Oncology/Radiotherapy

BREAST CANCER SURVIVAL: A HOSPITAL-BASED STUDY IN REGIONAL CANCER CENTRE, BENGALURU

Dr. Vijay C R	Associate Professor, Department of Epidemiology and Biostatistics, Kidwai Memorial Institute of Oncology, Bangalore-29.
Dr. Ashalatha D	Assistant Professor, Department of Radiation Oncology, Kidwai Memorial Institute of Oncology, Bangalore-29.
Dr. Shobha K	Associate Professor, Department of Gynaec Oncology, Kidwai Memorial Institute of Oncology, Bangalore-29.
Dr. P Sridhar*	Associate Professor, Department of Radiation Oncology, Kidwai Memorial Institute of Oncology, Bangalore-29.*Corresponding Author
Mr. Venkatesh K	Statistical Assistant, Department of Epidemiology and Biostatistics, Kidwai Memorial Institute of Oncology, Bangalore-29.

ABSTRACT **Introduction:** Breast cancer is one of the most common cancer among Indian Women. The age adjusted rate (AAR) of Breast cancer is 42.1/100000 women in Bengaluru and it is the leading site of cancer in Bengalurian females. The hospital based cancer registry was established in 1983 and is registering around 800 Breast cancer cases per year. Most of them were diagnosed with late stage. The objective of this study is to evaluate Pattern of Care and estimate the Survival rate with respect to different stages, Treatment modalities, ER, PR, HER-2 Status of breast cancer treated only at Kidwai Cancer Institute. **Methodology** A retrospective cohort study was carried out with 191 Carcinoma Breast cases at a Regional Cancer Centre (Kidwai Memorial Institute of Oncology), Bengaluru. The study started from 2006-2007 and was followed-up until the end of 2020. Five-year survival (60 Months) probabilities were estimated using the Kaplan-Meier and loss adjusted survival analysis method for less than 80% follow-up group for ten years. The log rank test was used to compare the survival between the factors. **Results** The overall observed survival rates at 5years (60 months) was 72.7%. When analysis was conducted for specific stages, Stage II, Stage III and Stage IV survival rates are 95%, 67% and 17% respectively and is statistically significant (p<0.001), 39 Patients were dead and 13 Patients were lost for follow-up. The overall survival rate at 10 years was 62.4% and lost for follow-up was 26.5% and death was 27.7%, the Kaplan Meier analysis was unable to be carried out as more than 20% censored cases were seen, hence loss adjusted survival analysis was carried out for 10 years. 89 Patients were alive, 52 patients were dead and 50 patients were lost for follow-up at 10 years. **Conclusion:** In surgical histopathological finding Estrogen receptor, Progesterone receptor and HER-2 status did not have significant impact on survival of patients. The post-operative Radiotherapy and combination of modalities of treatment had significant effect on the long term survival of the patients after adjusting for disease stage.

KEYWORDS : Breast Cancer, Loss-adjusted Survival analysis, Kaplan Meier analysis, Estrogen receptor, Progesterone receptor

Introduction:

Breast cancer is one of the most common cancer among Indian women (1). National Cancer Disease Informatics and Research (NCDIR) projected 179790 newly diagnosed breast cancer cases for the end of 2020. The age adjusted rate (AAR) of breast cancer was 42.1/100000 women in Bengaluru and it is the leading site of cancer in Bengalurian females (2). AAR increased significantly over the 30 years period from 15.9 to 36.2 (1). The hospital based cancer registry established in 1983 and registering around 800 breast cancer cases per year. Most of them are diagnosed with late stage. More than 50% of breast cancer patients were registering with advanced disease (3), about 35% of the breast cancer patients registered in the Institute had already undergone treatment in other hospital and about 45% of the patients are taking Cancer directed treatment only at Kidwai Cancer Institute. Most of these studies have shown that variations in overall survival depend on the different stage of breast cancer, stage has been a strong predicting factor for breast cancer survival, with the survival declining as stage increases (4,5).

