Prognostic factors affecting local recurrence and systemic metastasis in early stage breast cancer

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Abstract

Objective: Breast cancer is the most common cancer in women. Mortality in breast cancer is associated with recurrence and metastases. The aim of this study was to determine the causes of local recurrence and metastasis in operated early stage breast cancer.

Material and Methods: The files of the patients diagnosed with operated early stage breast cancer followed up at Dicle University Medical Faculty Medical Oncology Department between 2001-2010 were analyzed retrospectively. The group of patients with recurrence was referred to as the relapse-metastasis group and the other patients were called the remission group. Between these two groups, age, sex, tumor histology, size, presence of lymphovascular invasion, tumor grade molecular properties such as, ER, PR, HER, staging studies; time characteristics, surgical characteristics, time between surgery-chemotherapy and surgery-radiotherapy; The relapse-metastasis group and the remission group were compared in terms of chemotherapy. SPSS 22 was used for statistical analysis. $p < 0.05$ was considered significant.

Results: 479 patients were included in the study. The number of patients in the remission and relapse-metastasis group was 343 and 136, respectively. Tumor diameter was 3.33 cm in the remission group and 4.58 cm in the relapse-metastasis group, and the difference was statistically significant ($p < 0.01$). The percentage of involvement of more than 4 lymph nodes were 30.45% and 55.7% in the remission and relapse-metastasis groups, respectively ($p < 0.01$). The percentage of the lymphovascular invasions were remission group and relapse-metastasis group 46.4% and 80% respectively. The percentage of patients with surgery-chemotherapy time> 1 month was 9.7% and 24% in the remission and relapse-metastasis group, respectively. In remission group 30.9%; relapse-metastasis group 47.7% of the patients had incomplete staging at the time of diagnosis.

Conclusion: The factors determining the recurrence in patients with operated early stage breast cancer were tumor size, number of lymph node involvement, incomplete staging at the time of diagnosis, start chemotherapy later than 1 month.

Keywords: early stage breast cancer, recurrence, metastasis

Introduction

Breast cancer is a major health problem for women worldwide. One in 8 women gets breast cancer during their lifetime. It is the most common cancer in women in the United States; is the second leading cause of cancer -related deaths. According to annual cancer statistics, 26% of new cancer cases are breast cancer; it is estimated that 15% of cancer-related deaths will be breast cancer (1,2).

Early diagnostic procedures, adjuvant chemotherapy and hormonal therapy reduced mortality in breast cancer (3). As in the world, the most common cancer in women in our country is breast cancer (4).

Recurrence and metastases are the cause of mortality in early stage breast cancer (5).

Tumor sizes, poor histologic structure, lymphovascular invasion at diagnosis, local advanced diseases were known features for recurrence-metastasis (6).

Factors other than these risk factors have not been fully clarified in the literature.

The aim of this study was to determine the causes of local recurrence and metastasis in operated early stage breast cancer.

Material and Methods

The files of breast cancer patients admitted to Dicle University Medical Faculty Hospital Medical Oncology Department between 2001 and 2010 were reviewed retrospectively. Patients with metastasis at the first diagnosis were excluded. Operated patients were included in the study. Relapse-metastasis group was defined as relapse patients during follow-up and remission group was called as other patients. Between these two groups, age, sex, histology of tumor, tumor size, presence of positive lymph node, lymphovascular invasion, ER, PR, HER status were recorded. Staging studies at the time of diagnosis (such as chest radiography, abdominal USG, scintigraphy, tomography), surgical characteristics (surgical site, mode of operation), time of adjuvant treatments (time(month) between surgery-chemotherapy and surgery-radiotherapy relapse-metastasis group and remission group were compared.

Statistical analyses were performed using the SPSS software version 21. Variables were expressed as means ± standard deviations (SDs), and categorical variables were expressed as counts and percentages. The chi-square test or Fisher's exact test was used to compare these proportions in different groups. The results were evaluated with 95% confidence interval and p <0.05 significance level.

Results

After screening, 479 patients were included in the study. In the remission and relapse-metastasis group there were 343 and 136 patients, respectively. The mean age in the remission group was 48.7 years (18-79), and the mean age in the relapse-metastasis group was 47.9 years (23-77) (p> 0.05). The most common histological structure was ductal adeno-ca in both groups. Most patients in the recurrence-metastasis group had ductal histology and were statistically nearly significant (p:0.061).

Tumor diameter was 3.33 cm in the remission group and 4.58 cm in the relapse-metastasis group, and the difference was statistically significant (p<0.01).

The tumor diameter was T2 (2-5 cm) in most patients. There were 234 patients (73.8%) in the remission group and 83 patients (26.2%) in the relapse-metastasis group.

There were a significant difference between the two groups in terms of tumor diameter (p <0.01). The tumor diameter was greater in the relapse-metastasis group (p <0.01).The percentage of N0 patients in our study was 39% in the remission group; and 14% in the relapse-metastasis group.

The percentage of involvement of more than 4 lymph nodes were 30.45% and 55.7% in the remission and relapse-metastasis groups, respectively (p <0.01). The percentage of lymphovascular invasion remission group and relapse-metastasis group were 46.4%, 80% respectively (Table 1).

There was no statistically significant difference between ER, PR and HER between the two groups. When the patients were analyzed in terms of the mode of operation, it was seen that 90.2% of the patients who developed recurrence-metastasis underwent MRM.

