

An Autopsy Study of Metastatic Sites of Breast Cancer¹

Enrico Viadana, Richard Cotter, John W. Pickren, and Irwin D. J. Bross

Departments of Biostatistics and Pathology, Department of Health, State of New York, Roswell Park Memorial Institute, Buffalo, New York 14203

SUMMARY

A total of 374 women with cancer of the breast died and were autopsied at Roswell Park Memorial Institute. This patient population was examined with regard to age at the time of onset of symptoms, duration of disease, and distribution of metastases in various organs. The distribution of metastases in a younger and older age group in relation to the duration of the disease was analyzed. It appears that, with 50 years of age as the dividing point, cancer of the breast is more aggressive in its metastatic spread in younger women than in older women; however, age difference is not a factor when younger women survive more than 5 years.

INTRODUCTION

The purpose of this study is to ascertain whether the distribution of metastases from cancer of the breast is related to the age of the patient. Data were obtained from the charts of 374 women with primary breast carcinoma who died and were autopsied at Roswell Park Memorial Institute between 1955 and 1967. The sites of the metastatic lesions were obtained from the autopsy records, and this information was placed on cards for computer analysis.

MATERIALS AND METHODS

In order to separate women with higher and lower degrees of ovarian activity, an age split was necessary. Since the age at menopause was not recorded in the autopsy charts, an equivalent age was obtained from a follow-up study of 2637 primary breast carcinomas from the National Surgical Adjuvant Breast Project. In this cooperative study, almost 100% of the patients younger than age 50 were still menstruating. The converse held true for women above 50 years of age. Thus, we chose age 50 years as a dividing line in our study to separate the patients into groups of women with higher and lower ovarian activity.

The duration of the disease in months from the time of symptoms to death was also used as a criterion for dividing the patients into 2 groups: those surviving less than 5 years and those surviving more than 5 years. This division was made because this period of time is often used by physicians to calculate a so-called "cure rate."

The sites of metastases were listed as shown in Table 1. These sites are separated according to organs or tissues in the body. Metastases were common in the respiratory system, including the pleura and lungs, and in the digestive system, including the liver. Metastases were also fairly common in lymph nodes of the neck, thorax, abdomen, and pelvis. Endocrine organs were quite frequently seeded by tumor: thyroid, adrenals, and together the pituitary and/or parathyroid. Two other broad metastatic subdivisions are the osseous system and CNS² (the latter included 11 sites).

RESULTS

The total number of metastases including each site and in the CNS only were the first factors analyzed. The survival of the patients (subdivided in a less than 5-year or more than a 5-year period) and age of the patients at time of onset of symptoms (subdivided into under 50 years and 50 years and over) were taken into consideration.

All the possible comparisons for each variable are shown in Table 2. A consistent pattern emerges. The younger women have a more generalized disease. The median of the number of metastases below age 50 years is 9, compared to a median of 7 in the older group. A similar difference is found when the women surviving less than 5 years are considered. The same holds true if the comparison is made between the 2 survival periods in the younger age group with a median of 9 *versus* 7. The difference between the 2 age groups seems to disappear in women who survive more than 5 years. No difference was detectable in the older women with regard to the number of metastases by years of survival.

The metastatic behavior of the CNS did not show any of the differences found in the previous comparisons except in patients below age 50 years. Here a significant difference exists between the 1st 5 years and the subsequent time period.

The frequency of metastases in the various sites is generally higher in patients below age 50 years (Table 1). A few sites showed a significant difference by comparing the frequency of metastasis in the 2 age groups below and above 50 years and, particularly, by taking into account, besides the age at onset of symptoms, the 1st 5 years of survival. The liver, the bones, the endocrine system (adrenals, thyroid, and pituitary, and/or parathyroid), and the osseous system exhibited a striking difference in number of metastases in the 2 aforementioned comparisons. There was also a significant difference in the

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²The abbreviation used is: CNS, central nervous system.

