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Positive predictive values by mammographic density and screening mode in the Norwegian Breast Cancer Screening Program

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ABSTRACT

Objective: To investigate the probability of breast cancer among women recalled due to abnormal findings on the screening mammograms (PPV-1) and among women who underwent an invasive procedure (PPV-2) by mammographic density (MD), screening mode and age.
Methods: We used information about 28,826 recall examinations from 26,951 subsequently screened women in the Norwegian Breast Cancer Screening Program, 1996–2010. The radiologists who performed the recall examinations subjectively classified MD on the mammograms into three categories: fatty (<30% fibroglandular tissue); medium dense (30-70%) and dense (>70%). Screening mode was defined as screen-film mammography (SFM) and full-field digital mammography (FFDM). We examined trends of PPVs by MD, screening mode and age. We used logistic regression to estimate odds ratio (OR) of screen-detected breast cancer associated with MD among women recalled, adjusting for screening mode and age.
Results: PPV-1 and PPV-2 decreased by increasing MD, regardless of screening mode (p for trend <0.05 for both PPVs). PPV-1 and PPV-2 were statistically significantly higher for FFDM compared with SFM for women with fatty breasts. Among women recalled, the adjusted OR of breast cancer decreased with increasing MD. Compared with women with fatty breasts, the OR was 0.90 (95% CI: 0.84–0.96) for those with medium dense breasts and 0.85 (95% CI: 0.76–0.95) for those with dense breasts.
Conclusion: PPVs decreased by increasing MD. Fewer women needed to be recalled or undergo an invasive procedure to detect one breast cancer among those with fatty versus dense breasts in the screening program in Norway, 1996–2010.

1. Introduction

Positive predictive value (PPV) of screening mammography corresponds to the probability that women with a positive screening test truly have breast cancer. The probability of breast cancer among women recalled due to abnormal findings on the screening mammogram is referred to as PPV-1, while PPV-2 indicates the probability of breast cancer among women who underwent an invasive procedure due to the abnormal findings [1].

PPV is considered an early performance measure of the radiologists' performance and thus an indicator of the effectiveness of screening programs [1–3]. A high PPV implies high sensitivity of the radiologists' performance and consequently a low proportion of false positive screening tests. Women attending mammographic screening who are recalled for further assessment which turns out to be negative have a false positive screening result [1]. False positive results might be associated with anxiety and distress among participating women and are considered a harm of mammographic screening [1,4]. PPV and the rate of false positive screening results

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are influenced by the screening procedures (i.e., one or two views, single or double reading), the radiologists' experience, screening interval, and characteristics of the women, such as mammographic density (MD) [2–5].

MD represents the amount of the fibroglandular tissue that is allocated in the breast and visualized on the mammogram [1]. MD is known to decrease the sensitivity of the reader performance and thus the screening program [3,6–9].

PPV is an early performance measure and a quality assurance parameter commonly used for comparison of screening performance in different programs [10]. However, there appears to be a limited number of published studies on PPVs by MD conducted with data from organized screening programs [11]. During the last decade, full-field digital mammography (FFDM) has replaced screen-film mammography (SFM) as screening mode [12]. To date, there is still insufficient knowledge on how MD influences early performance measures in screening programs using FFDM [13]. Such knowledge is important to maintain and improve the quality of screening programs.

Data related to the screening process are collected as a part of the quality assurance of the Norwegian Breast Cancer Screening Program (NBCSP) and information about MD is available for all recall examinations. We took advantage of these data and investigated the PPVs by MD, screening mode and age at screening. We also estimated the number of women needed to be recalled or undergo an invasive procedure to detect one breast cancer.

2. Material and methods

2.1. Norwegian Breast Cancer Screening Program

The NBCSP started in four of the 19 Norwegian counties in 1996 and became nationwide in 2005. The program is administered by the Cancer Registry of Norway and run according to the European guidelines [1]. The program targets women aged 50–69 years. The women are invited by a personal letter with stated time and place to two-view mammography every second year. The annual participation rate is 75%, and 84% of the invited women participated once or more during the study period, 1996–2010.

