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BREAST IMAGING

ORIGINAL ARTICLE

Bahcesehir long-term population-based screening compared to National Breast Cancer Registry Data: effectiveness of screening in an emerging country

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PURPOSE
We aimed to show the effects of long-term screening on clinical, pathologic, and survival outcomes in patients with screen-detected breast cancer and compare these findings with breast cancer patients registered in the National Breast Cancer Registry Data (NBCRD).

METHODS
Women aged 40–69 years, living in Bahcesehir county, Istanbul, Turkey, were screened every 2 years using bilateral mammography. The Bahcesehir National Breast Cancer Registry Data (BMSP) data were collected during a 10-year screening period (five rounds of screening). BMSP data were compared with the NBCRD regarding age, cancer stage, types of surgery, tumor size, lymph node status, molecular subtypes, and survival rates.

RESULTS
During the 10-year screening period, 8758 women were screened with 22621 mammograms. Breast cancer was detected in 130 patients; 51 (39.2%) were aged 40–49 years. The comparison of breast cancer patients in the two programs revealed that BMSP patients had earlier stages, higher breast-conserving surgery rates, smaller tumor size, more frequent negative axillary nodal status, lower histologic grade, and higher ductal carcinoma in situ rates than NBCRD patients ($p = 0.001$, for all).

CONCLUSION
These results indicate the feasibility of successful population-based screening in middle-income countries.

Breast cancer is the most frequent cancer and cause of cancer-related deaths among Turkish women, as well as globally (1–5). Although the incidence of breast cancer increases every year, mortality rates are decreasing in developed countries because of nationwide screening programs and modern treatment options (5, 6). An invited mammography screening program for women aged between 40 and 69 years revealed a 60% reduction in cancer-related 10-year mortality in a landmark study (7). A systematic review of Myers et al. (8) showed that breast cancer screening reduced mortality by 20% in average-risk women of all age groups. However, this review did not evaluate the differences between annual and biannual mammographic screening.

In 2004, the Cancer Control Department of Turkey recommended biannual mammographic screening for women aged 50–69 years, based on European Guidelines. The population of Turkey is relatively young, and almost half of all breast cancer patients in Turkey are younger than 50 years. According to and National Breast Cancer Registry Data (NBCRD) reports, the starting age for mammography screening was set as 40 years. The Bahcesehir Mammographic Screening Program (BMSP) was the first organized population-based 10-year (2009–2019) mammography screening program in Turkey, a middle-income country.

Turkish Federation of Breast Diseases Societies started a voluntary data registry program that was provided by breast surgeons working in secondary or tertiary hospitals. This program aimed to collect detailed information of breast cancer patients and to pool comprehensive country-specific breast cancer data. This registry, namely the NBCRD, was the first specified database on breast cancer in the country and was started in 2005, before the

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BMSP (9). Data from 36 centers were collected for 10 years. However, the cancer registry is a standard database containing general information as defined by the International Agency for Research on Cancer standards.

The aim of this study was to show the feasibility of a population-based breast cancer screening program in an emerging, middle-income country, Turkey. The objective of our study was to evaluate the effectiveness of a population-based breast cancer screening program by comparing it with NBCRD data.

Methods

The population in the project area was 126 837 (5 districts in Bahcesehir, Istanbul, Turkey) in 2009; among these, the total number of women between the ages of 40 and 69 years was 4257 according to the Turkish Statistics Institute. All women aged 40–69 years who lived in Bahcesehir county were invited to Bahcesehir Breast Center (MEMEDER) by letter, e-mail, or telephone during the five-round (10-year) screening program. A list of the citizens was provided from the Turkish Statistical Institute's address-based population registration system. The list was renewed every two years (for each screening round) between January 2009 and January 2019. All women who were screened following the invitation were included in the study. Each eligible woman signed a written informed consent form. The exclusion criteria were as follows: (*i*) already having a diagnosis of breast cancer, (*ii*) having a mammogram within the past year or a breast biopsy within 6 months, (*iii*) current pregnancy. In the first round (the first two-year period), 3758 (88.3%) women were successfully screened (10). During the 10-year period, once every two years, women who turned age 40 in the region were included in the screening, and women aged over 69 years were excluded. During the screen, movers into and out of the region were updated every two years. The total number of women screened by the end of five rounds reached 8758. The acceptance rate for screening after invitation was 71.7%.

