ORIGINAL ARTICLE

Screening ultrasonography revealed 15% of mammographically occult breast cancers

Ken Uchida · Akinori Yamashita · Kazumi Kawase · Kentarou Kamiya

Abstract

Background Mammography and physical examination (PE) are the recommended modalities for breast-cancer screening for women 40 years and older in Japan. Mammography, however, cannot detect lesions in dense breast tissue, which is common in Japanese women. Breast screening by ultrasound (US) is popular in Japan. We studied which modality or combinations of modalities optimize breast cancer detection for Japanese women.

Methods From April 1993 through March 2005 we found 97 breast cancers in 9,082 women by screening examinations with mammography, US, and PE. We compared the detection rates of these three modalities for breast cancer.

Results The detection rates of mammography, US, and PE for breast cancer were 83.5 (81 of 97 cancers), 75.3 (73 of 97 cancers), and 60.8% (59 of 97 cancers), respectively. The detection rates of the combinations of mammography and US, mammography and PE, and US and PE were 99.0 (96 of 97 cancers), 88.7 (86 of 97 cancers), and 81.4% (79 of 97 cancers), respectively. Ultrasonography detected 15% of the mammographically occult breast cancers.

Conclusion Screening with the combination of mammography and US significantly increases the detection rate of breast cancer. These results suggest that screening with mammography and US would optimize cancer detection in Japanese women.

Introduction

Breast cancer screening with mammography and physical examination (PE) was recommended for women 40 years or older by the Japanese Ministry of Health, Labour and Welfare in April 2004. This caused a marked increase of the breast cancer detection rate compared with PE alone. In the West mammography has reduced breast cancer mortality rates in screened populations. Can a similar reduction in mortality be expected in Japanese women? One disadvantage of mammography is its difficulty in detecting lesions in dense breast tissue, which is common in Japanese women. On the other hand, ultrasonography (US) has been accepted widely in Japan and is better able to detect lesions in dense breast tissue. The performance of screening US and that of screening mammography have not been compared in a population. Therefore, in the present study we studied which modality or combination of modalities optimizes cancer detection.

Patients and methods

Patients

A total of 9,082 women were examined for 12 years from April 1993 through March 2005 at our medical check-up center. Ninety-seven breast cancers were found.

K. Uchida (✉) · A. Yamashita · K. Kawase
Department of Breast and Endocrine Surgery,
The Jikei University School of Medicine,
3-25-8 Nishi-Shinbashi, Minato-ku, Tokyo 105-8461, Japan
e-mail: kenucd@jikei.ac.jp

K. Kamiya
Department of Surgery, Showa University, Tokyo, Japan

Mammography

Mammography was performed with a Mammomat 1000 scanner (Siemens Medical Systems, PA, USA) or a Lorad M-IV series mammography system (Lorad, MA, USA) with dedicated cassettes (Min-R 2000; Eastman Kodak Co., Rochester, NY, USA). The mediolateral-oblique and cranio-caudal views were obtained routinely. Magnified spot views were added if necessary when a mammogram was judged as category 3. We made efforts to reduce the number of category 3 cases and the recall rate. Two examiners checked all mammograms according to the Mammography Guidelines [1]. Patients with category 3 or higher lesions were recalled to a breast clinic.

US

US was performed by technicians specializing in US of the breast using SSA-340A, 7.5-MHz probes (Toshiba Medical Systems Corp., Tokyo, Japan), HDI-3500, 5- to 10-MHz probes (Philips Medical Systems, Eindhoven, The Netherlands), and SSD-1000, 10-MHz probes (Aloka Co., Ltd., Tokyo, Japan). The recall criteria for US were 5 mm or lager masses or non-mass-forming abnormalities.

PE

PE of the breast was performed by four medical doctors who were not blinded to the results of mammography and US.

Statistical methods

The chi-square test was used to explore the associations among the three modalities. A *P*-value less than 0.05 was considered statistically significant.

Results

Ninety-seven breast cancers were found. The overall detection rate of breast cancer was 1.07% (97 cancers in 9,082 patients). The detection rates with the patients' first, second, and third or later examinations were 0.74 (67 cancers), 0.14 (13 cancers) and 0.19% (17 cancers), respectively. Patients in the 30s, 40s, 50s, 60s and 70s accounted for 15, 22, 38, 26, and 7% of all patients, respectively. The breast cancer detection rates in these age groups were 0.37, 1.10, 1.27, 1.13, and 1.80% , respectively.

