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Significance and positive predictive values of mammographic findings in the Asia-Pacific region: a single-centre study in Taiwan

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AIM: To report positive predictive values (PPVs) of mammographic findings (MFs) of a screening cohort in Taiwan with a view to providing radiologists around the world with adequate information for assessing MFs before recommending biopsy for Asian women.

MATERIALS AND METHODS: Between January 2014 and June 2017, 18,449 women received screening mammography at Tri-Service General Hospital (TSGH). Of these women, 1,622 exhibited specific MFs, namely mass (n=518), microcalcification (n=668), focal asymmetry (FA; n=462), and architectural distortion (AD; n=117). The distribution and PPVs of each MF were calculated after stratification based on cancer type, age, and breast density.

RESULTS: The age group with the highest proportion of women was 50–59 years (48.1%), and most women presented with dense breasts (68.6%). The most common MF in the recalled women was microcalcification (41.2%) and the least common was AD (7.2%). AD was the most predictive MF for overall breast cancers, invasive carcinomas, and carcinomas in situ. Microcalcification was the second most predictive MF among recalled women for predicting overall breast cancers; however, it was less predictive than mass and FA in women who received a biopsy recommendation or underwent biopsy.

CONCLUSION: AD can indicate the likelihood of breast cancer development in Asian women with abnormal screening results. Benign breast diseases are more likely to occur in women recommended for or receiving breast biopsy owing to microcalcification than to mass or FA.

Introduction

Mammography is the most commonly used imaging technique for breast cancer screening,[1] and has been shown to reduce breast-cancer-associated mortality.[2,3] As previously reported, the estimated sensitivity of mammography for detecting breast cancer varies between 77% and 95%[4]; however, sensitivity can be 26% lower in extremely dense breasts than in entirely fatty breasts.[5] The American College of Radiology Breast Imaging Reporting and Data System (ACR BI-RADS), fifth edition, recommends that women who have received a diagnoses of abnormal mammographic findings (MFs), namely mass, microcalcification,

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architectural distortion (AD), or focal asymmetry (FA), should be recalled for additional imaging tests or interventions.[5] Radiologists should understand the positive predictive values (PPVs) of MFs before recommending additional imaging tests or interventions to women who have received breast screening. Thus far, the PPVs of MFs have been reported in the USA; however, such values have rarely been reported among women receiving breast cancer screening in the Asia-Pacific region.

In most related studies, reported the PPVs of MFs have been limited to women who had undergone biopsy, resulting in so-called "verification bias." The PPVs of MFs from screening registries were first described in a Singaporean population; microcalcification was reported as a reliable predictor of ductal carcinomas in situ in this population[6,7]; however, one of these studies was limited to screening examinations followed by biopsy recommendations, and the other was limited to screening examinations followed by open biopsy. Another large retrospective analysis of MFs conducted in San Francisco demonstrated that mass, microcalcification, AD, and developing asymmetry had comparable PPVs in the study's screening population[8]; however, the PPVs of MFs among women in the Asia-Pacific region are not identical to those among women in the USA because of inherent differences in the biological characteristics of breast cancers in the two locations.[9]

In the present study, cases of women participating in the national breast cancer screening programme were examined retrospectively. The distribution of mass, microcalcification, AD, and FA based on age and breast density (BD) were reported and the PPVs of the specific MFs calculated in the diagnosis of overall breast cancers, invasive carcinomas, and carcinomas in situ. The present results could assist radiologists in obtaining a deeper understanding of screening populations in Taiwan and could serve as a reference for radiologists in other countries in the Asia-Pacific region. The aim of this study was to provide a reliable reference to radiologists assessing MFs among Asian women not only in the Asia–Pacific region, but also elsewhere around the world in breast cancer screening programmes.