Ethical approval from the Institutional Review Board of Istanbul University was obtained (Application No.: 2007/152, Date: 24.01.2007/01). The national health authorities were informed and approval was obtained. All eligible women invited to the study were informed and written consents were obtained from those who accepted to participate in the study.

Main points

- The Bahcesehir Mammographic Screening Program (BMSP) demonstrates the feasibility of a mammography screening program in a country with limited resources.
- Mammography screening may significantly shift the stage distribution of breast cancer.
- At least one screening after the age of 40 years may be beneficial for countries with limited resources where a long-term screening program cannot be held.
- The patients in BMSP had earlier stages, higher breast-conserving surgery rates, smaller tumor size, less frequent axillary nodal involvement, lower histologic grades, and higher DCIS rates compared with the National Breast Cancer Registry Data.

Screen procedure

Full-field digital mammographic equipment was used in the study (Selenia, Hologic). Mediolateral oblique (MLO) and craniocaudal (CC) projections were obtained and read by two expert radiologists with more than 5 years of experience. In cases of discordance, a third radiologist, who has over 20 years of experience in breast imaging, evaluated the images for the final decision. Mammographic findings and breast parenchymal patterns were assessed in accordance with the 4th edition of Breast Imaging-Reporting and Data System of the American College of Radiology (BIRADS of ACR) (11). Women with BIRADS 0 result were recalled for additional examinations including spot compression, magnification views, ultrasonography or magnetic resonance imaging (MRI). Women with mammograms categorized as BIRADS 4 and 5 were referred to the university hospitals for biopsy and histopathologic evaluation. Patients were monitored and followed up in the center continuously and periodically as a different cohort after being diagnosed and treated.

Definitions

Operational definitions related with a breast cancer diagnosis in the screening program were determined according to the standards of the European Union Breast Cancer Screening Quality Guidelines: 1) The date of diagnosis was established according to cytology or histopathology result; 2) Intermediate cancer was detected on a mammogram performed out of sequence with the screening interval mammogram (e.g., at 6 or 12 months), as a result of the screening test. Cancer following screening, detected at intermediate mammography was regarded as screen-detected cancer (not interval cancer); 3) Interval cancer was defined as the detection of primary breast cancer in a woman referred to the screening center with symptoms within 2 years following the final round screening with a negative mammogram with/without further assessment; 4) Missed cancer was defined as the diagnosis of cancer after a false-negative mammogram; 5) The breast cancer detection rate was the number of pathologically proven malignant lesions (both in situ and invasive) detected in a screening round, per 1000 women screened. Cancers detected at intermediate mammography were regarded as screen-detected cancers and thus were included in the cancer detection rate. This rate differed for initial (prevalence rate) versus subsequent (incidence rate) screening examinations (12).

Data collection

The BMSP data were collected during the 10-year screening period (5 rounds of screening) with a specific screening database created for the study. These data were compared with the breast cancer data of NBCRD including age, cancer stage, types of surgery, tumor size, lymph node status, molecular subtypes, and survival rates.

Statistical analysis

Descriptive statistics were expressed as median, minimum and maximum value, mean and standard deviation for continuous variables and number and percentage for categorical data. The Kolmogorov-Smirnov test was used for evaluating the normality of continuous variables. Non-normally distributed continuous variables were presented as median, together with minimum and maximum. Chi-square test was used to compare categorical variables. Kaplan-Meier survival analyses were performed and presented with 95% confidence intervals (95% CI). In this population-based screening study, length of follow-up was also evaluated. Kruskal-Wallis test was used to determine statistically significant differences between two or more groups of an independent variable on a continuous or ordinal dependent variable. SPSS (SPSS Statistics for Windows, Version 21.0, IBM Corp.) software and the Epi Info™ (CDC) were used

for data analysis. A two sided *p* value less than to 0.05 was considered statistically significant.

