Pattern and Prognosis of Breast Cancer: Data from the Eastern Province of Saudi Arabia

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With invasive breast cancer were retrospectively reviewed. The patients' mean age (± SD) was 43.4 (± 12.1) years; Saudis constituted 61.5%. The patients showed a mean primary tumour size (± SD) of 3.34 (± 3.91) cm. While only 22% of patients had stage I disease, almost 78% had stage II-IV. Of patients with known nodal status, only 22% were node-negative and the rest were positive nodes. The overall median survival (± SE) of all 130 months with a survival probability of 79% (± 4%) at 3 years. The Cox (regression) model has identified the advanced stages (III or IV) and presence of positive nodes as the only poor prognostic factors that adversely affect survival. In conclusion, the derived hazards proportional hazard model of Cox was applied to the study data to identify certain independent variables that affect the outcome of breast cancer in Saudi Arabia.

The prevalence of breast cancer in Saudi Arabia was 17%. The incidence of breast cancer in the country is significant among women. In a large epidemiologic survey conducted in the country, where 4734 female cancer patients were studied, breast cancer was the most frequent site with a crude relative frequency of 17%.

Materials and Methods

The medical records of all female patients with invasive breast cancer who were referred to the medical oncology unit of King Fahd Hospital of the University between April 1981 and September 1989, were retrospectively reviewed.
reviewed. The unit provides service for Saudi and non-Saudi patients who live in the eastern province. The total population of the province is approximately 500,000 inhabitants. With the exception of Dhahran Health Center—which receives only a particular group of patients and their dependents—no other oncology unit exists in the province. While some patients are referred to oncology units in Riyadh, others come to our unit from other regions and from outside the country. The lack of population-based regional or national cancer registry data precluded accurate estimation of the proportion of various groups of patients in various medical facilities.

All patients had a complete history and physical examination, radiologic studies and routine laboratory work-up. Disease staging was categorized based on the TNM system of the Union Internationale Contre le Cancer (UICC) with group clinical and pathologic staging according to the American Joint Committee on Cancer (AJCC). Objective assessment of response for both measurable and unmeasurable disease was defined according to the criteria proposed by De Lena et al. For those with operable breast cancer who received adjuvant chemotherapy using CMF or CMFVP protocols (cyclophosphamide, methotrexate, 5-fluorouracil, vincristine, prednisone), the effect of the actually received dose-intensity was evaluated. Calculation of the average dose intensity was made according to the method proposed by Hryniuk & Levine that utilizes the CMFVP treatment used by Cooper et al. as a reference regimen.

Data analysis and statistical methods
Survival was estimated using the Kaplan & Meier method. The log-rank test of Breslow (generalized Wilcoxon) was used to assess the significance of unadjusted differences in survival. Identifying variables for their independent prognostic significance on survival was carried out using the multivariate regression model of Cox. Determining the independent prognostic variables that influenced the likelihood of relapse was carried out using a stepwise logistic regression procedure. All data analyses were carried out using P1D, P4F, PLR, P1L, and P2L programs of the BMDP Statistical Software.

Results
Of the identified 146 women with invasive breast cancer, 16 were excluded from further analysis for the following reasons: nine patients were lost early to follow-up after diagnosis and no survival data could be obtained; and seven non-Saudi patients returned to their countries so there was no follow-up information. The remaining 130 patients were evaluable and they constituted the basis of this report.

The mean age (± SD) was 43.4 (± 12.1) years. Saudi patients constituted 61.5% (80 patients). The median duration of symptoms prior to diagnosis was 9.7 months (range, 1–72 months). However, further analysis failed to show any significant correlation between the duration of symptoms and the size of primary tumour, presence or absence of involved lymphadenopathy, or the number of involved lymph nodes.

Detailed disease characteristics are shown in Table 1. The mean (± SD) for the largest diameter of the primary tumour was 5.34 (± 3.91) cm with a range of 1–16 cm. Modified radical mastectomy (MRM) was the most frequently performed surgery (48%, 62 of 130 patients). Radical mastectomy was performed in only 9% of patients. Adjuvant radiotherapy, tamoxifen, and chemotherapy were given to 50 (38%), 55 (42%) and 62 (48%) of patients, respectively. Most of those who received adjuvant radiotherapy or tamoxifen and all those given adjuvant chemotherapy were node-positive patients.

Survival analysis
At the time of the analysis, 33 patients (25%) were dead and their death was either attributed to progressive breast cancer disease (32 patients) or to its therapy (one patient). Of the remaining 97 patients, 72 (75%) and 25 (22%) were still alive without or with evidence of disease, respectively. The outcome of all patients categorized according to their initial AJCC clinical stages (I and II vs III and IV) is shown in Table 2.