Table 1
 Percentages of patients with metastases at various sites
 Autopsy data are of 374 women with primary carcinoma of the breast.

Sites	Survival status					
	All patients			Patients surviving <5 yr		
	Age at diagnosis (%)		<i>p</i> ^a	Age at diagnosis (%)		<i>p</i>
	1-50 yr	50+ yr		1-50 yr	50+ yr	
Pleura	55	57	N.S. ^b	59	57	N.S.
Lungs	70	62	N.S.	71	64	N.S.
Liver	69	62	N.S.	80	56	<0.01
Thyroid	30	17	<0.01	33	15	<0.01
Adrenals	30	23	N.S.	33	26	N.S.
Pituitary ^c	26	17	<0.05	28	17	<0.05
Endocrine system ^d	57	40	<0.01	63	40	<0.05
Diaphragm	28	27	N.S.	31	29	N.S.
Peritoneum	33	23	<0.05	32	20	<0.05
Bones	79	65	<0.01	81	65	<0.01
Cerebrum	20	12	<0.05	21	15	N.S.
Choroid plexus	03	00	<0.05	03	00	N.S.
Leptomeninges	07	02	<0.01	04	06	N.S.
Dura	26	19	N.S.	23	17	N.S.

^a Chi square test.
^b N.S., not significant.
^c And/or parathyroid.
^d Adrenals, thyroid, pituitary, and/or parathyroid.

Table 2
 Comparison of the number of overall metastases and number of metastases in the CNS by age in years at time of diagnosis of 374 primary carcinomas of the breast (autopsy data)

Variable	Survival (yr)	Medians		<i>p</i> ^a
		Under 50 yr	Over 50 yr	
No. of metastases		8.5	7	<0.05
No. of metastases	1-5	9	7	<0.01
No. of metastases	5+	7	7	N.S.
No. of CNS metastases		1	1	N.S.
No. of CNS metastases	1-5	2	1	N.S.
No. of CNS metastases	5+	1	1	N.S.

Variable	Age at diagnosis (yr)	Medians		<i>p</i> ^a
		Under 5 yr	Over 5 yr	
No. of metastases	1-50	9	7	<0.05
No. of metastases	50+	7	7	N.S.
No. of CNS metastases	1-50	2	1	<0.05
No. of CNS metastases	50+	1	1	N.S.

^a Wilcoxon test.

metastatic frequencies of the endocrine system and liver in patients below age 50 years in accordance with the length of their survival (*i.e.*, below or above 5 years). Metastasis in the choroid plexus and leptomeninges seemed to be more frequent

in women below 50 years. The peritoneum, the pituitary gland, and cerebrum showed differences with borderline probability values. The pattern for either only the number of metastases or the various sites is rather consistent.

DISCUSSION

The difference in the number of metastases between an older and younger age group divided at age 50 years points toward a greater tendency in younger women with fatal breast cancer to show a more generalized and extensive metastatic disease. The 1st 5 years appears to be particularly crucial. When the data are expanded to the time beyond the 1st 5 years, the spread of cancer in the 2 age groups is not significantly different. Another feature (Table 1) is the consistently higher percentage of involvement in most metastatic sites for the younger age group.

The data do not show significant results in the comparison of the 2 age groups for those patients who survived more than 5 years. Several factors can account for such an outcome. First, the sample size of young women who survived more than 5 years (42 women) is quite small. In other words, in order to detect a significant difference in a sample size this small, the magnitude of the effect would have to be very large. Another factor that may account for the similar metastatic behavior of the 2 age groups after the 1st 5 years is the possibility that women enter menopause after diagnosis and thereby gain a more favorable status. The more generalized disease in the younger age group might suggest a more frequent lymphohematogenous spread or a faster tumor-doubling time. This difference may be related to a decrease in the host defense system that might be dependent on hormonal factors. Such consideration is only speculative since the difference may also be related to the tumor itself or to difference in the circulatory system in older and younger patients. Both circulations are affected by age.

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