PAPERS AND ORIGINALS

The curability of breast cancer

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Summary

The age-correlated survival rates for 982 women treated for localised breast cancer were analysed retrospectively. Analysis by size of the primary cancer showed that those with smaller cancers had a significantly higher survival rate and a significantly reduced probability of dying of cancer. Cured groups of patients were identified for all but those with the smallest tumours—2·0 cm in diameter or smaller. A longer period of follow-up (to 25 years) is necessary to establish the presence of a large cured group in such cases.

Introduction

Many women with breast cancer may look forward to a long period of survival after treatment, but arguments continue about whether prolonged survival can be regarded as evidence of definitive cure and about the importance of early diagnosis and management in determining prognosis. Bond[1] concluded that "breast carcinoma should be regarded as a disseminated disease, the metastases remaining dormant, or growing at a very slow rate until they present clinically. Although the condition is not necessarily lethal, cure in the sense of its total elimination is impossible by present methods."

In 1968 Brinkley and Haybittle[2] presented the results of an 18-year follow-up of 704 women with breast cancer of all stages. After 16 years the crude survival rate appeared to parallel that of the normal population, suggesting that there was a "cured" group whose mortality rate was similar to that of the controls, but they rightly stated that a longer period of follow-up was necessary to confirm this impression. Recently they reported a further analysis of the series with survival data to 25 years, which seemed to show that parallelism of the observed and expected survival curves might be evident after 21 years.[3] They noted, however, that the probability of long-term survivors dying of breast cancer continued to be much greater than in the normal population.

Meuller and Jeffries[4] studied two groups of patients with all stages of breast cancer—1513 women followed up for at least 15 years and 3225 women followed up for 10 years. They concluded that 80-85% of all women who develop breast cancer die of the disease. They also reported that the proportion of women dying of breast cancer each year was constant over at least 15 years. They pessimistically consider that treatment of breast cancer should not be proposed as a means of influencing either time of death or cause of death.

To attempt to evaluate the probability of a definitive cure in breast cancer a retrospective survey was carried out in a series of women with cancer apparently localised to the breast. They were followed up for 20 years after treatment and their survival rates compared with those of the normal population. It has been suggested that when the mortality rate of a group of patients with cancer after treatment is similar to that of a normal population a cured group may be defined and the size of this group determined.[5] This hypothesis assumes that at the time after which the treated group of patients has a normal expectation of life the cancer for which they were treated no longer influences their mortality rate. This premise has to be considered in the light of the results presented here and earlier studies described above.

Methods

The series consisted of 988 consecutive women with breast cancer referred to the radiotherapy department in Edinburgh between 1943 and 1953 and followed up for a minimum of 20 years. Six patients were excluded from the analysis. No treatment was advised in four patients because of advanced age or the presence of serious intercurrent illness, and two patients refused treatment and so were excluded.

All the tumours were confined to the breast, some with involvement of the overlying skin but none with deep fixation. There was no clinical evidence of spread to the regional lymph nodes or of distant metastases. The size of the primary tumour was determined by

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palpation and measurement against a rule and was recorded for all patients. The sizes ranged from 0·5 cm to 13·5 cm in diameter. The frequency distribution (fig 1) of the recorded tumour sizes showed that non-integer measurements were recorded much less often than integer measurements. The non-integer measurements were rounded-up and the resultant distribution was smoother, with a mode of 3·0 cm and a long tail to the right. Hereafter, tumour size will be referred to as a whole number, which will, by definition, include the rounded-up sizes —for example, 3·0 includes 2·5-cm tumours.

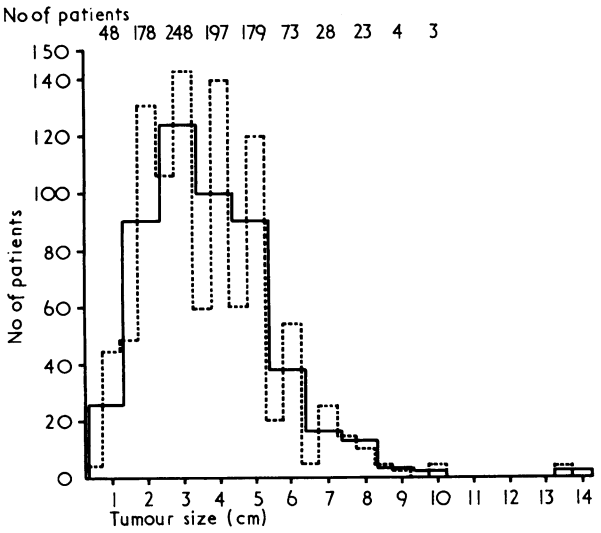

FIG 1—Frequency distribution of tumour size. Broken lines show actual distribution, solid lines show distribution when non-integer measurements were rounded up. Numbers of patients in each "rounded-up" tumour-size group are shown.

