PAPERS AND SHORT REPORTS

Long term prognosis of women with breast cancer in New Zealand: study of survival to 30 years

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Abstract

The long term prognosis of women with breast cancer was studied by analysing retrospectively the 30 year survival of 2019 women with histologically proved breast cancer recorded at the National Cancer Registry in New Zealand between 1950 and 1954. Excess mortality rates for successive five year survival cohorts were calculated from the survival data. From the total cohort the excess mortality rate fell rapidly during the first 10 years and then became low after 20 years. There were no significant differences in excess mortality for the age cohorts. Most of the excess mortality for 20 years was due to deaths from breast cancer.

In this study the prognosis for women with breast cancer approached normal after 20 years and the improvement in prognosis resulted from decreasing death rates from breast cancer.

Introduction

Assessing the prognosis of women with breast cancer is important because it is needed to decide treatment and counsel the patient. Although some prognostic factors are known, such as metastases in axillary lymph nodes,¹ size of the cancer,² and hormone receptor state,³ the long term prognosis is an open question. There are two main difficulties—(a) the insufficient length of follow up in most studies,⁴⁻⁷ and (b) the use of the word “cure” applied to long term survivors.⁴⁻⁵⁻⁸⁻⁹ This word is confusing because researchers have claimed to detect a group of “cured” women yet found that mortality from breast cancer is

higher than expected in that group.⁶⁻⁸ We think that prognosis is a more appropriate word. In this study we report the 30 year survival of 2019 women with breast cancer who had been registered at the National Cancer Registry in New Zealand between 1950 and 1954. We asked: What is the long term prognosis of women with breast cancer? and is this determined by their age at diagnosis?

Subjects and methods

The cohort consisted of 2019 women with breast cancer who had been registered at the National Cancer Registry between 1950 and 1954. All diagnoses had been proved histologically by a pathologist at the time of diagnosis. We corrected for the double registration of one woman who had had two primary cancers between 1950 and 1954. This cohort comprised about 80% of the total incidence between 1950 and 1954 estimated from death certificates of unregistered women.¹⁰

The women were managed in public hospitals and cancer consultation clinics but those managed in private hospitals were excluded because they were not notified to the registry. For early breast cancer the conventional treatment was modified radical mastectomy with or without radiotherapy to the chest wall and axilla. For advanced disease the systemic treatment was endocrinological surgery or chemotherapy, while radiotherapy and mastectomy were used to treat the residual breast cancer.

Medical clerks recorded data about crude survival, age at diagnosis, and cause of death from the medical record, which was written by a medical practitioner, on punch cards which were stored at the National Cancer Registry. These formed the data base for this study. The data for the first two variables were complete to 30 years, but information on cause of death was incomplete in 45 women (2.2%) and recorded to 20 years. Data were also recorded about clinical staging and treatment but we disregarded these because they were largely incomplete.

At the end of 1980 there were 174 women who had not been notified to the registry as dead. We verified that these women were alive by checking the national death registry, electoral rolls, and marriage rolls. Six women were last known to be alive in 1978, 160 in 1980, and eight were untraced. These eight were excluded because there was no evidence that they were alive. For the remaining 2011 there were 30 year survival data for 1860 and survival data between 26 and 29 years for 151, depending on their year of entry into the cohort.

To determine the effect of age at diagnosis on prognosis we divided the total cohort into five age cohorts: 20-34 years (n=60), 35-44 (n=276), 45-54 (n=463), 55-64 (n=452), and 65 and over (n=760). We calculated crude survival probabilities in annual intervals to 30 years

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for each age cohort and the total cohort and then estimated survival rates for equivalent cohorts of normal women from the New Zealand life tables.^{11,12} To correct for increased life expectancy during the 30 years life tables were used from the appropriate time period for each successive five years.¹³⁻¹⁸ We used these survival rates for normal women to calculate expected mortality rates for successive five year intervals in the 30 year study.

To examine the prognosis of women with breast cancer with increasing survival we calculated excess mortality rates per 100 women for successive five year intervals to 30 years for the total cohort and each age cohort. The excess mortality ($M_{t,t+5}$) for any cohort during an interval ($t,t+5$) was defined as the difference between the observed number of deaths ($O_{t,t+5}$) and expected number of deaths ($E_{t,t+5}$), multiplied by 100 and divided by the number of women with breast cancer alive at the start of the interval (N_t). Thus $M_{t,t+5} = (O_{t,t+5} - E_{t,t+5}) \times 100 / N_t$. The expected mortality for a five year interval was the sum of the yearly expected mortalities for normal women with the same age distribution as the women with breast cancer alive that year. The excess mortality for a five year interval measured the mortality of women with breast cancer over and above that expected in the normal population of the same age distribution. Decreasing excess mortality over time indicated improved prognosis for survivor cohorts relative to other women.