Figure 1 shows the overall survival curve for all 130 patients. The actuarial overall median survival (± SE) was 85.7 (± 0.04) months. The curve also demonstrates that the probability of survival (± SE) at 3 years was 79% (± 4%). To identify the independent effect of baseline prognostic factors on survival, the multivariate proportional hazard model of Cox was estimated. The procedure was first carried out on all 130 patients without including data on nodal status as it was not available for all patients. The second model was then tested only on those 97 patients who have data on their nodal status with inclusion of the latter as one of the independent covariates.

Table 2

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Stage no. (%)</th>
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<tbody>
<tr>
<td></td>
<td>I &amp; II</td>
</tr>
<tr>
<td>Alive NED</td>
<td>51 (66)</td>
</tr>
<tr>
<td>Alive with ED</td>
<td>15 (19)</td>
</tr>
<tr>
<td>Dead</td>
<td>12 (15)</td>
</tr>
<tr>
<td>Total</td>
<td>78 (100)</td>
</tr>
</tbody>
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NED: no evidence of disease; ED: evidence of disease. AJCC: American Joint Committee on Cancer.
Table 3 shows that AJCC stages III or IV alone (first model) or together with node-positive status (second model) were found to influence survival adversely. To illustrate the effect of stages, Fig. 2 was constructed to depict the survival curves of AJCC stages I and II vs stages III and IV together. The median survival of the first group has not been reached with a survival probability (± SE) at 3 years of 88% (± 4%). On the other hand, the survival probability for stages III and IV at 3 years was 61% (± 9%). The difference in survival between stages I and II vs III and IV was highly significant (p < 0.001).

Over a median follow-up in excess of 30 months, the median survival has not been reached at the time of analysis. However, the survival probability (± SE) at 36 months was estimated as 78% (± 8%). The multivariate regression analysis of Cox has shown that only clinical stage III, four or more lymph nodes positive and low average dose intensity of less than 0.75 were significantly related to survival.
has been shown to have a deleterious influence on survival, that adverse effect seems to diminish substantially if the duration of pretreatment symptoms increased beyond 6 months.

Our patients demonstrated a high incidence of risk criteria. First, they showed a significantly higher percentage of node-positive patients (88%) compared to that of 50% commonly quoted in Western literature. Second, about 35% of patients had stage III or IV disease. Third, they often presented with a large primary tumour with its estimated mean diameter greater than 5 cm. Survival analysis of all 130 patients has shown that advanced clinical stage (III or IV) and involvement of lymph nodes were the only independent adverse factors of survival. The adverse effect on survival of locally advanced or disseminated disease, and positive-node disease is consistent with available data. Due to the small size of the current series, different disease characteristics, variability of offered therapeutic modalities and relatively short follow-up comparing the attained overall survival with that reported in Western literature would not be appropriate.

Analysis of relapse data, however, in premenopausal patients have identified several risk variables that predicted higher relapse rate. Younger women (less than 35 years) relapsed more frequently. The latter pattern was consistent with recently published data about the poor outcome of that age group. The relation between higher relapse rates and positive lymphadenopathy or larger primary tumour size was expected. Furthermore, the association between low relapse incidence and adjuvant radiotherapy or chemotherapy was in keeping with the available data. For postmenopausal patients, the adverse effect of larger primary tumour and the protective influence of adjuvant tamoxifen was also shown.

Subgroup analysis of those patients who received adjuvant chemotherapy has shown the adverse prognostic effect of the following variables: locally advanced disease, presence of four or more positive lymph nodes, and low average dose-intensity (<0.75). The adverse influence of the presence of four or more positive lymph nodes is in keeping with the accepted concepts of prognosis in breast cancer. Despite the small size of the present sample, prognostic role of dose-intensity in this study was in keeping with recently published data. The 3-year survival of this subgroup was 78% (±8%) which is inferior to other adjuvant chemotherapy data. However, several factors could have contributed to that lower survival rate. A relatively high percentage of patients had stage III disease (26%), the mean largest diameter for their primary tumour was 6 cm (range, 1–16), and the mean number of positive lymph nodes was 4.5 nodes (range, 1–15).

Conclusion
Despite the small number of patients in the current analysis, and the short follow-up, an interesting pattern has been preserved. The identified patient and disease characteristics should mark the nature of the disease in Saudi Arabia. The prognostic factors for survival and relapse which were identified should facilitate future comparisons of data derived from prospective trials from major oncology units throughout the Kingdom.

References