Article published online: 2021-05-24

Original Article

Outcomes of Breast Cancer Management from an Urban Specialist Breast Center in South India

Naga Amulya Mullapudi, Kabeer Katherine Kirti, Naveen Padmanaban[1], Ramesh Nimmagadda[2], Selvi Radhakrishna

Department of Oncoplastic Breast Surgery, Chennai Breast Centre, [2]Department of Medical Oncology, Apollo Speciality Hospital, Chennai, Tamil Nadu, [1]Department of Surgical Oncology, AIIMS, New Delhi, India

Abstract

Context and Aims: The disease pattern and presentation of breast cancer in India are thought to differ from the West. The purpose of this study is to describe and to discuss the presentation, clinicopathological data, and survival from an urban specialist breast center in Southern India. **Materials and Methods:** Prospectively collected data were analyzed for clinicopathological details, treatment variables, and survival outcomes were analyzed. Cumulative survival curves were estimated using the Kaplan–Meier method for patients treated from 2007 to 2011. **Results:** A total of 1671 patients were operated at our center from January 2007 to December 2016. Average age at diagnosis was 54.2 years. Over 70% had Stage I and Stage II disease, infiltrating duct carcinoma was predominant in 88.2%. Average clinical tumor size was three centimeters. Breast conservation was performed in 22.4%. Sentinel lymph node biopsy was performed in 44.6%. Estrogen-receptor positivity was seen in 64.6%, 22.2% were Her2Neu positive. Triple negative disease was seen in 19.1%. Survival analysis was done using the Kaplan–Meier curves for 540 patients treated from 2007 to 2011. The median follow-up of surviving patients was 70 months with 10% lost to follow-up. In our study population, the 5 years overall survival rate is 88.3% and disease-free survival is 85.7%. **Conclusion:** Our study reflects a higher percentage of early breast cancer with outcomes comparable to the West. More research is required to understand the genetic predisposition in our population.

Keywords: *Breast cancer, breast cancer in India, breast cancer management, breast cancer outcomes, specialist breast center*

Introduction

The greatest rise in the incidence of breast cancer has been noted in the developing nations, particularly in India. The trend of rising incidence rates of breast cancer in India is likely to continue.[1] The mortality also is higher in India due to late stage at presentation and disparities in cancer care.[2] Indian Council of Medical Research has published guidelines for breast cancer management with minimum required standards in India.[3,4] The purpose of our study is to describe and discuss the disease pattern, clinicopathological presentation, and management outcomes of breast cancer from a specialist breast center in an urban setting in South India.

Materials and Methods

Prospectively collected data from January 2007 to December 2016 were analyzed. Clinicopathological details such as age, tumor size, grade, stage, hormone receptors and Her2 status, treatment variables such as breast conservation therapy (BCT) rates, sentinel lymph node biopsy (SLNB), and survival outcomes were analyzed. Survival analysis was done using the Kaplan–Meier curves for patients treated from 2007 to 2011, for they had a median follow-up of 70 months.

Statistical analysis

Data were collected using OncoCollect software and analyzed using Medcalc software for statistical analysis. Disease-free survival (DFS) was defined as the interval from the date of diagnosis to relapse, or death, whichever occurred first. Overall survival (OS) was defined as the interval from the date of diagnosis to death. Cumulative survival curves were estimated using the Kaplan–Meier method. Two-tailed $P = 0.05$ were considered statistically significant.

Results

A total of 1671 patients were operated at our center from January 2007 to December 2016. Patients who had primary

How to cite this article: Mullapudi NA, Kirti KK, Padmanaban N, Nimmagadda R, Radhakrishna S. Outcomes of breast cancer management from an urban specialist breast center in South India. Indian J Med Paediatr Oncol 2019;40:S102-8.