We calculated excess deaths due to breast cancer for each five year interval by subtracting the expected number of deaths from breast cancer for normal women from the actual number of such deaths in the cohort of women with breast cancer.

Results

CRUDE SURVIVAL RATES

The figure shows the crude survival rates over 30 years for each age cohort and the total cohort of women with breast cancer. For comparison the figure also shows the expected survival rates for equivalent cohorts of normal women. The 30 year crude survival rate (and median survival time) for the total cohort was 7.5% (3.3 years); for the age cohorts the figures were: age 20-34 years 31.5% (4.5 years), 35-44 years 20.0% (6.0 years), 45-54 years 13.3% (4.8 years), 55-64 years 2.8% (3.2 years), and 65 and over 0% (3.3 years). All curves for women with breast cancer showed a high mortality in the first 10 years and then decreasing mortality in the next 20 years. Relative survival, as measured by the ratio of the crude survival rate of the breast cancer cohort and the normal cohort, appeared to flatten out after 10 years in the cohort aged 20-34 years and after 20 years in the other age cohorts and the total cohort (table I). This suggests that the survival rates of women with breast cancer who were alive after that time approached normal.

TABLE I—Relative survival of women with breast cancer

Age cohort (years)	Time from diagnosis (years)					
	5	10	15	20	25	30
20-34 (n = 60)	0.4870	0.3728	0.3773	0.3499	0.3604	0.3556
35-44 (n = 276)	0.5450	0.4179	0.3537	0.3190	0.2960	0.2733
45-54 (n = 463)	0.5104	0.4109	0.3403	0.3133	0.2979	0.2746
55-64 (n = 452)	0.4353	0.3395	0.2671	0.2240	0.2301	0.1930
≥ 65 (n = 760)	0.4347	0.3418	0.2462	0.2147	0.2484	0.0000
Total (n = 2011)	0.4910	0.3758	0.3078	0.2852	0.2865	0.2622

EXCESS MORTALITY

Table II shows the excess mortality per 100 women for successive five year intervals, conditional on survival to the start of each interval. The table shows, firstly, that the total cohort and all age cohorts had a rapid fall in excess mortality over the 30 years; secondly, that in the total cohort the excess mortality after 20 years was very small (roughly one excess death per 100 women a year for the next 10 years); and, thirdly, that all age cohorts had a similar trend in excess mortality to the total cohort, although in six intervals the excess mortality was negative. We attach little importance to these negative values because the occurrence of only one more death in each interval would have resulted in a positive value in five intervals and a negative value of only 0.2 in the other. Furthermore, in the 20-34 age cohort the excess mortality was near zero after 10 years in contrast with the other age cohorts.

As an approximate test of the equality of excess mortality rates in the different age cohorts for each time interval the excess mortalities for each age cohort were compared by a χ^2 goodness of fit using the total excess for that time interval to generate the expected values. Values of χ^2 were then summed across time periods. This analysis showed that a model based on the excess mortality rates for the total cohort was sufficient for the data in table II. This implies that the excess mortality rates for each age cohort were similar and that each age cohort showed a similar improvement in prognosis with time.

CAUSE OF EXCESS MORTALITY

Table III shows the excess mortality due to breast cancer or other causes in the total cohort per 100 women for each five year interval up to 20 years from diagnosis. It shows that breast cancer accounted for the majority of excess deaths in all intervals up to 20 years and that the other causes accounted for a small part. There was almost a one to one correspondence between the total excess mortality and the excess mortality due to breast cancer. Furthermore, there was a near constant

Cumulative percentage survival curves for total cohort and each age cohort of women with breast cancer. For comparison each graph shows survival of equivalent cohort of normal women. — — — Women with breast cancer. — Normal women.

TABLE II—Excess mortality per 100 women per five year interval. (Figures in parentheses are numbers of women at beginning of each interval)

Age cohort (years)	Time from diagnosis (years)					
	0-5	6-10	11-15	16-20	21-25	26-30
20-34	51.2 (60)	23.3 (29)	-1.3 (22)	7.1 (22)	-2.9 (20)	2.1 (20)
35-44	45.2 (276)	23.1 (148)	15.2 (111)	9.6 (91)	7.3 (78)	6.8 (67)
45-54	48.3 (463)	19.1 (228)	16.8 (175)	7.8 (135)	4.7 (111)	5.3 (88)
55-64	54.8 (452)	21.1 (181)	20.3 (125)	16.7 (81)	-2.4 (50)	-3.2 (31)
≥ 65	51.5 (760)	21.8 (226)	14.5 (116)	12.8 (47)	-0.5 (18)	-3.2 (6)
Total	50.6 (2011)	21.2 (812)	16.1 (549)	10.7 (376)	3.7 (277)	4.0 (212)

