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Original Article

Correlation between clinicopathological features and postoperative prognosis in patients with breast cancer

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Abstract: Objective: To analyze the correlation between the clinicopathological features and postoperative prognosis in patients with breast cancer. Methods: The clinical data and follow-up data were analyzed retrospectively in 120 female patients with breast cancer who were naïve to treatment and received treatment at our hospital from January 2007 to December 2009. Kaplan-Meier method was used for survival analysis, and univariate and multivariate Cox regression analyses were also performed to screen and identify the risk factors associating with postoperative prognosis. Results: All the patients were followed up for 10 months to 82 months, with a median period of 49 months. During the follow-up period, 16 patients died and 26 patients relapsed that yield an overall survival (OS) of 75.92±1.49 months, and a disease-free survival (DFS) of 69.25±2.24 months. Univariate Cox regression analysis showed that tumor size, lymph node metastasis, number of metastatic lymph node, clinical stage and hormone receptor expression constituted the risk factors associating with the postoperative prognosis in breast cancer patients ($P<0.05$). Multivariate Cox regression analysis further confirmed that tumor size, lymph node metastasis, and hormone receptor expression constituted the independent risk factors associating with the postoperative prognosis of breast cancer patients ($P<0.05$). And the large-sized tumor, positive to lymph node metastasis, and large numbers of metastatic lymph node predicted a poor clinical prognosis, while, that positive to hormone receptor expressions predicted a good clinical prognosis. Conclusion: The tumor size, lymph node metastasis, number of metastatic lymph node and the expression of hormone receptors ER and PR could be used as the prognostic markers in the treatment of breast cancer.

Keywords: Breast cancer, clinicopathological features, prognosis, risk factors

Introduction

Breast cancer is the most common malignant tumor in women, with the mortality rate ranks the fifth highest in female cancer worldly [1-3]. In 2009, China National Cancer Center reported that the incidence of breast cancer reached 42.55/10 million, accounting for 16.81% of women with cancer, and the death toll was 10.24/10 million, which accounted for 7.54% of all cancer-related deaths in women [4]. Therefore, even though the incidence of breast cancer in China is relatively low when compared with that of western countries, the development of breast cancer showed an increasing trend in recent years, for example, it is reported that breast cancer presents a peak age of 50 years old in China, which is earlier than that in United States with the peak age of 75-79 years old [5, 6].

In recent years, with the progression and development achieved on the screening and diagnostic technology at molecular level, most breast cancer patients have received radical surgery at early stage, but the prognosis is not very optimistic. Still a number of patients died of postoperative recurrence and metastasis [7, 8]. Thus far, the clinicopathological characteristics are still the most widely used parameters for prognosis prediction in breast cancer, including tumor size, TNM stage, lymph node metastasis, distant metastasis and tumor-related molecular markers, such as estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2).

The aim of this study was to further clarify the correlation between clinicopathological characteristics in patients with breast cancer and the clinical prognosis after surgery.

Materials and methods

Participants

This study was approved by the ethics committee of our hospital, and all patients had provided informed consent form for the sample examination and data analysis.

A total of 120 women with breast cancer were enrolled in this study, who received surgery from January 2007 to December 2009 at our hospital. All the patients underwent chest X-ray examination, liver ultrasound, and whole-body bone scan before surgery to exclude distant metastasis. The clinical and pathological parameters were collected from all the patients, including age, tumor size, clinical stage, lymph node metastasis, number of metastatic lymph node, expressional status of hormone receptor (ER), progesterone receptor (PR) and HER2.

Inclusion criteria: Patients were naïve to cancer treatment; patients were pathologically diagnosed of unilateral invasive ductal carcinoma; patients had no distant metastasis; patients received no radiotherapy and neoadjuvant chemotherapy before surgery; patients received standard adjuvant chemotherapy and endocrine therapy postoperatively; patients had complete clinicopathological and follow-up data.

Exclusion criteria: Male patients had breast cancer; patients had bilateral breast cancer; patients had ductal carcinoma in situ; patients had lobular carcinoma, sarcoma, breast cystosarcoma phyllodes, breast lymphoma and other rare tumors; patients were concomitant with other primary tumor; patients had received anti-tumor treatment previously.

Follow-up

After surgery, the patients were followed up by telephone with an interval of 3 months for the first year after surgery, and an interval of 6 months after that. The patients were followed up until May 2014. Data including the recurrence, metastasis and death were all recorded.

Clinicopathological parameters

Clinicopathological parameters included age, tumor size, clinical stage, lymph node metastasis, number of metastatic lymph node, expressional status of ER, PR and HER2 were recorded and analyzed.