Materials and methods

Study design and population

Approval from the institutional review board was obtained through the institution's human investigations committee, which admitted that informed consent could be waived. A total of 18,449 Asian women participated in the national breast cancer screening programme at the TSGH between January 2014 and June 2017. Relevant data were accessed from the institutional screening database. The study inclusion criteria were based on age and family history of breast cancer. Accordingly, women were included in this study if they were of the age 45–70 years (without a family history of breast cancer) or >40 years (with a family history of breast cancer). No specific exclusion criteria were set for this analysis. Each screening mammography was reported according to the regulations of ACR BI-RADS, fifth edition. To understand the cancer risk associated with specific MFs, analyses were limited to all examination results interpreted as abnormal and for which specific MFs were recorded.

Mammographic systems and examination parameters

At the TSGH, bilateral two-view mammograms were obtained by Selenia or Dimensions Digital Mammography (Hologic-Lorad Inc. Bedford, MA, USA). All mammograms were performed by three competent technologists who were qualified and had been involved in the breast cancer screening programme for >6 years. As to examination parameters, the appropriate voltage setting was selected automatically by the machine and could be adjusted manually (range: 24–32 kVp). The glandular dosage of each screening mammography was <3 mGy, following the ACR BI-RADS guidelines.

Mammogram interpretation and management

All screening mammograms were reported in a single reading by four qualified radiologists in this study. The durations of experience of these radiologists in interpreting breast images were 20, 10, 5, and 4 years. All screening mammograms were evaluated in accordance with the regulations of ACR BI-RADS, fifth edition. BD was assessed by each radiologist visually and subjectively, and categorised as dense or non-dense breast. Women with suspicious imaging findings were recalled. The suspicious MFs of mass, microcalcification, FA, and AD were the focus, which corresponded to ACR BI-RADS categories 0, 3, 4, and 5, respectively. When two or more MFs were identified in a single mammogram, the MFs were categorised in separate columns so that individualised PPV could be calculated for each MF. Subsequently, additional imaging evaluation tools, such as mammography (spot magnification, spot compression, or digital breast tomosynthesis), ultrasound, or both were recommended. Biopsy was recommended for women whose lesions corresponded to ACR BI-RADS categories 4a, 4b, 4c, or 5. We excluded women who were recalled owing to other imaging findings (e.g., enlarged axillary lymph node) or lost to follow-up for any subsequent procedures.

Variable definitions

Demographic and self-reported breast health history data were recorded at each mammographic screening examination. The women were classified into two groups, namely, the recalled group and biopsy-recommended group. The collected data were stratified based on age, BD, the initial and final ACR BI-RADS categories, and the results of histopathological examinations of biopsy specimens, which were obtained by the 14 G biopsy system (MAX-CORE, Bard, Covington, Louisiana, USA). Histopathology was undertaken by pathologists with an average of 6 years of experience. In addition, one pathologist, with >20 years of experience, reviewed equivocal cases. Each breast cancer

was classified as an invasive carcinoma or carcinoma in situ. Other benign histopathological results, such as fibrocystic change, sclerosing adenosis, papilloma, or atypical ductal hyperplasia were excluded from the analyses.

Statistical analysis

The present study followed the rules of the medical audit of ACR BI-RADS. PPV_1 was the ratio of diagnosed cancers to the abnormal mammographic results of a specific MF. PPV_2 was the ratio of diagnosed cancers to the number of women to whom biopsy was recommended. PPV_3 was the ratio of diagnosed cancers to biopsied specimens. All PPVs were calculated separately for mass, microcalcification, AD, and FA for overall breast cancers and were stratified based on the histopathological findings (invasive carcinomas or carcinomas in situ). Besides, the PPVs of each MF were stratified based on age (with decade intervals) and BD (dense versus non-dense).

The distribution of BD stratified by age was calculated and analysed using the Pearson chi-squared test in Excel (Office 2016, Microsoft, Redmond, Washington, USA). The odds ratio of age and mammographic findings to be associated with overall breast cancers were calculated with Logistic regression in the SPSS software (version 16.0, IBM, Armonk, New York, USA). Results associated with p-values of <0.001 were considered statistically significant. This paper also described the frequencies of MFs in each subgroup and the overall distribution of MFs according to the ACR BI-RADS categories among all women to whom biopsy was recommended.