Figure 1 shows the age distribution of all examined women and of women with detected breast cancers.

The detection rates with mammography, US, and PE were 83.5 (81 of 97 cancers), 75.3 (73 of 97 cancers), and 60.8% (59 of 97 cancers), respectively (Table 1).

The total recall rates of mammography, US, and PE were 1.96 (178/9082), 3.90 (355/9082), and 0.72% (65/9082) respectively. The specificity of mammography, US, and PE were 98.0, 96.0, and 99.3% respectively. The positive predictive value of these modalities were 45.5 (81/178), 20.6 (73/355), and 90.8% (59/65), respectively.

The percentage of breast cancer cases missed by a single modality was 16.4% (16 of 97 cancers) for mammography, 24.7% (24 of 97 cancers) for US, and 39.2% (38 of 97 cancers) for PE. Table 2 shows the 16 breast cancers missed by mammography alone. However, 15 of these 16 breast cancers were found with US. Only one case, a non-palpable breast cancer with bloody nipple discharge, was not detected by mammography or US.

The mean age of patients with these mammographically occult breast cancers was 56.5 years (range, 44–73 years). The ratio of menopausal to pre-menopausal patients was one to one. The mean diameter of these cancers on US was 1.2 ± 0.5 cm (range, 0.5–2.5 cm). The overlooked breast cancers were of small size, but 81% were invasive.

The detection rates of combined modalities were 99.0% (96 of 97 lesions) with mammography and US, 88.7% (86 of 97 cancers) with mammography and PE, and 81.4% (79 of 97 cancers) with US and PE (Table 3). In other words, mammography and US missed 1 breast cancer (1%), mammography and PE missed 11 breast cancers (11%), and US and PE missed 18 breast cancers (19%).
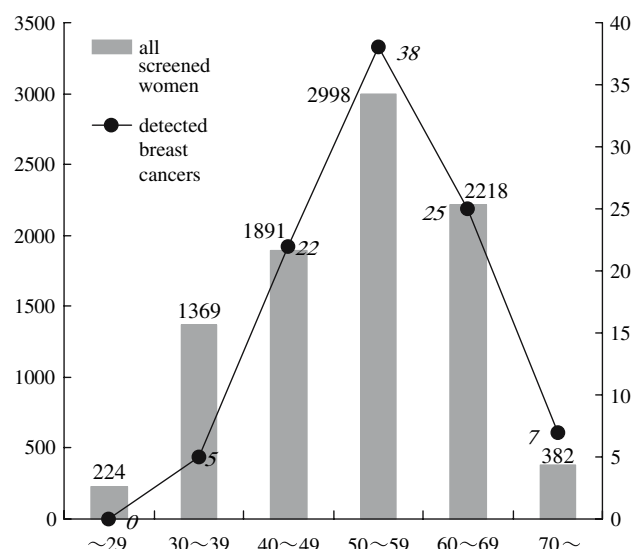
Fig. 1 All screened women and detected breast cancers

Table 1 Detection rates of each modality

Modality	Detection rates (detected cases/all cases)
Mammography	83.5% (81 of 97)*
US	75.3% (73 of 97)*
PE	60.8% (59 of 97)*

*$P < 0.0001$

Table 2 Sixteen breast cancers were missed with mammography alone

No.	Age	US size (cm)	Histology	Menopause status
1	44	0.7	Invasive ductal cancer	Pre
2	46	1.0	Ductal caucinoma in situ	Pre
3	46	1.3	Invasive ductal cancer	Pre
4	49	1.4	Invasive ductal cancer	Pre
5[a]	50	–	Medullary carcinoma	Pre
6	51	1.4	Invasive ductal cancer	Pre
7	51	0.7	Tubular carcinoma	Pre
8	54	0.8	Invasive ductal cancer	Post
9	57	2.5	Invasive ductal cancer	Post
10	64	1.3	Ductal caucinoma in situ	Post
11	66	0.5	Invasive ductal cancer	Post
12	66	1.8	Invasive ductal cancer	Post
13	70	0.6	Invasive ductal cancer	Post
14	73	1.0	Ductal caucinoma in situ	Post
15	51	1.4	Invasive ductal cancer	Pre
16	66	1.0	Invasive ductal cancer	Post

[a] No.5: nipple discharge

Table 3 Detection rates of combined modalities

Combined modalities	Detection rates (detected cases/all cases)
Mammography + PE	88.7% (86 of 97)*
US + PE	81.4% (79 of 97)*
Mammography + US	99.0% (96 of 97)*

*$P < 0.0001$

The mean age of patients with breast cancers detected by mammography and US was 54.9 and 55.3 years, respectively. The percentage of menopausal patients with mammography and US detected breast cancers was 58 and 56%, respectively. Age and menopausal status did not statistically affect the detection rates of the two modalities.