Most patients in the series were treated by the McWhirter policy of simple mastectomy followed by deep *x*-ray treatment. In these cases the histological stage of the axillary lymph nodes was unknown. Forty-five patients were managed by radical mastectomy only. In all patients primary carcinoma of the breast was histologically confirmed and in the case of those patients treated by radical mastectomy the axillary lymph nodes examined histologically were not affected by tumour.

All except 11 patients were followed up for 20 years; five patients were lost to follow-up after 13, 13, 17, 18, and 18 years; and two were dismissed from follow-up after 17 years, three after 18 years, and one after 19 years.

Four of the 982 treated patients died after operation, and they were considered in the analysis to have died of breast cancer.

The follow-up data on the cause of death are extremely good. For only thirty-four of the 735 patients who died was the certified cause of death given as breast cancer when there was no previous clinical confirmation of recurrent or metastatic disease. These cases were equally distributed throughout the groups examined and so could not have introduced any significant error into the analysis.

Survival data

Life tables of comparable groups of the female population were prepared and then used to correct the crude survival rates for the effects of age. When the age-corrected survival rate becomes constant —that is, parallel to the time axis—the treated group of patients may be regarded as having a normal expectation of life, and those of the treated group still surviving are often considered to be a cured group.

The survival data were first analysed for all individual groups of tumour sizes. It became clear that we could consider groups in 1-cm stages up to 6·0 cm and then validly consider together as one group cancers measuring over 6·0 cm in diameter.

The age-corrected survival curves for the larger tumours (over 3·0 cm in diameter) are shown in fig 2. There was no real difference between these groups although the survival rate of the patients with

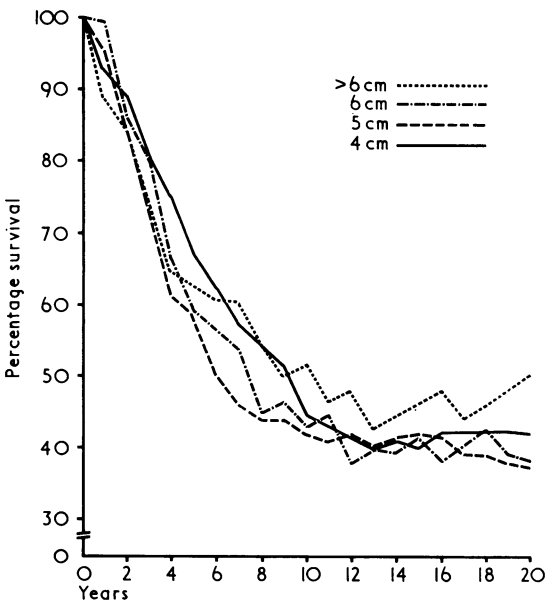

FIG 2—Age-corrected survival rates for women treated for breast cancers over 3·0 cm in diameter.

cancers over 6·0 cm in diameter was marginally better than of the others. In all groups there was a rapid fall in survival in the first five years after treatment to about 60%. After about 10 years the curves were parallel to the time axis, and about 40% then had a normal expectation of life.

Fig 3 shows the age-corrected survival curves for the smaller tumours. Here the differences were clear-cut. For patients with 3·0-cm tumours the survival curve became horizontal after the 13th year —at a level of 50%. In the two groups with the smallest tumours the age-corrected survival curves never settled parallel to the time axis, and there was a considerable drop in survival in the 1·0-cm tumour group between the 15th and 20th year. In both these groups cure might have been assumed if the follow-up period had been only 15 years.

The differences between 20-year survival rates for the 1·0- and 2·0-cm groups and for the 2·0- and 3·0-cm groups were significant at the 5% level. For the other adjacent groups the differences were not significant.

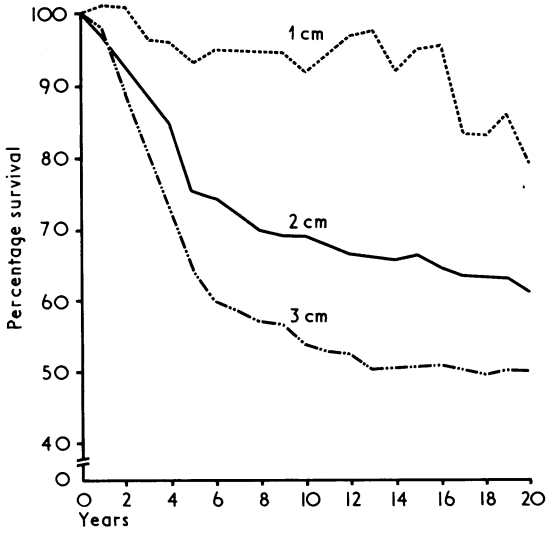

FIG 3—Age-corrected survival rates for women treated for breast cancers up to 3·0 cm in diameter.

Clearly, in this series the results in terms of survival were greatly influenced by treatment when the primary lesion was less than 3·0 cm in diameter, as measured clinically, and when there was no evidence of spread of disease beyond the breast. Yet while 80% age-corrected survival rates at 20 years have been shown for cancers 1·0 cm in diameter, the rates were only 60% for patients with growths of 2·0 cm and only 50% for patients with growths of 3·0 cm in diameter.

