Evaluation of Prognostic Factors In Patients with Metastatic Breast Cancer

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Abstract

Purpose: Metastatic breast cancer has remained as an incurable disease. The main objectives of treatments include alleviating of symptoms, delaying disease progression and increasing survival without any adverse effect on the quality of life. The main purpose of this study was to investigate the effects of some clinocopathological factors on the survival of patients with metastatic breast carcinoma in our institute.

Patients and Methods: In this retrospective cohort study, we reviewed the files of patients who were metastatic at presentation or became metastatic during follow-up and were referred to oncology department of Omid Hospital affiliated to Mashhad University of Medical Sciences from 1997 to 2007. The information regarding clinicopathological characteristics were recorded. The first line chemotherapy regimen was as follows: 79 CAF (cyclophosphamide, doxurobicine, 5FU), 25 CMF (cyclophosphamide, methotrexate, 5FU) and 11 Taxene based; AT (doxorubicin, paclitaxol) or TAC (taxene, doxurobicine, cyclophosphamide).

Results: 115 patients with a median age of 45 (range, 25-78) were investigated. The median follow-up time for all patients from diagnosis was 21 months (range, 5-74 months) and from metastatic manifestation was 12 months (5-36 months). The sites of recurrence or metastasis were as follows: 18 (15.7%) local recurrence, 23(20%) bone and 74 (64.3%) visceral metastases. The median and 2- year overall survival for all patients with metastatic disease were 15 months and 44.6% ± 6% respectively. Patients with bone metastasis had a significantly better overall survival compared to those with visceral metastasis. (74.2%vs.36.1%, P= 0.04) Among those patients who were non-metastatic at the time of referral, the time left to metastasis had a significant effect on the overall survival from metastasis manifestation. In comparison with premenopausal patients, the overall survival was relatively better in postmenopausal cases. (59.4% vs. 38.5%, P=0.1)

Conclusion: In our study, disease free survival (DFS) was the most important factor for overall survival in patients with metastatic breast cancer. The patients with longer DFS (>18month) had better overall survival. Overall the patients with bone metastasis had better survival than visceral metastasis.

Keywords: prognostic factors, metastatic breast cancer, disease free survival

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Introduction

In spite of outstanding progress in screening and treatment methods for early breast cancer, there has been little improvement in survival for the patients with metastatic breast carcinoma in recent years. The patients with metastatic breast carcinoma have a median survival of 18 t0 24 months. In a study on 250 metastatic cases, the median survival after symptom manifestation was 2.7 years and only 2% of patients lived more than 10 years. In this study, 75% of patients were metastatic at presentation. The metastatic breast cancer has remained an incurable disease. However, it is estimated that about 10% of patients may live more than 10 years with new systemic treatments.(1)The main objectives of treatments include alleviating of symptoms, delaying disease progression and increasing survival without any adverse effect on the quality of life. Systemic treatments based on anthracyclines and taxens as the most active agents are frequently used for metastatic breast carcinoma. However, multiple randomized trials have revealed that despite higher therapeutic responses with new agents, minor improvement in the overall survival has obtained.(2)The main purpose of this study was to

investigate the effects of some clinocopathological factors on the survival of patients with metastatic breast carcinoma in our institute.

Patients and Methods

In this retrospective cohort study, we reviewed the files of patients who were metastatic at presentation or became metastatic during follow-up and were referred to oncology department of Omid Hospital affiliated to Mashhad University of Medical Sciences from 1997 to 2007.The information regarding clinicopathological characteristics were recorded. The first line chemotherapy regimen was as follows: 79 CAF (cyclophosphamide, doxurobicine, 5FU), 25 CMF (cyclophosphamide, methotrexate, 5FU) and 11 Taxene based; AT (doxorubicin, paclitaxol) or TAC (taxene, doxorubicine, cyclophosphamide). The overall survival was calculated from the time of metastatic manifestation to the time of death using Kaplan-Meyer method. The Log rank test was utilized for comparing survival curves between groups .P values below 0.05 were considered as significant.

Results

115 patients with a median age of 45 (range, 25-78) were investigated. The median follow-up time for all patients from diagnosis was 21 months (range, 5-74 months) and from metastatic manifestation was 12 months (5-36 months). The sites of recurrence or metastasis were as follows: 18 (15.7%) local recurrence, 23(20%) bone and 74 (64.3%) visceral metastases. The median and 2- year overall survival for all patients with metastatic disease were 15 months and 44.6% ± 6% respectively. Table-1

reveals the effects of some clinicopathological characteristics on the overall survival. The patients with bone metastasis had a significantly better overall survival compared to those with visceral metastasis. (74.2%vs.36.1%, P= 0.04)(Figure-1)Among those patients who were non-metastatic at the time of referral, the time left to metastasis had a significant effect on the overall survival from metastasis manifestation. In comparison with premenopausal patients, the overall survival was relatively better in postmenopausal cases. (59.4% vs. 38.5%, P=0.1)(Figure2)

Discussion

In this study, we found a significantly worse overall survival for the patients with metastatic breast carcinoma with visceral recurrences compared to those with bone metastasis. In addition, overall survival in the cases with shorter disease free interval (less than 18 months) was significantly lower than those with longer disease free interval. In comparison with premenopausal patients, overall survival was relatively better in postmenopausal cases. The metastatic breast carcinoma is an incurable disease. The main purpose of treatment is to extend survival while preserving quality of life. In patients with the metastatic breast carcinoma, disease free interval, location of metastasis (visceral versus bone), hormone receptor status, menopausal status and history of previous treatment have been suggested to affect the survival.

