RESEARCH COMMUNICATION

Estimation of Survival Rates of Breast Cancer Patients - an Hospital-Based Study from Mumbai

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Abstract

Purpose: To estimate the survival rates of breast cancer patients with reference to various factors like age, literacy status, residential status, T-stage and treatment. This is because there are very few studies reported from Indian subcontinent. Methods: Survival rates were obtained by using the actuarial method and loss-adjusted survival rate method (LAR) for the above factors and the rates were compared. The present study carried out at the Tata Memorial Hospital (TMH), includes newly diagnosed (who were not treated elsewhere before attending TMH) primary breast cancer patients and having completed the initial treatment. Results: The survival rates, actuarial survival and rates corrected for losses to follow-up (LAR) are presented. It showed that younger patients (≤50 yrs) had a better 5-year survival (81%) than the older patients (> 50 years), with statistical significance (p=0.024). There was no variation in survival with regard to the residential status but literate patients had a better (non-significant) survival (77%) than their illiterate counterparts. T3-stage patients had the worst prognosis showing a 5-year survival of 60% (p=0.0002). Survival for those treated with surgery as the only modality and also in combination with other modalities did not show any remarkable differences except for the group that were treated with 'surgery in combination with chemotherapy'. The 5-year survival for those treated with surgery as the only modality was 83%. This study yielded useful information on breast cancer survival, especially in a situation with incomplete follow-up. The method applied (LAR) also clearly demonstrates the bias in estimates obtained by direct application of the standard actuarial method.

Key Words: Breast cancer - survival rate - LAR - India - T stage - literacy

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Introduction

The study of cause and effect relationships is a basis of research and measurement of survival time is necessary for evaluation of chronic diseases. There are several publications on breast cancer survival from all over the world, but from India there are few. This is mainly because of lack of adequate follow-up which is the key for estimating survival rates.

Globally, breast cancer is the leading cancer among females and the incidence rates are very high in the West. Breast cancer incidences are highest in North America (at around 99.4 per 100,000)(Parkin et al., 2005). In India, the highest incidence rates in the year 2001 are from Mumbai (ASR= 33.1 per 100,0000) as reported by the Mumbai Cancer Registry (Kurkure et al, 2005). There are other registries from India like Chennai, which has recently reported breast cancer as the leading site of cancer in their registry. Although there has not been any substantial increase in the breast cancer incidence rates in Mumbai in the last decade, the number of cases has surely increased.

There has been an increase in the incidence rates in various parts of the world, especially in the urban areas. The increase has been attributed to changing life-style. Incidence rates vary with age. Women of higher socioeconomic status and women living in urban areas have higher incidence rates. The reproductive factors are often thought to affect the risk of breast cancer by their effects on a woman's hormonal status. It is known that certain reproductive events, and the age at which they occur, are strong determinants of subsequent breast cancer risk. Nulliparity, age at first full-term pregnancy, age at menarche, age at menopause and breast feeding have well been established as determinants of risk of breast cancer. Dietary fat consumption have been a major focus in attempting to explain some of the international and geographical differences in breast cancer incidence. A few studies reported a weak increase in breast cancer risk among women consuming high fat diets, while several large prospective studies that evaluated effects of adult dietary fat intake showed little if any association (Hunter and Willett, 1993).

Length of survival of cancer patients is an important

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Table 1. Characteristics of the Study Population

	Number	%
Total Cases	471	100.0
Age (in years) at diagnosis		
≤ 50	324	68.8
> 50	147	31.2
Place of residence		
Non Mumbai	395	83.8
Mumbai	76	16.2
Education		
Illiterate	99	21.0
Literate	372	79.0
T-Stage of disease		
T1	91	19.3
T2	193	41.0
T3	187	39.7
Treatment		
Only Surgery	32	6.8
Surgery + Chemotherapy	42	8.9
Surgery + Radiotherapy + Chemotherapy	155	32.9
Surgery + Chemotherapy + Hormone therapy	40	8.5
Surgery + Radiotherapy + Chemotherapy+Hormone therapy	164	34.8
Other*	38	8.1

* Includes those treated with chemotherapy or radiotherapy alone or in combination

indicator for knowing the outcome of treatment in any study. There are very few studies conducted on breast cancer in India unlike in other parts of the world. But to conduct a survival study requires a long term active follow-up. Follow up is a very difficult task in India as in other developing countries for various reasons viz. patients are from rural areas and travel time is too long to reach health care centre, lack of awareness about the implications of the disease progress, and poor financial status. Yet, with all these limitations, a study was conducted at Tata Memorial Hospital (TMH), Mumbai, India. The study reports the survival rates according to various characteristics viz. age, literacy, residential status, stage of disease and treatment.

