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Original Article

Factors related to survival rates for breast cancer patients

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Abstract: This study is to analyze the relationship between clinical parameters and prognosis and survival rates of breast cancer patients. A total of 1541 cases of breast cancer were retrospectively reviewed with respect to clinical parameters and the correlation with prognosis and survival rates. Among these patients, follow-up investigation was performed for 1381 cases. Clinical parameters including disease sites (the lesion quadrant), incidences, the number of axillary lymph node metastasis, maximum diameter of tumor, tumor regional lymph node metastasis (TNM) stages, pathological types were investigated. The estrogen receptor, progesterone receptor, Human Epidermal Growth Factor Receptor-2 levels were correlated with long term disease-free survival. Lymph node metastases, tumor diameter, TNM stage, and hormone receptor status are correlated with survival rates of breast cancer patients.

Keywords: Breast cancer, breast cancer prognosis factors, clinical parameters, retrospective analysis

Introduction

Breast cancer has become one of the most common malignancies of women worldwide. Every year, over one million females are diagnosed [1]. Breast cancer is the leading cause of female cancer mortality in China. Breast cancer is a heterogeneous disease, including 5 subtypes: 1) luminal A (ER positive (ER+) and/or PR positive (PR+); 2) HER-2 negative (HER-2-); 3) luminal B (ER+) and/or PR+, HER-2 positive (HER-2+); 4) HER-2 positive (HER-2+, ER-, PR-); and 5) basal-like (ER-, PR-, HER-2-, cytokeratin 5/6 positive (CK5/6+) and/or HER-1positive (EGFR). It is well established that patients with different subtypes of breast cancers have different prognosis [2, 3]. Clinicopathological parameters such as tumor staging, lymph node involvement, as well as tumor receptor status [4, 5] are well-known prognostic markers for breast cancer, but the relationship between these prognostics markers and survival in the Chinese population is still not clear. In this study, the diagnosis and treatment information of 1541 consecutive breast cancer patients were analyzed for independent prognostic factors of breast cancers.

Materials and methods

Patients

A total of 1541 consecutive breast cancer patients were retrospectively investigated. Disease lesions, incidences, the number of axillary lymph node metastasis, maximum diameter of tumor, Tumor regional lymph node metastasis stages (TNM), pathological types, estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (HER-2) levels were collected. HER-2 levels was determined by immunohistochemical (IHC) staining in tumor tissue: IHC 3+ and IHC 2+ with confirmative FISH+ were classified as HER-2 positive tumor; IHC 2+ but confirmative FISH- or IHC 1+ or IHC- were classified as HER-2 negative tumor [6]. There are total seven variables. All cases were pathologically diagnosed by biopsy or surgery. Distant metastases were determined by radiological examination such as computed tomography, magnetic resonance

Table 1. Information of breast cancer patients

Clinical parameters	Disease-free Survival (Years)				Survival period median (month?)	*P*-values between groups
	1	3	5	10		
Gender					0.287	0.5922
female	94.88	88.73	80.70	56.21	154.93	
Male	100	71.43	71.43		60+	
Age of onset					12.212	0.0158
≤ 35	87.33	75.27	75.27	61.59	184.51	
36-45	96.37	89.31	80.90	53.34	147.38	
46-55	98.77	98.77	81.63	81.63	300+	
56-65	94.72	87.06	81.40	78.79	206.86	
> 66	97.81	90.27	76.03	34.48	104.16	
Blood types					4.559	0.2036
A	94.25	89.71	73.76	59.01	174.49	
B	100	100	100		72+	
O	93.94	85.77	85.77		96+	
AB	100	100	0		66	
Family history					1.235	0.2664
No	95.29	88.74	81.44	58.74	169.44	
Yes	96.93	90.38	86.27	49.3	107.77	
Other comorbidities					10.374	0.0653
None	95.69	89.67	81.74	51.08	144.82	
Endocrine disease	94.81	94.81	79.00	52.67	132+	
Cardiovascular disease	87.56	82.45	73.15	73.15	191.39	

imaging, ultrasound, and bone scintigraphy. The patient's information is given in **Table 1**.

Following-up investigation

Among these patients, 1381 patients received following-up investigation in a period of 2.5-335 months after treatment for breast cancer.

Statistical analysis

SPSS version 13.0 software was used for statistical analysis. Survival curves are drawn using Life-tables and survival rates comparison were done by using the Chi-squared test. Cox regression model analysis and multivariate analysis were performed to determine prognostic factors. A *p*-value of less than 0.05 was considered as statistically significant. The study endpoints were 5-year and 10-year disease-free survival.

Results

Following-up investigation

To determine the relationship between clinical parameters and survival rates of breast cancer patients, 1381 of the 1541 consecutive breast cancer patients were investigated during the following-up investigation after treatments. The overall survival rates of 1-year, 3-years, 5-years, and 10-years for the 1381 cases were 94.91%, 88.64%, 80.64%, and 56.17%, respectively, with a median survival period of 154.87 months.

