**Original Article** | Breast Imaging

eISSN 2005-8330
https://doi.org/10.3348/kjr.2019.0747
Korean J Radiol 2020;21(9):1027-1035

Korean Journal of Radiology
KJR

# Follow-Up Intervals for Breast Imaging Reporting and Data System Category 3 Lesions on Screening Ultrasound in Screening and Tertiary Referral Centers

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**Objective:** To assess the appropriate follow-up interval, and rate and timepoint of cancer detection in women with Breast Imaging Reporting and Data System (BI-RADS) 3 lesions on screening ultrasonography (US) according to the type of institution.
**Materials and Methods:** A total of 1451 asymptomatic women who had negative or benign findings on screening mammogram, BI-RADS 3 assessment on screening US, and at least 6 months of follow-up were included. The median follow-up interval was 30.8 months (range, 6.8–52.9 months). The cancer detection rate, cancer detection timepoint, risk factors, and clinicopathological characteristics were compared between the screening and tertiary centers. Nominal variables were compared using the chi-square or Fisher's exact test and continuous variables were compared using the independent *t* test or Mann-Whitney U test.
**Results:** In 1451 women, 19 cancers (1.3%) were detected; two (0.1%) were diagnosed at 6 months and 17 (1.2%) were diagnosed after 12.3 months. The malignancy rates were both 1.3% in the screening (9 of 699) and tertiary (10 of 752) centers. In the screening center, all nine cancers were invasive cancers and diagnosed after 12.3 months. In the tertiary center, two were ductal carcinomas *in situ* and eight were invasive cancers. Two of the invasive cancers were diagnosed at 6 months and the remaining eight cancers newly developed after 13.1 months.
**Conclusion:** One-year follow-up rather than 6-month follow-up may be suitable for BI-RADS 3 lesions on screening US found in screening centers. However, more caution is needed regarding similar findings in tertiary centers where 6-month follow-up may be more appropriate.
**Keywords:** *Screening; Breast cancer; Ultrasound; Mammography*

## INTRODUCTION

Breast cancer screening focuses on detecting occult cancer in its early stages without lymph node metastasis and distant spread (1). Although mammography is the only screening method proven to reduce mortality so far, its sensitivity varies, ranging 80–98% in women with fatty breast tissue to 30–48% in women with dense breast tissue (2, 3). Breast ultrasonography (US) is an attractive supplemental screening tool in women with dense breast tissue and the addition of US to screening mammography increases cancer detection yield by 1.9 to 6.8 cancers per 1000 women (2, 4-12). However, adding screening US results in increased cost, increased false-positive US examination findings, and higher benign biopsy rates (13-16). One reason for false-positive US results is the category 3 assessment of the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) (17). The BI-RADS 3 assessment comprises 14.6–41.4% of all screening US (11, 15, 16, 18-21). However, the overall

**Received:** October 8, 2019 **Revised:** March 10, 2020
**Accepted:** March 12, 2020
This study was supported by a faculty research grant of Yonsei University College of Medicine (6-2017-0045).
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malignancy rate of BI-RADS 3 lesions is low, ranging from 0.2% to 1.7% (11, 15, 16, 18, 22, 23). Cancers initially assessed as BI-RADS 3 and detected during follow-up are still in the early stage of malignancy while being small in size, ranging from 2 mm to 18 mm in size (11, 15, 16, 18, 22, 23). Most cases in past studies have had no axillary lymph node metastasis (11, 15, 16, 18, 22). Therefore, previous reports suggested one-year follow-up for women with BI-RADS 3 lesions on screening US (11, 16, 21, 22), and criteria to downgrade the initial BI-RADS category 3 assessment to category 2 (24).

In tertiary referral centers, screening breast US is performed for asymptomatic women with negative or benign findings on their screening mammogram. Community hospitals and private clinics selectively refer women to tertiary centers for screening US. Asymptomatic women with gynecological malignancies, including ovarian cancer, or receiving hormonal replacement therapy undergo screening US at tertiary centers. The characteristics of women who undergo screening US at screening centers may be different from those of women screened at tertiary centers. To our knowledge, no study has compared follow-up intervals and follow-up results in women with BI-RADS 3 lesions on screening US between screening and tertiary centers.