Results

During the 10-year period, a total of 8758 women aged 40–69 years who lived in Bahcesehir county were screened. A total of 22 621 screening examinations were performed during the study period. Breast cancer was detected in 130 women; 51 (39.2%) of whom were 40–49 years of age. The mean age at diagnosis was 53.3±7.8 years (median, 52 years; range, 40–69 years). The mean age of patients with ductal carcinoma in situ (DCIS) and invasive breast cancer was 50.8±7.1 years (median, 49 years; range, 44–69 years) and 53.7±7.8 years (median, 53 years; range, 40–69 years), respectively. The distribution of tumor size according to the age groups were similar ($p = 0.378$): mean tumor size was 16.2±9.3 mm (median, 14.0 mm; range, 4.0–50.0 mm) in patients aged 40–49 years, 14.6±8.5 mm (median, 12.0 mm; range, 1.0–40.0 mm) in patients aged 50–59 years, 14.9±7.5 mm (median, 13.6 mm; range, 3.0–35.0 mm) in patients aged 60–69 years. The diameter of tumor in all age groups were smaller in our study group compared to the data of the NBCRD ($p = 0.001$).

The overall recall rate for additional spot views, ultrasonography (US) examination, and MRI was 15.2%. Additional spot views were recommended in 9.8%, US was recommended in 12.3%, and MRI in 1.1% of cases, and spot views and US examinations were both recommended in 6.9%. Besides these, MRI was recommended together with US and spot views in 1.1% of the patients. Table 1 gives the recall counts (BI-RADS 0) with BI-RADS scores for each round.

There were 22 (16.9%) intermediate, 9 (6.9%) missed, and 15 (11.5%) interval cancers. The rate of cancers that were not detected with mammography (missed cancers) was 6.9%. Of these cases, one was detected with MRI, one with a clinical examination, and seven with US examinations (Table 2). The median time to diagnosis for intermediate, interval, and missed cancers was 8.0 months (range, 3.0–20.0 months), 11.5 months (range, 3.0–23.0 months), and 10.0 months (range, 3.0–23.0 months), respectively ($p = 0.439$). However, interval, intermediate, and missed cancers were seen frequently in the first half of the routine follow-up of 2 years. There was no statistically significant relationship between the cancer detection time and age distribution or mammographic density (Table 2).

Table 1. BI-RADS scores at screening and after diagnostic tests

		Screening rounds (Every two years)					
	BI-RADS	1	2	3	4	5	Total
Screening BIRADS scores[a]	0	1912	680	397	251	202	3442
	1	3494	2381	1383	1008	701	8967
	2	3909	2235	1464	1373	1231	10212
	Total	9315	5296	3244	2632	2134	22621
BIRADS scores after diagnostic tests[b]	0	113	47	43	30	19	252
	1	3494	2381	1383	1008	701	8967
	2	3909	2235	1464	1373	1231	10212
	3	1680	607	337	207	169	3000
	4	101	20	13	13	10	157
	5	18	6	4	1	4	33
	Total	9315	5296	3244	2632	2134	22621

[a]Results of BIRADS of women screened for 10 years.
[b]Results of BIRADS of women after diagnostic tests.

Table 2. Relation of cancer detection with age distribution, mammography density, and examination type

		Screen-detected + Intermediate	Interval + Missed	
		n (%)	n (%)	*p*
Breast density	1+2	77 (72.6)	19 (79.2)	0.689[a]
	3+4	29 (27.4	5 (20.8)	
Age	40–49 years	41 (38.7)	10 (41.7)	0.969[a]
	50–69 years	65 (61.3)	14 (58.3)	
MMG		97(91.5)	11(45.8)	[b]
US		5 (4.7)	2 (8.3)	[b]
MRI		- (-)	1 (4.2)	[b]
Clinical examination		4 (3.8)	10 (41.7)	[b]

MMG, mammography; US, ultrasonography.
[a]Chi-square analysis.
[b]Due to Cochran rules chi-square analysis could not be performed.

Table 3 shows the clinical stages of patients according to different age groups. Stage 1 and 2 invasive cancers were the most frequent cancers in all age groups. Seventeen of the detected cancers were DCIS (13.1%), whereas the remaining were invasive breast cancer. The DCIS rate was two-fold higher in younger women (40–49 years) than in women aged 50–69 years (11 vs. 6 out of 17 patients). The frequency of invasive lobular cancers was remarkably higher among women aged 50–59 years (9/19, 47.3%). Additionally, the frequency of invasive ductal cancers was slightly higher in women aged 50–69 years (20/85, 23.5%). However, these differences were not statistically significant (Table 3).

