Ten-year survival outcome of breast cancer patients in India

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Abstract:
INTRODUCTION: Breast cancer is the most frequently diagnosed cancer among women in India; however, there are no studies addressing long-term survival (10 years and above). This study sought to evaluate long-term oncological outcome among women with breast cancer treated with a curative intent.

MATERIALS AND METHODS: This is a retrospective cohort analysis of 1301 breast cancer patients of all stages who had received primary treatment with curative intent from 2004 to 2010 at a single cancer institution of India.

RESULTS: A total of 1301 breast cancer patients were available for final analysis. The median age was 51 years (range, 21–86 years). 70.25% of the patients had early breast cancer (EBC), 21.9% had locally advanced breast cancer, and 7.85% of the patients with de novo metastatic disease also underwent surgery. 56.5% of the patients had hormone-sensitive tumors, human epidermal growth factor receptor 2 over expression was seen in 17%, and triple-negative tumors accounted for 26.2% of the patients. The 5- and 10-year overall survival (OS) of the entire cohort was 79% and 66%, and the 5- and 10-year breast cancer-specific survival (BCSS) was 79% and 70%, respectively. OS and BCSS were 51% and 58%, respectively, at 15-year follow-up after primary cancer treatment. On multivariate analysis, the factors associated with prolonged survival were age ≤50 years, EBC, and treatment during the later period (2008–2010).

CONCLUSION: Difference between OS and BCSS was found to have an increasing trend during 10–15-year follow-up, the difference being 4% at 10 years and 7% at 15 years. Age ≤50 years, early-stage disease at presentation, and primary cancer treatment in later years (2008–2010) were favorable predictors for 10-year survival.

Keywords: 10 years, breast cancer, India, long-term survival, oncological outcome after treatment

Introduction
Breast cancer is one of the most common cancers and a major health problem in the world. Breast cancer is a rising health problem and the most common cancer in India.¹ As per GLOBOCAN 2018 data, annually, there were approximately 162,468 new cases and 87,090 deaths in India because of breast cancer.² Published data suggest a disparity in age and stage of breast cancer at diagnosis for Indian population in comparison with the Western population. This may affect the oncological outcome.³,⁴ The survival rate for breast cancer patients in low-to-middle-income countries is likely to have differences because of lack of awareness, access to health-care facilities, and nationwide screening programs.⁵–⁷ In India, there is no national mammographic screening program for breast cancer. Kerala is the top ranking state of India in terms of overall health performance, according to the second health index launched by NITI Aayog. The possible contributing factors include a high literacy rate, increased public awareness, a sustained focus on health by...
successive state governments, and a good footprint of the private sector.

Breast cancer recurrence can occur even after 5 years in many patients. Available data from India are mainly on 5-year survival figures from some of the major cancer treatment centers. Many patients are lost to follow-up after 5 years of primary treatment at oncology centers, even after the importance of follow-up visit is explained.

Development of molecular classification of breast cancer led to a better understanding of prognosis in breast cancer. Most published data analyzing molecular classification as a predicting factor for long-term oncological outcome are from high-income countries. Luminal type is more likely to have long-term failures compared to triple negatives where the failures are most often within the first 5 years. Long-term oncological outcome is needed in breast cancer to provide a better understanding of disease prognosis and influencing factors.

In this study, we report the long-term survival outcome (minimum of 10-year follow-up) in a cohort of breast cancer patients treated at the Amrita Institute of Medical Sciences, Kochi, Kerala (South India), from 2004 to 2010. This is the first publication of long-term survival (>10 years) from India.

Materials and Methods

Data collection

This is a retrospective cohort analysis of breast cancer patients who had received primary treatment with curative intent from a single institution of India. We have included all women with breast cancer who underwent surgical treatment from 2004 to 2010 to ensure at least 10-year follow-up for the study group. Patients with oligometastasis and bone-only metastasis who were treated with a curative intent based on volume of metastases, response to initial chemotherapy, and age and performance status of patients were also included in this study. Details of patients’ characteristics, clinicopathological details, and follow-up after surgery were collected from the hospital-based electronic medical record system. Hospital-based cancer registry helped us to complete inadequate details of last follow-up and survival status by telephonic or postal communication.