Therefore, we aimed to assess the appropriate follow-up interval, and rate and timepoint of cancer detection in women with BI-RADS 3 lesions on screening US according to the type of institution.

## MATERIALS AND METHODS

The Institutional Review Board approved this retrospective study and required neither patient approval nor informed consent for our review of patient images and medical records.

### Study Population

In our institution, the screening center is a separate facility and at a separate site from the main institution which is a tertiary center. From March 2013 to February 2015, 4776 screening US examinations were performed in the screening center and 1118 women (23.4%) without prior breast cancer surgery were initially assessed as BI-RADS 3. Among them, 349 women without at least 6 months of follow-up and 70 women with probably benign lesions on screening mammogram and/or additional mammogram were excluded. A total of 699 women with negative or benign mammogram findings (n = 664) or without mammogram examinations (n = 35) were included in our study.

In the tertiary center, the purpose of the US examination was recorded on the radiologic report. Screening US was defined as US examinations performed for asymptomatic women with negative or benign assessment of screening mammograms at outside hospitals or who did not undergo mammography, asymptomatic women with negative or benign assessment on previous US and mammography at our institution, or asymptomatic women with gynecological disease or receiving hormonal replacement therapy with negative or benign screening mammograms. Breast US examinations performed on women who had undergone prior breast cancer surgery were not defined as screening US. Among 43950 US examinations performed in the tertiary center, 8846 US examinations were performed in the screening setting. Of 828 women with BI-RADS 3 assessment on screening US (9.4%), 52 women without at least 6 months of follow-up and 24 with probably benign lesions on mammograms were excluded. Finally, 752 women with negative or benign mammogram results (n = 663) or who did not undergo mammographic examination (n = 89) were included in our study.

### Mammographic and US Examinations

In the screening center, screening US examinations and mammogram interpretations were performed by five board-certified radiologists with 3 to 7 years of experiences in breast imaging. Two of the radiologists had completed one year of fellowship training for breast imaging while the other three had only completed their residency training. Mammograms were obtained using dedicated equipment for digital mammography (Lorad Selenia, Hologic, Danbury, CT, USA). Mammography was usually performed on the same day as the screening US. US examinations were performed using high-resolution US equipment (iU22, Phillips-Advanced Technology Laboratories, Bothell, WA, USA) with a 5–12-MHz linear array transducer.

In the tertiary center, screening US examination and mammogram interpretation were performed by 11 board-certified radiologists dedicated to breast imaging with 1 to 20 years of experience in breast imaging. Mammograms were obtained using dedicated equipment for digital mammography (Senographe DS, GE Healthcare, Milwaukee, WI, USA; Lorad Selenia) and digital tomosynthesis (Selenia Dimensions, Hologic). In the screening setting, only 2-dimensional mammograms were obtained, with no


https://doi.org/10.3348/kjr.2019.0747

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tomosynthesis. High-resolution US equipment (iU22; LOGIQ 9, GE Healthcare) and 5–12- or 7–12-MHz linear array transducers were used. Mammograms and US examinations were originally reported according to the ACR BI-RADS in both centers (17).

In both the tertiary and screening centers, standard mediolateral oblique and craniocaudal views were obtained. Additional views were obtained when needed. For this study, an available mammogram was defined as a mammogram obtained 6 months before or after the screening US. Screening US included bilateral whole breasts and the axillae. Lesions were assessed as category 3 on US based on the following features: an oval circumscribed bordered mass parallel to the skin and no or minimal posterior enhancement, a hyperechoic mass with central hypo- or anechogenity suggesting fat necrosis, a hypoechoic mass with a homogeneous low-level internal echo, and a clustered microcyst (13, 16, 17). Orthogonal images with and without calipers were documented for all lesions detected on US, and Doppler US was used for lesion characterization. After 6 months, follow-up breast US was performed. If cancer was diagnosed at this time, mammography or tomosynthesis was additionally performed. At 12 months, both follow-up US and mammography were performed. Follow-up breast US at 6 and 12 months included bilateral whole breasts and axillae.

In both centers, the radiologists or clinicians checked each patient's family history of breast cancer and history of hormone replacement therapy and wrote in the radiologic reports or electronic medical records. We reviewed both for all patients included in this study.

