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Breast Cancer in Israel, 1960–1975. II. Effects of Age and Origin on Survival*

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Abstract—*The effect of age and origin on survival, measured by the life table method, was examined for* 10,702 *breast cancer patients diagnosed in Israel between* 1960 *and* 1975. *In contrast to a major American study, we found no differences in survival between younger and older women with breast cancer.*

In stages II, III *and* IV, *immigrants of Western origin survived significantly longer than native-born Israeli women and immigrants from other Asian or North African countries. This suggests that the different disease patterns (slow-growing, 'insidious' vs fast-growing, 'fulminant') may be distributed unequally among the several population groups, favoring women of Western origin. Factors accounting for this unequal distribution are undoubtedly genetic and environmental combined.*

The identification of groups of women with more aggresive disease may influence decisions about the use of more aggressive therapy.

INTRODUCTION

IN ISRAEL, cancer of the breast is the largest single cause of cancer death among women. Each year there are over 1000 new cases and 400 deaths from this disease [1].

Survival of cancer patients has traditionally been expressed in terms of fixed-time survivorship. This technique has been criticized [2] because it focuses only on survivors, deleting from the analysis entirely those who have died or were lost to follow-up.

An alternative way to look at survival, the life table method [2–4], has the important advantage of including in the analysis all patients, each according to the amount of time he lived following the diagnosis. It also permits inclusion of patients followed for only a portion of the follow-up period.

In this report we describe the outcome of breast cancer cases diagnosed in Israel during the period 1960–75 in terms of rate of dying, computed by the life table method, and examine the influence of age and origin on the rate of dying.

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Population of Israel

Israel is a country of immigrants, the result of waves of immigration from over 100 countries in the last 60 yr [5]. Half the 3,000,000 Jews of Israel are immigrants, and of the half who are native-born only 20% are second generation Israelis. In addition, there are 600,000 non-Jews, of whom 75% are Moslem Arabs. Among the immigrants to Israel, 55% came from Western countries (Europe, the Americas, South Africa, Australia, New Zealand), 25% from North African countries and 20% from Asia and other parts of the Middle East [6].

The risk of developing cancer varies among the different immigrant groups. Immigrants from Western countries are at higher risk of developing most cancers than immigrants from Asian or North African countries, a generalization which is particularly true in breast cancer [7]. For the years 1960–75, the average annual incidence of breast cancer for every age group was 2–3 times higher in European–American ('Western') immigrants than in Asian and North African immigrants. The incidence in native-born Israeli women fell between the two groups, but was nearer to that of the European–Americans [8]. Arabs showed the lowest breast cancer incidence of all groups [7].

MATERIALS AND METHODS

Since its inception in 1960, the Central Cancer Registry of the Israel Ministry of Health [9] has collected data on all cases of cancer in Israel. Registry personnel routinely extract demographic information and diagnostic data from reports received and assign stage to each new case according to a uniform set of criteria, on the basis of the clinical and pathological information available.

The staging scheme of the Cancer Registry for the entire 16-yr period employed the following criteria:

Stage I. Cancer confined to the breast.
Stage II. Cancer found also in axillary lymph nodes.
Stage III. Cancer spread to adjacent tissues (e.g., skin, chest wall) or spread to axillary nodes in the case of a medial breast tumor.
Stage IV. Distant metastases.
Unstaged. Insufficient information available for staging by the above scheme.

In 91% of breast cancer cases the diagnosis was confirmed histologically.

Because active annual follow-up of cases by the Cancer Registry was not feasible, it was necessary for us to check the adequacy and reliability of Cancer Registry data for use in survival studies. We cross-checked a sample of 200 breast cancer patients listed as "living" by the Cancer Registry against recently updated Population Registry files. We found that less than 2% of women under age 76 who were listed as living by the Cancer Registry were deceased according to Population Registry information. The percentage was higher for women 76 and older, and for this reason, women were considered 'lost to follow-up' at age 76. This necessitated our excluding from the survival analysis 554 women diagnosed after age 75. In addition to these, 130 were excluded because year of birth was unknown and seven others because of miscellaneous errors.

Cause of death was decided on the basis of information available. This included hospital case summaries, autopsy reports and, where no other information was available, death certificates. In the survival analysis, patients dying from causes other than breast cancer and from unknown causes were considered 'lost to follow-up' at the time of death.

The survival analysis was accomplished with the use of SPSS Procedure Survival [10], which incorporates the method of Lee and Desu [11] for the chi-square comparison of pairs of survival curves. This is a non-parametric method which evaluates differences between whole curves rather than between individual points on the curves.

