Evaluation of population-based breast cancer screening program in Turkey: Preliminary results

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Abstract

Introduction: In Turkey, a population-based breast cancer screening program for women aged 40 to 69 years old was recently introduced. The goal of this study was to document early outcomes and assess the program's success.

Method: This study looked at the 348,638 women who were screened in 2016. For end results, all data was gathered from the national centralized reporting system and the Cancer Registry database. For benign discoveries, Breast Imaging-Reporting and Data System (BI-RADS) 1-2 were applied, and for recalls, BI-RADS 0, 4, or 5 were utilized, depending on the level of suspicion. The study looked at the age distribution, recall rate, cancer detection, and interval cancer rates. The stages of identified malignancies were examined and compared to those of the non-screened group throughout the same time frame.

Results: In the screening population, 43.2 percent of women were between the ages of 40 and 49, and 56.8% were between the ages of 50 and 69. The age range of 50–69 was responsible for 70% of screen-detected malignancies. The total recall rate (n = 19,607) was 5.6 percent. The malignancy rate for BI-RADS 5 recalls was 70.2 percent, 19.2 percent for BI-RADS 4, and 1.7 percent for BI-RADS 0 recalls. Screen-discovered malignancies were detected at a rate of 3.2 per 1000 screening exams (n = 1,120). When compared to the non-screened group, the screened group had a larger percentage of early-stage illness (54.3%). (46.7 percent). Interval cancers were discovered in 231 women (0.66 per 1000 screened women).

Conclusion: Turkey's recently launched population-based breast cancer screening program appears to be viable and successful, according to preliminary results. According to this study, the breast cancer screening program should be sustained, with coverage of the target group rising.

Keywords: Breast cancer, Early detection, Mammography, Screening, Population-based, Clinical, Turkey
Introduction

Breast cancer is the most frequent malignancy in women and one of the main causes of death. With an increasing number of new cases and deaths, it is not only a health problem in wealthy countries, but also in developing and underdeveloped countries (1). Mammography is the primary method for population-based breast cancer screening, and multiple randomized controlled trials have shown that it reduces mortality by at least 20%. (2,3). According to the International Agency for Research on Cancer (IARC), women aged 50–69 years have a 40% lower risk of dying from cancer (4).

Many countries have successfully developed nationwide breast cancer screening programs. In terms of beginning age and intervals, the guidelines and implementation of mass screening programs vary per country. According to European Guidelines, women aged 50 to 69 are invited to a screening in most European nations (5,6). Screening recommendations for those aged 40–49 are not standard and vary depending on the practice (7-9).

Breast cancer affects one out of every four Turkish women, and the incidence varies by age group, with the incidence being higher at younger ages (10). Population-based screening programs began as a pilot study in 2004 with the European Union's approved criteria, and Standards for National Screening Programs were released in 2007. (11). According to the Turkish breast cancer registry program, nearly half of all women diagnosed with breast cancer are premenopausal and under 50 years old. This program was updated in 2012, and the age group was extended between 40 and 69 with two-year intervals because nearly half of all women diagnosed with breast cancer are premenopausal and under 50 years old (12). Over time, the number of dedicated screening facilities (Cancer Early Diagnosis, Screening and Education Centers-KETEMs), including mobile units, has grown, and the National Centralized Reporting System (MM Screen, which is the generic name used for mammography screening) was developed in 2016. The reports are finished in ten days, and women who are recalled and require additional evaluation are referred to diagnostic centers (11). The purpose of this research was to investigate a recently installed breast cancer screening program and get some preliminary results for future direction.