The objective of this study was to evaluate Pattern of care and estimate the Survival rate with respect to different stages, Treatment modalities, ER, PR, HER-2 Status of breast cancer treated only at Kidwai Cancer Institute.

Materials and Methods:

A total of 191 Histopathologically proven female breast cancer cases were registered for this study, only Bengaluru residents were considered from a Regional Cancer Centre. All cases were diagnosed of primary site of breast cancer during 1 January 2006 to 31 December 2007, histological confirmed and Treated only at research Institute for the analysis. Patient were followed upto 10year (120) months for clinical or demographic data. For Kaplan Meier analysis 5-year follow-up was considered. Very advanced stage and Incomplete treatment of breast cancer cases were not considered for the study.

The TNM system takes into account information on tumor size and tumor extension (T), regional lymph node involvement (N) and the evidence of distant metastasis (M). The grouped TNM stage in this data included the pathologic stage grouping also.

The data was analyzed using the R Software Version 4.2.2 (2022). Survival estimated by Kaplan- Meier method and differences in survival were compared by the log-rank test. Since the follow-up percentage was less than theoretical bound (80%) to apply regular method, hence loss adjusted survival analysis was also carried out parallely to confirm any discrepancy in results. Cox's proportional hazard models were investigated, the prognostic factors, hazard ratio and the associated 95% confidence level were presented.

Results:

Table-1: Shows the Patient characteristics of the study. The mean age of the patients in this study was 49 years. 58.1% of the cases were '<50 years' of age and 41.9% were '>50 years' of age. 30.4% were Stage II disease, 63.4% & 6.3% patients were Stage III and Stage IV disease respectively. In 57.8% patient's estrogen receptor is positive and in 42.2% estrogen receptor is negative. Out of 147 patients, among 67% of patients and 33% of patients Progesterone receptor was positive and negative respectively. Her-2 status was positive in 50.6% and negative in 49.4% out of 89 patients. Patients were treated with Surgery, Radiotherapy, Chemotherapy, Hormone therapy and also a combination of these therapies. A majority of the cases (88%) had undergone surgery with or without combination of treatment.

The overall survival rate at 10 years was 62.4% and lost for follow-up was 26.5% and death was 27.7%, the Kaplan Meier analysis was unable to carried out due to more than 20% censored cases, hence loss adjusted survival analysis was carried out for 10 years.

Table no1: Summary Statistics of Patients Demographic Detail

Variable	Number	Percentage
Age at Diagnosis		
< 50	111	58.1
> 50	80	41.9
Stage		
II	58	30.4
III	121	63.4
IV	12	6.3
Surgical Histopath Findings		
ER+	85	57.8
ER-	62	42.2
PR+	97	66.9
PR-	48	33.1
Her2+	45	50.6
Her2-	44	49.4
Surgery	168	88
Simple Mastectomy +Axillary clearance	164	97.6
Simple Mastectomy	2	1.2
Toilet Mastectomy	2	1.2
Radiotherapy (R)	89	46.6
Chemotherapy (C)	152	79.6
Neo-adjuvant	76	50
Concurrent	5	3.3
Adjuvant	71	46.7
Hormone Therapy (H)	88	46.1
Tamoxifen	64	72.7
Aromatase Inhibitors	21	23.9

Out of 191 cases, 139 (72.7%) cases were alive at the end of December 2012 and 39 (20.4%) were dead. About 7% patients were lost for the follow-up period on the closing date.

The age group distribution is represented in Table- 2: and although the number of deaths in age group 2 (more than 50 years) was higher compared to age group 1, there is no statistically significant difference between the age groups with respect to survival. Survival was examined stage by stage, and significant differences were discovered between broad stages with a 5% level of significance. ER, PR, and Her-2 status were examined, but no statistical significance in survival was observed.