Results

Of the 18,449 Asian women who had undergone screening mammography at Tri-Service General Hospital during the study reference period, 1,635 had abnormal MFs and 13 women were excluded from the analyses because they were recalled owing to diagnoses of enlarged axillary lymph nodes during screening mammography. The age group with the highest proportion of recruited women was 50–59 years (48.1%) and presented with dense breast parenchyma (68.6%). In the present study, women aged 60–70 years were more likely to present with non-dense breast parenchyma than were those aged 40–49 years ($p<0.001$; Table 1). Among the women to whom biopsy was recommended, 432, 96, 38, and two were classified under categories 4a, 4b, 4c, and 5, respectively. The distributions of the MFs were presented according to the ACR BI-RADS categories. The MFs were most commonly reported under category 4a, followed by category 4b and then category 4c. A lower reporting rate of mass than of microcalcification was noted in category 4a lesions and a higher reporting rate of mass than of microcalcification was noted in category 4c lesions (Fig 1).

Among the women who had positive findings on screening mammography, microcalcification (41.2%) and mass (31.9%) were the most commonly detected MFs, followed by FA (28.5%) and AD (7.2%; Table 2). Of the 467 women who had undergone biopsy, 130 (27.8%) exhibited malignant lesions; of these, 76 (16.3%) had invasive carcinomas and 54 (11.6%) had carcinomas in situ. Microcalcification was the most common MF among overall breast cancers and was the most predominant presentation among women with carcinomas in situ. In addition, mass and AD were more commonly presented in invasive carcinomas than in carcinomas in situ (Table 3). AD was the strongest predictor of overall breast cancers, invasive carcinomas, and carcinomas in situ. Microcalcification was secondary to AD in predicting carcinomas in situ. Microcalcification also exhibited a higher PPV than did mass and FA for overall breast cancers among recalled women; however, microcalcification showed a lower PPV than did mass and FA among women who had received recommendations for or had undergone biopsy (Table 2). In addition, mass exhibited a higher PPV for invasive carcinomas than for carcinomas in situ, whereas the PPV of microcalcification was comparable for both malignancies (Table 3).

In the present cohort, women aged 50–59 years or with dense breasts were more likely to be recalled owing to positive MFs or to receive a biopsy recommendation

Table 1
Age-stratified distribution of mammographic density.

Age-stratified group (years)	Women with dense breasts (n=1112)	Women with non-dense breasts (n=510)	p-Value
40–49 (n=427)	361 (84.5)	66 (15.5)	<0.001
50–59 (n=780)	530 (67.9)	250 (32.1)	
60–70 (n=415)	221 (53.3)	194 (46.7)	

Data are numbers of women. The numbers in parentheses are percentages within each age group.
The p-value was calculated using the Pearson chi-squared test.

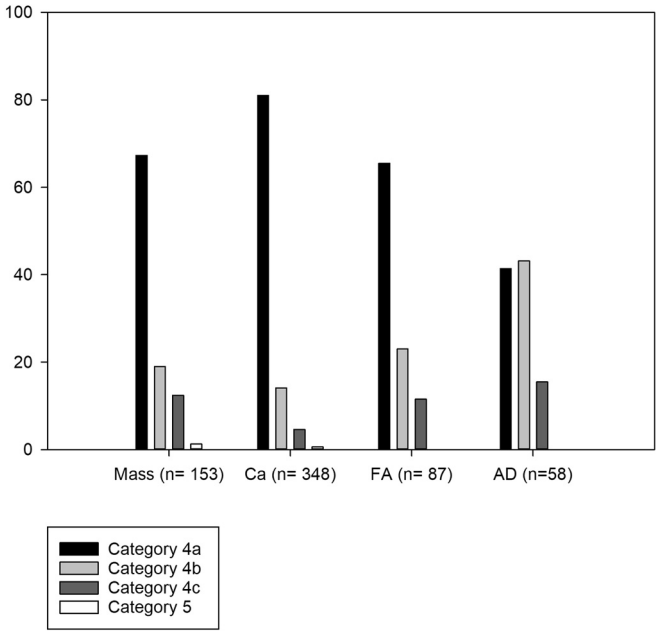


Figure 1 Distribution of mammographic findings according BI-RADS categories among women recommended to undergo biopsy.