The overall survival (OS) is defined as the time from the date of surgery to any cause of death or the deadline of follow-up. The disease-free survival (DFS) refers to the time from surgery to disease progression (tumor recurrence, metastasis, or a new tumor) or cancer-related death.

Statistical analysis

SPSS 19.0 was used for statistical analysis. Measurement data were expressed as mean ± SD and count data were expressed as rate. Kaplan-Meier method was used for survival analysis. Risk factors associating with clinical prognosis were screened by using univariate Cox regression analysis. Then the risk factors with $P<0.1$ were further analyzed by using multivariate Cox regression analysis to identify the independent risk factors associating with prognosis. A $P<0.05$ was considered statistically significant.

Results

Clinicopathological characteristics

In this study, the average age of the 120 enrolled patients at the time of surgery was 53.61±13.06 years old, including 50 (41.7%) patients younger than 50 years old, and 70 (58.3%) older than years old. In the meanwhile, there were 36 (30%) cases at stage I, 61 (50.8%) at stage II, and 23 (19.2%) at stage III. For tumor size, there were 43 (35.8%) patients with tumor size<2 cm, 51 (42.5%) with tumor size ranging from 2 to 5 cm, and 26 (21.7%) with tumor size>5 cm. For axillary lymph node metastasis, there were 69 (56.7%) cases without axillary lymph node metastasis, and 51 (43.3%) cases with axillary lymph node metastasis. For the number of metastatic axillary lymph node, there were 19 (37.2%) cases with 1-3 metastatic lymph nodes, 16 (31.4%) cases with 4-9 metastatic lymph nodes and 16 (31.4%) cases with over 10 metastatic lymph nodes. And there were 66 (55%) patients with ER (+), 50 (41.7%) with PR (+), 76 (63.3%) with HER2 (+), and 33 (27.5%) with three negative breast cancer (TNBC). See **Table 1**.

Survival analysis

The patients were followed-up from 10 months to 82 months until May 2014, with a median

Table 1. Cliniopathological characteristics

Mean age (year)	53.61±13.06
Range of age (n/%)	
<50 years	50 (41.7)
≥50 years	70 (58.3)
Clinical stage (n/%)	
I	36 (30.0)
II	61 (50.8)
III	23 (19.2)
Axillary lymph node metastasis (n/%)	
Yes	69 (56.7)
No	51 (43.3)
Number of metastatic axillary lymph node (n/%)	
1-3	19 (37.2)
4-9	16 (31.4)
≥10	16 (31.4)
Tumor size (n/%)	
<2 cm	43 (35.8)
2-5 cm	51 (42.5)
>5 cm	26 (21.7)
Status of ER expression (n/%)	
Positive	66 (55.0)
Negative	54 (45.0)
Status of PR expression (n/%)	
Positive	50 (41.7)
Negative	70 (48.3)
Status of HER2 expression (n/%)	
Positive	76 (63.3)
Negative	44 (36.7)
TNBC (n/%)	
Yes	33 (27.5)
No	87 (72.5)

follow-up period of 49 months. During the follow-up, 16 patients died and 26 patients recurred. The OS and the DFS of the patients were 75.92±1.49 months and 9.25±2.24 months, respectively. See **Figures 1** and **2**.

Risk factors associating the postoperative prognosis in breast cancer patients

As shown in **Table 2**, tumor size, lymph node metastasis, number of metastatic lymph nodes, clinical stage and ER and PR expression levels were risk factors associating with the clinical prognosis of patients with breast cancer, while age and HER2 expression did not associate with the postoperative prognosis.

Furthermore, multivariate Cox regression analysis indicated that tumor size, lymph node metastasis, number of metastatic lymph node and ER and PR expression levels were independent risk factors associating with the clinical prognosis of breast cancer patients. See **Table 3**.

Discussion

Currently, radical surgery is still the most effective method in the treatment of breast cancer as most breast cancer patients are able to be detected and treated at early stage with the extensive progression achieved on the diagnosis and treatment technology [9, 10]. However, still some patients died of tumor recurrence and metastasis. Moreover, the risk factors associating with the prognosis of patients with breast cancer after surgery are very complex, and the exact mechanism underlying breast cancer is still unclear [11]. Clinically, the clinicopathological parameters are still the most commonly used and the most recognized indicators for the prognostic prediction in the patients with breast cancer.