Compatible with the results of our study, some other trials reported more indolent disease courses in the patients with bone metastases compared with

Table 1: The effect of some clinicopathological features on the overall survival of patients with metastatic breast carcinoma

Characteristics	Number	2-year overall survival	Log-rank p-value
Menopausal status:			
Postmenopause	42	59.4%	0.1
premenopause	73	38.5%	
ER status:			
ER positive	33	52.4%	0.32
ER negative	45	42.8%	
undefined	37		
Metastatic site:			
Bone	23	74.2%	0.04
visceral	74	36.1%	
Stage at referral:			
Metastatic	45	47.3%	0.22
Non-metastatic	70	42.4%	
Time to recurrence*			
≤18 months	22	28.9%	0.04
>18 months	48	61.8%	

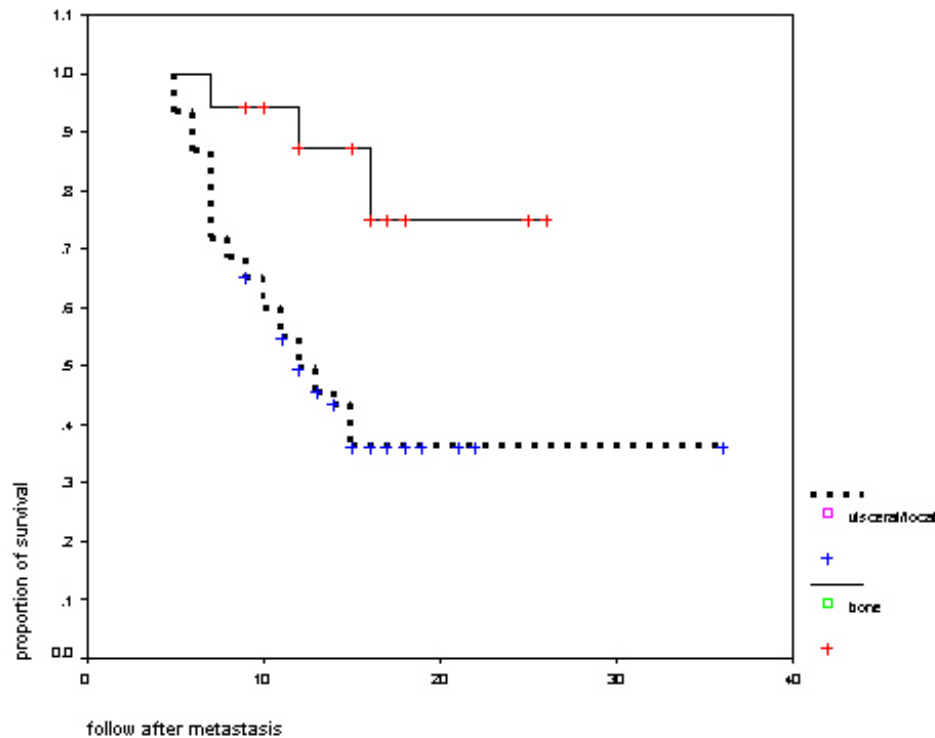*: The time from diagnosis to recurrence in non-metastatic cases at referral

Figure 1: Overall survival of patients with bone metastases versus visceral metastases (P=0.04)

those with visceral involvements. (3-4)The adverse effect of shorter disease free interval on prognosis has also been suggested in the other series. In contrast to other results (5-6), we did not find any association between hormone receptor status and survival rate in the metastatic breast carcinoma. In the study by Yamamoto et al, History of adjuvant chemotherapy, hepatic involvement, disease free interval of less than 24 months and serum LDH level were considered as prognostic indexes and accordingly patients were categorized into three risk groups of low, intermediate and high. The median survival in low, intermediate and high risk groups was 45.5, 24.6 and 10.6 months respectively (p<0.0001). (7)

In our study, although postmenopausal cases had relatively better survival compared to premenopausal ones, the difference did not reach to statistical significance. In the study by Ezzat et al on 1289 nonmetastatic breast carcinoma patients, cases were categorized based on age of less than 40, 40 to 50 and more than 50. They did not found a significant effect of age on overall survival and disease free survival (DFS). (8)

Venturini et al. designed a trial to evaluate the effect of previous adjuvant chemotherapy on overall survival, progression free survival and objective response rates in the metastatic breast carcinoma

patients treated with CEF (cyclophosphamide, epirobicine, and 5FU). Besides to higher objective response rate ((p=0.02), Chemotherapy naive cases had significantly longer median survival (21.1 months) compared to those with a history of adjuvant CMF –based chemotherapy (15.3 months) or anthracycline based chemotherapy (15.8 months). In multivariate analysis, the history of adjuvant chemotherapy proved to be a significant prognostic factor. (9) In our study all the patients who were nonmetastatic at the diagnosis had received adjuvant chemotherapy. There was no significant difference in survival between metastatic cases at diagnosis and nonmetastatic patients who experienced recurrence during follow-up. Although metastatic cases at the diagnosis had no history of chemotherapy, the diagnosis of the metastasis at presentation may indicate a more aggressive course.

Conclusion

In our study, disease free survival (DFS) was the most important factor for overall survival in the patients with metastatic breast cancer. The patients with longer DFS (>18month) had better overall survival. Overall the patients with bone metastasis had better survival than visceral metastasis.

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