Table 2
Distribution of mammographic findings and PPVs for overall breast cancers.

Mammographic findings	Recalled women		Women recommended for biopsy		Women undergoing biopsy	
	No. (n=1,622)	PPV_1 (%)	No. (n=568)	PPV_2 (%)	No. (n=467)	PPV_3 (%)
Mass	518 (31.9)	8.7	153 (26.9)	29.4	122 (26.1)	36.9
Microcalcification	668 (41.2)	11.3	348 (61.3)	21.6	283 (60.6)	26.5
FA	462 (28.5)	4.5	87 (15.3)	24.1	79 (16.9)	26.6
AD	117 (7.2)	28.2	58 (10.2)	56.9	56 (12)	58.9

Numbers in parentheses are percentages rounded up or down. The PPVs are calculated for overall breast cancers composed of invasive carcinomas and in situ carcinomas.
PPV, positive predictive value; FA, focal asymmetry; AD, architectural distortion.

Table 3
PPVs of mammographic findings stratified based on cancer type.

Mammographic findings	Invasive carcinoma				*In situ* carcinoma			
	No. of women (n=76)	PPV_1 (%)	PPV_2 (%)	PPV_3 (%)	No. of women (n=54)	PPV_1 (%)	PPV_2 (%)	PPV_3 (%)
Mass	35 (46.1)	6.8	22.9	28.7	10 (18.2)	1.9	6.5	8.2
Microcalcification	36 (47.4)	5.4	10.3	12.7	39 (72.2)	5.8	11.2	13.8
FA	15 (19.7)	3.2	17.2	19	6 (11.1)	1.3	6.9	7.6
AD	23 (30.3)	19.7	39.7	41	10 (18.5)	8.5	17.2	17.9

Each mammogram appears only once, and all cancers are linked to only one mammogram. The numbers in parentheses are percentages rounded up or down.
PPV, positive predictive value; FA, focal asymmetry; AD, architectural distortion.

because of suspicious or malignant MFs. Almost all MFs showed the highest PPV_1 and PPV_2 among women aged 60–70 years. Higher PPV_1s of microcalcification and AD and higher PPV_2s of all MFs were reported in women with non-dense breasts than in women with dense breasts. Overall, AD was the most predictive MF of overall breast cancers in all women stratified based on age intervals and BD. Microcalcification was more predictive of overall breast cancers than was mass in recalled women but less predictive of overall breast cancers than was mass in women who had received a biopsy recommendation, except in the subgroup of women with non-dense breasts (Table 4). Finally, the risk factors were assessed, namely age, BD, and specific MFs, for overall breast cancers in the screening population. Notably, neither age nor BD was significantly associated with the risk of overall breast cancers in the present analysis (Table 5).

Discussion

To the authors' knowledge, this is the first cohort study to analyse PPVs (PPV_1, PPV_2, and PPV_3) of MFs among a single-screening population. According to the medical audit of ACR BI-RADS, the PPV_1, PPV_2, and PPV_3 of each MF reflect the clinical value to be recalled, clinical value to be

Table 4
Yield of cancer for mammographic findings according to participants' factors on screening mammograms.

