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Effect of chemotherapy on survival in metastatic breast cancer

Alexander H.G. Paterson, M.D., Olga Szafran, B.Sc., Faye Cornish, B.Sc., Alan W. Lees, M.D., John Hanson, M.Sc.
Breast Unit, Departments of Medicine, Radiation Oncology and Biostatistics, Cross Cancer Institute and University of Alberta, Edmonton, Alberta, Canada

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Summary

In order to assess the impact of modern combination chemotherapy on overall survival of metastatic breast cancer patients, we retrospectively analysed survival data of those patients who presented with breast cancer and developed metastases at our clinic from 1971–78 inclusive. Our results indicate a trend towards improved survival from onset of first distant metastasis after 1975. Assessment of survival by treatment modality revealed significantly longer survival from first metastasis for those patients receiving predominantly endocrine treatment compared to chemotherapy, median survival being 32.5 versus 23 months for endocrine therapy and chemotherapy respectively. Patients receiving adriamycin in combination with other drugs, had longer survival from first metastasis than those patients receiving chemotherapy without adriamycin (median survival being 25 versus 18.5 months respectively). These differences are most probably due to patient selection. On the basis of these results it would appear that chemotherapy may be improving short-term survival in some patients, but is making no major impact on long-term survival.

Introduction

Despite the increased use of more aggressive combination chemotherapy for metastatic breast cancer with treatment starting earlier in the course of the disease, it is difficult to demonstrate that there has been a significant improvement in survival compared to less aggressive approaches, such as sequential single agent therapy (1, 2). With their variable impact on quality of life, we must carefully examine the effect of these treatment policies on survival, not only within clinical trials, but within the setting of an ordinary clinical practice over a period of time. Metastatic breast cancer encompasses a spectrum of disease with such a variable natural history, that a patient's ultimate survival after disease recurrence may depend as much on the biology of the disease as on the influence of systemic treatment.

The therapeutic management of metastatic breast cancer has evolved from the introduction of oophorectomy in the late 1800s to other endocrine ablative procedures, additive hormones and anti-hormones, single agent sequential chemotherapy and most recently, combination che-

Address for reprints: Dr. A.H.G. Paterson, Dept. of Medicine, Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta, Canada T6G 1Z2.

motherapy (3, 4, 5, 6, 7). Combination chemotherapy is curative in certain malignancies such as Hodgkin's disease, with early demonstrable improvements in survival of patients (8). Principles of chemotherapy, derived from cell kinetics have been rigorously applied to the chemotherapy of breast cancer but it is now clear that metastatic breast cancer is rarely curable. Patients with metastatic breast cancer who respond to treatment have consistently been shown to have longer survival than non-responders (9), yet a significant improvement in the overall survival of a patient population has not been convincingly demonstrated. Most survival data are not easy to interpret since they are presented from start of systemic treatment and are thus biased by institutional management policies and referral patterns.

The range of survival in untreated breast cancer patients is known to be considerable (10). A small proportion of metastatic patients with osseous or soft-tissue metastases survive many years with only symptomatic treatment. In contrast, there are those who die from rapidly progressive visceral metastases within three to six months. In most clinics a particular therapy is selected by assessing the patient with regard to prognostic factors such as bulk of disease, sites of disease, and estrogen receptor status (11, 12). Cytotoxic chemotherapy has contributed to effective symptom palliation and produced high response rates, but in many patients, significant side-effects and toxicity occur and the quality of life is variable. Based on evidence from response rates, many centers, particularly in North America, have suggested that treatment policy should evolve toward more aggressive combination chemotherapy started earlier in the course of the disease. Such a policy may have serious implications for the quality of life in many metastatic patients since the opportunity for a high quality endocrine remission may be foregone. In patients who do respond to chemotherapy, the role of maintenance treatment is largely unknown and some patients may be overtreated. Prolonged administration of cytotoxic chemotherapy may lead to chronic toxicity in those patients who may have survived just as long or longer on other therapies, thereby having an adverse effect on long-term survival. The adverse effects of acute toxicity of cytotoxic chemotherapy on some metastatic patients who may be quite frail may have been underplayed.

To assess the impact of modern combination chemotherapy on survival of metastatic breast cancer patients we retrospectively analysed survival data of those patients presenting for primary treatment at the Cross Cancer Institute, Edmonton, Alberta, during two sequential time periods when treatment policies changed. All of the patients studied developed metastases from 1971 to 1978 inclusive. It was our expectation that patients receiving chemotherapy for metastatic disease during 1975–1978 would have at least the same or better overall survival from the time of first metastasis when compared to those receiving chemotherapy during 1971–74, due to the institution of chemotherapy earlier in the course of the disease and the more frequent use of chemotherapy combinations containing adriamycin during 1975–78.

We also retrospectively analysed the survival of patients by the predominant type of treatment received. In this way, we compared survival of patients who received combinations containing adriamycin to those who did not receive adriamycin. In addition, the survival of patients receiving predominantly hormone therapy was compared to those receiving predominantly chemotherapy.

To gain an overview of the impact of chemotherapy on survival rates in breast cancer compared to Hodgkin's disease (where significant improvements in survival have been made) we compared the 3 and 5 year survival rates from 1963 to 1979 of patients with these two diseases registered in the Provincial Cancer Registry.

Patients and methods

1. Comparison of survival in Hodgkin's disease and breast cancer: 1963–79