The comparison of outcomes of breast cancer patients in BMSP data with patients from the NBCRD is shown in Table 4. The patients in BMSP had earlier stages, higher breast-conserving surgery rates, smaller tumor size, less frequent axillary nodal involvement, lower histologic grades, and higher DCIS rates ($p = 0.001$, for all). In patients with invasive cancers (n=113), mean tumor size was 15.9±9.0 mm (median, 14.0 mm; range, 1.0–60.0 mm) in the BMSP data and the diameter of tumors in all age groups was smaller in our study group than that of the cases in the NBCRD data ($p = 0.001$).

A comparison of prevalent cancers with incident cancers showed a significant dif-

Table 3. Distribution of clinical stages according to the age groups

	Clinical stage					
	Stage 0 in situ	Stage I	Stage II	Stage III	Stage IV	Total*
Age groups	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
40–49 years	11 (21.6)	17 (33.3)	15 (29.4)	6 (11.8)	2 (3.9)	51 (100)
50–59 years	4 (8.4)	29 (60.4)	10 (20.8)	5 (10.4)	0 (0)	48 (100)
60–69 years	2 (6.5)	16 (51.6)	9 (29.0)	4 (12.9)	0 (0)	31 (100)
Total	17 (13.1)	62 (47.7)	34 (26.2)	15 (11.5)	2 (1.5)	130 (100)

Combining boxes in the table was not considered, as it is clinically important to present the findings as they are.
*Due to Cochran rules chi-square analysis could not be done.

ference in the age at detection (p = 0.001). Prevalent cancers were more frequent in women aged 40–49 years (57.9%), whereas the incident cancer rate was higher in those aged 50–59 years (47.9%). Some 64.7% of women aged 40–49 years had cancers detected in the first round. This proportion was 93% in women aged 40–44 years (13/14) and 40.5% in women aged 45–49 years (15/37). There were no other statistical differences between the two groups in terms of cancer stage, molecular subtype, and histopathologic type, histologic grade, lymph node status, tumor size, and type of surgery. DCIS was higher in frequency in the prevalent cancer group (19.3% vs. 8.3%), although the difference was not statistically significant (Table 4).

The mean follow-up time in BMSP was 4.6 years (range, 1.4–9.3 years); only four patients among our cohort died of disease progression during the 10-year period. In the Kaplan-Meier survival analysis, the average survival time was 8.9 years (95% CI, 8.7–9.2 years); 5-year overall survival (OS) was 98.5% and 10-year OS was 96.9%. The mean follow-up time was 4.3 years in the NBCRD, with 5- and 10-year OS rates of 86% and 76%, respectively.

Discussion

Population-based screening for breast cancer is well documented and shows a significant impact on reducing mortality related to breast cancer (13–19). However, these studies were conducted in high-income countries and there are limited data regarding the feasibility of a population-based screening program in countries with limited resources. The detection of breast cancer in early stages is the main important benchmark for an improved outcome in patients. A recent multinational study showed that breast cancer stage was higher and tumor size was larger in countries with limited resources in which population-based screening was not held (20). The same study illustrated the obstacles in implementing quality measures and good medical practice in breast imaging and stated different deficiencies depending on the infrastructure and resources of limited income countries, implying great challenges in establishing a population-based screening program. BMSP was the first population-based screening program in Turkey and showed the feasibility of the screening program in a country with limited resources, but with constant belief and perseverance, with high manpower, and an internationally competent screening team. During the 10-year period, the same quality was maintained, with continuous evaluation monitoring, which are the main pillars of a successful screening program.

The initial highly cited randomized clinical screening trials came from high-income countries with a higher incidence of breast cancer (13–19). The incidence of breast cancer in North America and Western Europe is higher than 85–94 per 100 000 women (21, 22). Although the incidence of breast cancer in Turkey has increased almost two-fold in the last two decades (from 24/100 000 in 1994 to 43.8/100 000 in 2015), it is still significantly lower than in countries where initial screening trials were held (9). This increase can be explained by Westernization of lifestyle, aging of the population, increasing breast cancer awareness, and opportunistic breast cancer screening.