Address for correspondence:
Dr. Selvi Radhakrishna, Old No. 47, New No. 16, South Beach Avenue, 1st Street, MRC Nagar, Chennai - 600 028, Tamil Nadu, India.
E-mail: selvi.breastclinic@gmail.com

Access this article online

Website: www.ijmpo.org

DOI: 10.4103/ijmpo.ijmpo_206_17

Quick Response Code:

hormone therapy and those who had metastatic disease at presentation were not included in this study. Average age at diagnosis was 54.2 years (median age – 54 years, range 20–95) and 13.1% of them were under 40 years of age. Opportunistic screening accounted for 7% whereas the rest were symptomatic.

Over 70% had Stage I and Stage II disease (14% and 56%, respectively). Infiltrating duct carcinoma was the predominant pathology in 88.2% of our patients, and 4.8% (81) had ductal carcinoma *in situ* (DCIS) only, of whom 24 were screen detected. The average clinical tumor size was 3 cm. BCT was performed in 22.4% of patients. Local recurrence after BCT was seen in eight patients (2%).

Axillary lymph node dissection (ALND) was done in 997 (59.6%) patients. Average number of nodes removed was 19. Thirty-four percent of patients who underwent axillary lymph node clearance were node negative. Lymphedema was noted in 45 (4.5%) patients.

SLNB was performed in 746 (44.6%) patients. SNLB with mastectomy was performed in 455 (61%) patients. Breast conservation and SLNB were performed in 291 (39%) patients. An average of 3.2 sentinel lymph nodes (SLNs) was removed. SLN was positive in 170 (22.7%) patients, 71.7% of which were mastectomy, and 28.3% were with breast conservation surgery. SLN were reported negative on frozen section (FS) but positive on H and E in 16 (2.1%) patients. There were no regional recurrences in patients who underwent SLNB. Isolated axillary recurrence after axillary clearance was seen in three patients; all operated upfront and two patients with triple-negative breast cancer (TNBC).

The majority of tumors were Grade 2 and 3 (38.5% and 40.5%, respectively). Fifty-one percent were node negative. 64.6% were estrogen receptor (ER) positive, and 22.2% were Her2 positive. Over 62.7% (1048 patients) had chemotherapy. A combination of anthracyclines and taxane was given in 448 patients, anthracyclines-based chemotherapy schedule was given in 216 patients, taxane-based regime was given to 327 patients, and taxane plus carboplatin was given to 50 patients. Five patients received cyclophosphamide methotrexate fluorouracil (CMF) regime. Among 372 patients who were Her2 positive, 161 (43%) received trastuzumab. TNBC was seen in 19.1% [Table 1].

Survival analysis was done using the Kaplan–Meier curves for 540 patients treated from 2007 to 2011. The median follow-up of surviving patients was 70 months with 10% lost to follow-up. The DFS and OS outcomes from our data are comparable to the West [Table 2].

Table 1: Clinicopathological data

Clinico-pathological details	*n*	%
Patients from 2007 to 2016	1671	100
Menstrual status		
Pre	587	35.1
Post	1063	63.6
T status		
Tx, T0, Tis	105	6.2
T1	469	28
T2	975	58.3
T3	108	6.4
Node positive	688	41.1
LVI	316	18.9
Surgery		
BCS	381	22.8
Mastectomy	1290	77.2
Chemotherapy	1048	62.7
Endocrine therapy	1050	62.8
Metastasis		
Yes	158	9.4
Site of metastasis		
Liver	50	31.6
Lung	52	32.9
Bone	49	31
Brain	20	12.6
Loco-regional	32	20.2

Discussion

Age

The average age of patients in six hospital-based registries ranges from 44.2 to 49.6 years. In our cohort, the average age was 54.2 years. It has been noted that breast cancer in Indian women occurs a decade earlier than the West.[1] This is probably a reflection of the higher younger population rather an increase in the age-specific incidence.

In comparison to the 5% incidence of breast cancer, diagnosed in the below 40 age group in the West, we find that there is a higher percentage of (13.1%) patients diagnosed under the age of 40 years. Similar trends were seen at Tata Memorial Hospital (TMH) with 11% of their patients <40 years of age and 26% in SGPGIMS Lucknow, younger than 35 years of age. It is unclear if there are any genetic differences or other factors accounting for the young age at presentation. There are very few reports concerning the prevalence of BRCA 1 and 2 in India.[5-8]

Screen-detected breast cancer

Majority of our patients were symptomatic breast cancers with only 7% being screen detected. The average size of a screen-detected lesion in this group was 2 cm, which is considerably large for screen-detected lesions. DCIS was seen in 20.5%, and invasive disease was seen in 79.4%. Thirty-five percent of screen-detected tumors were lower grade, and 72.6% were node negative.

