RESEARCH COMMUNICATION

Effect of Comprehensive Breast Care on Breast Cancer Outcomes: A Community Hospital Based Study from Mumbai, India

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Abstract

Breast cancer is the second most common cancer in women in India and the disease burden is increasing annually. The lack of awareness initiatives, structured screening, and affordable treatment facilities continue to result in poor survival. We present a breast cancer survival scenario, in urban population in India, where standardised care is distributed equitably and free of charge through an employees' healthcare scheme. We studied 99 patients who were treated at our hospital during the period 2005 to 2010 and our follow-up rates were 95.95%. Patients received evidence-based standardised care in line with the tertiary cancer centre in Mumbai. One-, three- and five-year survival rates were calculated using Kaplan-Meier method. Socio-demographic, reproductive and tumor factors, relevant to survival, were analysed. Mortality hazard ratios (HR) were calculated using Cox proportional hazard method. Survival in this series was compared to that in registries across India and discrepancies were discussed. Patients mean age was 56 years, mean tumor size was 3.2 cms, 85% of the tumors belonged to T1 and T2 stages, and 45% of the patients belonged to the composite stages I and IIA. Overall 5-year survival was 74.9%. Patients who presented with large-sized tumors (HR 3.06; 95% CI 0.4-9.0), higher composite stage (HR 1.91; 0.55-6.58) and undergone mastectomy (HR 2.94; 0.63- 13.62) had a higher risk of mortality than women who had higher levels of education (HR 0.25; 0.05-1.16), although none of these results reached the significant statistical level. We observed 25% better survival compared to other Indian populations. Our results are comparable to those from the European Union and North America, owing to early presentation, equitable access to standardised free healthcare and complete follow-up ensured under the scheme. This emphasises that equitable and affordable delivery of standardised healthcare can translate into early presentation and better survival in India.

Keywords: Breast cancer - breast awareness - healthcare - prognosis factors - survival rate - India

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Introduction

Breast cancer has become an important public health problem and is the second most common cause of cancer incidence (115,251 cases) and cancer deaths (53,592 deaths) in women in India (Ferlay et al., 2010), accounting for an estimated 22% of cancer cases and 17% of the cancer deaths annually in women in India. Despite the fact that India contributes 8% of global burden of disease, there are no large-scale breast screening programs in the country or public health policies aiming at effective integration of awareness and screening in any region of India. More than 50-80% of breast cancer patients in different regions of India present in advanced clinical stages with less than half of the patients surviving longer than 5 years (Sankaranarayanan et al., 2011). Improved awareness, infrastructure, and efficient health services, for early detection and treatment of breast cancers leading to cure and longer survival, is fundamental for breast cancer control.

Clinical stage at presentation is a very important predictor for long-term survival. Five-year survival from breast cancer diagnosed at a localized stage is above 70% in most regions of India, whereas that of regional breast cancers varies between 23% and 49% (Dikshit et al., 2011; Jayalekshmi et al., 2011; Swaminathan et al., 2011; Yeole et al., 2011).

The main reasons for the poor survival in the different regions are lack of early detection initiatives, poor awareness among physicians and the public, advanced clinical disease at diagnosis and inadequate access to treatment, namely surgery, radiotherapy and chemotherapy and their permutation combinations integrated in specific protocols (Sankaranarayanan et al., 2010). The prognostic value of stage at presentation may vary in different populations due to other determinants such as socio-

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economic factors, age at presentation (general health, competing morbidity), availability, accessibility and affordability to and of effective treatment and varying adherence to prescribed treatment and follow-up care. In this manuscript, we describe the survival experience of breast cancer patients treated in an urban hospital serving an urban community covered under a healthcare system and receiving free and equitable healthcare services.