Materials and Methods

The present study was carried out at the Tata Memorial Hospital (TMH), Mumbai, India. The hospital registered 1,866 cases of breast cancer in the year 2001 (Dinshaw and Ganesh, 2005). Of these 1,294 cases were treated in TMH. Out of these, 591 cases had already received some form of treatment before coming to TMH. The remaining 703 cases were considered for inclusion in the study. There were quite a few cases which were not staged (unstaged) and these were excluded from the analysis. The following were the criteria for inclusion of cases in the present study.

(a) Registered in the year 2001
(b) Diagnosed as primary breast cancer
(c) those who are not treated elsewhere before attending TMH
(d) those for whom staging of disease is recorded
(e) those who have completed the initial treatment fully.

The total number of such cases eligible for analysis in the present study was 471. A regular follow-up was done periodically for all the cases. Patients who missed their appointments/ do not attend for follow-up visits were sent pre-paid post cards enquiring their health status. Follow-up information was updated through hospital visits/ letters/ telephones/Mumbai Cancer Registry. All Mumbai resident deaths were matched with the Mumbai cancer registry.

Statistical Methods

The actuarial method (ACM) (i.e. life-table) (Berkson and Gage,1950) was used to calculate survival rates. The proportion of lost to follow-up was high and varied within and between groups. Also the risk of losses and deaths were not independent, which violated the assumption of the actuarial method. Thus Loss-Adjusted Survival Rate (LAR) proposed by Ganesh (1995) was applied to obtain the corrected survival rates for various groups. This method takes into account the losses in different strata by adjustment to obtain the corrected survival rates. Estimated deaths are obtained by logistic regression method in those with complete follow-up and then subsequently these estimates were applied to those with incomplete follow-up. Thus by applying the LAR method, survival rates were obtained for each of the categories.

Results

Table 1 shows the patient characteristics of the study population. 31.2% of the cases were '>50 years' of age and 68.8% were '≤50 years' of age. Thus the study population was young. 83.8% were non-residents i.e. from outside Mumbai city. But the literacy rate was quite high (79%). Patients were treated with surgery, radiotherapy, chemotherapy and also a combination of these therapies. With regard to staging of disease, 19.3% were diagnosed at T1, 41% at T2 and 39.7% at T3. A majority of the cases had undergone surgery with or without combinative treatment.

The proportion of deaths and losses to follow-up were similar within each subcategory. The losses to follow-up varied between 35-43% in different sub categories. Survival rates calculated by the Actuarial method (ACM) and loss-adjusted (LAR) method are shown in Table 2. The overall survival rate at the end of five years for 'total cases' was 83% by ACM and 77% by LAR method. The 5-year survival rates for age group ''≤ 50 yrs' was 81% compared to '>50 years' (67%), showed that younger patients had better survival than older patients, irrespective of ACM or LAR method. The difference in survival between the two age groups was statistically significant ($p = 0.024$) But in '> 50 years', the effect of lost to follow-up showed remarkable changes in estimation of survival rates, as is evident in the difference between the Actuarial and LAR rates at the end of five years. Survival rates were similar for Mumbai patients and non-Mumbai patients (76%) indicating that there is no difference between the residence status did not have any bearing on the outcome.

Literacy was another factor which showed differences in survival rates. The literate had a better 5-year survival

Table 2. Five Year Survival Rates of Breast Cancer Patients Treated at TMH in the Year 2001