Opportunistic screening has gained popularity in the urban metros in the last decade among the upper and middle socioeconomic groups of women. Achieving quality

Table 2: Survival outcomes of breast cancer by stage from our data

Survival→ Stage↓	OS 5 years	DFS 5 years
I	93.8%	93.7%
II A	91%	89.4%
II B	89.7%	85.2%
III A	87.3%	82.7%
III B	80.7%	80.7%
III C	70.6%	65.2%

standards in technology, technique, interpretation, and aftercare following mammographic screening is a challenge in our heterogeneous health structure. Nearly 40% the breast cancers in our population are under 50 years of age. The higher density of breast tissue in the younger age makes mammographic interpretation more challenging. While mammography screening debates are still ongoing, population-based mammographic screening is not viable and cost-effective in India, but opportunistic and high-risk mammographic screening should continue.

The role of clinical breast examination (CBE) for population-based screening is being explored. Results published by Sankaranarayanan *et al*. and TMH demonstrated downstaging with CBE for early detection and mortality benefit results are awaited.[9,10]

Stage distribution

Majority of the patients had Stage I and Stage II breast cancers in our cohort (14% and 56%) Stage 0 accounted for 4.8% and 22.4% were Stage III. There is a slight increase in the number of Stage I and Stage II cancers since 2007 and a decrease in Stage III cancers [Figure 1].

Most regional cancer institutes report a large proportion of locally advanced breast cancers.[2,5] In our study, a larger proportion of patients presented at an earlier stage than regional cancer institutions. This is probably a reflection of the socioeconomic advantage seen with patients in our practice with better awareness and access to diagnosis and treatment.

Breast conservation versus mastectomy

Institutional facilities, such as TMC and AIIMS, have higher rates of BCT than private facilities. In our cohort, although 74.8% were diagnosed with Stage 0, Stage I, and Stage II breast cancer, only 22.8% underwent BCT. Less than 20% of patients are covered by medical insurance and quite often the coverage is limited and not optimal to cover all modalities of treatment. Radiotherapy facilities are limited to metros and tier two cities, which increase the cost of stay, travel, and time off from work for the breadwinner. Therefore, having a mastectomy is seen as a convenient option.[2] Besides, mastectomy is perceived to be safer by the patients, their families, and the referring medical physicians.

Re-excisions are not received well by patients. It increases the anxiety, the cost of treatment, and delays adjuvant therapy. Re-excision for positive/close margins was done in 15 patients (3.9%), 18 patients underwent a mastectomy after positive margins. Local recurrence after breast BCT was seen in eight patients (2%).

Patients who underwent BCT did better than patients who had mastectomy although not statistically significant [Figures 2 and 3].

Using shorter duration of radiotherapy with hypofractionation might make it easier for more women to adopt BCT. A large study from the Netherlands shows that BCT may offer better survival rates over mastectomy.[11] The study findings defy the conventional belief that the two treatment interventions offer equal survival, with evidence to show that BCT gives superior results than mastectomy. It is possible that selection bias and the role of radiotherapy as the possible driver of the OS benefit. Although this study is retrospective and possible confounding factors exist, the results gained from this study will have the potential to greatly improve shared treatment decision-making for our patients.

Sentinel lymph node biopsy and axillary lymph node dissection

Axillary conservation has been the most significant surgical advancement made in breast surgery in the last two decades. SLNB has become the standard of care for clinically node-negative axilla in early breast cancer.