Patients who did not come back for any follow-up after the primary treatment or patients who did not complete all treatment were excluded. Patients who developed other cancers later and had inadequate clinicopathological and treatment details of the same (usually due to having treatment elsewhere for the second malignancy) were also excluded. Patients who went for alternative systems of medicine after surgery were also excluded. Patients who were treated earlier for breast cancer on one side and now developing a second primary in the opposite breast were included. The flow diagram depicts the selection process of the study population [Figure 1].

We followed TNM AJCC 7th edition guidelines for defining the stage of breast cancer. For molecular classification, all patient samples were examined histologically and stained for estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2). Fluorescence in situ hybridization (FISH) testing for HER2 2+ was done only when the patient was willing for anti-HER2 therapy. Ki-67 was not part of the work-up until 2010. Hence, patients till 2010 did not have Ki-67 done. We have analyzed data by dividing the whole study cohort based on different parameters such as the stage of disease (early breast cancer [EBC – up to cT2N1 and T3N0] vs. locally advanced breast cancer [LABC – T4 and N2 and above] and metastatic breast cancer); molecular classification (three categories: luminal, HER2-enriched, and triple-negative breast cancer [TNBC]); and age at diagnosis. The HER2 enriched had luminal and nonluminal subtypes.

Surgery was either modified radical mastectomy or breast-conserving surgery, with the majority being mastectomy. Primary reconstruction was done in <5% of the patients. Neoadjuvant chemotherapy (NACT) was given to patients with clinical N2 or N3 and those with T4 lesions. Patients with oligometastatic disease and bone-only mets were offered surgery if the response to neoadjuvant therapy was good or if the primary was ulcerated. Chemotherapy schedules used in most included four cycles of Adriamycin and cyclophosphamide (AC) with four cycles of paclitaxel/docetaxel or six cycles of 5-fluorouracil and AC (FAC); anti-HER2 therapy was also affordable only to a small minority (<10%), and hence, the majority of

Figure 1: Flow of patient accrual in the study
the patients with HER2 overexpression did not receive any anti-HER2 therapy. Radiotherapy schedule followed was either 50 Gy/25# or 40 Gy/15#; hormone therapy was with either tamoxifen or letrozole depending on menopausal status for a minimum period of 5 years; extended adjuvant hormone therapy was given in many patients, especially those with positive nodes.

**Statistical analysis**

Overall survival (OS) was considered as the length of time from either the date of diagnosis/surgery to the date of last follow-up or death. OS after excluding patients who died due to causes other than breast cancer is considered as breast cancer-specific survival (BCSS). BCSS was measured from the date of completion of primary cancer treatment to the date of breast cancer death or last follow-up. Patients who had no follow-up visit for over 1 year and could not be reached by telephonic or postal communications were considered as lost to follow-up.

To compare the baseline patient characteristics of women with breast cancer, Pearson’s Chi-square test was used. For parameters such as age, stage of the disease, and molecular classification, we analyzed the statistical significance of the difference in the survival probability with Kaplan–Meier analysis and comparison using a two-sided log-rank test. Survival analyses were done on time to event outcomes. The primary objective was to evaluate 10-year BCSS and OS for breast cancer patients undergoing treatment. Univariate analysis screening method was used to select covariates for performing multivariate Cox proportional hazards regression model. Initially performed univariate analysis for all variables with the dependent variable and those statistically significant variables ($P < 0.05$) were included in the multivariate modelIBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp was used for all statistical analyses.

**Results**

Between January 2004 and December 2010, 1450 patients were identified from the hospital-based cancer registry database who underwent surgery for breast cancer. Out of these, 1301 were eligible for the present study as per inclusion and exclusion criteria. Fourteen of these patients had been treated earlier for breast cancer on one side (period ranging from 1998 to 2003) and were now treated during the study period for a second primary in the opposite breast. The overall median follow-up period was 10.8 years. The whole study group was followed up to April 25, 2020, and the database was locked on April 30, 2020. The median age of the study population at the time of diagnosis of breast cancer was 51 years (range, 21–86 years). Among the study cohort, 482 (37%) patients had died, and 638 (49%) were alive. One hundred and eighty one (14%) were lost to follow-up, and follow-up details of these patients were as follows: 20 (11%) patients had follow-up available for 12–24 months, 49 (27.1%) patients had for 25–60 months, 26 (14.4%) patients had for 61–84 months, 54 (29.8%) patients had for 85–120 months, and 32 (17.7%) patients had for >120 months but were not traceable within 1 year of the locked date. The clinicopathological profile of these patients is depicted in Table 1.