	Year				
	1	2	3	4	5
All Cases					
No. of cases	471	407	346	296	263
Actuarial survival (%)	97	94	90	85	83
LAR by Regression(%)	97	91	87	81	77
Age at diagnosis					
≤ 50 yrs					
No. of cases	324	282	239	200	180
Actuarial survival (%)	98	94	89	85	84
LAR by regression (%)	98	93	88	82	81
> 50 yrs					
No. of cases	147	125	107	96	83
Actuarial survival (%)	96	90	87	83	78
LAR by regression (%)	90	84	80	74	67*
Place of residence					
Mumbai					
No. of cases	76	70	63	59	53
Actuarial survival (%)	97	96	93	88	84
LAR by Regression(%)	95	93	88	83	76
Non-Mumbai					
No. of cases	395	337	283	237	210
Actuarial survival(%)	97	92	88	84	82
LAR by Regression(%)	97	91	85	80	76
Education					
Literate					
No. of cases	372	324	279	240	213
Actuarial survival (%)	97	93	89	85	83
LAR by regression(%)	97	92	87	82	77
Illiterate					
No. of cases	99	83	67	56	50
Actuarial survival (%)	97	93	87	82	80
LAR by regression (%)	85	82	74	68	66
T-Stage of disease					
T1					
No.of cases	91	81	66	58	55
Actuarial survival (%)	98	91	91	90	88
LAR by regression (%)	98	90	90	88	84
T2					
No.of cases	193	172	156	138	123
Actuarial survival (%)	97	96	90	86	83
LAR by regression (%)	91	90	83	79	75
T3					
No.of cases	187	154	124	100	85
Actuarial survival (%)	97	90	86	80	78
LAR by regression (%)	85	78	73	64	60**
Treatment					
Surgery					
No. of cases	32	27	22	21	20
Actuarial survival (%)	93	90	86	86	86
LAR by regression (%)	91	88	83	83	83
Surgery + CT					
No.of cases	42	26	17	15	10
Actuarial survival (%)	89	74	69	59	59
LAR by regression (%)	91	75	68	51	51***
Surgery +RT+CT					
No. of cases	155	133	113	94	87
Actuarial survival (%)	99	92	86	83	82
LAR by regression (%)	99	92	85	81	80
Surgery +CT+HT					
No. of cases	40	35	33	31	27
Actuarial survival (%)	97	92	92	89	85
LAR by regression (%)	98	91	91	89	83
Surgery +RT+CT+HT					
No. of cases	164	154	130	108	93
Actuarial survival (%)	99	97	94	88	85
LAR by regression (%)	99	97	94	85	81

* p= 0.024, ** p = 0.0002, *** p=0.0001

rate (77%) than the illiterates (66%) and indicating better prognosis for those who are literate. The difference in survival rates was not statistically significant (p=0.084).

Survival rates obtained by actuarial and LAR method for different stages of disease indicate that the prognosis is poorer for late-stage disease patient (T3), compared to those diagnosed in early stage T1. The survival rates was 84%, 75% and 60% for T1, T2 and T3 stage respectively. The difference in survival rates between T1and T3 was statistically significant (p=0.0002). The difference in the rates between actuarial and LAR for T2 and T3 stage clearly shows how biased the estimates would have been if only actuarial rates had been calculated.

The treatment groups were analysed and the details are shown in the above table. Those treated with 'only surgery' and 'Surgery +CT+HT' showed best 5-year survival rates; the 5-year survival rates for S+CT, S+RT+CT and S+RT+CT+HT was 51%, 80% and 81% respectively. This indicates that the outcome due to combinative therapies in the treatment of breast cancer are better than a single-modality treatment. The difference in survival rates between those treated with 'only surgery' and 'Surgery + Chemotherapy' were statistically significant (p = 0.0001).

Discussion

Estimation of survival rate is of primary importance since it will indicate the effect of new treatment, if any, compared to standard treatment. Also the length of survival is the measure which is used for computing survival rates. Both of these require that the patients be followed-up over a period of time. Like in some Western countries, there is a centralized registration system across the country, which makes it a lot easier to obtain follow-up information. Such systems don't exist in most of the developing countries, including India. There have been very few reports on survival from cancer in India, mainly because of poor patient follow-up and incomplete system of registration of deaths. Although there are methods to improve the follow-up response, it is not feasible to obtain an 100% follow-up. In such situations, there are limitations to undertake survival studies. This is so, because the standard methods available in the literature for calculating survival rates are based on 'certain assumptions'. Violation of these assumptions will only result in wrong estimation of survival rates by direct application of standard methods, like the Actuarial method.

There are few studies on breast cancer survival reported from Indian subcontinent due to incomplete follow-up and thus an attempt has been to deal with the problem of follow-up in the analysis. The present study undertaken at the Tata Memorial Hospital addresses these issues and demonstrates the fallacies of applying the

standard actuarial method. As a result of this, the authors have applied the corrected method, Loss-Adjusted survival Rate (LAR) method suggested by Ganesh (1995). Although the LAR estimates obtained are not completely unbiased, this is the perhaps the best possible method that can be applied for obtaining survival rates, adjusting for losses-to-follow-up; the rates will at least be close to the true survival rates that would have been obtained if there was an hundred percent follow-up.

In the present study, the proportion of deaths and losses to follow-up were clearly related, meaning that those factors that were responsible for deaths were also responsible for losses to follow-up. The survival rates calculated by the standard actuarial method (ACM) and LAR method clearly indicate these differences. An attempt is made in the present study to understand the true survival rate which is clearly demonstrated by the use of appropriate method (LAR) for computing survival rates, in data with incomplete follow-up. The study adds to present knowledge of outcome in terms of survival of breast cancer patients. The study reports on survival for factors as age at diagnosis, education, residential status, T-stage and treatment.

