RESEARCH ARTICLE

Analysis of Mammographic Breast Density in a Group of Screening Chinese Women and Breast Cancer Patients

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Abstract

Background: A dense breast not only reduces the sensitivity of mammography but also is a moderate independent risk factor for breast cancer. The percentage of Western women with fat breast tissue is higher aged 40 years or older. To a certain extent, mammography as a first choice of screening imaging method for Western women of this group is reasonable. Hitherto, the frequency and age distribution of mammographic breast density patterns among Chinese women had not been characterized. The purpose of this study was to investigate the frequency and age distribution of mammographic breast density patterns among a group of Chinese screening women and breast cancer patients in order to provide useful information for age-specific guidelines for breast cancer screening in Chinese women. Methods: A retrospective review of a total of 3,394 screening women between August and December 2009 and 2,527 breast cancer patients between July 2011 and June 2012 was conducted. Descriptive analyses were used to examine the association between age and breast density. The significance of differences of breast density between the screening women and the breast cancer patients was examined using nonparametric tests. Results: There was a significant inverse relationship between age and breast density overall (r=-0.37, *p*< 0.01). Breast density of the breast cancer patients in the subgroups of 40-49 years old was greater compared with that of the screening women, the same in those aged 50-54 years and in those 55 years old or older, less than in the screening group. Conclusions: With regard to the Chinese women younger than 55 years old, the diagnostic efficiency of breast cancer screening imaging examinations may be potentially improved by combining screening mammography with ultrasound.

Keywords: Breast cancer - breast density - Chinese women – age dependence - screening

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Introduction

American Cancer Society (ACS) guidelines for the early detection of breast cancer recommended that routine screening mammography should be annually done at the beginning of 40 years old (Smith et al., 2014). ACS guidelines for breast cancer based on clear evidences indicate that screening reduces mortality (Smith et al., 2014). Recent years, the incidence of breast cancer has been rapidly increasing among women in China (Lin et al., 2009; Fan et al., 2009), especially among younger women (Yang et al., 2006). Breast cancer has been the second most common cause of incidence from cancer in Chinese women (Zhang et al., 2012). Because of lack of screening guidelines for Chinese women, the death rate of breast cancer is still high (Yang et al., 2005; Yang et al., 2006).

As an available, inexpensive screening imaging modality, there is no doubt that mammography plays an important role in detecting early stage breast cancer, especially which is suited to depict microcalcificatoins. However, limitations in sensitivity and specificity of mammography remain be well known, including breast with dense parenchyma. Dense breast reduces its sensitivity (Carney et al., 2003; Sardanelli et al., 2004). The research has revealed that the percents of western women with fat breast tissue were higher in 40 years old or older (Stomper et al., 1966). To a certain extent, mammography as a first choice of screening imaging method for western women in 40 years old or older is reasonable. On the other hand, increased mammographic breast density is also a moderate independent risk factor for breast cancer (McCormack et al., 2006). The research has indicated the relationship between breast density and ethnic differences (Del Carmen et al., 2007). Another studies reported that Asian women including Chinese women had the highest percent density (Nie et al., 2010; Zulfiqar et al., 2011). However, the frequency and age distribution of mammographic breast density patterns

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among Chinese women are not characterized.

Therefore, the objective of this study was to investigate the frequency and age distribution of mammographic breast density patterns among a group of Chinese screening women and breast cancer patients in order to provide some useful information to further make age-specific guidelines for breast cancer screening in Chinese women.