The results of this study revealed that population-based mammography screening detects breast cancer at an early stage and is associated with a survival benefit. Previous studies showed that screen-detected cancers were more frequently tumors of smaller size, low grade, without axillary involvement, and estrogen-receptor-positive compared with registry cancers (23–25). Likewise, the patients in BMSP had earlier stages with smaller tumor size and had higher breast-conserving surgery rates with less frequent axillary nodal involvement than patients in NBCRD. These results reveal the unquestionable positive effects of mammography screening in decreasing morbidity and increasing cosmetic outcomes in breast cancer patients. Furthermore, screen-detected cancers were more frequently Luminal A and B cancers compared with those of NBCRD registry cancers (p = 0.002), and DCIS was detected more frequently in the screening group (13.1% vs. 5.4%). On the other hand, the triple-negative cancer rate was higher in the NBCRD registry (11.8% vs. 2.6%). A similar association was seen in HER-2-enriched tumors (9.9% vs. 5.4%). These findings also support that non-screen-detected cancers have more aggressive biologic potential than screen-detected cancers (26).

Prevalent cancers were more frequent in the younger age group when compared with incident cancers or other age groups (p = 0.013). The prevalence peak is a well-known phenomenon that is expected with the initiation of breast cancer screening; it shows an initial high rate of cancer detection in a non-screened population. A higher rate of cancer incidence (prevalence peak) is expected because both clinically detectable and undetectable (small and in situ cancer) lesions can be recognized with the initiation of mammography screening (27). In this screening program, we found that 64.7% of cancers in women aged 40–49 years and 93% of cancers in women aged 40–44 years were detected in the first screening round. If intermediate cancers were included with the screen-detected tumors, the detection rate in the first two screening rounds would be 86.4%. This higher prevalence rate of breast cancer in women younger than 50 years implies the importance of at least one random screening after 40 years of age, particularly in those aged 40–44 years, notably in countries that cannot perform population-based screening program due to limited resources. Prevalent cancers also showed a higher rate of DCIS than incident cancers (19.3% vs. 8.3%). Our data showed smaller tumor size and lower stage at detection when compared with the NBCRD registry, both for prevalent and incident cancers (Table 4). Therefore, recommending a screening mammogram any time between age 40 and 49 years (particularly,

Table 4. BMSP and TFBDS-NBCRP results according to type of surgery, cancer stages, TNM classifications, and cancer types