SLNB was validated at our center in 20 patients with both SLNB and ALND with acceptable false negative and identification rates in 2007. Subsequently, patients with clinically node-negative axilla have undergone SLNB with dual technique using radioisotope and blue dye. Since 2015, we have adopted ultrasound (US) criteria and US-guided core needle biopsy of suspicious axillary lymph nodes to select patients for SLNB. The SLNs were subjected to FS analysis and clearance was performed if the nodes were positive. A total of 746 (44.6%) patients underwent SLNB. Breast-conserving surgery (BCS) with SLNB was done in 291 (39%) patients and mastectomy with SLNB in 455 (61%) patients. Sentinel nodes were positive on FS in 133 patients. There were 16 patients in whom FS analysis of sentinel nodes was negative, and the final histopathological examination was positive. Ten of these patients had mastectomy, and six had BCT.

Disease control comparable to complete axillary clearance with no increased morbidity was observed SLN-positive patients without further axillary clearance in ACOSOG-Z11 and EORTC-AMAROS trials that underwent BCT.[12,13] We have adopted axillary radiotherapy in patients undergoing BCT with <3 nodes positive disease on SLN biopsy deferring axillary clearance. Out of 40 patients who

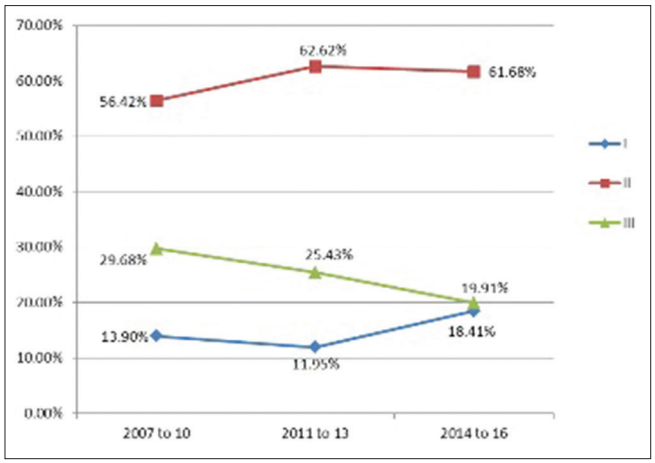

Figure 1: Line chart depicting the changing trends in breast cancer stage over 10 years at our center

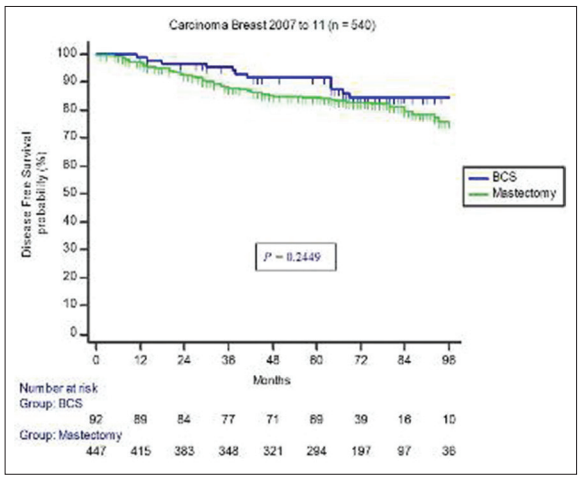

Figure 2: Five years disease-free survival (in months) in breast-conserving surgery versus Mastectomy was 91.8% and 84.8%, respectively

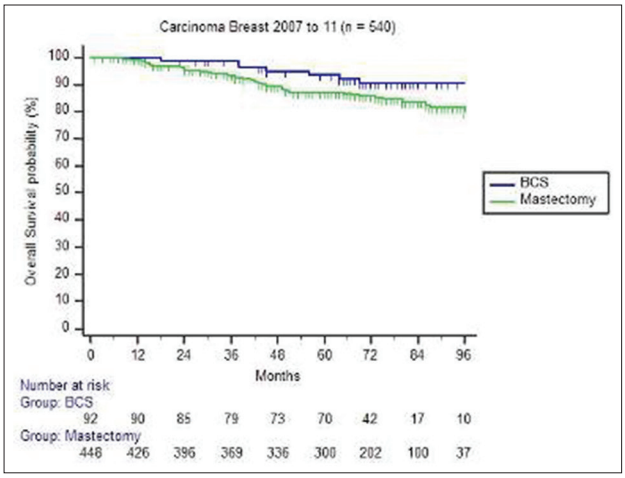

Figure 3: Five years overall survival (in months) in breast-conserving surgery versus Mastectomy was 93.7% and 87.1%, respectively

were FS positive with breast-conserving surgery, 24 had further axillary clearance, and 16 had axilla included with radiotherapy to the breast. There were no regional recurrences in patients who underwent SLNB.