Because of incomplete registration and less reliable reporting from the non-Jewish population [12], only data on Jewish women living in Israel have been included in this analysis.

RESULTS

During the 16 yr, 1960–75, 10,702 new cases of breast cancer were diagnosed in Jewish women. The distribution according to origin and age at diagnosis is presented in Table 1. Approximately 34.4%, of the population of new breast cancer cases were under 50 yr of age, 51% were between 50 and 69, and 13.4% were 70 and over. Among the women born in Israel, 61.4% were under 50, while 48.5% of the Asian and North African immigrants were under 50, compared to only 28.8% of the immigrants from Western countries.

Causes of death.

Of the 10,702 cases, 5383 (50.3%) were dead at the end of the study period. Table 2 shows the distribution of causes of death according to age at diagnosis. In 4415 (82%), cause of death was known. As has been shown in other studies, with advancing age at diagnosis the proportion of deaths from breast cancer fell and deaths from other causes, the 'competing risks,' increased. For the entire group, 86.5% died of breast cancer. Among women diagnosed under the age of 50, 90.7% died of breast cancer, while among women 70 and older, only 76.9% died of breast cancer.

Effect of age on rate of dying

Figure 1 compares the rates of dying in four age groups of breast cancer patients in our population, and Table 3 shows 20 and 50% mortality times for these age groups. Although there were significant differences in survival between pairs of age groups in each stage, these showed no consistency of direction. For example, in stages II and IV, the 50–59 age group had the worst survival, and in stage III, the best. In stage II, women 70 and older had the best survival, and in stage IV, the worst.

Effect of origin on rate of dying

Figure 2 compares the rates of dying among the four major Jewish population groups. In stage I, there were no differences in survival

Table. 1. *Distribution of new breast cancer cases in Jewish women in Israel*, 1960–1975, *according to place of birth and age at diagnosis*

Age (yr)	Israel	Asia	N. Africa	West	Unknown	Total
Under 50	468	467	337	2061	349	3682
50–59	133	230	174	2158	276	2971
60–69	101	187	107	1828	266	2489
70 plus	52	94	59	1069	156	1430
Unknown	8	2	1	9	110	130
Total	762	980	678	7152	1157	10,702

Table 2. *Causes of death in female breast cancer patients diagnosed in Israel*, 1960–1975

Age at diagnosis (yr)	Died of breast cancer No.	(Per cent)	Died of other cause No.	(Per cent)	Total dead of known cause No.	(Per cent)	Died, causes unknown	Total dead
Under 50	1411	(90.7)	145	(9.3)	1556	(100.0)	267	1823
50–59	1107	(88.8)	140	(11.2)	1247	(100.0)	244	1491
60–69	785	(83.7)	153	(16.3)	938	(100.0)	272	1210
70 plus	518	(76.9)	156	(23.1)	674	(100.0)	185	859
Total	3821	(86.5)	594	(13.5)	4415	(100.0)	968	5383

Table 3. *Twenty and* 50% *mortality times* in breast cancer patients, according to age at diagnosis*

	Number	20% mortality (yr)	50% mortality (yr)
Stage I			
Under 50	823	12.9	over 15
50–59	632	9.2	over 15
60–69	514	9.3	over 15
70 plus	151	over 5.7	—
Stage II			
Under 50†	1123	2.8	13.8
50–59	857	2.3	8.9
60–69†	637	3.0	11.8
70 plus†	158	3.7	over 5.7
Stage III			
Under 50	414	1.2	2.8
50–59‡	333	1.7	5.8
60–69	269	1.2	5.0
70 plus	97	1.5	3.5
Stage			
Under 50†	158	0.3	1.6
50–59	154	0.3	1.0
60–69	169	0.3	1.4
70 plus	65	0.2	0.9

*Deaths from breast cancer only.
†Survival significantly greater ($P<0.02$) than 50–59.
‡Survival significantly greater ($P<0.001$) than under 50.