A. Recalled group												
	Mass			Microcalcification			FA			AD		
	No. (n=518)	PPV_1 (%)	95% CI	No. (n=668)	PPV_1 (%)	95% CI	No. (n=462)	PPV_1 (%)	95% CI	No. (n=117)	PPV_1 (%)	95% CI
Age (years)												
40–49	136 (26.3)	8.1	3.5–12.7	183 (27.4)	10.9	6.4–15.4	113 (24.5)	2.7	0–5.7	32 (27.4)	21.9	7.6–36.2
50–59	208 (40.2)	7.2	3.7–10.7	348 (52.1)	8.6	5.7–11.5	221 (47.8)	4.1	1.5–6.7	52 (44.4)	30.8	18.3–43.3
60–70	153 (29.5)	12.4	7.2–17.6	187 (28)	18.5	12.9–24.1	128 (27.7)	7.0	2.6–11.4	33 (28.2)	30.3	14.6–46.0
BD												
Dense	299 (57.7)	8.7	5.5–11.9	530 (79.3)	10.0	7.4–12.6	290 (62.8)	5.2	2.6–7.8	91 (77.8)	23.1	14.4–31.8
Non-dense	219 (42.3)	8.7	5.0–12.4	138 (20.7)	15.9	9.8–22.0	172 (37.2)	3.5	0.8–6.2	26 (22.2)	46.2	27.0–65.4
B. Biopsy-Recommended Group												
	Mass			Microcalcification			FA			AD		
	No. (n=153)	PPV_2 (%)	95% CI	No. (n=348)	PPV_2 (%)	95% CI	No. (n=87)	PPV_2 (%)	95% CI	No. (n=58)	PPV_2 (%)	95% CI
Age (years)												
40–49	46 (30.1)	23.9	11.6–36.2	112 (32.2)	17.9	10.8–25.0	27 (31)	11.1	0–22.9	21 (36.2)	33.3	13.1–53.5
50–59	54 (35.3)	27.8	15.9–39.7	165 (37.4)	18.2	12.3–24.1	39 (44.8)	23.1	9.9–36.3	24 (41.4)	66.7	47.8–85.6
60–70	53 (34.6)	35.8	22.9–48.7	73 (21)	34.2	23.3–45.1	21 (24.1)	42.9	21.7–64.1	13 (22.4)	76.9	54.0–99.8
BD												
Dense	93 (60.8)	28.0	18.9–37.1	288 (82.8)	18.4	13.9–22.9	65 (74.7)	23.1	12.9–33.3	44 (75.9)	47.7	32.9–62.5
Non-dense	60 (39.2)	31.7	19.9–43.5	60 (17.2)	36.7	24.5–48.9	22 (25.3)	27.3	8.7–45.9	14 (24.1)	85.7	67.4–100

The numbers in parentheses are percentages rounded up or down.
CI, confidence interval; BD, breast density; PPV, positive predictive value; FA, focal asymmetry; AD, architectural distortion.

Table 5
Logistic regression analysis of risk factors for breast cancer on screening mammograms.

Variables	Univariate		Multivariate	
	OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
Age				
40–49	1.00 (reference)	0.990	1.00 (reference)	0.076
50–59	0.72 (0.48–1.10)		0.99 (0.60–1.63)	
60–70	0.98 (0.63–1.53)		1.64 (0.94–2.84)	
BD (dense versus non-dense)	1.11 (0.77–1.59)	0.594	1.03 (0.66–1.60)	0.911
Mammographic Findings				
Mass (yes versus no)	19.11 (13.20–26.67)	<0.001	20.78 (13.17–32.79)	<0.001
Microcalcification (yes versus no)	38.18 (26.89–54.23)	<0.001	39.08 (26.00–58.73)	<0.001
FA (yes versus no)	7.53 (4.68–12.11)	<0.001	7.05 (4.04–12.32)	<0.001
AD (yes versus no)	70.91 (45.32–110.95)	<0.001	37.44(21.26–65.91)	<0.001

OR, odds ratio; CI, confidence interval; BD, breast density; PPV, positive predictive value; FA, focal asymmetry; AD, architectural distortion.