Various centers in India have reported their results with SLNB. In low-resource settings, adopting a single dye technique and the practice of low axillary sampling could be effective alternatives for SLNB.[12,13] Three patients had who underwent BCS with SLNB had lymphedema, all three had RT to axilla as SLN were positive.

Lymph node positivity was seen in 41.1% (n = 688) of our patients. Among them, perinodal spread was reported in 41.8% (n = 288), Slightly more than half of the lymph node positive group 53% (n = 364) had N1 disease, N2 was documented in 26%, and N3 disease accounted for 19%. DFS rate was significantly better in the node-negative patients as expected [Figure 4].

Grade

In our study, we found a lower percentage, i.e. 40.5% of Grade 3 tumors. This differs with the data at a major cancer center in the city of Mumbai where 70% patients were reported as having Grade 3 disease.[14] Rangarajan *et al*. have noted an interesting fact about socioeconomic pattern and grade. In their review, they have made an observation that private hospitals treating patients from higher socioeconomic strata tend to have more Grade 2 tumors than major regional cancer centers, which cater more to patients from the lower socioeconomic strata.[15]

Estrogen-receptor positivity

ER, positivity was seen in 64.6% of our patients. The hormone-receptor expression in breast cancers in India is reported to be lower than the West.[1,16,17] The probable reason for the low-receptor expression in Indian patients may be due to younger age and higher grade of breast cancers. The lack of uniform standardization of basic procedures such as fixation and processing and immunohistochemistry (IHC) assays may also contribute to the low ER positivity rates in India. A study from a major hospital in Mumbai reported that the ER–/progesterone receptor (PR) + reported on IHC were actually due to suboptimal manual assays, and when the same tumors were evaluated using well-standardized international kits, the ER+/PR positivity rates were higher.[1]

Her2 status

Her2 status was reported as per the recommended ASCO guidelines 2007. Score zero and score one were considered as negative while score two and score three were considered as equivocal and positive, respectively.

Her2 positivity (IHC 3+) was seen in 22.2% of patients. Fluorescence *in situ* hybridization (FISH) test results were available only for 30% of Her2+ patients, as FISH test for Her2+ patients was not routinely performed in the earlier years. Nine percent of patients, who were Her2 equivocal,

were further tested with FISH, of whom 59% were reported Her2 positive.

Her2 positive disease has a poorer prognosis when compared to Her2-negative disease. However, the availability of trastuzumab has changed the outcomes with Her2-positive disease.

Targeted treatments for Her2 in the adjuvant setting are still beyond reach for the majority patients in the developing countries.[18] In a study from TMH, which is a publicly funded hospital, only 8.6% of patients were able to avail trastuzumab and nearly half of them were through patient participation in clinical trials.[16] In our study population, we noticed a rise in the number of patients receiving trastuzumab after the price drop in India in 2013 [Figure 5].

Triple-negative disease

It has been reported that the burden of TNBC is higher in India than the west.[19-21] A systematic review and meta-analysis of 17 cross-sectional studies that involved 7237 patients with breast cancer in India indicated a prevalence of TNBC in India ranged from 27% to 35% across studies, with a summary estimate of 31%.[18] This is comparable to the prevalence seen in African-American women and is more than twice the rate seen in caucasian women. The heterogeneity in the contributing studies in the definition of ER positivity and Her2 testing are possible limitations in the analysis in defining TNBC.