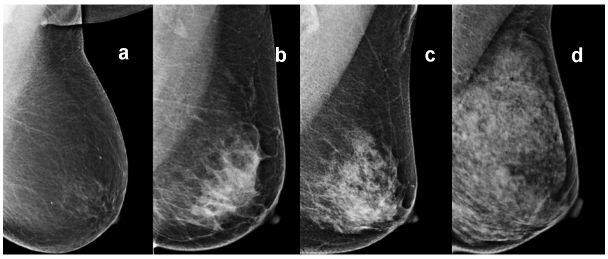

Figure 1. BI-RADS Density Types in Four Types. (a) Type 1: the breast is almost entirely fat, <25% fibroglandular breast tissues; (b) Type 2: there are scattered fibroglandular densities, approximately 25%–50% glandular; (c) Type 3: the breast tissue is heterogeneously dense, approximately 51%–75% glandular; (d) Type 4: the breast tissue is extremely dense, >75% glandular

Materials and Methods

We conducted a retrospective review of 3394 women who underwent screening mammography examinations between August and December 2009 and 2527 breast cancer patients proved by histopathology underwent diagnostic mammography examinations between July 2011 and June 2012 in the department of breast imaging diagnosis of Tianjin medical university cancer institute and hospital. Among 3394 women who did screening examination, the age range was 40-71 years (mean, 53 years). The age range of 2527 breast cancer patients was 21-87 years (mean, 51 years), 291 (11%) were aged younger than 40 years old, 2114 (84%) were aged 40-71 years old, 122 (5%) were aged older than 71 years old.

Craniocaudal (CC) and mediolateral oblique (MLO) views of bilateral mammograms were obtained using full-field digital mammography system (Senographe 2000D, General Electric Company, USA and Selenia Digital Mammography, Hologic Inc., USA).

Breast composition was described as four patterns according to the Breast Imaging Reporting and Data Systems (BI-RADS) of the American College of Radiology (ACR) as follows: type 1 (the breast is almost entirely fat, <25% glandular); type 2 (there are scattered fibroglandular densities, approximately 25%-50% glandular); type 3 (the breast tissue is heterogeneously dense, approximately 51%-75% glandular); and type 4 (the breast tissue is extremely dense, >75% glandular) (Figure 1) (D'Orsi et al., 2003). Mammographic densities of type 1 and type 2 were defined as low density, type 3 and type 4 were defined as high density.

All mammograms were interpreted by three radiologists to determine the mammographic breast density, respectively. For the breast cancer patients, no tumor side mammograms were selected to be assessed mammographic breast density. During assessment of the mammograms, the radiologists were blinded to all clinical and pathologic data. If interpretation differences occurred, the majority rating (two of three readers) was used. Descriptive analyses were used to examine the association between age and breast density. To evaluate the significance of a linear association, we conducted the analysis of variance with age as a continuous variable. The significance of differences of breast density between the screening women and the breast cancer patients was assessed by using nonparametric tests. All analyses were performed using SPSS software (version 12.0, SPSS). The reported p values were two-sided. P value less than 0.05 was set as the threshold for significance.

Results

The distribution of breast density among the screening women

A total of 3394 women who underwent screening mammography examination were divided into six subgroups by five-year age to be assessed mammographic breast densities. There were 24 (23%) women with low breast density and 79 (77%) women with high breast density in the subgroup of 40-44 years old, 194 (22%) and 672 (78%) in the subgroup of 45-49 years old, 402 (37%) and 679 (63%) in the subgroup of 50-54 years old, 455 (57%) and 346 (43%) in the subgroup of 55-59 years old, 314 (70%) and 135 (30%) in the subgroup of 60-64 years old, 72 (77%) and 22 (23%) in the subgroup of 65-71 years old. The results of the frequency and age distribution of breast density patterns in these screening women are summarized in Table 1 as well as Figure 2. Using analysis of variance, there was a significant inverse relationship between age and breast density (r=-0.37, $p<$

Table 1. Frequency and Age Distribution of Mammographic Breast Density Patterns among Screening Women and Breast Cancer Patients