In the west, based on the 1983-90 statistics, the five-year relative survival rates of breast cancer were 81.6 percent for white women and 65.8 percent for black women in the United States (Ries et al., 1994).

There are few studies on breast cancer survival from India, on a retrospective basis. A large breast cancer study was undertaken at Tata Memorial hospital by Dinshaw et al (2006) to study the various factors among those treated with breast conserving therapy (BCT). During 1980-2000, 1,022 pathological Stage I/II breast cancer patients (median age 43 years) underwent BCT were studied. The study showed an overall 5-year and 10-year actuarial survival of 87% and 77% respectively in this series. A population-based study of 1514 breast cancer patients published (Nandakumar et al, 1995) showed that the observed 5 year survival was 42.3% and the corresponding relative survival was 46.8%. The observed survival was 57.4% for localized disease, 45.8% for direct extension, 37% for those with regional node involvement, 14.2% for distant metastasis and 38.3% for those with un-staged disease. The clinical extent of disease were independent predictors of survival in this study. In an other study from India, analysis from 487 early breast cancer patients seen by Raina et al (1995) reported Five-year DFS and OS to be 73% and 78%, respectively.

A total of 2080 cases of invasive female breast cancer registered in MMTR, Chennai, (Gajalakshmi et al 1997) with a follow-up rate of 84% reported that observed survival rates at 1, 3 and 5 years were 80%, 58% and 48% respectively; the corresponding figures for relative survival were 81%, 61% and 51. In another study of 449 patients with breast carcinoma (Krishnan Nair et al 1993) showed that the overall 5-year survival rate was 40%.. On multivariate analysis, the following factors were found to significantly influence survival: response to treatment ($P < 0.001$), stage ($P < 0.01$), and regional nodal involvement ($P < 0.05$). Two-thirds of patients with advanced-stage disease on presentation accounted for the poor overall survival in this study.

The overall survival rate at the end of 5-year for 'total cases' was 77% by LAR method in the present study. The Overall five-year relative survival rate for US, White, was 90% (ACS, 2007). Shanta et al (2001) showed a survival rate of 57.2% at the end of three years. Also the 5-year survival rates for younger patients was better (81%) compared to older patients, '> 50 years' (67%), indicating better prognosis if diagnosed at an early age. This is in agreement with the report of Gajalakshmi et al (1997), showing prognosis becomes poorer with increase in age at diagnosis. A population-based study reported by Yeole et al (2001). They too reported that younger patients (< 35 years) had better survival than older patients The survival advantage of resident patients was to the extent of 6% for 'resident patients' (Mumbai) compared to 'non-residents'. Place of residence is considered mainly because the hospital registers a large proportion of cases from outside the city of Mumbai and this is important for determining the follow-up rates. Place of residence did not however show any survival differences. Literacy showed an advantage in survival over illiterate patients.

Stage at diagnosis is one of the important determinant of survival. The present study showed an inverse relationship of stage-of disease with survival which has been shown in earlier studies (Nair et al.,1993; Nandakumar et al., 1995; Gajalakshmi et al., 1997; Shanta et al., 1999; Yeole et al. , 1999). The 5-year survival rates were 85% for patients with T1, 63% for T2, 32% for T3, and 21% for T4 lesions. Those with N0 disease had a 68% 5-year survival rate. The survival rates were 90% for patients with Stage I, 65% for Stage II, 33% for Stage III, and 6% for Stage IV disease (Nair et al 1993). In a report published by the American Cancer Society 2007), the five-year relative survival rate among US Whites was 99% for localized disease , 85% for regional and 28% for distant metastases patients. The present study showed an 60% survival rate for T3 staged patients at the end of five years. The interpretation of international differences in cancer patient survival has been simplified by examining survival according to each disease stage at diagnosis which in the present study has been studied in terms of T-stage at diagnosis.

We know that retrospective studies do not give the answers regarding the efficacy of the treatment. Treatment by itself is not prognostic factor since it depends on the clinical extent of disease at presentation. In the present study, with regard to treatment, the group treated with 'only surgery' showed better survival (significant) than the other groups. The outcome due to different treatment was not very different except in those treated with 'surgery and chemotherapy as combination'. The increases in breast cancer patient survival could, in principle, could be attributed due to advancement in understanding the disease process through innovative research and also due to standardization of treatment across the board.

In conclusion, the present study reiterates that survival of breast cancer patients is dependent on age at diagnosis, literacy status and T-stage at presentation and are positive indicators of outcome in terms of survival. There are enough opportunities to study the disease process thereby

improving the treatment for better outcome.

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