 10-year follow-up data. Besides the down stage effect of mammography screening shown in previous studies [8, 14, 21–24], this study provided additional evidence on the stage-specific screening effect on mortality; the BC mortality reductions after screening were 42%, 36%, and 26% for patients diagnosed with localized, regional, and distant stages, respectively. A study conducted in Finland involving participants predominantly aged ≥ 40 years reported that patients with BC detected during a screening program had a 41% lower risk of BC death than those with BC detected outside the screening program after 15 years of follow-up[25]. Similarly, a large-scale study using data from the Swedish Cancer Registry highlighted that

40-69-year-old women who underwent mammography had a 41% lower risk of BC death within 10 years [24]. A 57% BC mortality rate reduction in women aged 50–69 years was reported by Kaplan et al. for 5-year survival [26], which is expected to have further reduced at 10 years as the effect of lead-time bias. Kalager et al. reported a 14% reduction in the BC mortality rate after the introduction of the screening program relative to that before the program [23], which is lower than that reported by our study and other mentioned studies [24, 25]. The main reason for the differences was that Kalager et al mainly divided the BC patients into 2 groups (pre-program and post-program) for the analysis without considering the participation status. Therefore, the effect of mammography on survival may have been underestimated, as some patients in the post-program group did not participate in the screening program.

Mammography screening among women younger than 50 years is controversial, as limited evidence supports the cost and effectiveness among this age group [27, 28]. Notwithstanding, some Asian countries have included women in their 40s in their screening guidelines, given the different epidemiological characteristics of the Asian population [3–5, 29]. In the current study, we found that the youngest age group of 40–49 years received the least benefit from mammography screening related to long-term survival (HR = 0.71, 95% CI = 0.62–0.81). The higher prevalence of dense breasts in younger women had been addressed by a Korean study, whereas the proportion of women with dense breasts was approximately more than 80% for women in their 40s attending mammography screening; this decreased in the older age groups [30]. The accuracy of mammography screening may be relatively lower for this age group [4, 31]. Therefore, screening for women in their 40s should have age-specific strategies including appropriate modality and screening interval [4, 27, 32–34]. The U.S. Preventive Services Task Force Recommendation indicated that screening at the age of 40 years should be based on the individual risk and benefits of mammography[32]. According to the recommendation of the American Cancer Society, 40-44-year old women can undergo mammography screening every year; however, women aged 45–54 and ≥ 55 years should screen annually and biannually, respectively [33]. The American College of Radiology also recommends annual mammography screening for women starting from 40 years old [34].

Overdiagnosis by BC screening is preferred for cases that are detected and diagnosed as BC but never progress to symptomatic and aggressive cancer cases. Therefore, the detection of these cases does not contribute to mortality reduction or cause more harm to patients such as psychological consequences or unnecessary treatments [35–37]. The DCIS cases are more likely to be associated with overdiagnosis due to screening than invasive BC cases [37, 38]. In the current study, we found a significantly higher proportion of DCIS cases among the screened group (13.9%) compared with the never-screened group (10.0%) but no significant reduction of the long-term BC mortality rate attributable to screening. While this can be associated with the successful treatment of early cancer, there may be several cases of overdiagnosis in this group. It is well known that DCIS patients have an excellent prognosis of more than 95% during the long-term follow-up [39, 40], which is consistent with the long-term survival rate of 96.4% in our study. Moreover, a study from SEER indicated that low-grade DCIS patients in the surgery and non-surgery groups had the same survival rates [41]. In contrast, women diagnosed with DCIS are not well aware of the risk of developing invasive cancer, which worsens their screening-related psychological issues [42–44]. Given the increasing trend of DCIS associated with the widespread implementation of

screening, it is essential to improve the understanding of DCIS in the population and the shared decision-making strategy for DCIS treatment between patients and physicians to minimize the risk of overdiagnosis and overtreatment.

Mammography screening has challenges that should be taken into careful consideration when evaluating its effectiveness. Firstly, the cancer cases detected by screening appear to have demonstrated longer survival, which is attributable to the earlier diagnosis, the so-called lead-time bias. In our cohort, the effect of lead-time bias may have been minimal due to the follow-up duration of at least 10 years for all patients. Secondly, the favorable outcomes for the screened population may have been attributable to the greater likelihood that slowly progressing cancers would be detected by screening. In addition, there is also the risk of selection bias stemming from the different baseline characteristics of people who show up for screening and those who do not. To partially control this in our study, we used several models with different population levels of adjustment of socioeconomic and tumor characteristics. Since the context of BC screening is universally provided with more than 80% of a lifetime screening rate [13], the selection bias would be small as indicated in the Handbook of Cancer Prevention by the International Agency for Research on Cancer (IARC) [45]. Additionally, we also used the formula suggested by the previous study design to address self-selection bias in a cohort study [20], and the calculated net benefit from mammography screening in our study was reported at 12.2% for invasive cancer only (Table 2) and 17.6% after excluding DCIS and distant cancer cases (Supplement Table S3).

Nevertheless, our study had several limitations. First, our study could not combine the opportunistic screening information for the screening history. The non-attendants of KNCSP may have already undergone opportunistic screening, which is often used during ultrasonography as a screening test. Therefore, the effect of BC screening through the KNCSP could be underestimated. Second, our study only assessed the extent of BC based on the summary stage classification by the SEER Cancer Statistics Review of the National Cancer Institute [19], which had limitations in investigating the stage-specific effect of screening compared with classification systems widely used for cancer treatment, such as the Tumor, Node, Metastasis (TNM) staging system [46]. Lastly, as our study covered all BC patients diagnosed in 2008 and 2009 in Korea, it was not possible to include information about treatment, which is a strong predictor of patient prognosis, in our analysis. However, we believe that the treatment statuses of the screened and never-screened groups are relatively similar at the same stage as all Korean residents are enrolled in the NHIS. Despite these limitations, this is one of the first studies evaluating the effect of mammography on the long-term survival of BC patients in Asia, to the best of our knowledge. Our study linked information at the individual level from 3 national databases with the nearly complete data on screening information, cancer information, and death information. This makes our findings relatively generalizable to the entire population of the country.