### Data and Statistical Analysis

Age, prevalence or incidence screening US, family history of breast cancer, hormone replacement therapy, malignancy rate, and follow-up interval from the date of initial BI-RADS 3 assessment to the date of last follow-up or cancer detection, and pathological characteristics of the detected cancers were compared between the two centers. For cancer cases, we classified detection intervals into two categories; "at 6 months," which included cancers detected 6–9 months after initial BI-RADS 3 assessment, and "after 12 months," which included cancers detected after 12 months. Women were subclassified and analyzed according to their mammographic breast density (fatty and dense mammography density) and whether they were 40 years or older. Of 1451 women, 124 did not have a mammogram available and were included in the dense mammographic density subgroup because 95 of the 124 women were younger than 40 years old. Nominal variables were compared using the chi-square or Fisher's exact test and continuous variables were compared using the independent *t* test or Mann-Whitney U test. Statistical analyses were performed using SPSS (version 23.0, IBM Corp., Armonk, NY, USA) software. A two-sided $p < 0.05$ was considered to indicate statistical significance.

## RESULTS

Mean age and mammographic density were not significantly different between the two centers ($p = 0.281$ and 0.223, respectively) (Table 1). The mean follow-up interval from the initial assessment to last contact or cancer diagnosis was longer in the tertiary center than in the screening center ($p < 0.001$). Prevalence screening US (76.7%, 536 of 699) was more frequently performed in the screening center than in the tertiary center (44.4%, 334 of 752) ($p < 0.001$). In the tertiary center, 72 women (9.6%) had a family history of breast cancer; in the screening center, 29 women (4.1%) had a family history of breast cancer ($p < 0.001$). In the tertiary center, 140 (18.6%) of 752 women underwent hormone replacement therapy, while in the screening center, 37 (5.3%) of 699 women underwent hormone replacement therapy ($p < 0.001$).

Of 1451 women, 19 cancers (1.3%) in 19 women were diagnosed during follow-up. Seventeen cancers were invasive and two cancers were *in situ*. Three cancers (0.2%) were BI-RADS 3 lesions progressing at 7.7, 12.4, and 21.2 months, and 16 cancers (1.1%) newly developed. Only two cancers (0.1%) were diagnosed at 6 months and 17 (1.2%) were diagnosed after 12 months. Nine cancers (1.3% of 699) were diagnosed at the screening center and 10 (1.3% of 752) at the tertiary center. The malignancy rates did not differ between the two centers ($p > 0.999$). Six cancers from the screening center were detected on prevalence US and eight cancers from the tertiary center were detected on incidence US, which was not significantly different between centers ($p = 0.070$).

When a cut-off age of 40 years was applied, the mean follow-up interval to last contact or cancer diagnosis was longer in the tertiary center (33.3 ± 11.4 months, $p = 0.001$) for 1138 women 40 years or older (Table 2). Of 1356 women with dense mammography density, the mean follow-up interval to last contact or cancer diagnosis was longer in the

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tertiary center (33.5 ± 11.3 months, $p < 0.001$) (Table 3).

The characteristics of the 19 cancers, including one case with axillary lymph node metastasis (5.3%, 1 of 19), are listed in Table 4. Median age, cancer diagnosis according to the cut-off age of 40 years, mean interval to cancer diagnosis, and diagnosis at 6 months or after 12 months