recommended for biopsy, and exact cancer yield rate of each MF, respectively. In the present study, AD was the least identified but most predictive MF for overall breast cancers, invasive carcinomas, and carcinomas in situ among recalled women who had received recommendations for or undergone biopsy (Tables 2 and 3). The present results were compared with a retrospective analysis conducted in San Francisco and identified a higher PPV_1 of AD for overall breast cancers (28.2% versus 10.2%), invasive carcinomas (19.7% versus 10.2%), and carcinomas in situ (8.5% versus 0%) in the present screening population than in the aforementioned study (Table 6)[8]; however, AD exhibited a lower PPV_3 for overall breast cancers (58.9% versus 67%) and invasive carcinomas (41% versus 61.9%) but a higher PPV_3 for carcinomas in situ (17.9% versus 5.1%) in the present study group than in another study group in the USA.[10] Thus, radiologists in Taiwan must recall women with AD identified at mammography screening.

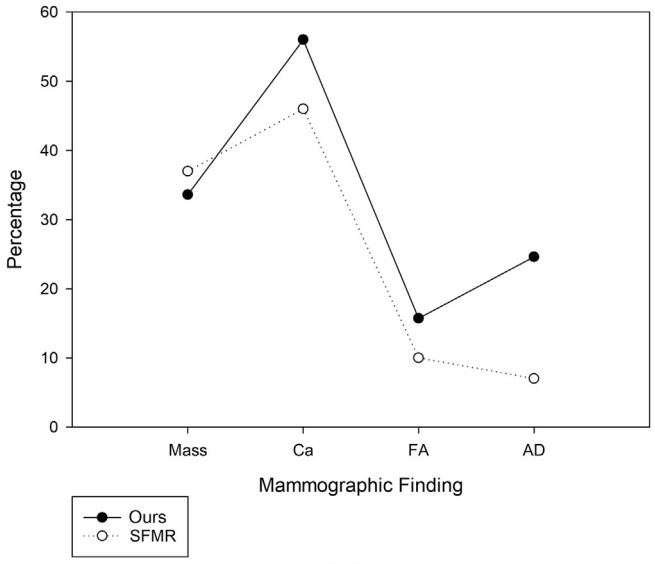
In the present analyses, the high PPV_1s of AD in the present study group were mostly related to the high likelihood of AD found in overall breast cancers, invasive carcinomas, and carcinomas in situ. The reporting rate of AD in the present screening population was comparable to that in the screening population in San Francisco (7.2% versus 7%, respectively)[8]; however, the percentages of AD found in breast cancers were significantly higher in the present study group than were those in the San Francisco study population (overall breast cancers: 24.6% versus 7%; invasive carcinomas: 30.3% versus 10%; and carcinomas in situ: 18.5% versus 0%; Fig 2). The reporting rates of the other MFs in the present population were comparable with those in the San Francisco study population (mass: 31.9% versus 35%; microcalcification: 41.2% versus 33%; and FA: 28.5% versus 25%), as acceptable annual recall and cancer detection rates were reported under the regulations of the ACR BI-RADS. To summarise, AD is a unique MF that was the best predictor of breast cancers in the present screening group and could also be in other screening groups of Asian descent around the world. Additional analyses from other countries in the Asia-Pacific region are welcomed to verify the present results.

In the present study, microcalcification exhibited higher PPV_1 but lower PPV_2 and PPV_3 for overall breast cancers than did mass and FA (Table 2). The PPVs of microcalcification in the present study were comparable with those in studies conducted in the USA.[8,11] The overall PPVs are believed to be the summation of PPVs of microcalcification in different morphologies (e.g., amorphous, coarse heterogeneous, and fine pleomorphic). A higher reporting rate of amorphous microcalcification (59.9% versus 34.9%) and a lower reporting rate of fine pleomorphic microcalcification (25% versus 34.2%) were identified in the present screening population than in a cohort study conducted in the USA.[11] Many previous studies have reported that amorphous microcalcification was less predictive of breast cancers than was fine pleomorphic microcalcification[5,12]; however, the present predictive trends of amorphous microcalcification over fine pleomorphic microcalcification differed from those reported in previous studies. In contrast to mass or FA, identifying the nature of microcalcification is difficult with imaging techniques other than mammography; this might lead to a comparatively high false-positive rate, thereby generating lower PPV_2s and PPV_3s for microcalcification than for mass