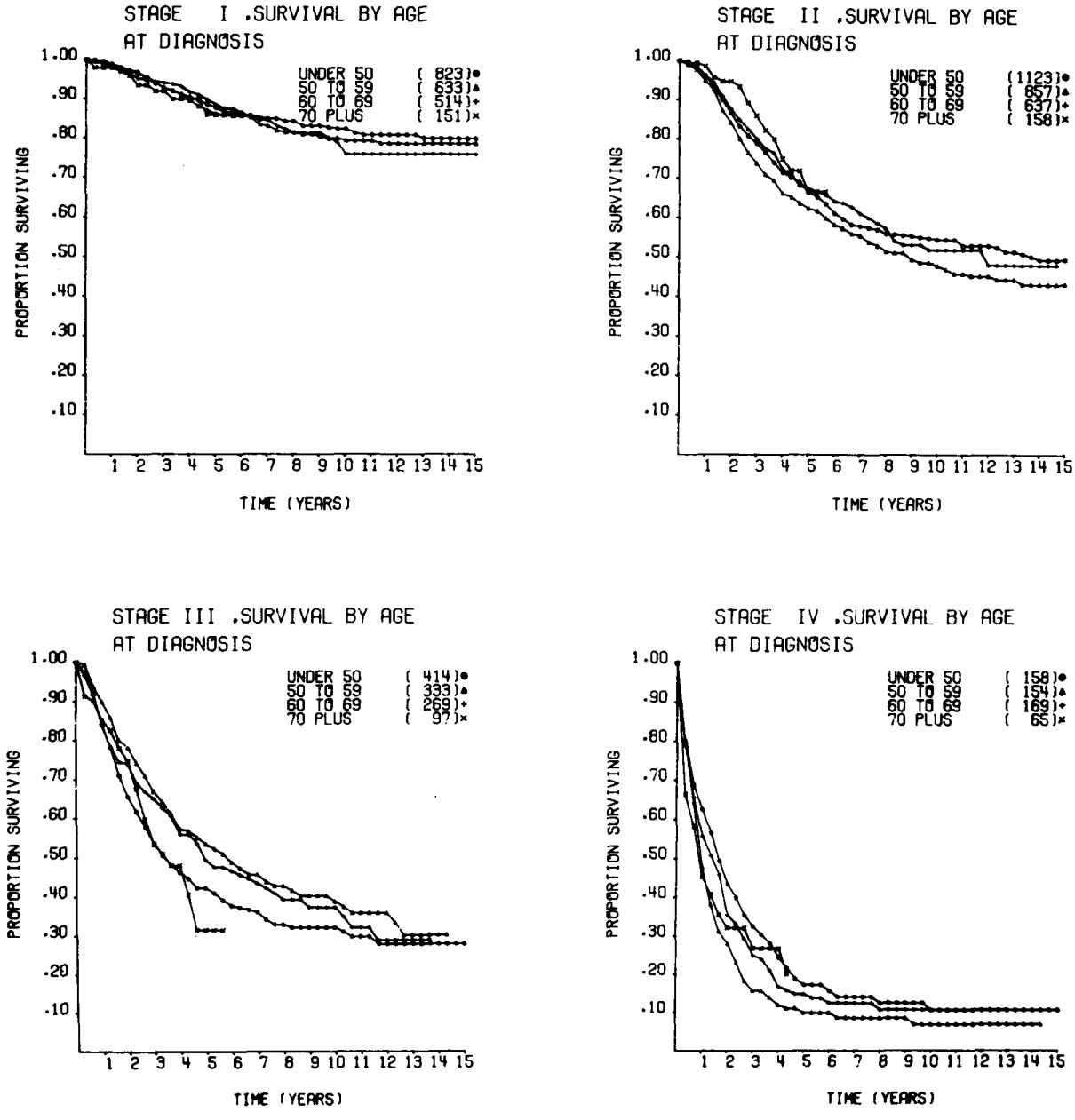

Fig. 1. Survival of breast cancer patients according to age at diagnosis, within each diagnostic stage. Numbers in parentheses represent initial number of cases in each category. Unstaged not shown. Age group '70 plus' includes only women 70–75.

among the four groups. In stages II, III and IV, immigrants from Western countries showed a longer survival compared to other groups, and North African immigrants generally had the shortest survival. Table 4 shows 20 and 50% mortality times for these population groups.

DISCUSSION

In a report on outcome in 3558 American women with breast cancer, Mueller *et al.* [2] showed that three age groups (21–50, 51–70, 71–100) died from their cancers at different rates, the younger women surviving significantly longer than the older women, leading these workers to conclude that breast cancer was "more rapidly lethal" in older women. Our data, on 10,702 Israeli women, fail to support their conclusions: no clear pattern of better or poorer survival emerged among the several age groups.