Factors related to survival rates in breast cancer patients

Analysis of tumor-related factors and prognosis for the 1381 breast cancer patients are given in **Table 2**. Univariate analyses of breast cancer patients with tumor-related factors indicated the incidences, disease lesions, and pathological breast cancer types have no significant correlation with long-term survival rates ($p > 0.05$). Factors such as the number of axillary lymph node metastasis, maximum diameter of tumor, TNM stage, and hormone receptor levels were significantly correlated with long-term disease-free survival rates ($p < 0.05$).

As shown in **Figure 1A**, the result of the Chi-square test was statistically significant ($\chi^2 = 18.524$, $p = 0.0001$). Axillary lymph node metastases had a significant negative correlation with the long-term disease-free survival

Table 2. Analysis of tumor-related factors and prognosis for 1381 breast cancer patients

Clinical parameters	Disease-free Survival (Years)				Survival period median (month)	*P*-values between groups
	1	3	5	10		
Incidences:					1.300	0.5220
Left breast	95.50	88.88	81.44	56.59	204 +	
Right breast	94.20	89.71	75.68	66.22	173.88	
Both breasts	100	93.55	80.18	80.18	148.52	
Disease site (lesion quadrant):					3.228	0.6650
Upper outer quadrant	94.46	88.22	81.23	52.54	145.45	
Lower outer quadrant	95.27	89.43	73.72	57.33	132.00 +	
Within the next quadrant	94.52	90.32	90.32	90.32	204 +	
Within the upper quadrant	99.19	91.96	74.76	58.15	132 +	
Central	94.20	89.72	89.72	89.72	144.0 +	
Both sides	100	50			48 +	
Axillary lymph node metastasis:					18.524	0.0001
≤ 4 cases	98.96	92.62	86.01	82.43	151.08	
5-9 cases	91.62	84.41	77.33	31.35	112.86	
≥ 10 cases or supraclavicular	86.14	76.19	58.78		82.76	
Maximum diameter of tumor:					19.971	0.0013
≤ 2 cm	98.66	94.17	89.01	74.59	151.91	
> 2 cm ≤ 5 cm	95.01	88.28	82.52	61.61	171.81	
> 5 m	68.77	81.83	54.55		84 +	
As long as the tumor size and chest wall invasion	66.67	66.64			24 +	
Single breast multifocal lesion	88.97	86.05	63.11		72 +	
Double breast lesions	85.7	85.71	85.71		65	
TNM stage:					58.210	< 0.001
0 stage	100	90.91			48 +	
I	98.87	95.44	89.99	89.99	212.00	
IIA	97.34	93.85	88.66	79.33	206.82	
IIB	99.16	92.26	86.83	81.57	153.29	
IIIA	95.66	84.77	72.40	33.79	114.24	
IIIB	63.35	63.35	63.35		72 +	
IIIC	87.35	81.78	66.05		98.53	
IV	69.33	69.33	55.47		36.98	
Pathological type:					4.932	0.1988
Carcinoma in situ +	98.02	92.65	87.5		120.57	
Invasive non-special cancer	95.92	89.7	80.42	58.81	172.18	
Invasive special cancer	93.96	90.33	90.33	90.33	149.36	
Other types	85.58	81.78	81.78	63.60	206.507	
Hormone receptor status					22.920	0.0009
ER+, PR+, HER-2+	100	100	100	100	246	
ER+, PR+, HER-2+	95.12	89.36	89.36	89.36	132 +	
ER or PR positive, HER-2+	98.52	93.41	84.32	67.08	240 +	
ER or PR+, HER-2+	96.43	93.04	93.34	82.81	156 +	
ER+, PR+, HER-2+	91.94	85.07	71.06	71.06	156 +	
ER+, PR+, HER-2+	90.58	73.42	63.11	44.05	105.57	
HER-2 (+2), regardless of ER and PR status	97.92	94.71	95.77		96 +	

rates. The high numbers of the lymph nodes were correlated to higher mortality rates.

As shown in **Figure 1B**, the Chi-square test indicated that tumor diameter and long-term disease-free survival was negatively correlated. A larger tumor diameter was related to a shorter long-term disease-free survival, with a statistically significant difference ($p < 0.01$). However, the 5-year disease-free survival of patients in this group was 34% lower than patients with a tumor diameter of less than 2 cm.

As shown in **Figure 1C**, the 10-year disease-free survival of phase I patients was approximately 90%, with a median survival of 212