In the study population, 613 (47.1%) out of 1301 patients were below the age of 50 years, and 670 (51.5%) patients had luminal-type breast cancer as per immunohistochemistry (IHC) staining. We could not collect details of IHC in 69 (5.3%) patients. Most of these had lumpectomy done outside with no residual tumor on surgery here, and slides and blocks were either of poor quality or not available. Nine hundred and fourteen (70.25%) patients in our study had EBC while 285 (21.9%) patients were with LABC. One hundred and two (7.85%) patients with metastatic breast cancer also underwent surgery. These were mostly patients with bone-only metastases, but also a few with visceral oligometastases who had complete response to NACT. About 10% of the EBC patients and almost 80% of the LABC patients and all the metastatic patients had some form of NACT. In this period, we usually offered surgery after four cycles of AC or three cycles of FAC. After 2010, we have moved to having all chemotherapy upfront.

In the entire study cohort, the median OS was 183 months (95% confidence interval [CI], 169.5–196.5 months). We excluded 93 patients who died because of reasons other than breast cancer for analyzing BCSS. In the present study, estimated BCSS for the remaining 1208 patients was 202 months (95% CI, 176.5–227.5 months). In our study population, the 10-year OS was 66%, and the 10-year BCSS was 70%. We also have 62 patients alive (patients treated in 2004 and early 2005) with more than 15-year follow-up, and the 15-year OS and BCSS were 51% and 58%, respectively. The OS rate for the whole study population irrespective of the cause of death and for patients who died because of breast cancer (BCSS) is presented in Table 2.

In all, we had 75 patients with some form of documented locoregional recurrence and 289 patients with documented distant failures. Some of the local recurrences were in the form of multiple skin nodules over the entire chest wall and many were in conjunction with systemic disease. This does not include the patients who already had metastatic disease at presentation or developed metastases while on or immediately after treatment. Furthermore, these figures may not be entirely accurate as some patients had telephonic follow-up and
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The median OS was significantly different for EBC, LABC, and metastatic breast cancer patients. The median OS for different molecular‑type groups according to stage and age are depicted in Figure 2. Both groups (≤50 years vs. >50 years) were comparable for IHC and stage of disease [Table 3].

Details regarding exact site of recurrence or metastases were not documented.

For analysis, we divided the study cohort into two groups with a cutoff of 50 years of age (≤50-year vs. >50-year groups). The median OS for patients with age ≤ 50 years was significantly better compared to patients with age >50 years (194 months vs. 150 (138–162) months, \( P = 0.005 \)). The upper limit and lower limit of OS for patients with age ≤ 50 years could not be defined because the survival function of the same group did not reach the 45th percentile. On analysis of BCSS, events in ≤50-year age cohort did not reach the median limit of the survival plot while it was 185 (165–205) months for patients with age >50 years [Figure 2]. Both groups (≤50 years vs. >50 years) were comparable for IHC and stage of disease [Table 3].

The median OS was significantly different for EBC, LABC, and metastatic breast cancer patients. The median OS for different breast cancer stages in descending order was as follows: 194 months for EBC patients; 130 (95% CI, 100.35–159.6) months for LABC patients; and 21 (95% CI, 15.7–26.26) months for metastatic breast cancer patients. For BCSS, patients with LABC had 154 (116.6–191.2) months and 22 (16.4–27.5) months for metastatic breast cancer. Survival function for EBC patients did not reach the 45th percentile, and this was the reason for missing median survival of EBC for the same group [Figure 2].

We evaluated the impact over survival outcome with improvement in treatment over two periods. All patients who received primary cancer treatment in 2004–2007 and 2008–2010 were divided into two separate groups for analysis. Patients from 2008 to 2010 had significantly better OS for the whole study cohort and BCSS analysis. The median OS for patients from 2004 to 2007 was 181 (95% CI, 166.7–195.2) months and 158 (95% CI, 137.5–178.2) months for patients in 2008–2010. On BCSS analysis, patients from 2004 to 2007 and 2008–2010 had median OS of 194 months and 202 (174.7–229.6) months, respectively. The upper limit and lower limit of OS for patients from 2004 to 2007 could not be defined because the survival function of the same group did not reach the 45th percentile [Figure 3].