Radiologists have to undergo special training to start working in the NBCSP [14]. The breast radiologists in the program read about 4000 screening examinations annually and conduct diagnostic mammography [15]. The screening mammograms are read independently by two radiologists and given a score for each breast, indicating the susceptibility of malignancies [16]. A score of one indicates a normal mammogram while a score of five indicates high susceptibility of breast cancer. All cases with a score of two or higher by one or both radiologists are discussed at a consensus meeting where the final decision whether or not to recall the women is made. About half of the cases discussed at the consensus meeting are dismissed [15]. The recall rate due to abnormal mammographic findings during the study period was 5.2% for women screened for the first time in the NBCSP, and 2.5% for women screened more than once in the program [15]. The recall rates in Norway are in accordance with the European guidelines and correspond to recall rates in many other European countries, which offer organized mammographic screening [10]. SFM was predominantly used in the NBCSP prior to 2004, while FFDM was gradually implemented during 2000–2011. All information related to screening invitations and participation is stored in a separate database, the NBCSP database. The program is described further elsewhere [16].

Cancer reporting is mandatory by law and the Cancer Registry has registered cancer cases since 1952 [17]. The Cancer Registry database is 99% complete for solid tumors, including breast cancer [18]. We used data solely from the NBCSP database for this study. The study was approved by the Regional committees for medical and health research ethics.

2.2. Study population

Data was available for all recall examinations in the NBCSP, except for those performed in 2.0% of the women who refused the Cancer Registry to use information related to their screening examination for quality assurance and research. The study initially included information about 39,427 recall examinations due to abnormal findings on the screening mammogram (recalls) among subsequently screened women (Fig. 1). A subsequent screening examination was defined as the second or later screening examination in the program. Information about recalls performed as part of the Oslo I [19] and Oslo II [20] studies was excluded because the women were screened both with SFM and FFDM [19] or randomized into SFM or FFDM [20], respectively ($n = 1038$). Further, we excluded information about recalls conducted during the transition period from SFM to FFDM ($n = 5315$). The transition period was defined as two years after implementation of FFDM. We also excluded recalls without information about MD ($n = 4248$).

The final study population included information from 28,826 recalls performed among 26,951 women. A total of 22,463 recalls were performed with SFM and 6363 with FFDM (Fig. 1). Further, 10,798 invasive procedures were performed and 5182 breast cancers were diagnosed (968 ductal carcinoma in situ (DCIS) and 4214 invasive breast cancer) among the recalls.

2.3. Mammographic density

At the recall examination, the radiologists considered all four screening mammograms of a recalled woman to classify MD subjectively into one of three categories: fatty (<30% of fibroglandular tissue), medium dense (30–70% of fibroglandular tissue), and dense (>70% of fibroglandular tissue). No information about MD was available for the whole population of screened women for the study period. An independent sensitivity analysis of available data from two Norwegian counties allowed us to compare the distribution of MD in the screened ($n = 11,462$) and recalled ($n = 244$) population for the period January–December 2007. Among the screened women, 35%, 54% and 11% had fatty, medium dense and dense breasts, respectively, whereas among the recalled women the percentages were 17%, 68% and 15% (p for comparison between screened and recalled <0.05). The recalled women had higher MD compared with the screened women.

2.4. Performance measures

Positive predictive value-1 (PPV-1) was calculated as the number of screen-detected breast cancer (DCIS or invasive breast cancer) divided by the total number of recalls. Positive predictive value-2 (PPV-2) was calculated as the number of screen-detected breast cancer divided by the number of recalls including an invasive procedure (fine-needle aspiration cytology or core needle biopsy). The number of women needed to be recalled and undergo an invasive procedure to detect one breast cancer was estimated by the inverse PPVs (1/PPV-1 and 1/PPV-2, respectively).

2.5. Statistical analyses

PPV-1, PPV-2 and the number of women needed to be recalled and undergo an invasive procedure to detect one breast cancer were presented as percentages and numbers, respectively. The PPVs were calculated by MD categories. The analyses were further stratified by screening mode (SFM and FFDM) and age groups (50–54, 55–59, 60–64, and 65–69 years). The results were presented with