Characteristics	BMSP (I) n (%)	BMSP prevalent cases (II) n (%)	BMSP incident cases (III) n (%)	TFBDS-NBCRP (IV) n (%)	*p* *p*1: I to IV *p*2: II to III *p*3: II to IV *p*4: III to IV
Age groups (years)	130 (100.0)	57 (100.0)	73 (100.0)	14162 (100.0)	*p*=0.013
40–49	51 (39.3)	33 (57.9)	18 (24.7)	5883 (41.6)	*p*1=0.638
50–59	48 (36.9)	13 (22.8)	35 (47.9)	5033 (35.5)	*p*2=0.003
60–69	31 (23.8)	11 (19.3)	20 (27.4)	3246 (22.9)	*p*3=0.054
					p4=0.020
Stage	130 (100.0)	57 (100.0)	73 (100.0)	7434 (100.0)	*p*=0.001
Stage 0	17 (13.1)	10 (17.5)	5 (6.8)	353 (4.7)	*p*1=0.001
Stage 1	62 (47.7)	27 (47.4)	37 (50.7)	2253 (30.3)	*p*2=0.137
Stage II	34 (26.2)	14 (24.5)	20 (27.4)	3515 (47.3)	*p*3=0.001
Stage III-IV	17 (13.0)	6 (10.6)	11 (15.1)	1313 (17.7)	*p*4=0.003
Surgery type	126 (100.0)[a]	55 (100.0)	71 (100.0)	11045 (100.0)	*p*=0.001
BCS	103 (81.2)	46 (83.6)	57 (80.3)	4384 (39.7)	*p*1=0.001
Mastectomy	23 (18.8)	9 (16.4)	14 (1972)	6661 (60.3)	*p*2=0.630
					*p*3=0.001
					*p*4=0.001
TM size	121(100.0)[b]	53 (100.0)	68 (100.0)	6471 (100.0)	*p*=0.001
T0	17 (14.1)	11 (20.7)	6 (8.8)	575 (8.9)	*p*1=0.001
T1	81 (66.9)	33 (62.3)	48 (70.6)	3016 (46.6)	*p*2=0.140
T2+T3	23 (19.0)	9 (15.8)	14 (19.2)	2880 (44.5)	*p*3=0.001
					p4=0.002
Lymph node	n (126)[a]	65 (100.0)	71 (100.0)	6055 (100.0)	p=0.001
N0	86 (68.3)	39 (70.9)	47 (66.2)	3179 (52.6)	*p*1=0.001
N1	28 (22.2)	12 (21.8)	16 (22.6)	1661 (27.4)	*p*2=0.463
N2+N3	12 (9.5)	4 (7.3)	8 (11.2)	1215 (20.0)	*p*3=0.003
					*p*4=0.017
Molecular subtypes	112 (100.0)[c]	46 (100.0)	66 (100.0)	4222 (100.0)	*p*=0.002
Lum A	66 (58.9)	26 (56.5)	40 (60.6)	2443 (57.8)	*p*1=0.016
Lum B	37 (33.1)	17 (37.0)	20 (30.3)	862 (20.5)	*p*2=0.962
Her 2	6 (5.4)	2 (4.3)	4 (6.1)	419 (9.9)	*p*3=0.128
TNBC	3 (2.6)	1 (2.2)	2 (3.0)	498 (11.8)	*p*4=0.062
Histological grade	109 (100.0)	34 (100.0)	65 (100)	5316 (100.0)	*p*=0.001
I	23 (21.1)	9 (20.5)	14 (21.5)	453 (8.5)	*p*1=0.001
II	58 (53.2)	24 (54.5)	34 (52.3)	2545 (47.9)	*p*2=0.996
III	28 (25.7)	11 (25.0)	17 (26.2)	2318 (43.6)	*p*3=0.001
					*p*4=0.001
Histopathological types	129 (100.0)[d]	57 (100.0)	72 (100.0)	10616 (100.0)	*p*=0.001
DCIS	17 (13.1)	11 (19.3)	6 (8.3)	575 (5.4)	*p*1=0.034
Invasive ductal cancer	83 (64.4)	5 (8.8)	14 (19.4)	7726 (72.8)	*p*2=0.659
Invasive lobular cancer	19 (14.7)	35 (61.4)	48 (66.7)	649 (6.1)	*p*3=0.003
Others	10 (7.8)	6 (10.5)	4 (5.6)	1666 (15.7)	*p*4=0.001

Chi square analysis was performed using the epi info program.
BMSP, Bahcesehir Mammographic Screening Program; BCS, breast-conserving surgery; DCIS, ductal carcinoma in situ; TFBDS- NBCRP, Turkish Federation of Breast Diseases Societies National Breast Cancer Registry Program; TNBC, triple-negative breast cancer.
[a]Four missing data: two metastatic disease with no surgery, one has not been operated on yet, and detailed pathological report of the other one could not be obtained.
[b]Nine missing data: nine neoadjuvant cases.
[c]18 missing data: 17 DCIS cases, one patient's detailed pathological report could not be obtained.
[d]One missing data: one patient's detailed pathological report could not be obtained.

starting at 40–44 years) once a decade may be a feasible approach for low- and middle-income countries (LMIC) that cannot afford long-term screening programs before 50 years of age (28).

The median time of diagnosis in the intermediate, interval, and missed cancers was 8.0, 11.5, and 10.0 months, respectively, without any significant differences (p = 0.439). Considering the median time for diagnosis of these interval cancers, which was less than 12 months after the prior mammogram, we can speculate that screening at 1-year intervals could be a better approach for more effective detection. Interval cancers have poor biologic behavior and larger tumor size compared with screen-detected cancers (29). We found no significant mammographic density difference between interval, intermediate, missed, and screen-detected cancers (p = 0.689) (Table 2). In other words, the interval cancer rate was the same in women with dense and fatty breasts. Radiologists harbor a fear of missing cancers in dense breasts and are more confident in reading fatty breasts. However, in this study, breast density was not a variable for interval or missed cancers. We believe that both dense and non-dense breasts should be evaluated with the same degree of caution (30). The definition of "interval breast cancer" differs between Europe and the United States because of the interval between two screening rounds. In the United States, an interval cancer occurs within 1 year after the last mammogram; however, in Europe, it is accepted as within two years. The interval cancer rate was between 0.084% and 0.213% of mammograms according to various studies (31). The interval cancer rate in our study was 0.086% of mammograms, which was consistent with previous literature.