In conclusion, our study found a significant reduction of the BC-specific mortality rate after mammography screening of BC patients during a long-term follow-up of 10 years. Our results also indicated a reduced effect of mammography among women in their 40s, who require more detailed and

specialized screening strategies. Future studies should have appropriate designs to directly address the overdiagnosis by mammography screening, especially among DCIS patients.

List Of Abbreviations

BC	Breast cancer
CI	Confidence interval
HR	Hazard ratio
ICD	International Classification of Diseases
KCCR	The Korea Central Cancer Registry
KNCSP	Korea National Cancer Screening Program
SEER	The Surveillance, Epidemiology, and End Results

Declarations

Ethics approval and consent to participate

The current retrospective study was approved by the Institutional Review Board of the National Cancer Center, Korea (No. NCCNCS08129). We used de-identified data of a relatively large population from the National Health Insurance Service database, and the requirement for informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

The data are not publicly available due to privacy and ethical restrictions. The datasets generated during and/or analysed during the current study are not publicly available due to privacy and ethical restrictions but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

XQL, JKJ, MS, and KSC made substantial contributions to the conception and design of study. XQL and KL performed data curation and formal analysis. The data resources were provided by KWJ and KSC. The manuscript was drafted by XQL, and was reviewed/edited by KSC. **All authors read and approved the final manuscript.**

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Figures

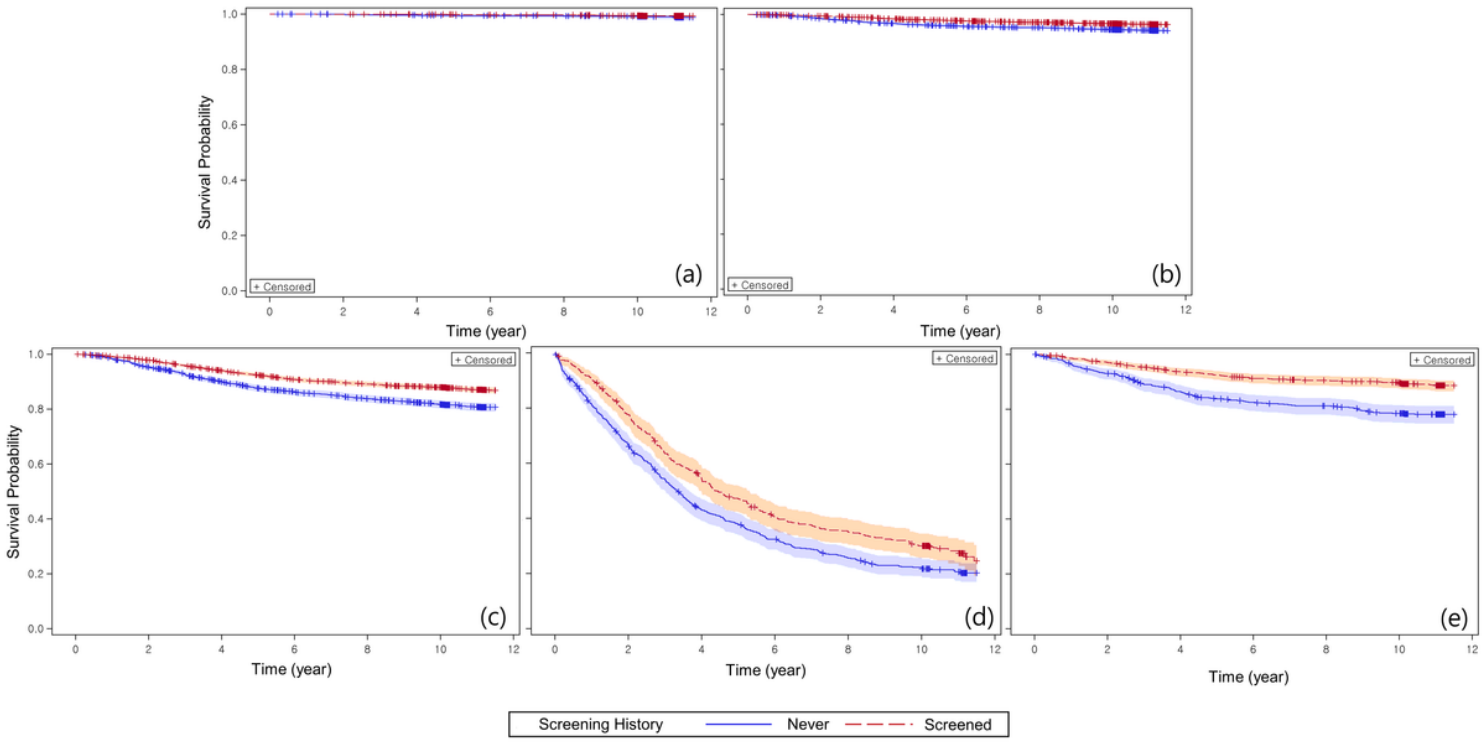

Figure 2

Product-limit breast cancer-specific survival estimates according to screening history-based SEER stages: (a) DCIS; (b) Localized; (c) Regional; (d) Distant; (e) Unknown.

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