Spectrum of Abnormal Mammographic Findings and Their Predictive Value for Malignancy in Singaporean Women from a Population Screening Trial

K W E Sng,*MB ChB (UK), MRCS (Edin), E H Ng,**FAMS, FRCS (Edin), F C Ng,***FAMS, FRCR (UK), P H Tan,****FAMS, FRCPA, S C Low,+FAMS, FRCS (Edin), G Chiang,++FAMS, FRCPA, G H Ho,+++FRCS (Edin), L T Ng,***FRCR, DMRD, C Wilde,***MD, DABR, K P Tan,***FAMS, FRCR (UK)

Abstract

***Introduction**: The ability to categorise mammographic features according to their likelihood of malignancy would be valuable in the management of women with abnormal mammograms. The aim of our study was to correlate abnormal mammographic features in a screened population with their histology to identify those features which are predictive of malignancy. The study also examined the spectrum of mammographic features in an Asian population. **Materials and Method**: This prospective study involved 28,231 women who were randomly selected from a population registry and underwent two-view screening mammography without physical examination. Women with suspicious lesions were recalled for further mammographic views or to a joint assessment clinic prior to biopsy. Mammographic abnormalities and their corresponding histology were assessed. **Results**: The spectrum of mammographic abnormalities was similar to that in Caucasian populations. The positive predictive value for malignancy was 44.1% of all biopsied cases. Mammographic features could be broadly classified into low-, moderate- and high-risk categories for malignancy. Those features which correspond to high malignancy rates (9.8% to 16.0%) include multiple abnormalities or parenchymal lesions with microcalcifications. The presence of microcalcifications was a good predictor of ductal carcinoma-in-situ (DCIS): 46% of lesions in which the microcalcifications were the sole abnormality were DCIS only. Further, 71% of cancers with any microcalcification on the mammogram had a focus of DCIS on histology. **Conclusion**: Mammographic abnormalities can be segregated into three risk groups for malignancy, and this in turn can improve the selection criteria for breast biopsy, hence reducing unnecessary intervention. Furthermore, the presence of microcalcifications denotes the presence of DCIS, and would be an important determinant of the extent of surgical excision.*

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Introduction

While screening mammography can detect early breast cancers, a significant proportion of asymptomatic women are subject to unnecessary workup and surgery when biopsies for abnormal mammograms are proven to be benign on histology. An accurate correlation between abnormal mammographic features detected on screening and their corresponding histology or predictive value for malignancy would considerably improve the selection criteria for biopsies, as well as therapeutic planning for definitive treatment. However, previous studies reporting such outcomes were for patients that had been referred for biopsies, and hence were subject to referral bias.[1-3] These studies do not adequately reflect the predictive value of specific mammographic features in the context of population screening. Fewer still were studies involving only Asian women, as the rising incidence of this disease in Asian communities as well as the adoption of screening mammography represent relatively recent phenomena.[4-6] We have completed a population screening mammography trial involving 28,231 women in Singapore and report here the outcomes of *all* women with abnormal mammographic features. These mammographic features are based on prevalence screening; subsequent incident rounds were

* *Medical Officer Specialist*
+++ *Registrar*
Department of Surgery, Singapore General Hospital
** *Consultant Surgeon, Private Practice*
Visiting Consultant, Department of Surgery, Singapore General Hospital and National Cancer Centre
*** *Senior Consultant*
Department of Diagnostic Radiology, Singapore General Hospital
**** *Consultant*
++ *Senior Consultant*
Department of Pathology, Singapore General Hospital
\+ *Consultant*
Department of Surgery, Changi General Hospital
Address for Reprints: Dr Eng-Hen Ng, #07-09 Mount Elizabeth Medical Centre, 3 Mount Elizabeth, Singapore 228510.

not done. We assessed the spectrum of mammographic abnormalities and classified lesions into varying risks and predictive values for malignancy. Our aim was to separate the overall risks of malignancy into broad categories. This study also correlated the presence of ductal carcinoma-in-situ (DCIS) or invasive components within the tumour based on mammographic features.

Materials and Methods

In this prospective study, 28,231 women aged 50 to 64 years randomly selected from a population registry were screened over a 29-month period between October 1994 and February 1997, as part of the Singapore Breast Screening Project. This was a study of population-based screening mammography[7] to determine whether mammography could pick up early stage breast cancers and subsequently reduce deaths among Singaporean women, and to assess the quality of screening that could be achieved in our local population. Screening was performed at two screening centres, predominantly by four radiologists.

Screening mammography without physical examination was performed using mediolateral oblique and craniocaudal views. The mammograms from this prevalence screening were subsequently reviewed by the radiologist, and abnormalities were classified as defined in Table I. While it has been recognised that different subtypes of microcalcifications have different predictive values, such subclassifications are subject to reader interpretation, and none were used in this study.