Materials and Methods

In this paper we present the data on survival in female breast cancer patients operated and treated at Bhabha Atomic Research Centre Hospital in Mumbai between 2005 and 2010. The hospital opened in 1976, has 390 beds with in-house diagnostic and therapeutic facilities and caters to a population of 90,000 employees under a health scheme. This scheme is supported by the central government of India and the health care is delivered equitably and free of charge. This being an exclusive scheme for the employees and their dependents, it ensures complete follow-up. All breast cancer cases treated at this hospital between 2005 and 2010 were included in this analysis. Each patient was treated within two weeks from the date of diagnosis. The treatment protocol was in line with the evidence based treatment guidelines followed by the Tata Memorial Centre, a tertiary referral centre in Mumbai. The patients were followed up actively through a breast cancer follow-up clinic run by the investigators once every three months for a year, once every six months up to a period of three years and once a year thereafter. All the cases were histological proven cancers. The demographic, clinical, and laboratory information was available on the computerised "Hospital Information Management System" (HIMS) and was retrieved for all the patients. The details were verified and any missing information was completed by checking the case files of concerned patients. We studied survival rates in these patients. The patient characteristics assessed in this study included socio-demographic and reproductive factors (including age, status of formal education and menopausal status), tumour characteristics (including type of surgery, histological grade, presence of ductal carcinoma in situ component on histology, lymph vascular emboli, tumor size, tumor stage (T), nodal status (N), composite stage, the Nottingham prognostic index (NPI), estrogen receptor status, and progesterone receptor status), and treatment given. Clinical composite stage at surgery of patients was categorized according to the stage categories of the UICC TNM Composite staging system as stages I, IIA, IIB, IIIA, IIIB, IIIC, or unknown (Wittekind et al., 2005). Nottingham Prognostic Index was calculated for prognostication (Rostgaard et al., 2001). Treatment given was grouped as none, surgery, radiotherapy only, chemotherapy only or a combination of these. Age-groups were dichotomised as < 50 and ≥ 50 years. Women with formal English education were grouped together and informal primary education and illiterate women were considered in a separate group. The patients were followed up till 31 December 2010. As the hospital also offers palliative care to its beneficiaries, death records were maintained in the HIMS and could be retrieved. The primary endpoint was death from breast cancer. The vital status of all included patients was established as dead, alive or lost to follow-up on 31 December 2010. Survival time was defined from the date of surgery to date of death, for the patients who had died, or date of last follow-up for those who were still alive or lost to follow-up. Cumulative observed survival was estimated using the Kaplan-Meier method and Cox proportional hazards regression was used to assess the effect of patient characteristics on patient survival after diagnosis. All analyses were done using STATA software package, version 11.0 (StataCorp, Lakeway Drive College Station, Texas, USA)

Results

We included 99 consecutive patients treated at our institution from 2005 to 2010 in the study. Records and follow ups were complete for 95 of these patients. Four of these patients were lost to follow-up after 6 months hence their vital status at the end of the study could not be ascertained. Follow-up compliance was 95.95%. Average age of the patients was 56.6 years (range 30-83 years) and mean tumor size at presentation was 3.2 cms (range 1-8 cms). Five (5.1%) of the patients presented in clinical stage I, 38 (38.4%) in IIA, 26 (26.3%) in IIB, 12 (12.2%) in IIIA, 5 (5.1%) in IIIB, 9 (9.1%) in IIIC and 4 (4.0%) with stage unknown.

The details of socio-demographic distribution, tumor characteristics and treatment received are given in Table 1. None of the socio-demographic or reproductive factors came out as definite predictors of survival because of the small sample size, but the crude estimates of some of these are worth mentioning due to their clinical and possibly biological significance. Higher age at diagnosis showed 43% reduced mortality as compared to the younger age group (HR=0.57 for those aged 50+ compared to those 30-49 years; and HR=0.46 for post menopausal compared to premenopausal women). Women who had received a formal English education had better survival rates compared with those who had lesser or informal levels of education (HR=0.25, 95% CI=0.05-1.16).

The following factors showed elevated risk of dying: modified radical mastectomy compared to breast conservation surgery (HR=2.9); patients with higher stage/sized tumors (HR=1.9 for those with tumor size >2 cm compared to those with ≤2 cm; HR=3.1 for those in clinical T2-T4 compared to T1-T2 stages); and a HR of 2.5 for those with estrogen receptors positive tumors compared to those with estrogen receptors negative tumors (Table 1).