Age Cohort	Breast Density in Screening Group			Breast Density in Breast Cancer Group				
	Type 1[a]+2[b]	Type 3[c]+4[d]	Total	Type 1[a]+2[b]	Type 3[c]+4[d]	Total	Z	P
40-44	24 (23%)	79 (77%)	103 (3%)	67 (20%)	275 (80%)	342 (16%)	-3.09	<0.01
45-49	194 (22%)	672 (78%)	866 (26%)	108 (23%)	371 (77%)	479 (23%)	-2.18	0.03
50-54	402 (37%)	679 (63%)	1081 (32%)	171 (42%)	241 (58%)	412 (19%)	-0.07	0.95
55-59	455 (57%)	346 (43%)	801 (24%)	280 (67%)	137 (33%)	417 (20%)	-3.89	<0.01
60-64	314 (70%)	135 (30%)	449 (13%)	239 (84%)	47 (16%)	286 (14%)	-5.10	<0.01
65-71	72 (77%)	22 (23%)	94 (2%)	159 (89%)	19 (11%)	178 (8%)	-2.47	0.01
Total	1461 (43%)	1933 (57%)	3394	1024 (48%)	1090 (52%)	2114	-2.47	0.01

[a]Predominantly fatty; [b]Scattered fibroglandular densities; [c]Heterogeneously dense; [d]Extremely dense

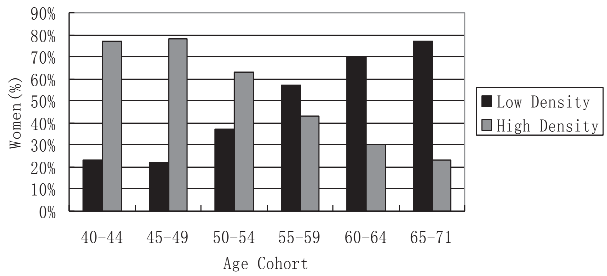

Figure 2. Bar Graph Shows Age Distribution of BI-RADS Types of Breast Density

Table 2. Mean Rank of Mammographic Breast Density among Screening Women and Breast Cancer Patients

Age Cohort	Mean Rank of Breast Density	
	Screening Group	Breast Cancer Group
40-44	192.9	232.1
45-49	659.1	698.2
50-54	747.4	746.0
55-59	635.2	560.1
60-64	396.8	322.8
65-71	151.4	128.6

0.01). From the results of Figure 2, it could be found that the distribution of breast density in the screening women reversed in 55 years old. In the subgroup of less than 55 years old, the percentages of women with high breast density were higher. In the subgroup of 55 years old or older, low breast density proportions were higher. There was a statistical significance of breast density between the above two age groups (z=-19.1, p< 0.05).

Comparison of the distribution of breast density between screening women and breast cancer patients

A total of 2114 breast cancer patients in the group of 40-71 years old were also divided into six subgroups in an age-matched subgroup of the above screening women. There were 67 (20%) with low breast density and 275 (80%) with high breast density in the subgroup of 40-44 years old, 108 (23%) and 371 (77%) in the subgroup of 45-49 years old, 171 (42%) and 241 (58%) in the subgroup of 50-54 years old, 280 (67%) and 137 (33%) in the subgroup of 55-59 years old, 239 (84%) and 47 (16%) in the subgroup of 60-64 years old, 159 (89%) and 19 (11%) in the subgroup of 65-71 years old (Table 1). In the group of 291 (11%) breast cancer patients younger than 40 years old and 122 (5%) older than 71 years old, there were 50 (17%), 113 (93%) with low breast density and 241 (83%), 9 (7%) with high breast density, respectively. Using nonparametric tests, there was a statistical significance in breast density between the screening women and the breast cancer patients in each age-matched cohort (p<0.05), except in the subgroup of 50-54 years old (p=0.95). From the results of the mean rank of breast density (Table 2), it could be inferred that breast density of the breast cancer group was denser than that of the screening group in the subgroup of 40-49 years old. Breast density of the screening and breast cancer group were similar in the subgroup of 50-54 years old. In the subgroup of 55 years old or older, breast density of the screening group was denser than that of the breast cancer group.