TABLE III—Excess mortality due to breast cancer or other causes per 100 women for five year interval. (Figures in parentheses are numbers of excess deaths in each interval)

Time from diagnosis (years)	Excess mortality/100 women	Excess mortality due to breast cancer/100 women	Excess mortality due to other causes/100 women
0-5	50.6 (1017.6)	48.6 (977.5)	2.0 (40.1)
6-10	21.2 (172.1)	19.0 (154.6)	2.2 (17.5)
11-15	16.1 (88.4)	10.5 (57.4)	5.6 (31.0)
16-20	10.7 (40.2)	7.5 (28.1)	3.2 (12.1)
Total	65.6 (1318.3)	60.6 (1217.5)	5.0 (100.8)

excess mortality due to causes other than breast cancer over the 20 years. Although cause of death is not always established with certainty it seems unlikely that errors and biases in the reported cause of death affected the trends shown in these data.

Discussion

In this study the prognosis of women with breast cancer who had survived for 20 years approached but never reached normal (fig, table I). The excess mortality of the total cohort, used to determine the prognosis of women with breast cancer, fell rapidly in the first 20 years from diagnosis and then approached normal in the next 10 years (table II). As expected, the excess mortality was largely due to deaths from breast cancer, though deaths from other causes also played a small part (table II). The pattern of the excess mortality of each age cohort was similar to that of the total cohort except that the youngest cohort may have approached a normal prognosis 10 years after diagnosis (table I). Studying relative survival rates for age cohorts gave the same trends in prognosis (fig, table I).

Some analyses of the long term prognosis of women with breast cancer are confusing because groups of women with normal life expectancy are detected yet deaths from breast cancer are more frequent than expected in these groups.⁶⁻⁸ We attempted to solve this by studying excess mortality rates for successive survivor cohorts. Our finding that after 20 years the excess mortality rate was very small (about one excess death per 100 women with breast cancer a year) implies that the prognosis of women with breast cancer after 20 years is almost normal. Their outlook may be further improved if other prognostic factors, such as axillary lymph node disease,¹ tumour size,² or hormone receptor state,³ are favourable.

We found that the excess mortality in each five year interval to 20 years was largely due to breast cancer (table III). Because there was a one to one correspondence between the estimated excess mortality in each interval and the excess mortality due to breast cancer, the improvement in prognosis for women with breast cancer was due to a reduced mortality from breast cancer.⁷⁻⁹ Unexpectedly, however, we found an excess mortality due to causes other than breast cancer, which contradicts the suggestion of Brinkley and Haybittle that women with breast cancer may die less frequently from causes other than breast cancer.⁶⁻⁸

Although age at diagnosis is a controversial prognostic factor,¹⁸⁻¹⁹ we found no apparent relation between age and excess mortality. The pattern of the excess mortality rate for each age cohort was similar (table II), although there were differences in crude survival rates (fig) between age cohorts. There may be, however, a more favourable prognosis for the cohort aged 20-34 because the excess mortality became low 10 years after diagnosis. We are cautious about this trend because of the small size of the group. This finding plus a similar one by Langlands *et al*⁵ raise the question about an improved prognosis for young women with breast cancer.

In conclusion, we emphasise the need for a prospective study of the long term prognosis in breast cancer with data about known prognostic factors. If the effect of these on survival were analysed simultaneously it might be possible to detect favourable prognostic groups and advise women with breast cancer accordingly.

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SORREL is under the dominion of Venus. It is prevalent in all hot diseases, to cool any inflammation and heat of blood in agues pestilential or choleric, or sickness and fainting, arising from heat, and to refresh the overspent spirits with the violence of furious or fiery fits of agues; to quench thirst, and procure an appetite in fainting or decaying stomachs: For it resists the putrefaction of the blood, kills worms, and is a cordial to the heart, which the seed doth more effectually, being more drying and binding, and thereby stays the hot fluxes of women's courses, or of humours in the bloody flux, or flux of the stomach. The root also in a decoction, or in powder, is effectual for all the said purposes. Both roots and seeds, as well as the herb, are held powerful to resist the poison of the scorpion. The decoction of the roots is taken to help the jaundice, and to expel the gravel and the stone in the reins or kidneys. The decoction of the flowers made with wine and drunk, helps the black jaundice, as also the inward ulcers of the body and bowels. A syrup made with the juice of Sorrel and fumitory, is a sovereign help to kill those sharp humours that cause the itch. The juice thereof, with a little vinegar, serves well to be used outwardly for the same cause, and is also profitable for tetters, ringworms, &c. It helps also to discuss the kernels in the throat; and the juice gargled in the mouth, helps the sores therein. The leaves wrapt in a colewort leaf and roasted in the embers, and applied to a hard imposthume, botch, boil, or plague sore, doth both ripen and break it. The distilled water of the herb is of much good use for all the purposes aforesaid. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)