Table-2: Age, Stage, ER, PR, Her-2 Status and Survival Analysis

Variable	No of Death	Kaplan Meier Survival %	Loss Adjusted Survival % for 10 Years	p-value
Age at Diagnosis				
Group-1 < 50years	14	77.8	77.9	0.368
Group-2 > 50years	39	69.4	70.2	
Stage				
II	6	95.1	88.0	0.001
III	41	66.8	51.2	
IV	6	16.8	14.3	
All stage	53	72.7	62.4	
Surgical Histopath Findings				
ER+	11	85.5	87.1	0.411
ER-	10	79.3	83.9	
PR+	15	80.3	75.3	0.324
PR-	18	87.5	60.5	
Her2+	33	84	76.5	0.737
Her2-	34	87	75.8	

Table-3: Explains survival with respect to a different modality of cancer treatment. A significant difference was found in the survival with a patient group that received Radiotherapy treatment after or before surgery compared with patients who underwent only surgery. A difference was observed in survival over multiple combinations of treatment compared to a single modality of treatment but the difference is not statistically significant with a 95% confidence level.

Table no3. Five year Survival rates of Breast Cancer with Treatment Combination

Treatment Modality	Number	Death	Survival %	p-value
Surgery				
Without RT	83	20	68.6	0.021
With RT	85	11	85.3	
Without CT	37	9	65.6	0.152
With CT	131	22	80.4	
Surgery+RT				
Without CT	8	2	66.7	0.270
With CT	77	9	86.9	
Surgery+RT+CT				
Without HT	32	6	77.8	0.085
With HT	45	3	93.2	

Cox- proportional hazard ratio was calculated by adjusting and without adjusting the stage of the disease. The impact of Radiotherapy and Hormone therapy treatment on the survival of Breast cancer was found to be significant with a 5% level of significance, the detailed results are given in table no4.

Table no 4. Crude and Adjusted Hazard Ratios of factor by Adjusting Stage

Variable	Crude Hazard ratio	Adjusted Hazard ratio	p-value
Age Group	0.89	0.88	0.365
Surgery	0.44	0.67	0.380
Radiotherapy	0.43	0.38	0.014
Chemotherapy	0.72	0.75	0.468
Hormone therapy	0.24	0.4	0.029

Discussion:
In females, Breast cancer is the most common cancer in the world; it accounts for about 2.26 million new cases estimated to be diagnosed every year (7). In India, around 1,79,790 cases of female breast cancer are diagnosed every year with an age-adjusted rate of around 26 per 100,000 population, accounting for 27% of all female cancers. Breast cancer is the first-leading site in the population-based cancer registry in Bengaluru (42 cases per 100,000 persons) (7,8) and the second leading site in the hospital-based cancer registry, KMIO. Every year, the trends in the incidence of Breast cancer across the registries in India show an increase in the incidence over the years. The PBCR, Bengaluru accounts for a 4.6% average annual percentage change (9).

The incidence has gone from 15 per 100,000 in 1982 to 42.1 per 100,000 in recent years and is likely to increase further. At KMIO, around 900 cases of Breast cancer are registered every year, accounting for 19% of all female cancers seen in KMIO. The matter of concern is that more than 50% of patients with Breast cancer are being diagnosed in advanced stage (10).

