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Breast cancer in young women of Chinese Han population: A retrospective study of patients under 25 years

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ABSTRACT

Background: Breast cancer has aggressive clinical and pathological features in younger women and is characterized by poorer prognosis than in older women. However, data on women <25 years are limited.
Objective: The aim of the present study was to evaluate the different pathological characteristics and prognostic factors in Chinese women with breast cancer <25 years at the time of diagnosis.
Methods: This retrospective study included 94 patients (aged <25) of Chinese Han population with operable breast cancer at the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences between January 1, 2000 and September 30, 2015. Univariate and multivariate Cox regression analysis were performed. The median follow-up duration was 64 months (range, 11–200 months).
Results: The HER2-positive and triple-negative groups had a higher T (P = 0.002) and N stage than the luminal A group (P = 0.014). The 5-year overall survival (OS) was 90.4%, and the disease-free survival (DFS) was 74.5%. The 5-year DFS varied among the four groups were 94.1 vs. 76.9 vs. 45.5 vs. 66.7%, respectively; P = 0.009. Multivariate analysis showed that only estrogen receptor (ER) status was a significant predictor of OS and DFS [Hazard ratio (HR) = 5.3, 95% confidence interval (CI) = 1.11-25.27, P = 0.036; HR = 2.712, 95%CI = 1.27-5.80, P = 0.01).
Conclusion: HER2-positive and triple-negative breast cancer are more likely to have poor prognosis in patients <25 years. Hence, ER status may be identified as an independent prognostic factor for predicting young women with breast cancer.

1. Introduction

Breast cancer is the most common type of cancer among women worldwide. According to the American Cancer Society, the incidence rate of breast cancer in the United States is more than 200,000 in 2010, accounting for 28% of all malignant tumors in women [1]. Approximately 6.6% of all patients with breast cancer are diagnosed in women <40 years, 2.4% in women <35 years, and 0.7% in women <30 years [2,3]. The proportion of patients with breast cancer <35 years is reported between 9.5 and 12 in Asia, which is higher than in Western countries [4–6]. Breast cancer is known to manifest more aggressive subtypes and biological characteristics in young women and is associated with a more unfavorable prognosis compared with older women [7–9]. Considering the poor clinical outcomes, and more complications in frequent long-term treatment, special consideration should be given to the development of adequate therapeutic approaches in young patients with breast cancer (YBC).

Several studies have concerned breast cancer in women <35 years. However, studies in YBC <25 years are very rare, these patients have low rate of pregnancy or marriage; hence, it is difficult to estimate the incidence rates and prognostic factors. The clinical and pathological characteristics feature of YBC remains, particularly in terms of each subtype. The present study was aimed to investigate the pathological characteristics and prognostic factors of Chinese women with breast cancer who were ≤25 year at the time of diagnosis.

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2. Methods

2.1. Patients

The medical records of 94 and 1795 female patients aged <25 who had breast cancer were treated with breast surgery at the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences between January 1, 2000 and September 30, 2015, were retrospectively reviewed. Patients with distant metastasis or T4 stage were excluded from this study.

2.2. Data collection

The clinical and pathological characteristics of patient were collected including a history of pregnancy, family history of breast cancer, information about therapy, tumor size, status of lymph node, pathological stage at diagnosis, histological, and immunohistochemical (IHC) characteristics of the primary tumor. The study was approved by the institutional review board (IRB) of Cancer Hospital, Chinese Academy of Medical Sciences, and Peking Union Medical College. All aspects of the study comply with the Declaration of Helsinki. Informed consent requirements were waived by the IRB since an honest advisor provided a de-identified dataset for the analysis.

2.3. Follow-up

Follow-up records were maintained by outpatient department and records of personal contact with the patients including routine correspondence and/or telephone calls, were used to follow the patients and determine the occurrence of loco-regional recurrence, distant metastasis or death. For deceased patients, the date and cause of death were obtained from the medical records. The end point of follow-up duration was September 30, 2015.

2.4. Clinical examination and treatment

All patients were required to have a complete physical examination, bilateral mammography, chest X-ray, electrocardiogram, ultrasonography of the breast, axillary, cervical region, and abdomen, and routine blood and biochemical tests prior to surgery, and adjuvant therapy when appropriate. All patients were staged per the guidelines of the American Joint Committee on Cancer, 2007 [10].