**Table 1. Comparisons of Clinic-Pathological Characteristics between Screening and Tertiary Center**

| Characteristics | Screening Center (n = 699) | Tertiary Referral Center (n = 752) | *P* |
|---|---|---|---|
| Mean age (years, SD) | 47.4 ± 9.3 | 47.9 ± 9.7 | 0.281 |
| Mean follow-up interval* (months, SD) | 30.9 ± 11.2 | 33.2 ± 11.5 | < 0.001 |
| Mammographic density (%) | | | 0.223 |
| Grade A and B (n = 95) | 52 (7.4) | 43 (5.7) | |
| Grade C and D (n = 1356) | 647 (92.6) | 709 (94.3) | |
| US screening (%) | | | < 0.001 |
| Prevalence (n = 870) | 536 (76.7) | 334 (44.4) | |
| Incidence (n = 581) | 163 (23.3) | 418 (55.6) | |
| Family history (%) | | | < 0.001 |
| Yes | 29 (4.1) | 72 (9.6) | |
| No | 670 (95.9) | 680 (90.4) | |
| Hormone replacement therapy (%) | | | < 0.001 |
| Yes | 37 (5.3) | 140 (18.6) | |
| No | 662 (94.7) | 612 (84.1) | |
| Cancer detection rate during follow-up (n = 19) (%) | 9 (1.3) | 10 (1.3) | > 0.999 |
| Cancer detection interval (%) | | | 0.500 |
| At 6 months (n = 2) | 0 (0) | 2 (0.3) | |
| After 12 months (n = 17) | 9 (1.3) | 8 (1.1) | |
| Cancer detection rate according to US screening (%) | | | 0.070 |
| Prevalence | 6 (0.9) | 2 (0.3) | |
| Incidence | 3 (0.4) | 8 (1.1) | |

*Follow-up to last contact or cancer diagnosis. SD = standard deviation, US = ultrasonography

**Table 2. Comparisons of Clinic-Pathological Characteristics according to Cut-Off Age of 40 Years**

| Characteristics | Less than 40 Years (n = 313) | | | Characteristics | 40 Years or Older (n = 1138) | | |
|---|---|---|---|---|---|---|---|
| | Screening Center (n = 161) | Tertiary Referral Center (n = 152) | *P* | | Screening Center (n = 538) | Tertiary Referral Center (n = 600) | *P* |
| Mean age (years, SD) | 34.8 ± 3.7 | 34.0 ± 4.3 | 0.093 | Mean age (years, SD) | 51.2 ± 6.9 | 51.4 ± 7.2 | 0.486 |
| Mean follow-up interval* (months, SD) | 30.5 ± 10.5 | 32.8 ± 11.7 | 0.074 | Mean follow-up interval* (months, SD) | 31.0 ± 11.4 | 33.3 ± 11.4 | 0.001 |
| Mammographic density (%) | | | > 0.999 | Grade on mammogram (%) | | | 0.190 |
| Grade A and B (n = 5) | 3 (1.9) | 2 (1.3) | | Grade A and B (n = 90) | 49 (9.1) | 41 (6.8) | |
| Grade C and D (n = 308) | 158 (98.1) | 150 (98.7) | | Grade C and D (n = 1048) | 489 (90.9) | 559 (93.2) | |
| Cancer detection rate during follow-up (n = 2) (%) | 2 (1.2) | 0 (0) | 0.499 | Malignancy rate (n = 17) (%) | 7 (1.3) | 10 (1.7) | 0.793 |

*Follow-up to last contact or cancer diagnosis.

**Table 3. Comparisons of Clinic-Pathological Characteristics according to Breast Density**

| Characteristics | Fatty Breast (n = 95) | | | Dense Breast (n = 1356) | | |
|---|---|---|---|---|---|---|
| | Screening Center (n = 52) | Tertiary Referral Center (n = 43) | *P* | Screening Center (n = 647) | Tertiary Referral Center (n = 709) | *P* |
| Mean age (years, SD) | 54.3 ± 9.2 | 54.9 ± 7.4 | 0.731 | 46.8 ± 9.1 | 47.5 ± 9.6 | 0.189 |
| Mean follow-up interval* (months, SD) | 34.0 ± 11.9 | 32.4 ± 13.0 | 0.551 | 30.8 ± 11.1 | 33.5 ± 11.3 | < 0.001 |
| Cancer detection rate during follow-up (%) | 1 (2.3) | 0 (0) | 0.453 | 9 (1.4) | 98 (1.3) | > 0.999 |

*Follow-up to last contact or cancer diagnosis.


https://doi.org/10.3348/kjr.2019.0747

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were not significantly different between the two centers (all $p > 0.05$) (Table 5). All nine cancers found in the screening center were invasive, a median 9 mm (range, 2–12 mm) in size, without lymph node metastasis and diagnosed after 12.3 months. No cancers were found at 6 months in the screening center. Even though two cancers in the screening center showed progression at 12.4 months and 21.2 months, they were invasive cancers 9 mm and 12 mm in size without lymph node metastasis. In the tertiary center, eight were invasive cancers and two were ductal carcinomas