Table 2 shows that the overall survival in our cohort was 98.9 %, 89.1% and 74.9% at the end of one, three and five years of follow-up, respectively. The observed 1-, 3- and 5-year survival estimates by categories of patient socio-demographic characteristics and tumor characteristics are given. Marked declines in survival were observed for women presenting with larger sized tumors, oestrogen receptor positive tumors, and patients who received modified radical mastectomy or had ductal carcinoma *in situ*. Additionally, marked survival declines

Table 1. Patient Socio-demographic and Tumor Characteristics and Treatment Received

Characteristic	No. Assessed	No. Dead (%)	Crude HR (95% CI)	p-value
Patients	99	11 (11.1)		
Patient socio-demographic characteristics				
Age				
30-49	23	3 (13.0)	1.00	
50+	73	8 (11.0)	0.57 (0.14-2.21)	0.41
Formal education				
No	49	9 (18.4)	1.00	
Had	49	2 (4.1)	0.25 (0.05-1.16)	0.08
Menopausal status				
Pre	18	3 (16.7)	1.00	
Post	79	8 (10.1)	0.46 (0.12-1.81)	0.27
Type of surgery				
Breast conserving	42	2 (4.8)	1.00	
Modified radical mastectomy	57	9 (15.8)	2.94 (0.63-13.62)	0.17
Predominant ductal carcinoma in situ component on histology				
Absent	45	4 (8.9)	1.00	
Present	50	7 (14.0)	1.42 (0.41-4.88)	0.58
Lymphovascular emboli				
Absent	69	7 (10.1)	1.00	
Present	26	4 (15.4)	1.41 (0.41-4.83)	0.59
Tumor size (cm)				
≤ 2	20	2 (10.0)	1.00	
> 2	68	8 (11.8)	1.9 (0.40-9.00)	0.42
Clinical Tumor stage				
T1-T2	81	7 (8.6)	1.00	
T3-T4	14	4 (28.6)	3.06 (0.89-10.52)	0.08
Clinical node stage				
N0	46	5 (10.9)	1.00	
N+	49	6 (12.2)	1.12 (0.34-3.67)	0.86
Clinical composite stage				
I-IIA	43	4 (9.3)	1.00	
IIB-IIIC	52	7 (13.5)	1.91 (0.55-6.58)	0.31
Nottingham Prognostic Index				
Good	4	0		
Moderate	45	7 (15.6)		
Poor	27	3 (11.1)		
Estrogen receptor				
Negative	37	2 (5.4)	1.00	
Positive	57	8 (14.0)	2.45 (0.52-11.57)	0.26
Progesterone receptor				
Negative	40	4 (10.0)	1.00	
Positive	54	6 (11.1)	1.08 (0.30-3.86)	0.90
Adjuvant treatment to surgery				
None	5	2 (40.0)		
Radiotherapy only	2	0		
Chemotherapy only	36	3 (8.3)	1.00	
Both	52	6 (11.5)	1.15 (0.29-4.59)	0.85

CI: confidence interval

were observed in patients with no formal education and pre-menopausal women. Nottingham prognostic index did not predict the survival. Patients with poor prognosis had higher survival rates than those with good and moderate prognosis.

Table 3 compares the survival in the present study with population-based cancer survival estimates reported by cancer registries from different locations in India. The present study shows up to 25% higher survival compared to other populations in India.