By subclassifying the study cohort according to IHC‑based molecular classification, there was no statistically significant difference found for estimated median OS and BCSS [Figure 3]. The median OS for HER2 and luminal with HER2 groups was not available as both groups did not reach the median limit of survival plot. The survival rate for different groups as per molecular classification and stage of the disease is presented in Table 2. One hundred and seventy (49.9%) patients aged ≤ 50 years. In the TNBC group, 254 (74.5%) patients were diagnosed at an early stage of disease; 56 (16.4%) patients had an advanced stage, and the remaining 31 (9.1%) had metastatic breast disease on presentation. Details for patients' distribution of different molecular-type groups according to stage and age are depicted in Table 3. The biological subtypes did not show a significant difference in survival at 10 years between luminal, HER2 enriched, and triple negative. However, as HER2‑directed therapy was not available for the vast majority due to cost considerations, and the patients with HER2 2+ did not have FISH testing unless they were scheduled to receive HER2‑directed therapy, we cannot comment on this.

For BCSS, patients from 2004 to 2007 and 2008–2010 had median OS of 194 months and 22 (16.4–27.5) months for metastatic breast cancer patients. Survival function for EBC patients did not reach the 45th percentile, and this was the reason for missing median survival of EBC for the same group [Figure 2].

Early‑stage breast cancer (\( P = 0.005 \)) and age ≤50 years (\( P = 0.0001 \)) had significantly better survival on multivariate Cox regression analysis. We did not get a \( P \) value on BCSS univariate analysis for ≤ 50 year age cohort because events in the same group did not reach the median limit of the survival plot. Hence, the hazard ratio for age was not available on multivariate Cox regression analysis for BCSS [Table 4].

### Table 1: Clinicopathological characteristics of the whole study group

| Characteristics | n (%) |
|-----------------|-------|
| Age (mean with range) | 52 (21-86) |
| Year (n=1301) | |
| 2004 | 139 (10.7) |
| 2005 | 160 (12.3) |
| 2006 | 142 (10.9) |
| 2007 | 172 (13.2) |
| 2008 | 202 (15.5) |
| 2009 | 280 (21.5) |
| 2010 | 206 (15.8) |
| Age (years) (n=1301) | |
| <40 | 194 (14.9) |
| 41-50 | 419 (32.2) |
| 51-60 | 403 (31) |
| 61-70 | 208 (16) |
| >70 | 77 (5.9) |
| IHC (n=1232) | |
| Luminal | 670 (51.5) |
| HER2 | 156 (12) |
| TNBC | 341 (26.2) |
| Luminal with HER2 | 65 (5) |
| Missing data | 69 (5.3) |
| Stage (n=1301) | |
| EBC | 914 (70.25) |
| LABC | 285 (21.9) |
| Metastatic | 102 (7.85) |
| Status (n=1301) | |
| Alive | 638 (49) |
| Dead | 482 (37) |
| Lost to follow-up | 181 (14) |

IHC: Immunohistochemistry, EBC: Early breast cancer, LABC: Locally advanced breast cancer, TNBC: Triple-negative breast cancer.

Details regarding exact site of recurrence or metastases were not documented.
In the present study, age ≤50 years and early stage breast cancer were significantly favorable predicting factors for 10-year survival. The association of IHC-based molecular subclassification with long-term survival outcome cannot be commented upon in our study, as in a vast majority, HER2 neu 2+ was not confirmed with FISH and HER2-directed therapy was not affordable. Although we had 47% of the patients below 50 years, there was no significant difference in the incidence of triple negative and luminal in the groups >50 or ≤50. To the best of our knowledge, this is the first publication from India having a median follow-up period of >10 years looking at 10-year and 15-year survival rate in breast cancer patients.

