Breast cancer in women younger than 25: clinicopathological features and prognostic factors

According to the statistics from American Cancer Society, 95% of new cases and 97% of breast cancer mortality occurred in women aged 40 and older during 2000–2004; in the same period, women aged 20–24 years had the lowest breast cancer incidence rate, 1.4 cases per 100,000 women [1]. The fact that breast cancer is a very rare disease in women younger than 25, therefore, has resulted in fewer studies reporting the outcomes of this cohort of patients and limited knowledge regarding the biological characteristics and clinical behavior [2, 3]. Many epidemiologic studies have demonstrated that younger women with breast cancer may potentially be related to more aggressive tumor biology such as larger tumor size, high histologic grade, positive lymph nodes, high proliferation rate, the presence of lymphovascular invasion, the absence of steroid receptors and high S-phase fraction [4–6]. Up to now, the prognosis and survival of young women with breast cancer remain a controversial issue.

We made a retrospective study of 54 patients histologically diagnosed with breast cancer at the age of ≤25 in the Cancer Hospital of China Academy of Medical Science and treated from January 1980 to December 2005. The case records of all patients were examined for details of their initial presentation and subsequent treatment. Details of local and disseminated recurrence of disease and overall survival were also obtained for all patients. The following data were evaluated regarding tumor size, the histological types, involvement of lymph nodes, estrogen receptors (ERs), progesterone receptors (PRs), receptors for c-erbB2 and lymphovascular invasion. The median follow-up was 52 months (ranging from 7 to 235 months). Three of the patients failed to be followed up and their information was only partial. The subjects alive at the end of follow-up (30 November 2007) and those that failed to follow up or were deceased from other causes were censored at the date of their last observation. Patients with stage IV disease were excluded from the statistical evaluation of recurrence and those with noninvasive carcinoma were excluded from statistical evaluation of survival. Disease-free survival (DFS) and overall survival (OS) estimates were calculated using the Kaplan–Meier method and differences between survival times were assessed by log-rank test. To determine prognostic factors for overall survival, a Cox proportional hazard model was used, with $P < 0.05$ accepted for each additional variable to enter. All statistical analyses were processed with SPSS software version 13.0 (SPSS, Chicago, IL).

This cohort of patients comprised 0.48% of all breast cancers (1,151 patients) during the same period in our institute. There were 12 patients with pregnancy–associated breast cancer. Metastatic disease was detected in two (3.7%) patients at their initial presentation. Seventeen patients (31.5%) presented with locally advanced breast cancers. The median duration of symptoms was 4 months (range 1 week to 2 years). Nine patients presented with a 1- to 2-year history of a palpable mass before diagnosis. In 34 (63.0%) cases, there was a delay of >3 months before the patients seeking medical attention. No history of breast or ovarian cancer was found in any of the 54 patients. Regarding the biological features, frequencies of ER and PR positivity were low (29.6% and 36.0%, respectively), and frequency of c-erbB2 positivity (22.2%) was high.

Treatment characteristics are shown in Table 1. Thirty-eight patients received adjuvant chemotherapy. Six patients were administrated with cyclophosphamide, methotrexate and 5-fluorouracil, 17 with 5-fluorouracil, doxorubicin and cyclophosphamide and another six patients with paclitaxel (Taxol, Bristol-Myers Squibb, USA) and doxorubicin and several other regimens. No dose-dense regimen or neo-adjuvant chemotherapy was administrated. Stratified analysis according to axillary lymph node status was carried out for the patients who had received chemotherapy. In lymph node-positive patients, chemotherapy can improve their 5-year OS significantly (Figure 1, $P = 0.007$). Only five patients with positive ER or PR received hormonal therapy in the form of either taking tamoxifen (TAM) for $>1$ year or oophorectomy.

The median OS was 55 months (range 17–313). Twenty-six (48.1%) out of all patients were dead by the end of this study. The 5- and 7-year OS for all patients were 55.5% and 48.9%, respectively. The 5- and 7-year DFS were 54.3% and 50.9%,
Survival related to patient delay was quantified in one of the patients in our study were II–III stages (75.9%). Decreased which is more consistent with the truth that as well as most of women under 25 years old. Most studies linked patient delay with more advanced staged breast cancer at diagnosis [7], changes and lower levels of suspicion of malignancy are the dense or nodular breast tissue subject to cyclical hormonal physical examination, inferior accuracy of mammography for months were significant prognostic factors (P = 0.007, P = 0.157). The updated Early Breast Cancer Clinical Trialists’ meta-analysis have shown beneficial effects of adjuvant TAM in younger women [11], as well as the findings from the International Breast Cancer Study Group (Trial 13-93) [12]. Nearly 50% of patients’ ER status is unclear and few patients received TAM >1 year in our study, so we did not observe any benefit from adjuvant endocrine therapy. The reason that patients did not persist on TAM maybe that suppression of ovarian function creates significant problems for very young women, including menopausal symptoms, psychological distress and the need to adjust personal and family plans. It should be mentioned that our patients were treated during a 25-year period, dating back to 1980, when the major advances in cancer management had not occurred. Therefore, the variation in treatments given to our patients in this study should no longer occur and all women should now be receiving optimal treatments. Although we do not have a direct comparison group of patients older than 25 years of age, it is interesting to compare the survival of our young patients with the reported 5-year OS for the 4396 patients of all ages treated in China National Breast Cancer Group in the similar period [13]. In our study, the 5-year OS of I, II, III and IV stages were 80%, 65.7%, 28.1% and 0%.

Table 1. Treatment characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n (%)</th>
<th>5-year OS (%)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Surgery Mastectomy</td>
<td>32 (65.3)</td>
<td>48.7</td>
<td>0.450</td>
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<td>Conservation Mastectomy</td>
<td>17 (34.7)</td>
<td>60.5</td>
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<td>Chemotherapy Yes</td>
<td>38 (70.4)</td>
<td>58.4</td>
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<td>No</td>
<td>16 (29.6)</td>
<td>47.1</td>
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<tr>
<td>Radiation therapy Yes</td>
<td>28 (51.9)</td>
<td>63.7</td>
<td>0.749</td>
</tr>
<tr>
<td>No</td>
<td>26 (48.1)</td>
<td>57.4</td>
<td></td>
</tr>
<tr>
<td>Hormone therapy Yes</td>
<td>5 (9.3)</td>
<td>80</td>
<td>0.161</td>
</tr>
<tr>
<td>No</td>
<td>49 (90.7)</td>
<td>52.8</td>
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</tbody>
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Figure 1. Overall survival for lymph node-positive patient with or without chemotherapy (CT). Lymph node-positive patients with CT had significantly better outcomes than patients without CT (P = 0.007).
and 0%, respectively, which were correspondingly 88.2%, 72.92%, 46.81% and 9.84% in the report, indicating that the local advanced diseases in our study had worse prognosis than the all aged group.

In conclusion, breast cancer is a rare condition in women aged ≤25. Invasive breast cancer occurring at this subgroup has more aggressive biological behaviors. Diagnostic delay >3 months and lymph node metastasis are considered adverse prognostic factors in the current study. The general principles of managing adolescents and very young women with breast cancer are different from those applying to older women in current study, but development of tailored treatment for this population is still crucial.

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references

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