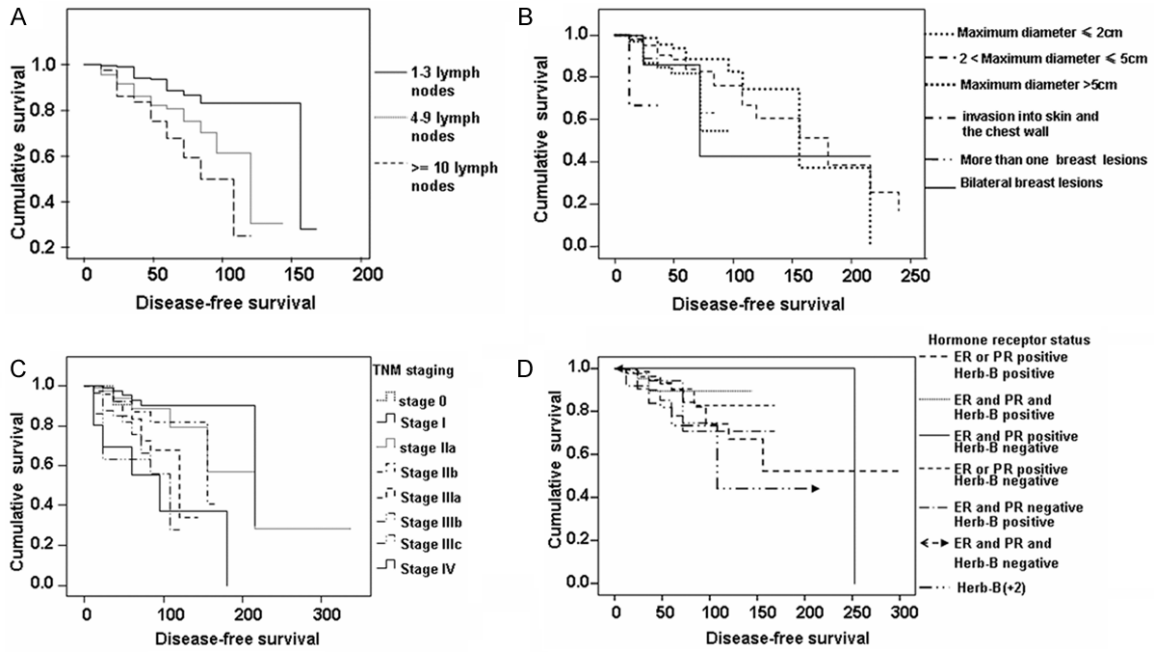

Figure 1. Factors related to survival rates of breast cancer patients. A. Relationship between axillary lymph node metastases and disease-free survival rates; B. Relationship between tumor diameter and survival rates; C. Relationship between TNMs staging and survival rates; D. Relationship between hormone receptor levels and survival rates.

months. Patients diagnosed at the later stages of the breast cancer had lower survival rates. The Chi-square test indicated that TNM staging and long-term survival are statistically significant ($\chi^2 = 58.21$, $P = 0.000$).

As shown in **Figure 1D**, hormone receptor levels were prognostic factors of breast cancer. According to the classification of ER, PR, HER-2 status in the results of the Chi-square test in this study, hormone receptor levels of breast cancer are significantly correlated with long-term disease-free survival rates ($\chi^2 = 22.92$, $P = 0.0009$). The 1-year and 3-year disease-free survival rates of triple negative breast cancer patients (ER, PR, and HER-2-negative) were slightly lower than all other subtypes of breast cancers, while the 5-and 10-year disease-free survival rates of these patients were much lower (63.11% and 44.05%, respectively). Altogether, the above results suggest that the axillary lymph node metastases, tumor diameter, TNM staging, and hormone receptor levels are factors related to survival rates of these patients.

Discussion

Factors related to survival rates of breast cancer patients were very important for patients. Roder et al. found several breast cancer-related risk factors, including tumor size, higher grade, positive nodal status, ER-negative status, as well as vascular invasion and multifocal [7]. Abbass et al thought that the tumor size and high histological grade are independent prognostic factors [8]. Study of 246 breast cancer patients demonstrated that breast cancer patients with a 5-year overall survival rate was dependent on menopausal status, tumor size, axillary lymph node metastasis and TNM stage [9]. It was found that nodal status is independently significant in univariate and multivariate analysis [10].

Our results that tumor sizes are related with the 5-year survival rates of patients are consistent with the above findings. Research indicates that 30% of all breast cancers are discovered in the advanced stages of the disease [11]. Early diagnosis of breast cancer contributes to the therapeutic efficacy and quality of life of patients. Therefore, the TNM staging of breast cancer patients plays a key role in the prognosis and treatment strategy. In multivariate analyses, advanced stage disease and negative hormone receptor status were independently associated with poor survival outcome [12]. This retrospective analysis of 1541 cases of

breast cancer reveals the absence of significant correlation between the pathological type and the long-term survival. The 5-year survival rate was negatively correlated with the TNM stage, implying that diagnosis of an earlier TNM stage leads to longer survival rates.

The expressions of ER, PR, HER-2 can help predict prognosis and provide guidance for selection of the most efficacious treatment [13]. Patients exhibiting a strong HER-2 expression indicate poor tissue differentiation and tumor prognosis. Blows et al [1] discovered the long-term survival rates of HER-2-negative patients had not changed drastically. Conversely, the 5-year survival rate of HER-2-positive patients was decreased and the 15-year disease-free survival rate of patients was decreased more significantly. In this study, single and multivariate factor analysis showed that the hormone receptor levels of breast cancer is significantly associated with long-term survival. The survival rates related to ER, PR, HER-2 were significantly different. This conclusion parallels the findings of Sirohi's study (64%) [14].

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Disclosure of conflict of interest

None.

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