Sathwara and Bobdey in their review looked at all Indian studies from 1990 to 2016 and included a total of 16 studies with details of survival outcome. Nine out of 16 studies were hospital-based retrospective studies looking at all treated breast cancer patients, and the remaining were population-based studies. They reported 5-year OS from 42% to 48% and 40%-45% for population-based and hospital-based studies, respectively. As per the ICMR data based on cumulative analysis of data from 13 institutions across the country, the cumulative 5-year survival rate was 51%.
survival of a cohort of 7609 patients was 73.8%.\[10\] Subsequently, there have been a few more studies which have looked at 5-year OS,\[9\] which showed better survival, but no Indian data looked at 10-year survival outcome and more. Globally, also there have been only a small number of studies looking at more than 10-year survival outcome from a single hospital. Most of the studies have been from population-based registry studies. One systematic review and meta-analysis for survival rate in breast cancer patients had searched all published studies till 2017 and found a total of 130 studies from 52 countries with a total of 776,431 women.\[15\] They found 32 global studies with adequate 10-year survival data. Their global estimate of the pooled 10-year survival data was 0.61 (95% CI, 0.54–0.67), which was similar to our finding.

On subgroup analysis, Maajani et al. concluded that survival rates varied according to different WHO regions, age and stage at diagnosis, year of study, and developmental status of the country. As in the meta-analysis, our data also showed a better survival in <50 age group compared to the more than 50 (70% vs. 63% at 10 years and 60% vs. 43.5% at 15 years),\[15\] but this is in contrast to the study reported from Sri Lanka.\[16\]

Stage of the disease is one of the most important factors influencing long-term survival. A Japanese study involving 13.4% of the whole country population reported 5- and 10-year survival of 97.3% and 93.7%, respectively, for EBC.\[17\] Subanalysis in our study found slightly less in comparison with Japanese data but comparable to global 5-year survival rate (0.82, 95% CI: 0.70–0.92) provided by systematic review and meta-analysis.\[15\] In the review of Sathwara and Bobdey, an average of 50% of the patients were shown to be in Stage III and IV.\[14\] However, in the state of Kerala in South India, we do have a higher proportion of patients with EBC. In our study, 70% of the patients were with EBC, and this may be one of the factors contributing to the improved long-term survival in comparison with other Indian data.\[14\]

When divided the cohort into two blocks based on year of treatment (2004–2007 and 2008–2010), there was a significant improvement in survival in the latter period. The department started functioning in September 2003 and radiotherapy from January 2004. The improvement in survival in the latter half is possibly a result of improvements in chemotherapy, radiotherapy, and
surgery techniques as the department grows in volume, equipment, and patient load.\[17\]

At 15-year follow-up, we observed a 3% (60% vs. 63%) difference between OS and BCSS for patients with age ≤50 years which was around 8.5% (43.5% vs. 52%) for the >50-year age group. This finding suggests a decrease in the probability of death due to breast cancer and increased probability of death due to older age for the >50-year age group.\[18\]

The molecular subtypes did not show a significant difference at 10 years between luminal, HER2 enriched, and triple negative. However, an interesting observation was that the HER2-enriched group did not show any fall in survival after 10 years, while the luminal and triple negative continued to fall.\[13\] This, however, has to be taken with caution as the number of HER2 positive was much lower when compared to the luminal group and very few patients received anti-HER2 therapy in this period. Furthermore, as anti-HER2 therapy was not available for the vast majority due to cost considerations, the patients with HER2 2+ did not have a FISH testing unless they were scheduled to receive anti-HER2 therapy. The proportion of HER2-positive patients receiving anti-HER2 therapy in the same setting has gone up to 40% by 2014–2015 and has been increasing after that with the falling prices of HER2-directed therapy and availability of biosimilars.\[19\] Missing data of IHC for 69 (5.3%) patients was one of the limitations and maybe the reason for bias in results.

We had to exclude 125 of the total 1450 patients operated in this period as they either did not come back for adjuvant treatment or preferred alternative therapies. This is always going to be an issue as alternative medicines such as Ayurveda and homeopathy are popular among some patients. A small number with other unrelated malignancies were excluded as the treatment protocols were different, and it was not possible sometimes to differentiate whether the metastases were from breast or another primary. The problems with retrospective studies in most developing countries include inadequate documentation, data retrieval, noncompliance to treatment, and loss to follow-up. In our case, we have shown that with a dedicated breast unit, treating around 500 patients annually, in a state like Kerala in South India, it is possible to maintain good documentation and ensure long-term follow-up. Our percentage of lost to follow-up after 12 months of primary care is about 14% (181 patients); even among these, only 69 patients (5.3%) had follow-up period <5 years. All
the others dropped follow-up after 5 years. They were all disease free at the time of the last visit. Distances they have to travel and the cost incurred for travel may be limiting factors for a follow-up visit.