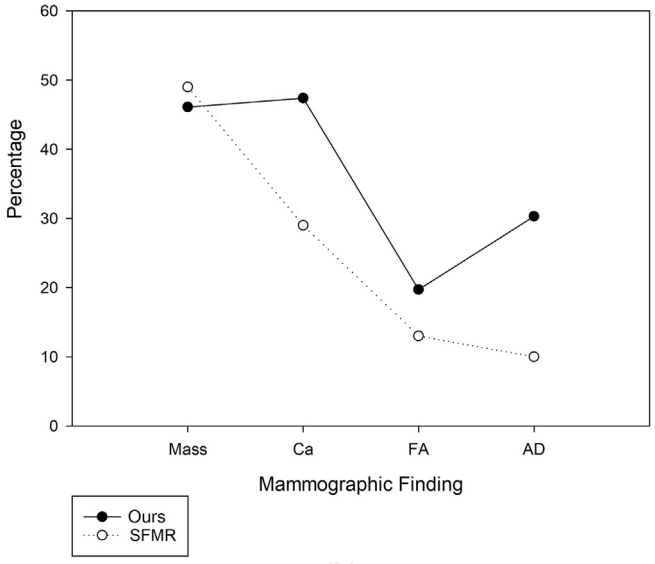
Table 6
The positive predictive values among recalled women between Taiwan and the United States.

Mammographic findings	Ours (n=1662)			SFMR (*n*=4025)		
	Overall breast cancers	Invasive carcinoma	*In situ* carcinoma	Overall breast cancers	Invasive carcinoma	*In situ* carcinoma
	PPV_1 (%)	PPV_1 (%)	PPV_1 (%)	PPV_1 (%)	PPV_1 (%)	PPV_1 (%)
Mass	8.7	6.8	1.9	9.7	9.5	0.2
microcalcification	11.3	5.4	5.8	12.7	5.9	6.8
FA	4.5	3.2	1.3	3.7	3.6	0.1
AD	28.2	19.7	8.5	10.2	10.2	0

Note: The numbers in parentheses are percentages rounded up or down. PPV = positive predictive value.
BD = breast density, microcalcification=microcalcification, FA = focal asymmetry, AD = architectural distortion, Ours = Our screening group, SFMR = San Francisco Mammography Registry.



(a)



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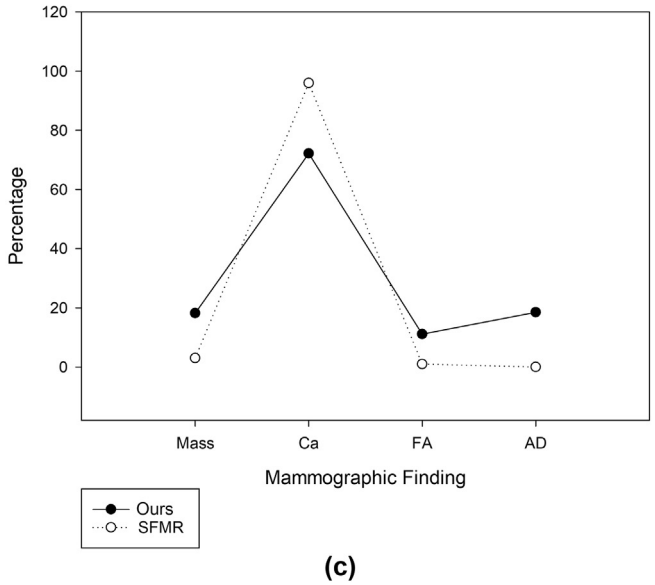

(c)

and FA. An increase in the use of new imaging techniques with low false-positive rates is expected for characterising microcalcification in women receiving breast cancer screening.