**Table 4. Clinicopathologic Features of 19 Detected Cancers from Breast Imaging Reporting and Data System Category 3**

| No. | Age (years) | Interval to Cancer (Months) | Symptoms at Cancer Diagnosis | Detection Center | Pathology | Size on Pathology (mm) | Node Status | Features of Cancer Detection |
|---|---|---|---|---|---|---|---|---|
| 1 | 57 | 12.3 | None | S | IDC | 9 | 0 | New<br>Non-visible on MG |
| 2 | 59 | 12.4 | Palpable | S | Metaplastic carcinoma | 9 | 0 | Increased size (4 mm to 14 mm)<br>Mass on MG |
| 3 | 49 | 21.2 | Palpable | S | IDC | 12* | Unknown | Increased size (10 mm to 12 mm)<br>Mass on MG |
| 4 | 46 | 26.1 | None | S | IDC | 12 | 0 | New<br>Non-visible on MG |
| 5 | 37 | 28.5 | Bloody nipple discharge | S | IDC | 2 | 0 | New<br>Non-visible on tomosynthesis |
| 6 | 37 | 31.8 | None | S | IDC | 8* | Unknown | New<br>Non-visible on MG |
| 7 | 49 | 33.1 | Palpable | S | IDC | 7 | 0 | New<br>Mass on MG |
| 8 | 60 | 35.9 | Palpable | S | IDC | 11 | 0 | New<br>Mass on MG |
| 9 | 40 | 36.9 | Palpable | S | IDC | 7 | 0 | New<br>Non-visible on MG |
| 10 | 44 | 6.8 | None | T | IDC | 16 | 1 | New<br>Mass on MG |
| 11 | 68 | 7.7 | None | T | IDC | 7 | 0 | Increased size (5 mm to 7 mm)<br>Non-visible on MG |
| 12 | 55 | 13.1 | None | T | ILC | 10 | 0 | New<br>Non-visible on MG |
| 13 | 47 | 16.5 | None | T | DCIS | 24 | 0 | New<br>Non-visible on MG |
| 14 | 61 | 18.2 | None | T | IDC | 22 | 0 | New<br>Microcalcifications on MG |
| 15 | 53 | 20.6 | None | T | DCIS | 10 | 0 | New<br>Mass on MG |
| 16 | 43 | 25.3 | None | T | IDC | 4 | 0 | New<br>Microcalcifications on MG |
| 17 | 47 | 35.1 | None | T | IDC | 7* | Unknown | New<br>Non-visible on MG |
| 18 | 49 | 37.8 | None | T | IDC | 6 | 0 | New<br>Mass on MG |
| 19 | 56 | 38.3 | None | T | IDC | 13 | 0 | New<br>Mass on MG |

*Surgery was not performed at outside institution and size on US at time of cancer diagnosis was described. DCIS = ductal carcinoma *in situ*, IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma, MG = mammography, New = newly developed suspicious lesion on US, S = screening center, T = tertiary referral center