On literature search, we found a study from India with the largest dataset of breast cancer patients having median follow-up period not more than 6 years; still, around 14% of the total population had lost follow-up within 12 months of surgery. Since we were looking to document survival statistics of all breast cancer patients treated with a curative intent, we have included patients with bone mets alone and also oligometastatic patients who had a complete response to chemotherapy. We have not included patients who have not taken adjuvant therapy or have gone for alternate medicines. This study was single centered and it does not represent a population but covers patients from all over the state.

The other strengths of our study include a fairly large number of patients, uniform treatment protocols, and good documentation in the majority. The limitations were missing IHC data for 69 patients, lack of standard treatment for HER2-positive disease, lack of confirmation of HER2 2+ with FISH, and inability to differentiate luminal A and B.

**Conclusion**

OS rate on 10- and 15-year follow-up for breast cancer is 66% and 51% while for BCSS 70% and 58%, respectively. Age ≤50 years, early stage of disease, and primary cancer treatment in later years (2008–2010) were favorable predictors for 10-year survival.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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**Table 3: Comparison of study group according to parameters such as age, immunohistochemistry, and stage of disease**

| Parameters | Luminal | HER2 | Triple negative | Luminal with HER2 | P     |
|------------|---------|------|----------------|------------------|-------|
| Stage      |         |      |                |                  |       |
| EBC        | 463 (69.1) | 112 (71.8) | 254 (74.5) | 45 (69.2) | 0.034 |
| LABC       | 168 (25.1) | 37 (23.7) | 56 (16.4) | 15 (23.1) |       |
| Metastatic | 39 (5.8) | 7 (4.5) | 31 (9.1) | 5 (7.7) |       |
| Age (years) | <40 | 219 (32.6) | 47 (30.1) | 105 (30.8) | 24 (36.9) | 0.086 |
|            | 41-50 | 208 (31.1) | 61 (39.1) | 96 (28.2) | 22 (33.8) |       |
|            | 51-60 | 112 (16.7) | 26 (16.7) | 52 (15.2) | 6 (9.2) |       |
|            | >70   | 44 (6.6) | 3 (1.9) | 23 (6.7) | 3 (4.6) |       |
| Status     | Alive | 317 (51.7) | 321 (46.7) | 0.288 |       |
|            | Dead  | 203 (33.1) | 279 (40.6) |       |       |
|            | Lost to follow-up | 93 (15.2) | 88 (12.8) |       |       |

**Table 4: Multivariate Cox regression analysis for estimating overall survival**

| Parameters | Category | Overall survival | P  | Breast cancer-specific survival |
|------------|----------|-----------------|----|--------------------------------|
|            |          | HR (95% CI)     |    |                                |
| Age (years) | ≤50 | Reference | 0.005 | N/A | N/A |
|            | >50 | 1.44 (1.19-1.73) | N/A | N/A |
| Stage      | EBC | Reference | <0.0001 | N/A | N/A |
|            | LABC | 2.17 (1.79-2.64) | 2.48 (1.99-3.08) | 14.19 (10.64-18.94) | <0.0001 |
|            | Metastatic | 12.3 (9.33-16.20) | 4.17 (3.40-5.00) | 14.19 (10.64-18.94) | <0.0001 |

IHC: Immunohistochemistry, EBC: Early breast cancer, LABC: Locally advanced breast cancer, HER2: Human epidermal growth factor receptor 2

Distribution of events according to the stage of disease (n=1301)

| Parameter | EBC | LABC | Metastatic | P |
|-----------|-----|------|------------|---|
| Status    | Alive | 558 (61.1) | 80 (28.1) | 0 (0) | <0.0001 |
|           | Dead  | 216 (23.6) | 166 (58.2) | 100 (35.8) | 14.19 (10.64-18.94) | <0.0001 |
|           | Lost to follow-up | 140 (15.3) | 39 (13.7) | 2 (1.9) | 8.12 (4.78-13.62) | <0.0001 |

EBC: Early breast cancer, LABC: Locally advanced breast cancer, HR: Hazard ratio, CI: Confidence interval, NA: Not available (as ≤50 years age group did not reach median limit [50th percentile] of on Kaplan-Meier analysis)
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