Among 120 patients with breast cancer in our study, 16 patients died and 26 patients recurred during the follow-up. The OS of the patients was 75.92±1.49 months, and the DFS was 69.25±2.24 months. Univariate Cox regression analysis showed that tumor size, lymph node metastasis, number of metastatic lymph node, clinical stage and the expressional status of ER and PR all were the risk factors associating with postoperative prognosis of breast cancer. And multivariate Cox regression analysis further confirmed that these indicators were independent risk factors associating with the clinical prognosis of patients with breast cancer.

In the previous studies, age is recognized as an important prognostic indicator for breast cancer [12, 13], which indicating that young breast

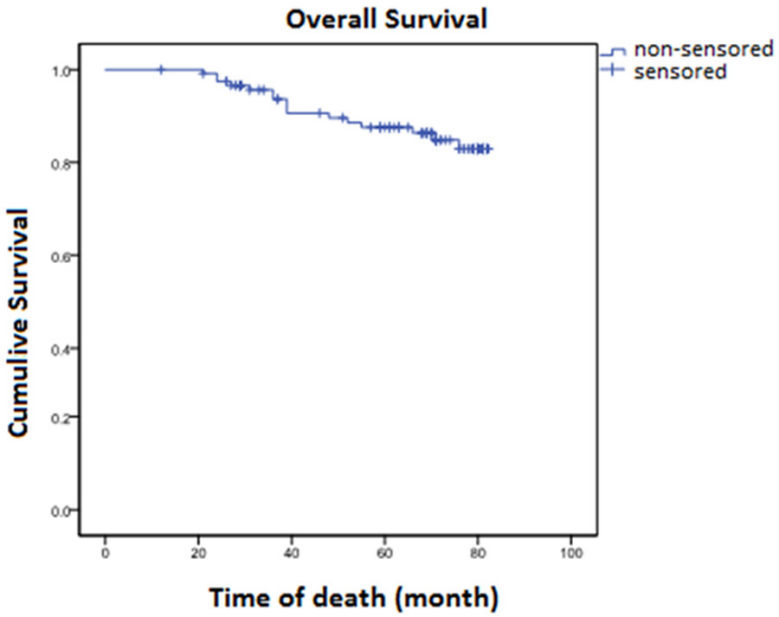

Figure 1. The overall survival of breast cancer patients.

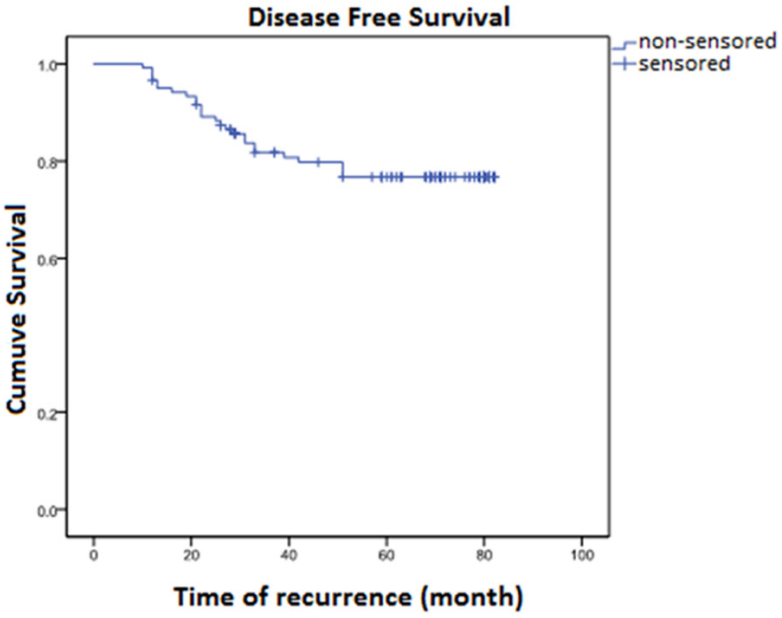

Figure 2. The disease-free survival of breast cancer patients.

cancer patients generally have a poorer prognosis by comparison with elderly patients at the same clinical stage [14, 15]. Albain et al. found that young age was the risk factor predicting a poor prognosis in newly diagnosed breast cancer patients, which was also confirmed by Love et al. [16, 17]. In order to further investigate the correlation of age and breast cancer prognosis of Chinese, in this study, all the enrolled patients were divided into two groups according to the age as breast cancer presented a peak age of 50 in China, and univariate Cox regression analysis showed that age was not the factor associating with the clinical prognosis in our study (P>0.05), which was consistent with the results of Wei et al. in Hong Kong who retrospectively analyzed the clinical prognosis of newly diagnosed breast cancer patients from 2003 to 2008 [18]. In their study, all the patients were divided into younger than 40 years old group, 41-69 years old group and older than 70 years old group and the results suggested that although young patients had more aggressive pathological types, the clinical prognosis in the three groups were very similar [18].