https://doi.org/10.3348/kjr.2019.0747

**Table 5. Characteristics of Detected Cancers**

| Characteristics | Screening Center (n = 9) | Tertiary Referral Center (n = 10) | *P* |
|---|---|---|---|
| Median age (years, range) | 49 (37–60) | 51 (43–68) | 0.400 |
| Women 40 years or older (n = 17) (%) | 7 (77.8) | 10 (100) | 0.211 |
| Women less than 40 years (n = 2) (%) | 2 (22.2) | 0 (0) | |
| Median interval of cancer detection (months, range) | 28.5 (12.3–36.9) | 19.4 (6.8–38.3) | 0.179 |
| Cancer detection interval | | | 0.474 |
| At 6 months (n = 2) (%) | 0 (0) | 2 (20.0) | |
| After 12 months (n = 18) (%) | 9 (100) | 8 (80.0) | |
| Mammographic density (%) | | | > 0.999 |
| Grade A and B (n = 1) | 0 (0) | 1 (10.0) | |
| Grade C and D (n = 18) | 9 (100) | 9 (90.0) | |
| Interval change of detected cancers (%) | | | 0.582 |
| Newly developed lesions (n = 16) | 7 (77.8) | 9 (90.0) | |
| Increased size of existing lesions (n = 3) | 2 (22.2) | 1 (10.0) | |
| Cancer type (%) | | | 0.474 |
| *In situ* cancer (DCIS) (n = 2) | 0 (0) | 2 (20.0) | |
| Invasive caner (n = 17) | 9 (100) | 8 (80.0) | |
| Symptom at cancer diagnosis (%) | | | 0.003 |
| Bloody nipple discharge (n = 1) | 1 (11.1) | 0 (0) | |
| Palpable lump (n = 5) | 5 (55.6) | 0 (0) | |
| Negative (n = 13) | 3 (33.3) | 10 (100) | |
| Pathology (n = 16)* | (n = 7) | (n = 9) | |
| Median invasive tumor size (mm) | 9 (2–12) | 10 (4–22) | 0.535 |
| T stage (%) | | | 0.475 |
| 0 (n = 2) | 0 (0) | 2 (22.2) | |
| T1 (n = 13) | 7 (100) | 6 (66.7) | |
| T2 (n = 1) | 0 (0) | 1 (11.1) | |
| N stage (%) | | | > 0.999 |
| 0 (n = 7) | 7 (100) | 8 (88.9) | |
| 1 (n = 1) | 0 (0) | 1 (11.1) | |

*Of 19 women with cancers, 16 underwent surgery in our institution.

*in situ*. Two cancers (0.3%, 2 of 752) in the tertiary center were diagnosed at 6.8 months and 7.7 months; one showing progression at 7.7 months was a 7-mm invasive cancer without lymph node metastasis (Fig. 1) and the other newly developing at 6.8 months was a 16-mm invasive cancer with one axillary lymph node metastasis (Fig. 2). The other eight cancers were newly developing cancers diagnosed after 13.1 months; six invasive cancers were 4 mm to 22 mm in size without lymph node metastasis and two were *in situ* cancers. At the time of cancer diagnosis, symptoms such as palpable lumps (n = 5) and bloody nipple discharge (n = 1) were more frequently present in the screening center (66.7% of 9 cancers) than in the tertiary center (0% of 10 cancers) ($p$ = 0.003). Of the 19 women with cancer, 16 underwent surgery at our institution. Tumor size on pathology, T stage, and N stage were not significantly different between the two centers (all $p$ > 0.05).

## DISCUSSION

In our study, the malignancy rates in women with the BI-RADS 3 assessment on screening US were both 1.3% in the screening and tertiary centers, which was less than the 2% of the recommended range (17) and comparable with previous studies (10, 11, 15-18, 22). Two cancers (0.1%) were diagnosed at 6 months; one progressed from a BI-RADS 3 lesion and the other was a new cancer. The remaining 17 (1.2%) were diagnosed after 12.3 months. At 6 months, the malignancy rates were 0% in the screening center and 0.3% in the tertiary center. Three cancers (0.2%) progressed from BI-RADS 3 lesions at 7.7, 12.4, and 21.2 months while the other 16 (1.1%) were newly developed cancers.

For BI-RADS 3 lesions on screening mammograms, such as non-calcified solid masses with round or oval


https://doi.org/10.3348/kjr.2019.0747

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shape, a solitary group of round microcalcifications, or focal asymmetry without associated calcifications (25-29), a 6-month follow-up is recommended due to the low malignancy rate, detection of mostly early-stage cancers after 6 months, and cost reduction with immediate biopsy (17, 25, 27, 30). Similar strategies are applied to BI-RADS 3 lesions identified on screening US (17). However, the effectiveness of a 6-months follow-up US is questionable (15, 16, 21, 22). Furthermore, the very low malignancy rates of 0.2% to 1.0% (11, 15, 16, 18, 21-23) and high