58% of the 191 patients were under the age of 50. Over the years, it has been observed that more young ladies are affected by breast cancer. The average age of patients with Breast cancer has shifted from 50–70 years old to 30–50 years old (11). Other cancer registries in India also reported that more than 80% of Indian patients are younger than 60 years of age. The average age of patients in six hospital-based cancer registries ranged from 44.2 years in Dibrugarh, 46.8 years in Delhi, 47 years in Jaipur and 49.6 years in Bangalore and Chennai. The average age of breast cancer patients has been reported to be 50–53 years in various population-based studies done in different parts of the country (12) and it is well known that these cancers in the young tend to be more aggressive (13). Approximately 63% of reported breast cancer patients are in stage 3, In a study from a large hospital in New Delhi, 80% of the patients treated for breast cancer over a period of 10 years had metastatic disease in the axillary lymph nodes (14). Estrogen (ER) and Progesterone receptors (PR) are found positive in only 57% and 67% of patients, respectively. Similar results were reported in Delhi, where only 35.5% of patients had receptor testing. ER-positive rates were reported to be lower in Indian patients than those in Western countries. As evident from the study, not all patients in India undergo hormonal receptor testing . The observed incidence of her-2 status was 50.6 and 49.4 percent positive and negative, respectively, the positivity of her-2 status in the Indian population is between 26 and 50% (15). 88% of the 191 patients underwent surgery, while 46.6%, 79.1% and 46.1% received radiotherapy, chemotherapy and hormone therapy treatment respectively.

The survival analysis was calculated for 191 breast cancer patients treated only at Kidwai Memorial Institute of Oncology. The date of diagnosis to the date of last follow-up or death was considered to calculate the overall survival analysis. Age cohorts were formed for analysis, with two groups: those under the age of 50 and those over the age of 50; the survival probabilities were 77% and 79% respectively. The result was not statistically significant; however, some studies reported that the median overall survival for patients aged less than 50 years was significantly higher than for patients aged > 50 years (16).

The stage of the disease is one of the most important factors influencing on Overall survival. Overall survival was found to be 72.7 percent at the end of five years. The stage of the disease in our study significantly impacted the probability of survival; since Kidwai Memorial Institute of Oncology is a referral tertiary care center, the proportion of stage 1 disease was minimal, hence excluded from the analysis. While proportions of stage 3 disease were commonly reported (63.4%) compared to stage 2 (30%) and stage 4 (6%), the symptomatic treatment group was excluded from the study (17). A similar study conducted at SGPGIMS Lucknow found that the 5-year overall survival rate was 62%. The 5-year actuarial survival has been 90% for stage I patients, 78% for stage II, 57% for stage III, and 22% for stage IV, though the survival data is available based on the follow-up information for only 75% of patients (18). Although there is no statistically significant difference in the overall breast cancer survival rate observed with respect to surgical, histopathological findings, some of the studies reported that the risk of metastasis increases over time for patients with Lymph node negative ER-positive breast cancer, especially for older patients or patients with larger tumours (19). The triple-negative subtype has the worst overall and disease-free survival rates (20).

Postoperative radiation has a significant effect on the overall survival of breast cancer, with patients who received radiotherapy after surgery having a significantly higher 5-year survival rate. It can be an optimal supplementary treatment for stage IV patients after surgery, especially for the Luminal subtype, TNBC, and patients with a low metastatic burden (21–22). The combination of cancer treatment modalities significantly increased survival after adjusting the stage of the disease. The use of trimodality therapy increased marginally with time, but there remain significant factors associated with differences in the use of trimodality treatment. Incomplete treatment or patient refusal to take treatment had a significant impact on the patient's 5-year survival and it is always detrimental. Counselling adequately for treatment completion still remains a challenge.

Conclusion:
The overall observed survival rates at 60 months was 72.7%. When analysis was conducted for specific stages, Stage II, Stage III and Stage IV survival rates are 95%, 67% and 17% respectively and is statistically significant (p<0.001). The overall survival rate at 10 years was 62.4% and lost for follow-up was 26.5% and death was 27.7%, the Kaplan Meier analysis was unable to be carried out as more than 20% censored cases was seen, hence loss adjusted survival analysis was carried out for 10 years. 89 Patients were alive, 52 patients were dead and 50 patients were lost for follow-up at 10 years.

In surgical histopathological finding Estrogen receptor, Progesterone receptor and HER-2 status did not have significant impact on survival of patient. The post-operative Radiotherapy and combination of modality of treatment significantly effects on long term survival of the patient after adjusting disease staging.

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