In our study, TNBC was seen in 19.1% of our patients. The majority (66.2%) had Grade 3 tumor. DFS was significantly lower in TNBC. Visceral metastasis occurred more commonly in the triple-negative subset. The DFS is 80.5% at 5 years, and OS is 84% [Figure 6]. Similar results were observed in a study published from AIIMS and SGPGI.[22,23]

Systemic therapy

Chemotherapy was given to 62.7% (n = 1048), of which 20.5% (n = 215) received neoadjuvant chemotherapy. Generic drugs for chemotherapy and hormone therapy have made systemic treatment more affordable. Most patients received a combination of anthracyclines and taxanes (448 patients), in 216 patients anthracyclines-based chemotherapy schedule was given, taxane-based regime was given to 327 patients, and taxane plus carboplatin was given to 50 patients. Five patients received CMF regime.

Receptor-positive patients (62.8%) received endocrine therapy, of which Tamoxifen accounted for 29.2% and aromatase inhibitors for 33.6%. Intramuscular depot progesterone 500 milligrams was given 5 days before surgery from the year 2014. This was based on evidence from the phase three study randomized controlled study published by Badwe *et al*. in which there was a statistically significant improvement of OS in the node-positive subset with a single dose of preoperative progesterone.[24]

Radiotherapy

Postoperative radiotherapy using LINAC to the breast or chest wall with or without lymph nodes has been given in 49.7% (n = 831) of our patients. Following the results of EBCTCG meta-analysis in breast cancer-specific mortality, we have selectively radiated chest wall in patients who are one to three nodes positive with unfavorable features such as extranodal involvement and lymphovascular invasion.[25] Patients undergoing BCT received 50 Gy in 25 daily fractions over 5 weeks with a boost to the tumor bed. Hypofractionated regime of 40 Gy in 15 fractions over 3 weeks has been adopted since 2016.

Hypofractionated regimes are equivalent to conventional regimes regarding disease control and survival and will reduce the machine time in our already overcrowded healthcare sector where radiotherapy facilities are inadequate. Besides, the acute and late breast toxicity is less with hypofractionated regimes.[26,27]

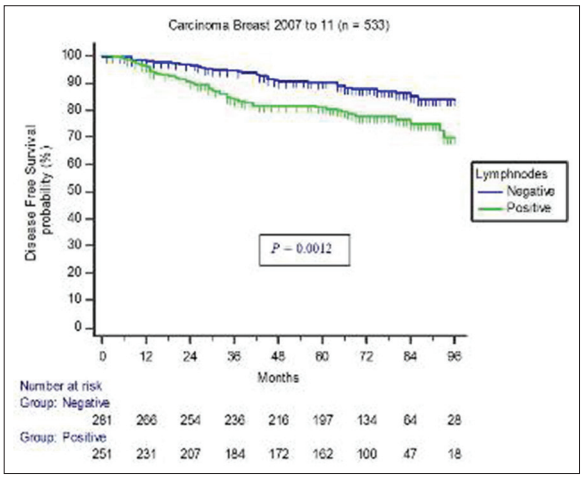

Figure 4: Five years disease-free survival in node-positive is 80.8% versus 90.6% in node negative disease

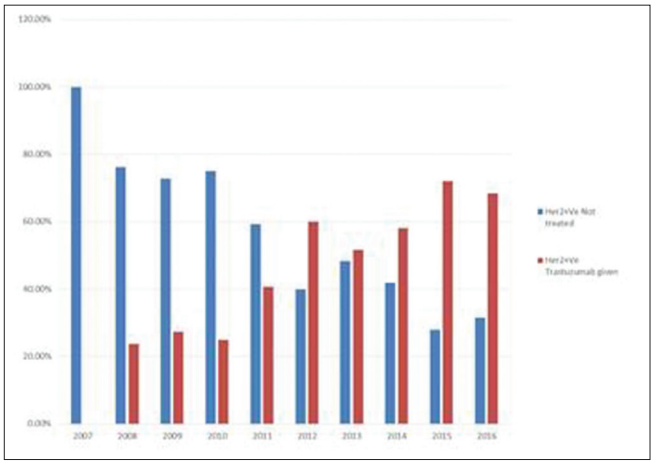

Figure 5: Graph depicting the gradual increase in the number of patients who received Trastuzumab over a decade

Survival

A review of published studies has reported a very low 5 years survival rate ranging from 40% to 45%. Raina *et al*. (OS 73% and DFS 78%) and Dinshaw *et al*. (OS 87% and DFS 76%) reported higher survival rates in patients with early breast cancer. In our study population, the 5 years OS is 88.3%, and DFS is 85.7%. Node-negative patients, and hormone receptor-positive patients did better than node negative and receptor-negative patients. Patients who underwent BCT did better than those with mastectomy. Triple-negative patients did worse than nontriple-negative patients [Figures 7-10].