TABLE I: MORPHOLOGIC CATEGORIES OF BREAST LESIONS DETECTED ON SCREENING MAMMOGRAPHY

Categories	Definition
Microcalcification only	Any type of microcalcification identified as the sole abnormality.
Parenchymal lesions	
Smooth mass	Ovoid or round lesions with a distinct edge; >80% of margins well-defined on mammography.
Smooth mass with microcalcification	
Irregular mass	Lesions with indistinct edges; <80% of margins defined on mammography e.g. stellate lesions.
Irregular mass with microcalcification	
Stromal distortion	No discrete mass lesion; tenting of parenchymal tissue.
Stromal distortion with microcalcification	
Asymmetric density	No discrete mass lesion; presence of opacity which is denser than the contralateral breast, or changes with different mammographic views.
Asymmetric density with microcalcification	
Multiple abnormalities	Presence of two or more of the above mammographic abnormalities.

Suspicious or indeterminate lesions were recalled for further mammographic views or for a joint assessment by a team of surgeons, radiologists and pathologists. Fine-needle aspiration cytology (FNAC) of palpable lumps or ultrasound-guided FNAC of non-palpable lumps was performed to ascertain histology. Definitive surgery was then recommended. For lesions with inconclusive FNACs, open biopsies were performed. In the case of impalpable lesions not visible on ultrasound, stereotaxic localisation was carried out prior to biopsy, and specimens were examined radiologically to confirm complete excision. Histologies of all resected specimens were reviewed and the presence of DCIS within the lesions specifically documented. Women who did not have biopsies were followed-up to detect any interval cancers. There was no subsequent incident screening performed on the study cohort; interval cancers were detected clinically. The women who were not subsequently diagnosed with interval cancers were deemed to have benign conditions.

Results

The racial composition of the 28,231 women screened was similar to that in the general population. Chinese predominated (84.2%) and Malays formed 5.6%; Indians 4.9%, and other ethnic groups accounting for the remaining 5.2%. Results for women aged between 50 to 64 years were analysed.

Three thousand (10.6%) abnormal lesions in 2662 women were detected on screening (Table II). The commonest abnormality detected on mammography was a smooth mass (4.9%). Microcalcification as the sole abnormality was the second commonest abnormality (2.3%). Lesions with multiple mammographic abnormalities were present in 1.5% of women screened.

After joint assessment, 290 biopsies were performed—9.7% of abnormal mammograms and 1% of all women screened. Eighty-three of these lesions (28.6%) were palpable. Of those biopsied, 162 lesions were benign and 128 were cancers, giving a positive predictive value of 44.1% for biopsies. Sixty of the cancers (46.9%) were clinically palpable lesions. Thirty-four of the cancers (26.6%) were DCIS, while the remaining 94 (73.4%) were invasive carcinomas. Ductal carcinoma (not otherwise-specified) was the predominant histological type (76 cases). 56.4% of these invasive cancers were associated with a component of DCIS.

At the last review, 28,099 women had completed two years of follow-up after the initial screen; this included women who had normal as well as those with abnormal mammograms at the first screening. Six interval cancers

TABLE II: RESULTS OF BREAST LESIONS DETECTED ON MAMMOGRAPHIC SCREENING BY MORPHOLOGIC CATEGORIES

Categories	Abnormal mammograms		Malignant lesions	
	No. (%) n = 3000	% screened n = 28231	No. n = 128	% of abnormal category
Smooth mass	1390 (46.3)	4.9	9	0.6
No microcalcification	1075 (35.8)	3.8	5	0.5
With microcalcification	315 (10.5)	1.1	4	1.3
Irregular mass	109 (3.6)	0.4	12	11.0
No microcalcification	59 (2.0)	0.2	4	6.8
With microcalcification	50 (1.7)	0.2	8	16.0
Microcalcification only	639 (21.3)	2.3	44	6.9
Stromal distortion	161 (5.4)	0.6	11	6.8
No microcalcification	110 (3.7)	0.4	6	5.5
With microcalcification	51 (1.7)	0.2	5	9.8
Asymmetric density	288 (9.6)	1.0	9	3.1
No microcalcification	257 (8.6)	0.9	5	1.9
With microcalcification	31 (1.0)	0.1	4	12.9
Multiple abnormalities	413 (13.8)	1.5	43	10.4
Total	3000 (100)	10.6	128	4.3
Microcalcification any	1203	4.0	87	7.2
Microcalcification none	1797	6.4	41	2.3

were detected in the first year of follow-up and 29 in the second year. The corresponding interval cancer rates per 10,000 women were 2.1 and 10.3, respectively.