Materials and methods

Primary health care physicians contacted women aged 40 to 69 years old and invited them to a nationwide screening via e-mail, phone, letter, or face-to-face invitations. Invited women from KETEM (Cancer Early Diagnosis, Screening and Education Centers) were given an appointment to either travel to a mobile truck or a fixed screening site. During registration on the day of the appointment, all women were asked if they had a palpable lump or any other breast-related symptoms. Symptomatic individuals and women with a personal history of breast cancer were excluded from the study and directed to a secondary health care facility. The mammograms were performed in 155 facilities, with 121 of them being digital (full field digital mammography, or FFDM) and 34 being traditional units with computed radiography units. Mammograms were taken from two different angles: MLO (mediolateral oblique) and CC (craniocaudal). There was no tomosynthesis conducted. All photographs were first reviewed for location and visual image quality before being sent to an Ankara-based central reporting center. Two blinded radiologists double-readed the mammograms. Mammographic screening was taught to all radiologists, and a continuous education program for radiologists and technicians was held. Mammograms were assessed using a one-of-a-kind web-based online system developed specifically for the nationwide screening program. The final assessment categories were Breast Imaging-Reporting and Data System (BI-RADS) 1-2 for negative mammograms, BI-RADS 0, BI-RADS 4, and BI-RADS 5 for positive mammograms, according to the ACR (American College of Radiology) BI-RADS vocabulary. If the first two radiologists disagree on the BI-RADS category, a third radiologist is chosen to make the final decision. To allow for possible prioritizing at diagnostic facilities, recalls were subcategorized as BI-RADS 0, 4, or 5, based on the degree of suspicious findings on screening mammography. In 2016, 348,638 women in Turkey were screened as part of a population-based screening program. All the data obtained from Turkey’s 81 provinces was examined retrospectively, and all the data used was anonymized. Furthermore, a national centralized reporting system was built, which utilizes a one-of-a-kind software application known as MM Screen in 2016. MM Screen is a database that allows for the double reading, reporting, and archiving of screening mammography. The final results of the recalled women were gathered from cancer registration (CanReg) records, which were designed for population-based cancer registration by WHO (World Health Organization) and IARC (International Agency for Research on Cancer). CanReg gave information regarding the patient's clinical characteristics and disease stage at the time of presentation.
The MM Screen database and the CanReg application, which are utilized for this purpose, provided all of the data used in this investigation. The results of women recalled for positive mammography findings (BI-RADS 0,4,5) between January 1, 2016, and December 31, 2016, were collected from the cancer registry database and matched for analysis. Women who had mammograms that came out negative (BI-RADS 1-2) had their outcomes studied as well. For statistical analysis, the SPSS 23 software was used. The frequency distribution and percentages were evaluated using descriptive statistics. The Chi-Square test was used to examine the differences in stage between the tested and non-screened groups (a value of 0.05 was accepted). The recall rate, cancer detection rate, cancer incidence distribution by age and breast pattern, and the interval cancer rate were all calculated in this study.

Results

The outcomes of a nationwide screening program were analyzed retrospectively. In 2016, 348,638 asymptomatic women were screened in either dedicated stationary centers or mobile trucks. A total of 5.6 percent of women (n =19,607) were recalled and sent to a diagnostic center for further testing. Women with BI-RADS 0 recalls made up 4.94 percent (n =17,237), BI-RADS 4 recalls made up 0.47 percent (n =1,649), and BI-RADS 5 recalls made up 0.21 percent (n = 721). (Fig 1). Cancer registry reports provided the final results of these recalls. Screen-detected malignancies were found in 70% of instances in people aged 50 and over. Only 30% of malignancies were found among women aged 40 to 49, despite the fact that 43.2 percent of women were screened in this age group. Patients between the ages of 50 and 54 were the most likely to be referred to a diagnostic facility following the recall, accounting for 22.5 percent (n = 4,413). This age group likewise had the highest rate of cancer diagnosis (23.1 percent, n = 259). Figure 2 shows the age distribution of women in the referred and diagnosed groups, with the cancer group having a median age of 54. (Figure 2).

The most common mammographic density pattern was type B both in recalled group for diagnostic examination (48.4%), and in group with cancer diagnosis (50.8%) (Table 1), followed by type C parenchymal pattern. Breast density patterns in patients with cancer diagnosis were varied related to age groups. 60% of women in 40-49 age group had dense breast tissue (BI-RADS C or D category), however at age 50 and older group only 31.7% had dense breast pattern. Breast density was type C in most women (54.9%) between the ages of 40 and 49, and type B in those aged 50 and over (56.7%), according to the BI-RADS parenchymal density categorization. The fact that thick breast patterns are more common among women between the ages of 40 and 49 who have been diagnosed with cancer is statistically significant. (p<0.001). (See Table 2)

The BI-RADS category from recalls of screening examination was BI-RADS 5 in 45.2 percent of patients (n=506), followed by BI-RADS 4 in 28.3 percent, and 26.5 percent in BI-RADS 0 in patients who received a cancer diagnosis (Table 3). On recall, 70.1 percent of lesions classified as BI-RADS 5 had malignancy, 19.2 percent had BI-RADS 4 lesions, and 1.7 percent had BI-RADS 0 lesions. 231 BI-RADS 1-2 cases developed cancer before the next screening cycle, resulting in an interval cancer rate of 0.66 per 1000 screening exams. Screen-discovered malignancies were detected at a rate of 3.2 per 1000 screening exams (n=1120). There was a stage evaluation on the data for 817 of these patients. More than half of the malignancies discovered by the screen were in situ or localized tumors in the early stages (54.3 percent). Non-screen cases accounted for 46.7 percent of all cases in Turkey's cancer database. The difference (p<0.001) is statistically significant (Table 4).