Table 2. Absolute Survival for the Breast Cancer Patients

		Absolute survival		
		1-year	3-year	5-year
Overall		98.8	89.1	74.9
Age:	30-49	100.0	87.9	73.3
	50+	98.4	89.6	76.3
Formal education:	No	100.0	84.4	61.5
	Had	97.5	94.0	94.0
Menopausal status:	Pre	100.0	85.9	68.7
	Post	98.4	89.9	76.7
Type of surgery:				
Breast conservation		100.0	95.7	85.0
Modified radical mastectomy		97.8	84.9	69.4
Predominant ductal carcinoma *in situ* component on histology				
	Absent:	97.6	90.3	83.9
	Present:	100	87.9	69.8
Lymphovascular emboli:	Absent	98.3	93.9	73.1
	Present	100.0	77.7	77.7
Tumor size (cm):	≤2	100.0	94.1	86.3
	>2	98.2	88.0	69.0
Clinical tumour stage:	T1-T2	98.6	90.7	79.5
	T3-T4	100	81.8	56.1
Clinical node stage:	N0	97.5	95.0	68.7
	N+	100.0	83.8	79.2
Clinical composite stage:	I	100.0	100.0	100.0
	II	98.3	92.0	74.9
	III	100.0	78.8	70.0
Nottingham Prognostic Index:	Good	97.7	92.2	70.4
	Poor	100.0	82.8	82.8
Estrogen receptor:	Ve-	96.8	93.1	93.1
	Ve+	100.0	88.4	66.6

Table 3. Absolute Survival for the Breast Cancer Patients from Different Locations in India

	Absolute survival		
	1-year	3-year	5-year
Current study	98.8	89.1	74.9
Barshi*	81.5	55.6	49.2
Bhopal*	83.1	62.1	30.7
Chennai*	79.2	54.7	43.7
Karunagapalli*	85.8	59.0	46.8
Mumbai*	77.9	56.6	46.0

*Sankaranarayanan and Swaminathan, 2011

Discussion

This paper attempts to understand breast cancer outcomes in a comprehensive health care system and some of the prognostic factors relevant to it. Our study showed higher survival as compared to other population studies in India mainly due to the large number of smaller tumors at presentation and to early detection. The women in our study being beneficiaries of the health scheme, the problems of incomplete treatment and affordability often seen in India are eliminated to a large extent. Also, the problem of migration and 'lost to follow up' are countered with lifelong registrations under the scheme.

In our study, stage at presentation has shown impact on the survival as is well documented in the literature, forming the basis of TNM and UICC staging of cancers. A significant finding in our study is that 85% of the cases

belonged to tumor stages I and II which is in contrast with the Indian and Asian scenario where large and advanced tumors are common findings. In a study from Karachi, only 51% of the patients belonged to T1, T2 category (Ahmad et al., 2009). Also, in a study from Tata Memorial Hospital in Mumbai, T1 and T2 tumors, grouped together represented 60% of the study population (Ganesh et al., 2008). A survival study from Kerala showed twice the number of patients in T3 and T4 group as compared to smaller tumors (Nair et al., 1993). Some of the large sample survival studies in India (Nandakumar et al., 1995; Gajalakshmi et al., 1997) do not present the stage subgroups at presentation.

Subsequent to these large numbers of T1 and T2 tumors, the survival observed in the present study is better as compared to the other studies in India (Table 3) .(Sankaranarayanan & Swaminathan 2011), Similarly, the study done on early breast cancers by Raina et al (2005), presents the overall survival of 78% comparable to that of our study. The comparable results are due to larger numbers of smaller tumors in our study making the study population similar to the group in Raina's study. Our results can be explained by the fact that the healthcare is given free of charge and equitably to all individuals of the population. Patients seek medical help in time and compliance in completing the treatment is high, resulting in better survival. The poor survival rates due to vastly different socioeconomic conditions prevalent in India, are countered by the presence of healthcare services. Our five year survival rates are comparable to those of the European Union (74%) and United States (81%). The meta-analysis done by Kogevinas et al from IARC, Lyon (Kogevinas & Porta, 1997) supports the findings where 19 out of 24 studies analysed showed poorer survival in subgroups of low socio-economic status, a condition similar to those prevalent in other populations in India. This is an important finding in the Indian context as an accessible and free healthcare service, given equitably in the population, could reflect into better survival in breast cancer patients.