The absolute aim of cancer screening is to decrease the mortality rate of the causal disease in subjects, the assumption being that early detection coupled with treatment slows or terminates the progression of the disease, whereas later treatment is probably less effective (32). Breast cancer-specific mortality in the group invited for screening is around 0.80 in general across all ages and methods. This suggests a 20% relative risk reduction with 11 years of mammography screening follow-up. However, a larger magnitude of risk reduction was demonstrated via longer follow-up, meaning that the full effect of mammography screening could only be observed after 20 years or more (8, 33–35). The studies that reported reduced mortality from breast cancer with mammography screening came from high-income countries (36). A life table method of investigation of 5-year breast cancer survival rates among 24 740 cases recorded in the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute revealed that survival rates ranged from 45.5% to 96.3% for tumors smaller than 2 cm and without axillary involvement (37). The longest follow-up was recorded as 39 years. According to the NBCRD data, the 5- and 10-year survival rates were 86% and 76%, respectively, with a mean 4.3 years of follow-up. Kaplan-Meier survival analysis revealed a mean survival rate of 26 years with 95% CI 24.6–28.3. In our study, the 10-year survival rate was as high as 96.9% with a mean 4.6 years of follow-up. Only 4 of the 130 breast cancer patients died of their disease within the 10-year screening period. We believe that this survival advantage will be more clearly demonstrated after a longer follow-up period.

The rate of compliance to screening after invitation was 71.7%, which is in line with the literature (13–19). One of the main reasons for noncompliance was the preference of women to have their screening in a private breast clinic or a clinic close to their work. Some women resisted mammography due to two reasons. First, some stated that they had experienced unpleasant pain due to compression of the breast during a previous examination and were reluctant to feel it repeatedly. Second, they were misinformed about radiation exposure and were anxious about having cancer as a result of this exposure. Some women moved from the county during the study period. Another reason was the lack of confidence in the screening center. This issue was overcome with time, following the first two rounds of screening in the county.

Other benefits of screening include the reduction in costs associated with treatment. Treatment for individuals diagnosed at an earlier stage is less invasive and less costly, which might reduce patient anxiety and improve prognosis (38). BMSP proved to be cost-effective showing that 82.89 life-years would be saved with an additional expense of $698 931 US dollars with an incremental cost-effectiveness ratio of $8433 US dollars per additional life year. Therefore, mammography screening may significantly shift the stage distribution of breast cancer, and organized population-based screening program would be cost-effective in Turkey, as well as in other low-middle-income countries (39). Furthermore, the benefits associated with earlier detection from the patient's perspective are as follows: (*i*) breast-conservation surgery instead of mastectomy, (*ii*) decreased chemotherapy, and (*iii*) less time off work. A decreased likelihood of axillary lymph node metastases with screening can also result in fewer axillary lymph node dissections and reduced risk of lymphedema (40).

There are some limitations of the present study. First, the study included only a small cohort of women who lived in one county. Consequently, the ability to generalize data from this study for the Turkish female population is limited. Also, the number of patients with screen-detected breast cancer is low in comparison with patients that were registered in the NBCRD. Third, the mean follow-up duration is too short to show a mortality benefit. However, we showed a mortality benefit greater than that of the NBCRD registry. Finally, we did not make a risk assessment to assess the rate of high-risk women.

In conclusion, the BMSP was the first population-based screening program in Turkey. It demonstrated the feasibility of a mammography screening program in a country with limited resources with a high compliance rate. The study demonstrated the impact of mammography screening in shifting the stage distribution of breast cancer in Turkey; detected tumors were smaller in size with less frequent axillary nodal involvement. Furthermore, our results revealed the feasibility of starting screening at 40 years of age. We believe that at least one screening after the age of 40 years would be beneficial for countries with limited resources where a screening program cannot be held.

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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