Discussion

Population-based screening programs have been effectively implemented in various countries, with high coverage and lower mortality rates (9,13-15). Turkey's population-based mammography breast cancer screening program is still relatively new, although it has improved since the establishment of a centralized reporting system in 2016. Since then, the number of people who have been screened has gradually increased over time. The recall rate was 5.6 percent, and the cancer detection rate was 3.2 per 1000 examined women, according to the first wave of screening results. The 40-49 age group accounted for 30% of all malignancies found, accounting for 43.2 percent of all women examined. 54.3 percent of patients had early-stage malignancies, such as localized breast cancer or cancer in situ. At the same time span from the cancer registry dataset, this percentage was 46.7 percent in the non-screened group. There is a statistically significant difference. The rate of interval cancer was 0.66 per 1000 women who were tested.

Recall rate (the proportion of screening mammograms returned for additional study), cancer detection rate (the number of identified cancers per 1000 women screened), and percentage of early-stage cancers are all performance indicators that have been set for successful screening. These characteristics must be monitored to evaluate the program.
Figure 1. The Breast Imaging-Reporting and Data System (BI-RADS) results of breast screening mammograms in Turkey in 2016.

Figure 2. Age prevalence in screening group and in diagnosis group comparatively.
Table 1. BI-RADS* parenchymal density patterns in recalled and cancer diagnosis group of women

<table>
<thead>
<tr>
<th>Breast Density*</th>
<th>Recalled women No (%)</th>
<th>Women with cancer diagnosis No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1383 (7.1)</td>
<td>101 (9.0)</td>
</tr>
<tr>
<td>B</td>
<td>9496 (48.4)</td>
<td>569 (50.8)</td>
</tr>
<tr>
<td>C</td>
<td>7683 (39.2)</td>
<td>415 (37.1)</td>
</tr>
<tr>
<td>D</td>
<td>1045 (5.3)</td>
<td>35 (3.1)</td>
</tr>
</tbody>
</table>

#: BI-RADS = Breast Imaging-Reporting and Data System.

*: Breast Density: A) Almost fatty, B) Scattered fibroglandular densities, C) Heterogeneously dense, D) Extremely dense

Table 2. Distribution of breast density according to age groups in cancer diagnosis

<table>
<thead>
<tr>
<th>Age group</th>
<th>Breast density</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>Total</th>
<th>( \chi^2 )</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td></td>
<td>10 (3.0%)</td>
<td>124 (37.0%)</td>
<td>184 (54.9%)</td>
<td>17 (5.1%)</td>
<td>335 (100.0%)</td>
<td>84.2</td>
<td>3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥50</td>
<td></td>
<td>91 (11.6%)</td>
<td>445 (56.7%)</td>
<td>231 (29.4%)</td>
<td>18 (2.3%)</td>
<td>785 (100.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
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</table>

Table 3. BI-RADS* category of lesions from recall with cancer diagnosis

<table>
<thead>
<tr>
<th>BI-RADS</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>BI-RADS 0</td>
<td>297</td>
<td>26.5</td>
</tr>
<tr>
<td>BI-RADS 4</td>
<td>317</td>
<td>28.3</td>
</tr>
<tr>
<td>BI-RADS 5</td>
<td>506</td>
<td>45.2</td>
</tr>
<tr>
<td>Total</td>
<td>1,120</td>
<td>100.0</td>
</tr>
</tbody>
</table>

*: BI-RADS = Breast Imaging-Reporting and Data System.

Table 4. Stage of cancers for screening and non-screening group of patients

<table>
<thead>
<tr>
<th>SEER* Stage</th>
<th>Screen detected cancer</th>
<th>Non-screen group</th>
<th>( \chi^2 )</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>In situ, Localized (00,01)</td>
<td>444 (54.3%)</td>
<td>5339 (46.7%)</td>
<td>45.0</td>
<td>2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regional (02,03,04,05)</td>
<td>334 (40.9%)</td>
<td>4696 (41.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distant (07)</td>
<td>39 (4.8%)</td>
<td>1389 (12.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>817 (100.0%)</td>
<td>11,424 (100.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Uunknown stage group was out of analyzing)

SEER* = Surveillance, Epidemiology, and End Results
Based on data from the Breast Cancer Screening Consortium (16), the minimum acceptable recall rate was established as 5–12%, and it has been suggested in numerous guidelines to be fewer than 10% of screened women (6,10,17). The recall rate in different European countries has been reported to range from 2.3 percent to 13 percent (9), and it was 5.6 percent in our screening investigation, which was close to those published. Grabler et al (18, on the other hand, recommended a recall rate of 12 to 14 percent for effective cancer detection.