Impact of education on the cancer survival has been studied by many investigators. Education is a key factor of the socio-economic status, influences lifestyles, behavioural patterns, reproductive factors like parity and even stage at presentation. The present study shows better survival in educated women as compared to those who had no formal education. Similar influence of education on survival is evident in other Indian studies (Gajalakshmi et al., 1997). A population-based survival study from Chennai has shown the hazard ratio of 0.54 in educated women with more than 12 years of education as compared to those who had no education. A hospital-based study in Mumbai (Ganesh et al., 2008) observed a similar trend of better survival in the educated group, but the difference was not statistically significant. Similar finding of higher survival in educated women were noted in population-based survival studies from Bangalore and Mumbai (Nandakumar et al., 1995; Yeole et al., 2004) where education was shown to be an independent prognostic indicator for survival. Similar findings have been shown in a large population based study from Sweden, where women with college education had 32% better survival than the women receiving lesser education (Hussain et al., 2008).

This emphasises the need for breast awareness programmes and educational material to be delivered in various local and regional languages for it to reach the less as well as uneducated and underserved women, in order to improve their survival.

Our results showed a favourable hazard ratio for the women above 50 years of age as compared to the younger women, but survival at the end of a five-year period was similar in both the age-groups. Recent studies from India reveal that age was a prognostic factor for survival and that younger women had better survival than the older women (Gajalakshmi et al., 1997; Yeole et al., 2004; Ganesh et al., 2008). Another hospital-based study in India (Nair et al., 1993), showed a similar drop in the survival at the extremes of ages and the best prognosis was between ages 35-49. Also, another large sample study from Norway (Host & Lund, 1986) described highest mortality at the extremes of ages ≤ 35 and ≥ 74 and the best prognosis for women was, here again, between 35 and 49 years of age. Our findings do not reveal advantage of age in terms of survival, probably because a larger sample size may be needed to make the prognostic significance apparent. Also, the rates being crude rates need to be interpreted with caution.

Our study showed better survival in the Breast Conservation Surgery (BCS) group, compared to the mastectomy group. Long-term results on correlation of type of surgery with survival are available in the literature (Jacobson et al., 1995; Poggi et al., 2003), which do not suggest any difference in the survival following mastectomy when compared with that of conservative surgery. Our results show that patients with breast conservation survived better, but as the numbers are small and the multivariate analysis could not be performed, the lack of adjustment for other factors may influence the findings. Nottingham prognostic Index did not predict the survival in our study, although it has shown good correlation in many studies where their Authors have advocated its routine use (Rostgaard et al., 2001; Okugawa et al., 2005; Ahmad et al., 2009).

The limitations of the study include small number of patients and deaths, whereas the long term and complete follow ups associated with standardised care are its main strengths.

This study emphasises the need of breast awareness programmes aimed at early diagnosis and treatment of breast cancer in India and the favourable impact of accessible, affordable and standardised healthcare on the survival from breast cancer in Indian women.

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References

Ahmad Z, Khurshid A, Qureshi A, et al (2009). Breast carcinoma grading, estimation of tumor size, axillary lymph node

status, staging, and nottingham prognostic index scoring on mastectomy specimens. *Indian J Pathol Microbiol*, **52**, 477-81.

Dikshit R, Kanhere S, Surange S (2011). Cancer survival in Bhopal, India, 1991-1995. In 'Cancer Survival in Africa, Asia, the Caribbean and Central America', Eds Sankaranarayanan R and Swaminathan R. International Agency for Research on Cancer, Lyon pp. 107-13.

Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM (2010) 'GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet].' International Agency for Research on Cancer: Lyon.

Gajalakshmi CK, Shanta V, Swaminathan R, et al (1997). A population-based survival study on female breast cancer in Madras, India. *Br J Cancer*, **75**, 771-5.

Ganesh B, Talole SD, Dikshit R, et al (2008). Estimation of survival rates of breast cancer patients--a hospital-based study from Mumbai. *Asian Pac J Cancer Prev*, **9**, 53-7.

Host H, Lund E (1986). Age as a prognostic factor in breast cancer. *Cancer*, **57**, 2217-21.