Predictive Value for Malignancy

Only 0.5% (5 per 1000) of smooth masses proved to be malignant. Similarly, a sole asymmetric density also had a low malignancy rate of 1.9%. Irregular masses and stromal distortions had slightly higher rates of malignancy of 6.8% and 5.5%, respectively. However, the predictive value for malignancy of a) multiple abnormalities, or b) a parenchymal lesion (irregular mass, stromal distortion and asymmetric density) associated with microcalcifications, was appreciable, with values ranging from 9.8% to 16% (Table II). In particular, we noted that the presence of microcalcifications within a lesion increased the malignancy rate three-fold (Table II; P <0.0005, Fisher's exact test).

Table III shows a reclassification of mammographic abnormalities into low, moderate and high-risk categories for malignancy. The low-risk group with a malignancy rate of 0.5% to 1.9% consisted of all smooth masses, and asymmetric densities without calcification. The moderate risk group, with malignancy rates of 5.5% to 6.9%, consisted of microcalcifications only, or irregular masses or stromal distortion without microcalcifications. The high-risk group had malignancy rates from 9.8% to 16% and consisted of those with multiple abnormalities, or parenchymal lesions with microcalcifications. The overall malignancy rates for each category were 0.9% for low-risk features, 6.7% for moderate-risk features, and 11.0% for high-risk features. The differences between the three groups were statistically significant (chi-square test for trend, P <0.0005). The corresponding positive predictive values after biopsy in each of categories are also shown in Table III.

Correlation with Histology

Table IV details our analysis of the correlation between mammographic abnormalities and histological diagnosis. 45.5% of lesions in which the mammographic abnormality was microcalcifications alone were DCIS lesions without any invasive component. This is significantly more than the 9.8% of DCIS in mammograms where a parenchymal lesion was the sole abnormality (P <0.0005, Fisher's exact test). Moreover, microcalcifications were found to indicate the likelihood of a DCIS component on histology: 71% of the cancers with any microcalcification on mammograms had DCIS on histology. In contrast, those without microcalcification on mammograms had only 39% associated DCIS (P = 0.001, Fisher's exact test). Conversely, a high rate of invasive carcinoma corresponded with parenchymal lesions on mammography. 54.5% of those without any parenchymal lesions had invasive carcinomas as compared to 83% of parenchymal lesions on mammography (P = 0.001, Fisher's exact test).

TABLE III: RISK STRATIFICATION OF MAMMOGRAPHIC ABNORMALITIES

Risk groups	No. of abnormal mammograms (n = 3000)	Malignancy rate[1] (%)	Overall malignancy rate for each category (%)	Biopsy rate[2] (%)	Positive predictive value[3] (%)
Low risk for malignancy					
Smooth mass					
No microcalcification	1075	0.5	0.9%	2.7	17
With microcalcification	315	1.3		3.5	36
Asymmetric density	257	1.9		4.2	50
Moderate risk for malignancy					
Stromal distortion	110	5.5	6.7%	10.0	54
Irregular mass	59	6.8		15.3	44
Microcalcification	639	6.9		20.3	34
High risk for malignancy					
Stromal distortion with microcalcification	51	9.8	11.0%	19.6	50
Multiple abnormalities	413	10.4		15.0	69
Asymmetric density with microcalcification	31	12.9		23.0	57
Irregular mass with microcalcification	50	16.0		20.0	80

[1] percentage of mammograms in each category which were malignant

[2] percentage of abnormal mammograms in each category which were biopsied

[3] percentage of biopsied lesions which were malignant

TABLE IV: CORRELATION BETWEEN MAMMOGRAPHIC ABNORMALITIES AND HISTOLOGY OF LESIONS

Mammographic abnormality	No. of carcinomas	DCIS only* No. (%)	Invasive carcinomas No. (%)	Presence of any DCIS No. (%)
Microcalcification only	44	20 (45.5)	24 (54.5)	39 (88.6)
Microcalcification any	87	30 (34.5)	57 (65.5)	62 (71.3)
Parenchymal lesion any	84	14 (16.7)	70 (83.3)	48 (57.1)
Parenchymal lesion only	41	4 (9.8)	37 (90.2)	16 (39.0)

*Ductal carcinoma-in-situ only i.e. non-invasive carcinomas

Discussion

The ability to accurately predict the corresponding histology of specific mammographic abnormalities would greatly enhance the effectiveness of breast screening programmes. While numerous studies conducted in Western countries have analysed abnormal mammographic findings in Caucasian women, scarce data exist for Asian women. The aim of this study was to look at the prevalence of mammographic abnormalities in an Asian population, and to correlate these with their predictive value for carcinoma, in order to identify those mammographic features which indicate an increased likelihood of malignancy. Our study population consisted of 28,231 women who were invited and screened in the Singapore Breast Screening Project and as such, the findings in this group of women would be representative of the local population. Moreover, this screening population eliminates any bias associated with a group that has been referred for surgical biopsy. Overall, our cancer detection rate for biopsied patients was 44.1%. This value is comparable with other population-based screening programmes[8] in Western populations, bearing in mind that the incidence of breast cancer is lower in Asian women. The low incidence of interval cancers is favourable compared with other series,[8] and indicates that the quality of screening was within acceptable limits.