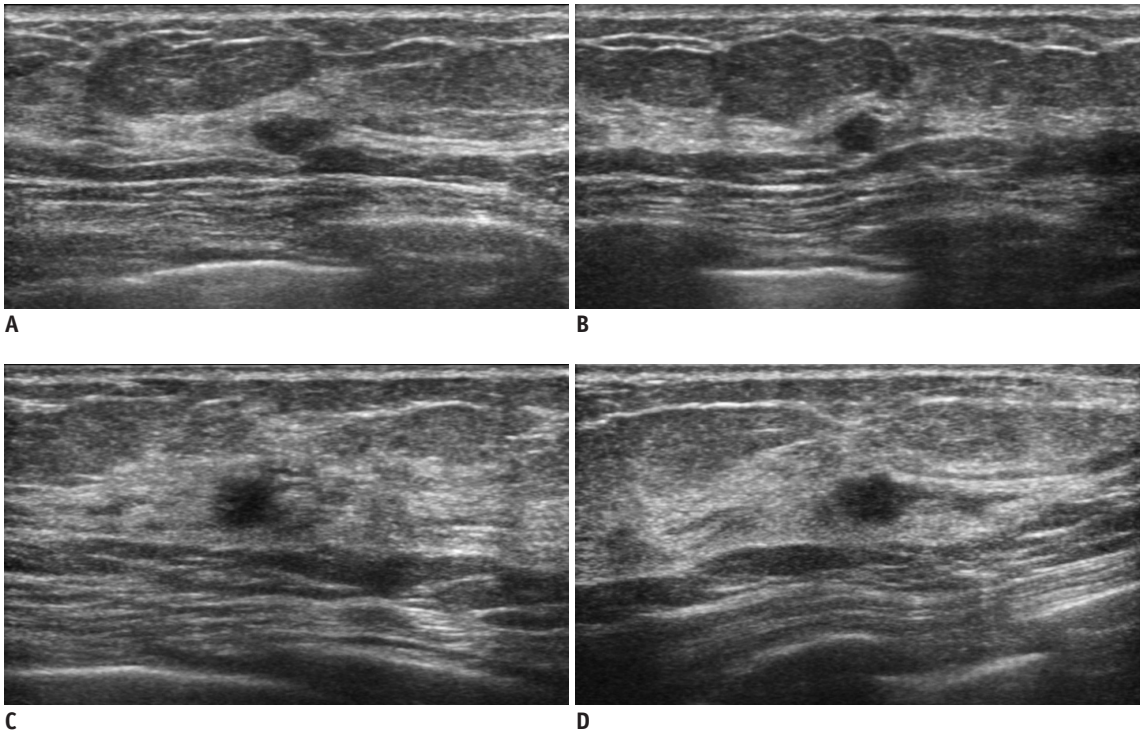


**Fig. 1. 68-year-old women with benign calcifications on screening mammogram and BI-RADS category 3 lesion on screening US performed at tertiary center.**
**A.** Initial transverse. **B.** Initial longitudinal scan. Initially, 5-mm-sized lesion was assessed as BI-RADS category 3. **C.** Follow-up transverse. **D.** Follow-up longitudinal scan. At 7.7 months of follow-up, lesion progressed to 7 mm in size with suspicious features. This change was not detected on mammogram at 7.7 months. It was 7-mm-sized triple-negative invasive ductal carcinoma with nuclear grade 2 and without axillary lymph node metastasis on surgical pathology. BI-RADS = Breast Imaging Reporting and Data System, US = ultrasonography