2.5. Pathology examination

The anatomopathological examination indicated the histological and IHC characteristics of the tumor. Block method were applied in pathology sampling. The mean size of DCIS cases were 18mmm (range 7–41 mm). All DCIS case specimens were serially sectioned consecutively along the long axis. Tissue sections were arranged and processed in sequence. The entire tissue of DCIS were examined (up to a total of 26 blocks), and the average thickness of each specimen slice was 0.3 cm.

The criteria defined by World Health Organization (2012) were used for histopathological diagnosis, classification and grading of DCIS and invasive carcinoma [11]. The nuclear grade of DCIS was classified as low, intermediate or high on the basis of nuclear size, pleomorphism, chromatin pattern, presence of nucleoli and mitotic activity. The grade of invasive carcinoma was classified as 1,2 or 3 based on the assessment of tubule/gland formation, nuclear pleomorphism and mitotic count. Tubular formation was assessed over the whole tumor; nuclear pleomorphism was evaluated in the area showing the highest degree of pleomorphism, and mitotic counting was performed in the area exhibiting most proliferation [11].

The original blocks were stained for estrogen receptor (ER), progesterone receptor (PR), and HER2 antigen. IHC staining positivity for ER and PR was defined as 1% or more nuclear staining. The HER2 assessment was performed per the guidelines of the American Society of Clinical Oncology and the College of American Pathologists. Samples were considered positive if they scored 3+ and were considered negative if they scored 1+. For patients with a 2+ score, the samples were further assayed using fluorescence in-situ hybridization and were considered positive if the ratio of HER2 signal to CEP17 was greater than 2.2 [11]. The four subtypes of tumor were defined per the IHC results: 1) luminal A: ER+ and/or PR+ and HER2-; 2) luminal B: ER+ and/or PR+ and HER2+; 3) HER2+: ER-, PR-, and HER2+; and 4) triple negative: ER-, PR-, and HER2- [9].

2.6. Statistical analysis

Statistical analysis was conducted using statistical package for social science, version 19.0 (SPSS Inc., Chicago, Illinois, United States of America). The association between variables was calculated using chi-square and the maximum likelihood ratio. The nonparametric Kruskal-Wallis rank test was used for ordinal categorical variables. Overall survival (OS) was defined as the time from the first diagnosis of primary breast cancer to the time of death by any cause. Disease-free survival (DFS) was defined as the time from the diagnosis of breast cancer to the development of any local recurrence or metastatic disease. Survival estimates were analyzed using Kaplan-Meier method. The log-rank model was used to compare survival curves per prognostic factors. Multivariate analysis was performed using Cox's proportional hazard regression model, and hazard ratios (HRs) were calculated based on 95% confidence intervals (CIs). All statistical tests were considered significant when the $P \leq 0.05$.

3. Results

3.1. Clinical and pathological characteristics

The median age of patient was 23 years (range, 14–25 years). The study patients were classified into four groups namely luminal A, and B, HER2-positive, and triple-negative. The number of patients in each group was 17, 39, 11, and 27, respectively. The patient characteristics of the four groups were summarized in Table 1.

Among the patients, 10 (10.6%) had a family history of breast cancer, 6 of which had a triple-negative subtype ($P = 0.034$, Table 1). 7 cases were carcinoma in situ, and 6 cases were luminal A like ($P < 0.001$, Table 1). 1 case was low-grade DCIS, 4 cases were intermediate-grade and 2 cases were high-grade. The HER2-positive and triple-negative groups had a higher T ($P = 0.002$) and N stage in comparison with the luminal A group ($P = 0.014$). More Grade III tumors were presented in the triple-negative group, whereas the difference was not statistically significant ($P = 0.166$).

According to the guidelines of the American Joint Committee on Cancer, The study patients were classified into Stage 0, Stage I, Stage II and Stage III groups. The number of each group is 7, 27, 42 and 18. The Stage III group included more patients with invasive carcinoma ($P < 0.001$) and more Grade III tumors ($P < 0.001$) in comparison with other stages. The patients characteristics of stages were summarized in Table 2.

Forty-five patients underwent breast-conserving surgery (BCS) and the other 49 patients underwent mastectomy. Among the latter group, nine patients underwent plastic surgery simultaneously. Eighteen patients received neoadjuvant chemotherapy, whereas 80 patients received adjuvant chemotherapy. Radiotherapy was indicated for 59 patients after conservative surgery or after mastectomy for lymph node involvement, or for T3 and T4 tumors. Eleven