To examine more closely the fate of these patients the pattern of local recurrence and distant metastases was studied.

The mean incidence of local recurrence was 8·2% and no statistically significant differences were found among the different groups. There was a surprisingly high recurrence rate (16·7%) among the 48 patients with growths of 1·0 cm in diameter, and no local recurrence was recorded in the eight patients with cancers over 8·0 cm in diameter but confined to the breast.

The incidence of distant metastases (table I) increased steadily with tumour size up to a peak at 6·0 cm; it then declined with larger tumours, indicating the special nature of these large cancers that remain localised to the breast. In this series the mean time from first treatment to the demonstration of metastases was 10·2 years for patients with tumours 1·0 cm or less; this was significantly longer than for all other tumour sizes (mean latent period 4·2 years).

TABLE I—*Percentage of patients developing metastatic disease according to size of primary tumour*

Tumour size (cm):	1	2	3	4	5	6	>6
Percentage of patients developing metastatic disease:	27	38	37	47	51	58	42

As expected, the proportion of deaths from breast cancer in each tumour-size group during the 20 years' follow-up closely followed the incidence of metastatic disease, but there were no significant differences between adjacent groups up to 4·0 cm. The differences between the proportion of deaths from breast cancer in the groups with 4·0-cm tumours and those with 5·0-cm tumours and between those with 6·0-cm tumours and those with tumours greater than 6·0 cm were both significant at the 5% level.

Fig 4 shows the proportion of deaths due to breast cancer compared with deaths from other causes in the treated groups of patients with breast cancer and the relative proportions to be expected in the control population. There was a progressive increase in mortality from breast cancer in patients with tumours up to 6·0 cm. In large tumours the rate declined significantly. The mortality from breast cancer in all groups was much higher than that in the control population. The proportion of deaths from breast cancer was also examined in quinquennial periods after treatment (table II). There was no significant difference in these proportions for tumours in the individual size groups. There was a statistically significant decrease in the probability of dying of breast cancer as the time from initial treatment increased, but even 15 to 19 years after treatment the death rate from breast cancer in the treated groups still exceeded that in the control population.

Conclusions

It has been shown that cured groups may be identified in female patients treated for primary cancer apparently localised to the breast. Normal life expectancy has been shown after the 12th year in all groups except those with tumours 2·0 cm in diameter or smaller.

Patients with these small tumours have significantly higher survival rates, and the failure to show a cured group at this time is considered to be due to the long latent period before metastatic disease emerges in these patients. From our data we predict that a normal mortality rate may be observed in these groups in the sixth quinquennium after treatment.

During 20 years' follow-up an excess mortality rate from

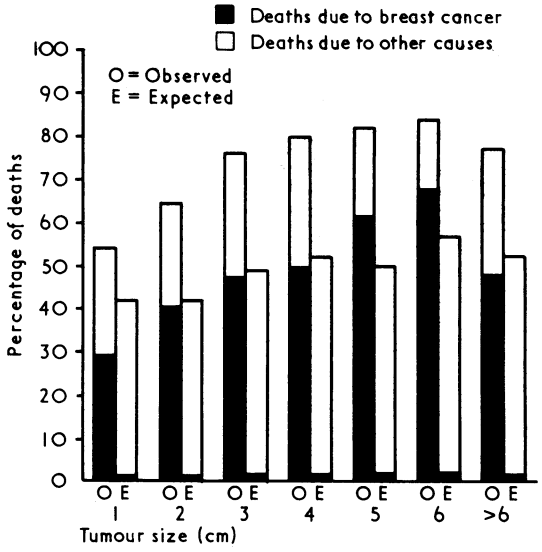

FIG 4—Percentages of patients dying of breast cancer or other causes during 20-year follow-up according to size of primary tumour compared with expected rates.

TABLE II—*Percentage of deaths due to breast cancer in quinquennial periods*

Years' survival:	<4	5–9	10–14	15–19
Percentage of deaths due to breast cancer:	78±4·1	65±7·0	45±10·7	30±10·5

breast cancer remained in all these treated groups irrespective of the size of the primary tumour. This excess mortality rate fell significantly, however, in each successive quinquennial period after treatment.

Early diagnosis, particularly the detection of primary cancers no greater than 3·0 cm in diameter without apparent spread of disease, is of prime importance in obtaining high survival rates and minimising the risk of death from breast cancer. It is therefore important to continue to develop and evaluate population screening programmes and techniques that are safe, consistent, and precise enough to detect small cancers in the breast.

Even in these apparently "early" cases a high proportion of patients treated by excision and radiotherapy will die of metastatic disease, and in this series of patients the number of deaths from breast cancer over the 20 years was about 20 times that expected in the normal population. Consequently it is essential to continue to evaluate effective methods of systemic management with low morbidity that now hold promise of further increasing the prospect of cure in a high proportion of women with primary breast cancer.

References

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