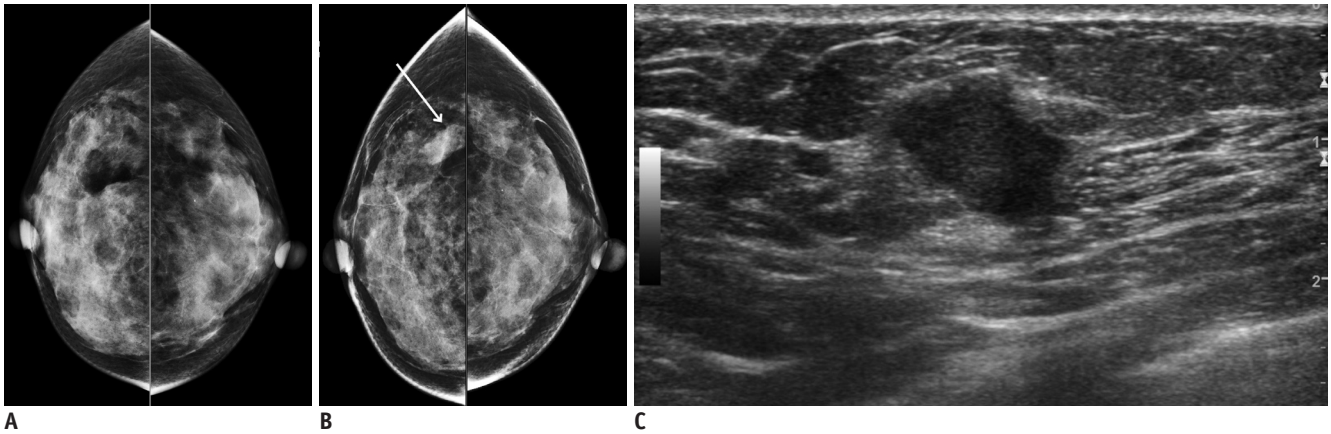


**Fig. 2. 48-year-old woman had benign findings on screening mammogram and BI-RADS category 3 lesions on screening US performed at tertiary center.**
**A.** Screening mammogram. **B.** Follow-up mammogram. **C.** Follow-up US. All BI-RADS 3 lesions showed no change on follow-up US at 6.8 months. However, new 14-mm-sized BI-RADS category 4C lesion was detected on both US and mammogram (arrow). It was 16-mm-sized luminal A type invasive ductal carcinoma with nuclear grade 2 and metastasis to one axillary lymph node on surgical pathology.


https://doi.org/10.3348/kjr.2019.0747

false-positive rates of US examinations during follow-up are problematic. A previous study found newly developed BI-RADS 3 lesions in 26.4%, 23.6%, and 24.6% of all cases in year 1, 2, and 3, respectively, despite the low malignancy rate (16). Prior reports recommended one year of follow-up for multiple bilateral circumscribed masses or BI-RADS 3 lesions on screening US (22, 31). Of 1451 women, only three cancers (0.2%) progressed from BI-RADS 3 lesions at 7.7, 12.4, and 21.2 months. In our screening center, the malignancy rate was 1.3% and all malignancies were diagnosed after 12.3 months. Therefore, a one-year follow-up might be recommended in the screening center. In the tertiary centers, two malignancies (0.3%) were diagnosed at the 6-month follow-up; therefore, more caution is needed in tertiary centers and a 6-month follow-up may remain appropriate.

Most cancers in previous studies diagnosed after initial BI-RADS 3 assessment on screening US were T1 stage (range, 2–18 mm) (11, 15, 16, 18, 22, 23) without lymph node metastasis (11, 15, 18, 22). In our screening center, all nine invasive cancers were detected after 12.3 months with a median tumor size of 9 mm (range, 2–12 mm) and without lymph node metastasis. Two malignancies with progression after the initial BI-RADS 3 assessment at 12.4 months and 21.2 months were 9-mm and 12-mm invasive cancers without lymph node metastasis. Therefore, in the screening center, a one-year follow-up might be cautiously recommended for BI-RADS 3 lesions. In the tertiary center, two invasive cancers were diagnosed at 6 months; one progressing from a BI-RADS 3 lesion was a 7-mm invasive cancer without axillary lymph node metastasis and the other was a new 16-mm invasive cancer with one axillary lymph node metastasis. In the tertiary center, more caution is needed and a 6-month-follow-up in the tertiary center may be appropriate.

Our study has some limitations. First, it was a retrospective study and 495 of 1946 women were excluded. A selection bias might exist, and malignancy rates might be overestimated. However, the overestimation would not change our results. Second, data from screening breast US performed at a single tertiary center and its branch screening center were included. A multicenter study is needed to generalize our findings. Third, US examinations were performed by 16 radiologists and inter-observer variability might exist. Inter-observer variability was not analyzed in this study. However, the inclusion of many radiologists with differing levels of experience is reflective of routine daily practice.

In conclusion, one-year follow-up rather than 6-month follow-up might be more appropriate for BI-RADS 3 lesions identified during screening US in screening centers. However, more caution is needed in tertiary centers where a 6-month follow-up may be more appropriate.

### Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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