Mueller's report, however, is enormously strengthened by active and nearly complete case follow-up, whereas ours, because of the absence of active follow-up, was based upon the assumption that a woman not reported to be dead was assumed, up to age 76, to be

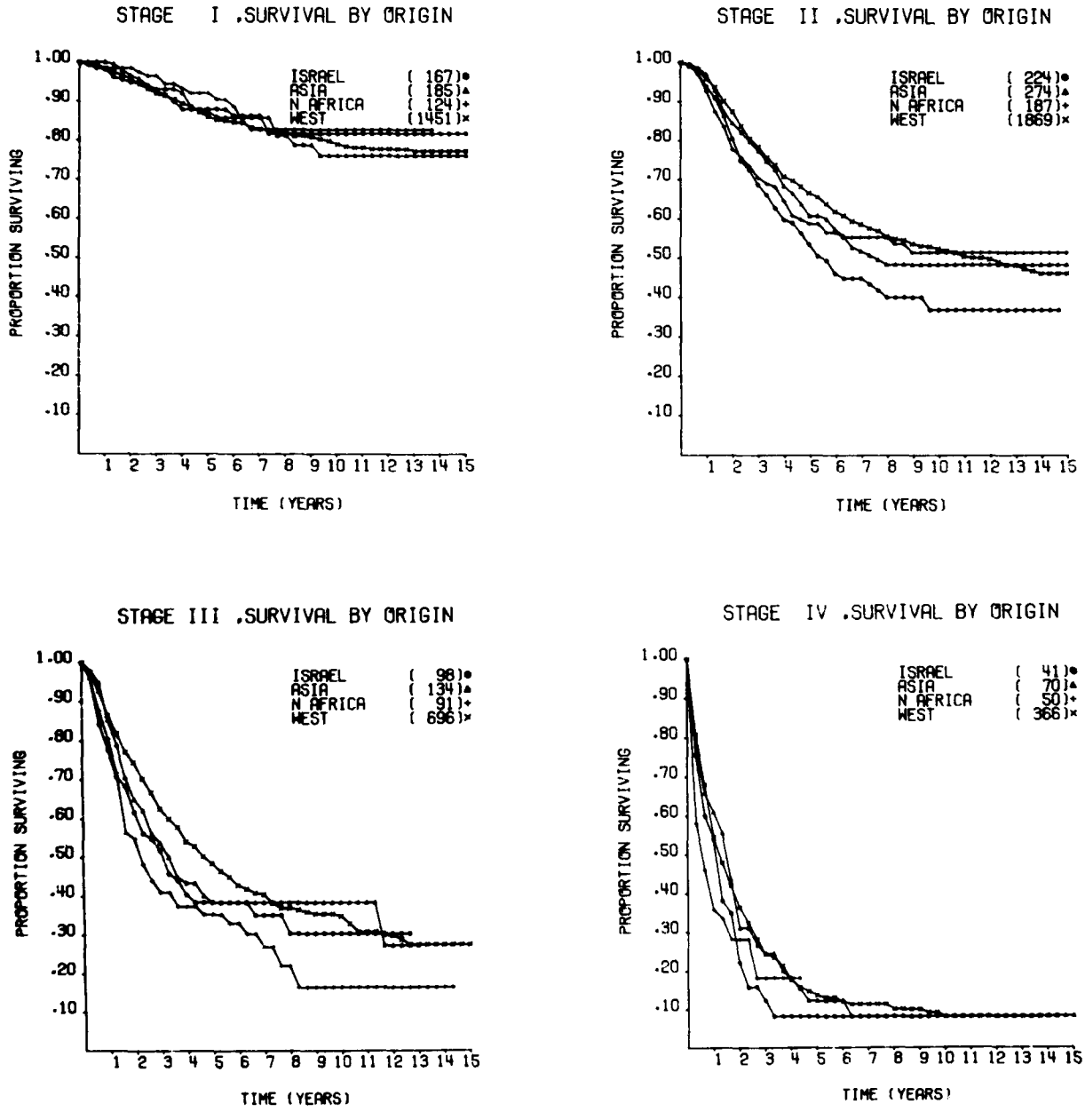

Fig. 2. Survival of breast cancer patients according to place of birth, within each diagnostic stage. Numbers in paretheses represent initial number of cases in each category. Unstaged not shown.

alive. We tested this assumption (see Materials and Methods) and found it to be valid, although we realize that active follow-up would have strengthened the validity of our findings by eliminating the need for this assumption and by enabling us to include women diagnosed after age 75.