In this context, approximately one-tenth of all women screened had at least one abnormality on mammography. Four per cent of such abnormalities will be malignant, and the overall prevalence of cancer among screened women is 4.5 per 10,000. These findings in an Asian population agree with figures published in other population-based screening programmes[8,9] and suggest that the spectrum of mammographic abnormalities does not appear to be influenced by ethnic origin. The predictive value of specific mammo-graphic features for malignancy appears also to be similar to previous reports involving women from Western populations.[2,10-12]

Since 96% of abnormal mammograms are benign lesions, the segregation of abnormal mammograms into varying risks for malignancy, as suggested in this study, would be

of help in advising patients and deciding if further work up or biopsy is necessary. Although each individual mammographic abnormality can be assigned a risk of malignancy, some of these would be very small, e.g. only 0.5% of smooth masses were malignant. We feel that in the context of large population screening, as in our study, it would be more helpful to broadly divide mammographic features into three groups according to their risks of malignancy. Our data indicate that smooth, well-defined masses or asymmetric densities have the lowest malignancy rate of 6 to 19 cancers per 1000 lesions. This low risk suggests that biopsy would not be indicated in the majority of women with such lesions detected on screening. However, they must continue to be followed up. In contrast, parenchymal lesions with microcalcifications or those with multiple abnormalities have the highest risk of malignancy. The positive predictive rate of these biopsies, ranging from 50% to 80%, indicates that these features are easily recognisable by the radiologist and surgeon, and were appropriately biopsied.[10,12]

The intermediate-risk group poses the greatest diagnostic difficulty. Improvements in the positive predictive rate for biopsies for this category of abnormalities — 34% to 54% in this study—would greatly improve the effectiveness of screening programmes. Similar to previous studies,[12-14] mammographic features consisting only of micro-calcifications continue to pose a challenge, as the predictive value for biopsy was only 34%, two-thirds of such biopsied lesions being benign. While certain characteristics have been identified that may indicate a higher risk of malignancy —i.e. clusters of more than five calcifications; fine calcifications or branched calcifications; variation in shape; a change from a previous mammogram[12,13,15]—none of these is pathognomonic of malignancy, and micro-calcifications continue to form the majority of indeterminate lesions requiring follow-up or biopsy. Subdividing microcalcifications into benign, suspicious or malignant groups have been shown to improve predictive values,[10] however, we felt that this subdivision would be subject to variations in interpretation between different radiologists. Furthermore, the objective of this study was to assess the overall rate of malignancy of various features in broad categories. As such, microcalcifications were grouped together in the data. However, we acknowledge that in mammograms where microcalcification is the sole abnormality, subcategorisation by an experienced radiologist would improve the predictive value. The use of stereotaxic large core biopsies, not used in this screening study, could also improve results in this group of women with intermediate risks.

The differences in histologies of sole mammographic abnormalities of microcalcifications and parenchymal lesions support the observation that malignancies identified by clustered calcifications are likely to be early, non-invasive carcinoma.[2,11,13,14] About 45% of patients with microcalcifications alone had only DCIS. Further, the presence of any microcalcification indicates the presence of a DCIS component within the tumour. These findings would be important in preoperative counselling and when considering the extent of excision in breast-conserving surgery. Indeed, others have shown that microcalcifications occupying an area greater than 3 cm in diameter are associated with extensive DCIS and recommended that such patients would not be appropriate candidates for breast conservation.[16] As expected, about 83% of parenchymal lesions, either as the sole abnormality or associated with other features on screening will be invasive carcinomas.[2,11,14]

In conclusion, the findings of this study suggest that the spectrum of abnormalities detected on mammographic screening in Asian women is similar to those in Western populations. These abnormalities can be broadly segregated into three risk groups for malignancy. The majority of women are in the lowest risk group with smooth masses and asymmetric densities. The highest risk group, those with multiple abnormalities or mixed lesions consisting of parenchymal distortion with microcalcification, is associated with high positive predictive rates after biopsies. An intermediate-risk group consisting of sole abnormalities of either microcalcification or parenchymal lesion presents the greater diagnostic challenge for effective breast screening. Finally, the presence of microcalcification denotes the presence of DCIS and would be an important determinant for the extent of surgical excision of the tumour.

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