Conclusion

Our study from an urban population reflects a higher percentage of early breast cancer with outcomes comparable to the West. The availability of generic chemotherapeutic and hormone therapy drugs has made these treatments affordable in India. Despite being a socioeconomically advantaged cohort, many women in our practice undergo mastectomy and few can afford targeted therapies. Wider adoption of hypofractionation technique will decrease the duration and cost of treatment and availability of radiotherapy facilities extensively will increase breast conservation rates. Studies to look at the efficacy of shorter versus longer duration of trastuzumab are necessary in our population. More research is required to understand the genetic predisposition in our population.

Acknowledgment

The authors would like to thank Ramesh Nimmagadda Cancer Foundation for their technical support and providing OncoCollect software for data collection and analysis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

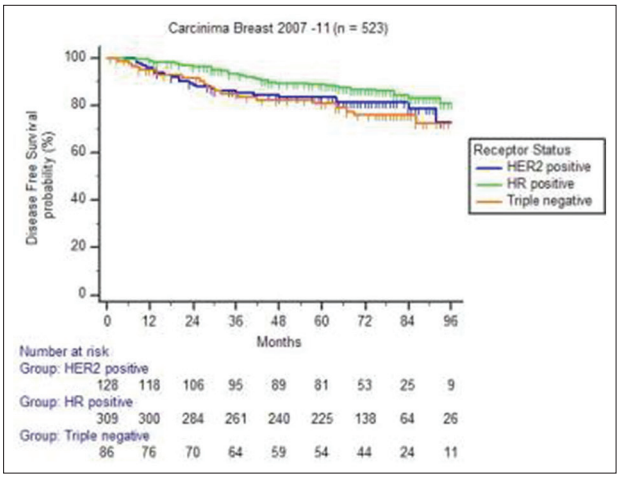

Figure 6: Five years disease-free survival in receptor positive, Her2 positive, and triple negative breast cancer patients