Hussain SK, Altieri A, Sundquist J, et al (2008). Influence of education level on breast cancer risk and survival in Sweden between 1990 and 2004. *Int J Cancer*, **122**, 165-9.

Jacobson JA, Danforth DN, Cowan KH, et al (1995). Ten-year results of a comparison of conservation with mastectomy in the treatment of stage I and II breast cancer. *N Engl J Med*, **332**, 907-11.

Jayalekshmi P, Gangadharan P, Sebastian P (2011). Cancer survival in Karunagappally, India, 1991-1997. In 'Cancer Survival in Africa, Asia, the Caribbean and Central America', Eds Sankaranarayanan R and Swaminathan R. International Agency for Research on Cancer, Lyon pp. 125-32.

Kogevinas M, Porta M (1997). Socioeconomic differences in cancer survival: a review of the evidence. In 'Social Inequalities and Cancer. IARC Scientific Publications, No 138.', Eds Kogevinas M, Pearce N, Susser M, and Boffetta P. International Agency for Research on Cancer, Lyon pp. 177-206.

Nair MK, Sankaranarayanan R, Nair KS, et al (1993). Overall survival from breast cancer in Kerala, India, in relation to menstrual, reproductive, and clinical factors. *Cancer*, **71**, 1791-6.

Nandakumar A, Anantha N, Venugopal TC, et al (1995). Survival in breast cancer: a population-based study in Bangalore, India. *Int J Cancer*, **60**, 593-6.

Okugawa H, Yamamoto D, Uemura Y, et al (2005). Prognostic factors in breast cancer: the value of the Nottingham Prognostic Index for patients treated in a single institution. *Surg Today*, **35**, 907-11.

Poggi MM, Danforth DN, Sciuto LC, et al (2003). Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial. *Cancer*, **98**, 697-702.

Raina V, Bhutani M, Bedi R, et al (2005). Clinical features and prognostic factors of early breast cancer at a major cancer center in North India. *Indian J Cancer*, **42**, 36-41.

Rostgaard K, Mouridsen HT, Vaeth M, et al (2001). A modified Nottingham prognostic index for breast cancer patients diagnosed in Denmark 1978-1994. *Acta Oncol*, **40**, 838-43.

Sankaranarayanan R, Ramadas K, Thara S, et al (2011). Clinical breast examination: preliminary results from a cluster randomized controlled trial in India. *J Natl Cancer Inst*, **103**, 1476-80.

Sankaranarayanan R, Swaminathan R (2011) 'Cancer Survival in Africa, Asia, the caribbean and Central America. IARC Scientific Publications No. 162.' International Agency for Research on Cancer: Lyon

Sankaranarayanan R, Swaminathan R, Brenner H, et al (2010). Cancer survival in Africa, Asia, and Central America: a population-based study. *Lancet Oncol*, **11**, 165-73.

Swaminathan R, Rama R, Nalini S, Shanta V (2011). Cancer survival in Chennai (Madras), India, 1990-1999. In 'Cancer Survival in Africa, Asia, the Caribbean and Central America', Eds Sankaranarayanan R and Swaminathan R. International Agency for Research on Cancer, Lyon pp. 115-24.

Wittekind C, Hutter R, Greene FL, Klimpfinger M, Sobin LH (2005) 'UICC. TNM Atlas: Illustrated Guide to the TNM Classification of Malignant Tumours, 5th edition.' John Wiley & Sons: Hoboken, New Jersey

Yeole BB, Kumar AV, Kurkure A, et al (2004). Population-based survival from cancers of breast, cervix and ovary in women in Mumbai, India. *Asian Pac J Cancer Prev*, **5**, 308-15.

Yeole BB, Kurkure AP, Sunny L (2011). Cancer survival in Mumbai (Bombay), India, 1992-1999. In 'Cancer Survival in Africa, Asia, the Caribbean and Central America', Eds Sankaranarayanan R and Swaminathan R. International Agency for Research on Cancer, Lyon pp. 133-42.