Similarly, we were unable to document cause of death in 18% of our patients. If there were a greater proportion of breast cancer deaths among the older women whose cause of death we did not know, compared to the younger women, a bias might have been introduced which would have suppressed faster rates of dying among the older women. This does not seem a likely possibility. On the contrary—deaths of older breast cancer patients are more likely to be due to 'competing risks' than among younger patients [13].

Therefore, despite the deficiencies in our material, we think our results, in our defined population, are valid. Before we can conclude that breast cancer is or is not a more rapidly lethal illness in older women, studies will need to be performed in different places on other populations.

We have also shown that breast cancer patients who immigrated from Western count-

Table 4. Twenty and 50% mortality times in breast cancer patients, according to origin*

	Number	20% mortality (yr)	50% mortality (yr)
Stage I			
Israel	167	over 15	—
Asia	185	8.2	over 15
N. Africa	124	over 13.7	—
West	1450	9.5	over 15
Stage II			
Israel	224	2.0	5.5
Asia	274	2.6	7.5
N. Africa	187	1.9	over 15
West†	1869	2.8	11.8
Stage III			
Israel	98	0.9	3.1
Asia	134	1.3	3.3
N. Africa	91	1.0	2.6
West†	696	1.5	4.7
Stage IV			
Israel	41	0.3	1.1
Asia‡	70	0.3	1.5
N. Africa	50	0.2	0.6
West‡	366	0.4	1.2

*Deaths from breast cancer only.
†Survival significantly greater ($P<0.02$) than Israel and N. Africa.
‡Survival significantly greater ($P<0.02$) than N. Africa.

ries lived longer than native-born Israelis and other immigrant groups. The reason for their improved survival in stages II, III and IV, is not clear. It is possible that they have increased access to medical care or make better use of it. In a chronic disease such as metastatic breast cancer, closer medical supervision or adherence to treatment regimens might well increase survival, and there is some evidence that immigrants to Israel from Western countries do, in fact, utilize medical services more effectively than other immigrant groups [14].

Modan [12] has described improved survival in Western immigrants to Israel suffering from gastric cancer. He rejected superior medical care as the sole explanation for their improved life expectancy and suggested the possibility that "different disease patterns (fulminating vs insidious)" developed in the various population sub-groups accounting, in part, for their different survival rates.

The existence of different patterns in breast cancer has been postulated by many investigators. Baum [15], quoting Haybittle, and Mueller and Jeffries [13], suggest the existence of two distinct groups in breast cancer, one group, the large majority of patients, dying at a rate of 8% per year (50% mortality: 6 yr) and a second, smaller group, with a more fulminant disease pattern, dying rapidly, 50% within 10 months of the diagnosis. This division cuts across the artificial boundaries set up by the process of staging and could explain the improved survival in our Western immigrants: among all patients diagnosed at apparently 'advanced' stages (II, III and IV), the patients of Western origin may contain a greater proportion with the slower-dying pattern compared to the other immigrant groups, the basis of this difference being the combined environmental and genetic background of the several ethnic groups.

We are in a period of rapidly changing ideas about the development, progression and treatment of breast cancer, the first such period in decades. Investigators are advocating less extensive surgery for some groups of

breast cancer patients and for others are recommending that chemotherapy be added to the primary surgical treatment of the disease.

Methods of distinguishing at the outset patients with poorer prognoses from those with better prognoses may ultimately assist clinicians to decide how to treat their breast cancer patients, decisions which have been more or less dictated by tradition since the end of the last century. It would seem to be of particular importance to clarify whether age influences prognosis, and we hope that future investigations will address themselves to this issue. Furthermore, since many countries, particularly in the Western world, contain large immigrant groups, it appears desirable, in view of our results, to examine the influence on prognosis of origin among other demographic features, in order to further refine the 'prognostic profile' which is emerging for breast cancer and other malignancies as well.

CONCLUSIONS

1. In 10,702 Israeli Jewish women with breast cancer, no differences in survival were seen between older and younger women, contradicting earlier reports which suggested that breast cancer was more rapidly lethal in older women.

2. In all but the earliest stages, immigrants from Western countries survived significantly longer than native-born Israelis or immigrants from Asian, Middle-Eastern and North African countries. These differences probably reflect a combination of disease pattern differences among the different origin groups and differences in the kind of medical care they receive.

3. Changing ideas about breast cancer treatment make it important to seek ways of distinguishing, at the time of diagnosis, patients with better prognoses from patients with poorer prognoses.

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