RESEARCH ARTICLE

Correlation Between Mammograghic Findings and Clinical/ Pathologic Features in Women with Small Invasive Breast Carcinomas

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Abstract

Background: To study the relationship between mammographic findings and clinical/pathologic features in women with 1-15mm sized invasive breast cancer. Materials and Methods: We investigated a consecutive series of 134 cases diagnosed in Tianjin Medical University Cancer Institute and Hospital in 2007. Mammographic findings were classified into five groups as follows :1) stellate mass without calcification; 2) non-stellate mass without calcification; 3) intermediate suspicious calcification with or without associated mass; 4) higher probability malignant calcification with or without associated mass; 5) focal asymmetry/distortion without associated calcification. Associations between mammographic and clinical/pathological features (menopause status/family history/histologic grade/lymph node status and ER/PR/HER2 status) was analyzed through logistic regression and chi square tests. Results: Compared to the stellate mass without calcification group, higher probability malignant calcification patients were associated significantly with a positive lymph node status, always presenting in patients who were non-menopausal and with a family history of carcinoma. Conclusions: Higher probability malignant calcifications with or without associated tumor masses are associated with clinical/pathologic features of poor prognosis.

Keywords: Mammography findings - breast carcinoma - clinical/pathologic features - calcification

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Introduction

Breast cancer is a major public health challenge, and the survival of breast cancer patients is improved by decreasing of tumor size. Although the prognosis of women with small breast cancer is generally excellent, some patients still die from breast cancer a few years later. Mammography increased the detective ability of small tumor, and the image reflects the alteration of breast anatomy and pathology. Tabar et al. (2000; 2004) revealed mammography features may correlate with prognosis of breast cancer patients.

Casting-type microcalcifications have been suggested to indicate patient at high risk of recurrence and death. But some research published after that showed conflictive results (Thurfjell et al., 2001; James et al., 2003; Peacock et al., 2004; Evans et al., 2006). In this retrospective study, we tried to find the relevence between mammography and clinical/pathologic features, in order to provide some information for the prognosis of small breast cancer.

Materials and Methods

Patients

A total of 134 women were initially diagnosed as 1-15mm primary invasive breast cancer in Tianjin Medical University Cancer Institute and Hospital from January 1 to December 31 in 2007.

Tumor classification by mammographic image, clinical/ pathologic features characteristics

According to Breast Imaging Reporting and Data System (BI-RADS), the mammographic appearance of the tumors in the current study was classified into five groups that was similar to Tabar et al (2000; 2004): 1) stellate mass without calcifications; 2) non-stellate mass without calcifications; 3) intermediate suspicious calcifications with or without associated mass; 4) higher probability malignant calcifications with or without associated mass; 5) focal asymmetry/distortion without associated calcifications. The forth group, higher probability

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Table 1. Association between Mammographic Appearance and Lymph Node Status

Mammographic Appearance	Lymph Node Status		OR (95%CI)	
	Negative	Positive	Crude	Adjusted[a]
Stellate mass	21	10	1	1
Non-stellate mass	44	9	0.701 (0.232-2.119)	0.904 (0.281-2.907)
intermediate suspicious calcifications	13	6	1.582 (0.439-5.705)	2.225 (0.551-8.980)
Higher probability malignant calcifications	6	7	4.000 (1.009-15.862)	4.922 (1.136-21.333)
focal asymmetry/distortion	13	5	1.319 (0.348-4.993)	0.641 (0.100-3.758)

*OR: odds ratio; 95% CI: 95% confidence interval; Adjusted for age, tumor size and histologic grade in continuous scale

Table 2. Association between Mammographic Appearance and Histologic Tumor Grade

Mammographic Appearance	Histologic Tumor Grade			OR (95%CI)	
	I	II	III	Crude	Adjusted[a]
Stellate mass	3	23	1	1	1
Non-stellate mass	7	35	2	0.76 (0.201 - 2.679)	0.78 (0.204 - 2.781)
intermediate suspicious calcifications	1	12	2	2.806 (0.473 - 17.535)	2.151 (0.355 - 13.859)
higher probability malignant calcifications	2	10	0	0.574 (0.106 - 3.377)	0.446 (0.076 - 2.805)
focal asymmetry/distortion	0	11	2	4.71 (0.781 - 29.440)	3.988 (0.623 - 26.506)

*OR: odds ratio; 95% CI: 95% confidence interval; Adjusted for age, tumor size and lymph node status in continuous scale

malignant calcifications with or without associated mass group, was equal to casting-type calcifications group in the Tabar studies.