Discussion

ACS guidelines for the early detection of breast cancer recommended that routine screening mammography should be annually done at the beginning of 40 years old (Smith et al., 2014). Breast cancer mortality rates declined about 2% per year over the period 1998 through 2009 (Smith et al., 2014). In addition to government "one-child" policy and the insufficient medical financial appropriation (Lu et al., 2010), Chinese women have their unique physiological features and epidemiological characteristics compared with women in some western developed countries (Han et al., 2011; Li et al., 2011). These lead to a controversy on the application of mammography as a single screening modality for Chinese women in the developing country. There is no doubt that screening mammography plays an important role in the detection of early stage breast cancer, especially in detecting calcifications which may be the only mammographic sign of ductal carcinoma in situ. However, there are quite a few lesions of early stage breast cancer shown as masses which may be obscured by increased parenchymal density on mammograms. The research revealed that the sensitivity and specificity of screening mammography in women with extremely dense breasts was 63% and 89%, respectively compared with 87% and 97% in women with predominately fatty breasts (Carney et al., 2003). Increased parenchymal density was of greater clinical significance as a cause of false-negative mammograms (Lehman et al., 1999). The study revealed the relationship between breast density and ethnic differences (Del Carmen et al., 2007). From the Stomper's research (Stomper et al., 1966), it could be found that the percentages of women with high breast density were higher in the group of younger than 40 years old. In the group of 40 years old or older, the percentages of women with low breast density were higher. It was revealed that the distribution of breast density in the western women reversed in 40 years old. Another studies reported that Asian women including Chinese women had the highest percent density (Nie et al., 2010; Zulfiqar et al., 2011). Our data revealed that the distribution of breast density in Chinese women reversed in 55 years old. In the group of less than 55 years old, the percentages of women with high breast density were higher. In the group of 55 years old or older, low breast density proportions were higher. Therefore, with regard to the Chinese women in younger than 55 years old, the addition of other modalities such as ultrasound may provide some potential benefits in the sensitivity, specificity as well as diagnostic accuracy of the detection and characterization of early stage breast cancer. A recent research (Wang et al., 2013) reported that ultrasonography was markedly more effective than mammography for most Chinese women who were younger than 55 years old. Recently, the State Legislatures of Connecticut, Texas, Virginia, California and New York passed laws requiring physicians to tell women whether they have dense tissue based on mammographic imaging. These laws specified that women should be told that dense breast tissue can hide tumors on mammograms, increase the risk of breast cancer, and require additional screening tests, such as breast MRI (Hollenbeck et al., 2013).

In addition, many researches demonstrated that increased mammographic breast density was also an independent risk factor for breast cancer, although it was controversial (Colin et al., 2013). Boyd et al (Boyd et al., 1995) indicated that there were statistically significant increases in breast cancer risk associated with increased mammographic density in the group of 40-49 years old and 50-59 years old. Results of this study revealed that breast density of the breast cancer patients was significantly difference from that of the screening women in each age-matched cohort, except in the subgroup of 50-54 years old. Breast density of the breast cancer patients in the subgroup of 40-49 years old and 50-54 years old was denser and similar, respectively compared with that of the screening women. In the subgroup of 55 years old or older, breast density of the screening women was denser than that of the breast cancer patients. Although the reason of the above results was unclear, it could be inferred that the addition of other imaging modalities such as ultrasound may be useful to improve the diagnostic accuracy of breast cancer in a meaningful population of Chinese women in younger than 55 years old, especially in younger than 50 years old. Further prospective studies will be explored with regard to this issue.

It should be noted that there were some limitations in this study. Visual estimation of mammographic density was subjective, although three experienced radiologists interpreted. In addition, several other factors which have previously been shown to correlate with breast density and breast cancer, such as weight, nutritional, age at first birth, parity, as well as menopausal status, were not taken into account this time (Asif et al., 2014; Kruk, 2014). This study was a preliminary study.

In summary, the age of the distribution reversal of breast density in Chinese women is 55 years old, compared with 40 years old in the western women. A meaningful population of Chinese women younger than 55 years old has denser breast tissue. With regard to the Chinese women less than 55 years old, the accuracy of the detection and characterization of early stage breast cancer may be potentially improved by basing on the screening mammography in combination with ultrasound.

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