Discussion

The recommendations for breast cancer screening by the Japanese Ministry of Health, Labour and Welfare were revised in April 2004. The main points of the official notice were the screening with mammography and PE and the lowering of the target age from 50 to 40 years or older. In several countries mammography has decreased breast cancer mortality rates by nearly 50% in screened populations [2]. The sensitivity of mammography is related to the radiographic density of the breast, being as high as 98% in women with predominantly fatty breasts to as low as 48% in women with extremely dense breasts [3].

Is breast cancer screening with mammography also appropriate for Japanese women? Japanese woman frequently have dense breasts that conceal small masses in mammary glands. Some breast cancers might be missed if screening involves only mammography and PE. To date, there has been no randomized controlled trial or sufficient evidence of a reduction in mortality due to mammographic screening in Japanese women. If mammography is not effective, which modality would be better?

In our study the overall detection rate of breast cancer was 1.07% (97 cancers in 9,082 patients). The detection rates with the patients' first, second, and third or later examinations were 0.74 (67 cancers), 0.14 (13 cancers) and 0.19% (17 cancers), respectively. The detection rate in our study was higher than that of other reports because of the combined screening method of mammography and US, screening of patients in their the 50s and 60s (57%) who have a high incidence of breast cancer, screening of women who live in urban settings, and screening by breast cancer specialists.

Our study of breast cancer screening with mammography, US, and PE found detection rates of 83.5 (81 of 97 cancers), 75.3 (73 of 97 cancers), and 60.8% (59 of 97 cancers), respectively. However, 16 breast cancers were missed by mammography alone. These breast cancers were small but invasive. The mean age of patients who had breast cancers missed with mammography was 56.5 years (range, 44–73 years), which was nearly identical to that of patients who had mammography-detected breast cancers (54.9 years range, 31–75 years).

Edeiken [4] has reported that the false-negative rates for palpable breast cancers on mammography were 22% for a series of 449 patients, 44% for patients 50 years and younger, and 13% for patients older than 50 years. Tarter et al. [5] reported that 11% (91 of 813) of breast cancer in their series could not be found with mammography. They also reported that false-negative results are associated with lower age, weight, and parity. Namba et al. [6] reported that 7% of 513 operable breast cancers could not be found even with re-examination of the mammogram, magnified spot films, or specimen mammography. They also reported that 72% of patients at 49 years and younger had cancers undetectable by mammography. Breast cancers in young women tend to be overlooked by mammography. Takahashi

et al. [7] reported that 72 (7.2%) of 987 palpable breast cancers were not detected with mammography; in particular, 12% of cancers in patients younger than 50 years were not detected. Our data on age and menopausal status did not support these studies. Ma et al. [8] reported that extensive parenchymal densities, lobular carcinoma, and tumors of small size were less likely to be detected.

US is a standard modality for diagnosing breast diseases [9]. Screening for breast cancer with US alone is popular in Japan. However, a randomized clinical trial to assess the efficacy of US screening in Japanese women has not been performed. Four recent trials [10] of breast US in the West from 1995 through 2002 enrolled 37,085 women. In these studies, cancers that were clinically or mammographically occult were detected at a rate of 0.34 per 1,000 patients. These cancers had a mean diameter of 9 mm and almost all (94.5%) showed invasion. According to the summary of previously published reports [11] of "ultrasound-only" cancers, breast cancer was detected in 0.10–2.7% of patients. Mammographically occult cancers in our study had a mean diameter of 1.2 ± 0.5 cm (range, 0.5–2.5 cm) and almost all (81%) showed invasion. US screening detects small breast cancers in the West and in Japanese women as well.

Several questions are associated with the use of US for breast cancer screening. These include its possible effects on breast cancer mortality, its financial cost, population selection, and technical disparities. Screening with US is less expensive than screening with mammography. Our study showed that screening US found 15% of mammographically occult breast cancers. For the present, we recommend both mammography and US for breast cancer screening except for patients with fatty breast.

We conclude that mammography missed 16% of breast cancers. Screening with mammography and US would optimize breast cancer detection.

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