The recorded clinical characteristics included menopause status and family history of carcinoma. The pathologic features included histological grade (WHO grading system), lymph node status, vessel cancer embolus, soft tissue involvement and the ER/PR/HER2 status.

Statistical methods

The association between mammographic findings and lymph node status with or without adjustment for patient age, tumor size and histologic grade, was analyzed using a logistic regression model. Unadjusted and adjusted odds ratios (ORs) and 95% confidence interval (95%CIs) were both estimated. The ORs for histologic grade were estimated using ordinal logistic regression. The Mantel-Haenszel chi-square test for trend was used to assess the association of clinical/pathological features between higher probability malignant calcifications patients and other patients.

Results

Overall, among tumors with the greatest dimension ranging from 1 to 15mm, 23.1% were stellate mass, 39.6% were non-stellate mass without associated calcifications, 14.2% were intermediate suspicious calcifications with or without associated tumor mass on mammogram, 9.7% were higher probability malignant calcifications with or without mammographically demonstrable tumor mass, and 13.4% were focal asymmetry or distortion. In this study, the pathological type of invasive cancer included 116 (86.6%) invasive ductal carcinomas, 11 (8.2%) invasive lobular carcinomas, and 7 (5.2%) invasive carcinoma of special types (including tubular carcinoma, mucinous carcinoma, medullary carcinoma and carcinoma with apocrine differentiation).

Table 1 shows the correlation between mammographic appearance and lymph node status. The ORs were adjusted for age, tumor size and histological grade by inclusion of these factors. For lymph node-positive disease with higher probability malignant calcifications, the crude OR was 4.000 (95% CI, 1.009-15.862) relative to stellate mass, while the adjusted ORs was 4.922 (1.136-21.333) after adjusted. No significant difference was found between stellate mass and higher probability malignant calcifications groups in histological tumor grade. Similarly, ORs adjusted for age, tumor size and lymph node status were shown in Table 2.

Table 3. Association between Mammographic Appearance and Survival Situation

Mammographic Appearance	Suivival No.	Death No.
Stellate mass	30	1
Non-stellate mass	52	1
Intermediate suspicious calcifications	19	0
Higher probability malignant calcifications	11	2
focal asymmetry/distortion	18	0
total	130	4

Table 4. Comparison of Clinical/Pathological Features between Higher Probability Malignant Calcifications Patients And Other Patients

		Higher Probability Malignant Calcifications Patients	Other Patients	*p*
Menopause status				0.041
Menopausal		4	73	
Nonmenopausal		9	48	
Family history	+	8	33	0.022
	-	5	88	
vessel cancer embolus	+	1	1	0.185
	-	12	120	
Soft tissue spread	+	3	8	0.075
	-	10	113	
ER	+	8	82	0.758
	-	5	39	
PR	+	9	93	0.509
	-	4	28	
HER2	0/+	10	110	0.138
	++/+++	3	11	

Table 3 showed the number of tumors fatalities by mammographic tumor characteristics. It seemed that higher probability malignant calcifications group was relative to the highest fatality rate (15.4%). In the group of women who had intermediate suspicious calcifications with or without associated tumor mass and the group of women who had focal asymmetry or distortion, none of the patients was dead (0% fatality) in the past 7 years.

As patients with higher probability malignant calcifications group had more positive lymph node, we compared the clinical/pathological features between the patients in higher probability malignant calcifications group and other groups. Table 4 showed higher probability malignant calcifications group always was present in patients who were nonmenopausal and with family history of carcinoma. Although there was no statistic significance existed, the risk of soft tissue involvement rate was higher in higher probability malignant calcifications group.