It was observed that breast conserving surgery was performed mostly in university hospitals (40%). The percentage of patients with surgery-chemotherapy time> 1 month was 9.7% and 24% in the remission and relapse-metastasis group, respectively.

Statistically significant difference was found between the two groups. In remission group 30.9%; recurrence-metastasis group 47.7% of the patients had incomplete staging at the time of diagnosis(Table 1).

	Remission group	Relapse-metastasis group	p value
n: 479	343	136	
Gender (F/M)	341/2	133/3	
Mean age (years)	48.7(18-79)	47.9(23-77)	>0.05
Ductal carcinoma	81.2%	87.3%	>0.05
Tumor diameter (cm)	3.3	4.58	<0.01
T2 (2-5cm) tumor	73.8%	26.2%	<0.01
Lymphovascular invasion	46.4%	80%	<0.01
Percentageof NO patients	39%	14%	<0.01
>4 lymphnode involvement	30.4%	55.7%	<0.01
Modified radicalmastectomy	80.4%	90.2%	<0.01
Surgery-chemotheraphy time (>1 month)	9.7%	24%	<0.01
Incomplete staging in initial diagnosis	30.9%	47.7%	<0.01

Discussion

In this study, the most important finding is that in the breast cancer incomplete staging at the time of diagnosis, start chemotherapy later than 1 month were found to be associated with recurrence.

Breast cancer is the main health problem for women in the world. The most common cancer in women in our country is breast cancer. Local recurrence and distant metastasis in breast cancer are associated with mortality. Due to the increased scans, most patients are diagnosed at an early stage. Chemotherapy and hormonal therapy in breast cancer reduces recurrence and mortality (7).

The larger tumor in breast cancer, worsens the prognosis. There is a direct correlation between tumor size and recurrence and distant metastasis. In a study by Rosen et al. which examined the relationship between 20-year tumor size and recurrence-metastasis survival, disease-free survival was shortened as tumor size increased (8). In our study, tumor size was found to be larger in the relapse-metastasis group.

Survival rates of those with tumors less than two centimeters are high. Carter and colleagues found that tumor size was an independent prognostic factor for survival in the study of 24,740 breast cancer patients. The 5-year survival rate was 96.3% in patients with tumor size less than 2 cm; in patients with a tumor size of 5 cm and over, this rate was 45.5% (9).

In retrospective prognostic index determination study performed by Galea et al. in 387 breast cancer patients, tumor size was found to be a prognostic factor (10). In our study, mean tumor diameter in the remission group was 3.33 cm and 4.58 cm in the relapse-metastasis group and statistically significant. In our study, the percentage of patients with tumor diameter 2 cm and over was 88.2% in the relapse-metastasis group; whereas in the remission group this rate was 76% and statistically significant (p <0.001). Consistent with the literature, in our study, the recurrence-metastasis rate increased as the tumor diameter increased.

The number of metastatic lymph nodes is also a factor that affects the prognosis negatively. In patients with one to three lymph node positive patients, recurrence rate is lower than in patients with four or more lymph node positive patients and the likelihood of long-term survival is higher. The 5-year survival rate in nod negative patients is 70-80%, while the 5- year recurrence rate is approximately 20%. In the American National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program, 24740 patients were examined and it was determined that as the lymph node involvement increased, the likelihood of recurrence increased and survival decreased and this correlation was found to be directly proportional to the increase in tumor size (9). The percentage of N0 patients in our study was 39% in the remission group; and 14% in the relapse-metastasis group. The percentage of patients with the number of involvement nodes 4 or more was 30.4% in the remission group and 55.7% in there relapse-metastasis group and was statistically significant.

The recurrent-metastasis rate increased as the number of involvement nodes increased.

Adjuvant chemotherapy usually begins 4-6 weeks after the operation. The benefit of starting earlier has not been shown; however, it has been reported that it is harmful to start late than 12 weeks. In the retrospective analysis of Danish breast cancer group with 5003 patients, it was found that starting from the first 3 weeks in terms of survival analysis grouped as first three weeks, 1-3 months and after 3 months, according to chemotherapy patients, it did not provide additional benefit; delay after three months was found to have a negative effect on survival (11). In our study, the time to start chemotherapy was designed as 1 month and before or after 1 month. In the remission group, 90.3% of patients who received early chemotherapy; it was found to be 76% in the relapse-metastasis group and was statistically significant. Most of the patients in the remission group had chemotherapy started early.

Currently, surgical treatment of breast cancer includes breast conserving surgery and modified radical mastectomy (12). When the patients were evaluated in terms of operation type, breast conserving surgery was performed mostly in the remission group; modified radical mastectomy was performed in patients in the relapse-metastasis group. There was a statistically significant difference between the mode of operation and recurrence. Recurrence was more common in MRM patients. This may be related to the progression of relapse patients at the time of diagnosis. The limitations of our study were retrospective design.

Conclusion

The factors determining the recurrence in patients with operated early stage breast cancer were tumor size, number of lymph node involvement, incomplete staging at the time of diagnosis, start chemotherapy later than 1 month.

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: AI: Research concept, Design and Revision; ZP: Data collecting, Preparation of article, and Revisions. All authors approved the final version of the manuscript

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