Lymph node metastasis is widely accepted risk factor associating with the clinical prognosis of cancer. And the current study also showed that axillary lymph node metastasis was the main factor associating with the prognosis of breast cancer. In addition, the number of metastatic lymph node was closely related with the prognosis of patients with lymph node metastasis. This study also indicated that the clinical stage was an important prognostic factor and the higher clinical stage predicted a worse prognosis. The results were similar to these reported by the National Cancer Institute, whose report showed that patients with localized breast cancer often had a better prognosis than those with metastatic breast cancer [19].

Increasing number of evidences prove that different molecular types represent different biological behaviors and clinical features in breast

Table 2. Risk factors associating with the postoperative prognosis in breast cancer patients by using univariate Cox regression analysis

Risk factors	DFS		OS	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age (≥50 vs. <50)	0.681 (0336~1.960)	0.391	0.519 (0.109~1.366)	0.239
Tumor size (>5 vs. ≤5)	0.198 (0.069~1.371)	0.029	0.129 (0.066~1.201)	0.033
Lymph node metastasis (yes vs. no)	0.181 (0.091~0.886)	0.010	0.209 (0.099~0.866)	0.012
Number of metastatic lynph nodes (>10 vs. ≤10)	0.211 (0.096~1.010)	0.009	0.310 (0.106~0.966)	0.016
Clinical stage (I-II vs. III)	0.188 (0.081~0.960)	0.008	0.131 (0.060~0.566)	0.009
ER (positive vs. negative)	0.198 (0.069~1.002)	0.005	0.218 (0.059~1.018)	0.003
PR (positive vs. negative)	0.196 (0.091~0.610)	0.033	0.198 (0.066~0.655)	0.010
HER2 (positive vs. negative)	0.811 (0.416~2.210)	0.601	0.862 (0.339~1.696)	0.501

Table 3. Independent risk factors associating with the postoperative prognosis in breast cancer patients by using multivariate Cox regression analysis

Risk factors	DFS		OS	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Tumor size (>5 vs. ≤5)	0.261 (0.109~0.890)	0.006	0.202 (0.077~0.966)	0.033
Lymph node metastasis (yes vs. no)	0.190 (0.088~0.820)	0.019	0.221 (0.090~0.899)	0.021
Number of metastatic lynph nodes (>10 vs. ≤10)	0.112 (0.069~1.200)	0.008	0.262 (0.139~0.812)	0.008
ER (positive vs. negative)	0.313 (0.098~1.008)	0.012	0.319 (0.089~1.360)	0.002
PR (positive vs. negative)	0.160 (0.081~0.819)	0.013	0.098 (0.036~0.661)	0.001

cancer. Molecular classification is an endogenous typing of breast cancer via immunohistochemical detection of the tumor cell-expressed molecules of ER, PR and Her2, which is similar to the molecular typing by gene sequencing that has been proved to be a vital prognostic factor for breast cancer [20]. Mammary gland is one of the most important target organs of estrogen and progesterone. Previous studies demonstrated that breast cancer with positive ER and PR had a better prognosis [21, 22]. Breast cancer with ER (-) had a 1.5 to 2-fold higher mortality than those with ER (+). In our study, we found that the expression levels of hormone receptors ER and PR in tumor tissues were important prognostic factors for breast cancer, which were consistent with previous studies. However, the expression of HER2 in tumor tissues often indicates a poor prognosis. The results of our study showed that there was no significant correlation between the expression of HER2 and the clinical prognosis, which might be due to the use of molecular targeted therapy after surgery.

Clinically, it is necessary to strengthen the postoperative monitoring and tracing of patients with high risks, and to optimize the perioperative adjuvant therapy to reduce the local recurrence and distant metastasis, so as to further improve the long-term survival of patients with breast cancer.

Additionally, this study still has some limitations. Firstly, the number of patients included in this study was limited. Secondly, only relationship between clinicopathological features and prognosis was analyzed. With the in-depth research, increasing attentions have been paid on the study of tumor molecular markers, such as PI3K, Akt, mTOR and other predictors on the prognosis of patients with breast cancer, therefore, we will expand the sample size in future studies and screen more biomarkers that have the potential to predict the prognosis of breast cancer after surgery.

In conclusion, the tumor size, lymph node metastasis, number of metastatic lymph node and the expression levels of hormone receptors ER and PR are the independent risk factors associating with the postoperative prognosis of breast cancer surgery, which can be applied as the prognostic markers in the treatment of breast cancer.

Disclosure of conflict of interest

None.

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