Discussion

In 2000 and 2004, Tabar et al. (2000; 2004) suggested that radiological features provide prognostic information. They found that masses with malignant stellate detected in mammographic screening was accompanied with an excellent outcome, while the presence of mammographic comedo calcifications was a poor prognostic factor in women with 1-14 mm invasive breast carcinoma. But others have ventured conflicting opinions that casting calcifications was not yet used as a prognostic factor in clinical application (Thurfjell et al., 2001; James et al., 2003; Peacock et al., 2004; Evans et al., 2006). In this retrospective study, we evaluated the correlation between mammographic findings and clinical/pathologic feature in hope of providing more information for the clinical application of higher probability malignant calcifications.

In this study, we divided all patients into five groups: 1) stellate mass without calcifications; 2) non-stellate mass without calcifications; 3) intermediate suspicious calcifications with or without associated mass; 4) higher probability malignant calcifications with or without associated mass; 5) focal asymmetry/distortion without associated calcifications. Among them, higher probability malignant calcifications with or without associated mass group was equal to casting-type calcifications group in Tabar' study.

In this study, patients with speculated masses were used as a reference group. Compared with the reference group, higher probability malignant calcifications group was associated with more lymph nodes involvement with statistic significance, while other groups have no statistic significance. Axillary nodal status always remains one of the most important prognostic indicators in breast cancer (Goodman et al., 2014; Karimi et al., 2014). Knowing the status of the lymph nodes is important for accurate staging and appropriate selection of subsequent treatment in breast cancer. Generally, breast cancer with more positive lymph node implies poor outcome. Although, histological grade in breast cancer is not included in tumor staging, but recent study (Schwartz et al., 2014) proved that it remained a prognostic factor for breast cancer regardless of the number of positive lymph nodes and tumor size. However, our study do not prove that higher probability malignant calcifications with or without associated mass group has high histological grade. That may be attributed to the limitation of the small sample size due to the rarity of patients presenting with mammographic microcalcifications.

Based on the research results above, we divided all patients into two groups: higher probability malignant calcifications with or without associated mass group and other group, and attempted to find difference in clinical/pathological features of these two groups. The result was higher probability malignant calcifications group always developed in patients who were nonmenopausal and with family history of carcinoma. Tabar's study (Tabar et al., 2004) also revealed that tumors associated with casting-type calcifications appeared to occur more frequently in women age less than 50 years old. Dubsky et al. (2002) found that juvenility was an independent adverse prognostic factor in premenopausal patients with T1a and T1b tumors. Furthermore, oncologists have reached an agreement that breast cancer in young patients often show more aggressive biologic behavior, such as advanced stage, less ER positive expression, higher histological grade and more peritumoral vascular invasion. All these features indicate a bad prognosis of young patients (Anders et al., 2008; Cancello et al., 2010; Thapa et al., 2013).

In the past several decades, estrogen (E) and progesterone (P) receptor were believed to play an important role in the prognosis of breast cancer. As we known, ER/PR positive tumors always associate with higher cell differentiation and slower tumor coefficient of multiplication. Previous study showed that 5-year survival rate of ER and PR positive patients was higher than negative patients (Falck et al., 2013) . Human epidermal growth factor receptor 2 (ErbB-2/HER2), a major player in the breast cancer scenario, which belongs to one of the members of the ErbB family of membrane receptor tyrosine kinases, is low-expression in normal breast tissue while over expression is only present in 20%-30% breast cancer (Victorino et al., 2014). Studies have indicated that a HER2-positive status is one of the most powerful poor prognostic factors (Guarneri et al., 2013). Moreover, no significant correlation was found between mammograghic features and ER/PR/HER2 in the current study. And that was concordance with the study of Mansson's study et al. (2009).

At the end of the follow-up, there were 4 patients died, including 2 patients of higher probability malignant calcification. These results were also in accord with published data (Malik et al., 2000; Zunzunegui et al., 2003). In others' study with a larger sample size, 20-year overall survival rate of this group was only 55%, lower than other groups (>87%).

In conclusion, in this retrospective study of women with 1-15mm invasive breast cancer, we found that higher probability malignant calcifications group had high positive rate of lymph nodes and family history of cancer. Meanwhile, most of the patients were nonmenopausal. Because of these entire clinical/

pathologic factors mentioned above, higher probability malignant calcifications patients have a poor prognosis in this study.

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