The ladies who had been referred were sent to diagnostic centers for further evaluation, which included tissue diagnosis if necessary. A comprehensive BI-RADS categorization is not used in the screening setting, and differentiating cases that require recall is sufficient. However, in our practice, we classified referred cases as BI-RADS 0, 4, or 5 depending on the amount of suspicion for diagnostic center prioritization. In the Dutch breast cancer screening program, similar segmentation of referred cases was done, and significant disparities in PPV were discovered according to BI-RADS categories (19).

The cancer detection rate is a significant performance metric for population-based screening programs, and the predicted value for prevalent screening is 6–10 per 1000 tested women (20). The threshold for poor cancer detection performance was set at 2.5 per 1000 interpretations (16). Our screening group had a cancer detection rate of 3.2 per 1000 screening examinations. The inclusion of the 40–49 age bracket, in which cancer rates are lower, could explain the significantly lower incidence of this number. Only 30% of the malignancies detected in our screening group occurred in women aged 40 to 49, accounting for 43.2 percent of all women screened.

The screening of 40–49-year-old women is a contentious issue, with recommendations differing amongst countries' breast cancer screening guidelines. The American College of Radiology recommends that screening begin at the age of 40, whereas the American Cancer Society suggests that screening begin at the age of 45. (3, 21). National screening programs in Europe span a variety of age categories and intervals, with the majority of countries screening every 50-69 years at 2-year intervals (9). Turkey's population is relatively youthful, and over half of all breast cancer patients in the country are under the age of 50 (11). The findings of a pilot screening study conducted in Istanbul's Bahcesehir county demonstrated the viability of starting screening at the age of 40. (22). As a result, the existing screening program included age groups beginning at 40. In this study, approximately a third of the malignancies detected on screens were found in women under the age of 50. The main issues with screening in the 40–49-year-old age group are the possibility of greater recall rates and false positive results. The memory rates for this age group were not significantly different from those for earlier age groups, according to our findings.

Most of the screened women and patients with cancer diagnoses between the ages of 40 and 49 exhibited dense breast patterns, BI-RADS C or D, in this study. Although dense breast tissue is the main concern when screening younger age groups (23), the introduction of digital mammography has enhanced mammography sensitivity and is now frequently used in screening. The Digital Mammography Imaging Screening Trial (DMIST) found that employing a digital mammography approach improves accuracy for women over 50, women who are pre- or peri-menopausal, and women who have thick mammographic breast tissue (24).

Breast cancer screening programs for the general public are designed to detect breast cancer at an early stage and reduce mortality rates. An efficient screening program must meet a number of criteria, one of which is an increase in the incidence of early-stage malignancies coupled by a decrease in the incidence of advanced-stage cancers. Some tumors, however, may be metastatic at the time of standard screening due to their aggressive nature (25). On the other hand, early diagnosis of precursor lesions is likely to reduce the incidence of invasive malignancies. Since the introduction of screening mammography, the prevalence of DCIS (ductal carcinoma in situ) has been demonstrated to increase (26). In order to meet minimum quality standards for screening mammography, the combined rate of in situ and early-stage malignancies must be greater than 50%. (20). In this study, the stage distribution of tumors diagnosed was favorable, with 54.3 percent of early tumours being in situ or localized breast cancer. At the same time span from the cancer registry dataset, this percentage was 46.7 percent in the nonscreened group. There is a statistically significant difference. In this study, the rates of DCIS were similar in the screened and nonscreened groups. The limited number of screened populations and the lack of experience of interpreting radiologists at the start of the program could explain these results.

After a negative screening, but before the next planned screening, interval cancers may be discovered. The interval cancer rate is thought to be a good predictor of screening quality. Interval malignancies should account for less than 10% of all cancers in a good screening program, and the maximum interval cancer rate during 24 months (screened women) should be less than 1.2/1000. (4,27). The cancer rate was 0.66
per 1000 tested women, which is within the acceptable range, according to our early findings. A thorough examination of interval cancers is being proposed, and it would be helpful in documenting the causes of false negative results. This is the first data from Turkey's population-based national screening program, which dates back to the first round of screening in 2016. In the years that followed, the number of women who were screened climbed until the COVID-19 pandemic. It is also vital to obtain this information on a regular basis and to evaluate the long-term results in the following years. The study does, however, have significant drawbacks. First, at the start of the coordinated screening program, the target population only encompasses a one-year period. Second, there hasn't been a thorough examination of histopathological and clinical management concerns. However, these findings show that the breast cancer screening program is effective, and that it should be sustained, with coverage of the target group increased.

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