In the present analysis, a major proportion of women with the MF mass (70.5%) on screening mammography had received diagnoses of negative or benign diseases after evaluation through additional imaging (Table 2). The false-positive rate of mass in additional imaging tests was low in the present study. Moreover, the hierarchy of assessed ACR BI-RADS categories of mass was higher than that of microcalcification among women who had received a biopsy recommendation (Fig 1). Therefore, the PPV_2 and PPV_3 of mass were higher than those of microcalcification. In the present study, mass was more predictive of invasive carcinomas than of carcinomas in situ, whereas calcification exhibited similar PPVs for both carcinoma types (Table 3). The present results were consistent with those of previous studies.[13,14] In previous studies, microcalcification was the only MF that predicted carcinomas in situ.[7,8] Few reports have described the high PPVs of mass for carcinomas in situ. Biological differences in carcinomas in situ between Asian women and women from Western countries play a crucial role in determining the PPVs of MFs.[15] Carcinomas in situ more commonly present as mass in addition to AD among women in Taiwan than among those in Western countries (Fig. 2C). The results indicate the need for other highly sensitive imaging tools (e.g., sonography) to detect mass lesions in dense breasts, which are commonly presented among women in the Asia-Pacific region.

The present results revealed that the PPV_1s of microcalcification and AD decreased with BD and increased with age (Table 4). These results were consistent with a retrospective study of a Norwegian screening cancer registry.[16] The author of that study explained that these trends were observed because of superimposition, which is related to overlapping tissue and should be distinguished from the masking effect that occurs due to mammographic densities.[17] High BD hindered the distinction between normal and abnormal MFs; in such cases, additional imaging tools might facilitate confirmation of the presence or absence of abnormal MFs in dense areas. Consistent with the results of previous studies,[18] women aged 60–70 years were more likely to have non-dense breasts in the present study (Table 1). The effect of superimposition was relatively less visible among women in this age group; thus, the PPV_1 of all MFs were high in this age group. Superimposition also explains the lower PPV_2 of MFs among women with dense breasts because such women received recommendations for biopsy more often than did the women with non-dense breasts in the present screening population. Because age and BD were not significant risk factors for breast cancers in the present screening population (Table 5), the PPV_1 and

Figure 2 Percentages of mammographic findings found in (a) overall breast cancers, (b) invasive carcinomas, and (c) in situ carcinomas in the screening group and San Francisco Mammography Registry (SFMR). Note that higher percentages of AD were found in all breast cancers of the present screening group than those of SFMR.

PPV_2 of the MFs were mostly related to superimposition in the present study.

Strengths and limitations

Information was collected from screened women of Asian descent and aged 40–70 years at the TSGH. In the present study, all radiologists were well trained and experienced in interpreting screening mammograms; the radiologists generated an annual recall rate of 8–10% and cancer detection rate of 6–8%. To the authors' knowledge, this was the first retrospective cohort study to investigate the PPVs of MFs stratified based on age and BD in the Asia-Pacific region. The study design considered the fact that information of age and BD was collected and available only for women recalled in the present study.

The present study had several limitations. First, this study was conducted at a single academic radiological centre, and thus, the results may not be generalisable to other institutions. Second, the variables of women who had a family history of breast cancer or manifested other risk factors for breast cancer were not controlled. Third, symptomatic women were probably enrolled in the present screening examination (i.e., contamination), and this might have generated so-called "verification bias." Fourth, the histopathological results were obtained only from the database in the pathological department at the TSGH. In total, 17.8% of cases recommended for biopsy did not undergo biopsy at the TSGH. Thus, some false-negative errors were present in the calculations of PPV_1 and PPV_2 of the MFs in the present analyses.

In the present study's Asian population, AD was strongly associated with malignancy in the screened population. Microcalcification was more predictive of overall breast cancers than mass and FA in recalled women, but less predictive of malignancy in the group who proceeded to biopsy following further imaging. Compared to Western populations, AD and mass were more likely to be associated with carcinoma in situ.

Conflicts of interest

None declared.

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