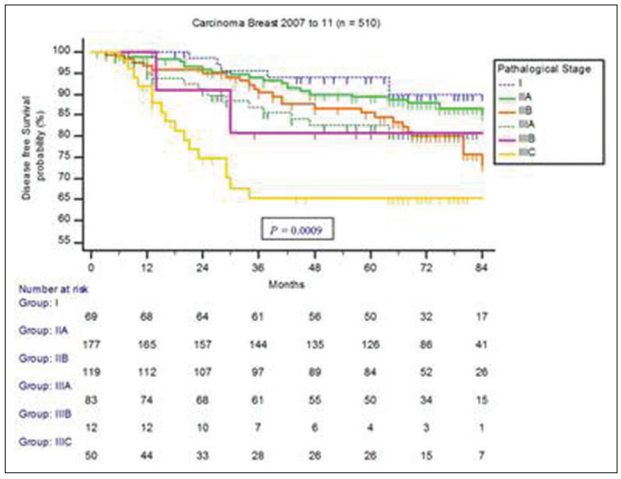

Figure 7: Five years disease-free survival for Stage I, II, and III

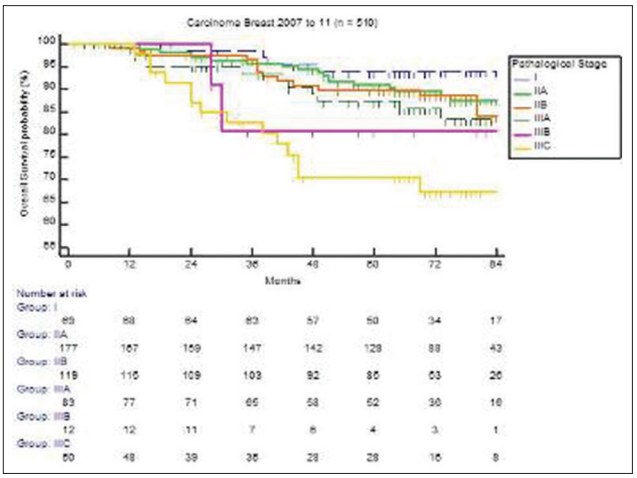

Figure 8: Five years overall survival for Stage I, II, and III

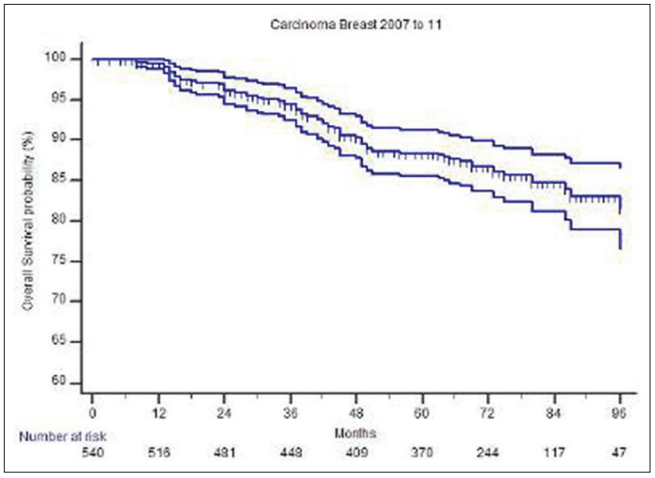

Figure 9: Graph depicting the 5 years overall survival with a confidence interval of breast cancer patients in our study

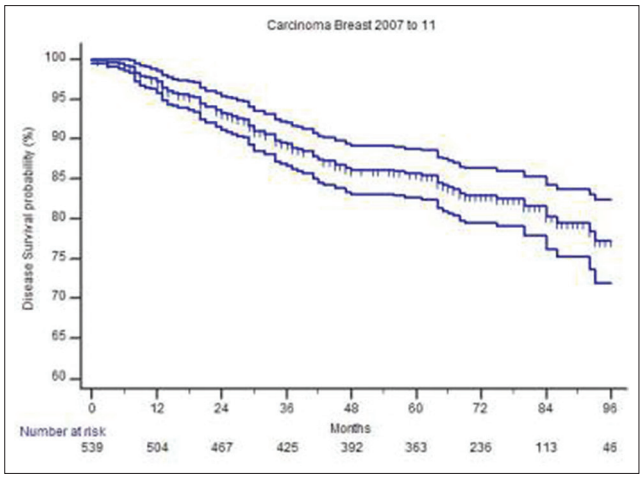

Figure 10: Graph depicting the 5 years disease-free survival percentage with confidence interval of breast cancer patients in our study

References

1. Khokhar A. Breast cancer in India: Where do we stand and where do we go? Asian Pac J Cancer Prev 2012;13:4861-6.
2. Agarwal G, Ramakant P. Breast cancer care in India: The current scenario and the challenges for the future. Breast Care (Basel) 2008;3:21-7.
3. Agarwal G, Pradeep PV, Aggarwal V, Yip CH, Cheung PS. Spectrum of breast cancer in Asian women. World J Surg 2007;31:1031-40.
4. ICMR Subcommittee on Breast Cancer. Consensus Document for Management of Breast Cancer 2016; 2016.
5. Saxena S, Rekhi B, Bansal A, Bagga A, Chintamani C, Murthy NS, *et al.* Clinico-morphological patterns of breast cancer including family history in a New Delhi hospital, India – A cross-sectional study. World J Surg Oncol 2005;3:67.
6. Kumar BV, Lakhotia S, Ankathil R, Madhavan J, Jayaprakash PG, Nair MK, *et al.* Germline BRCA1 mutation analysis in Indian breast/ovarian cancer families. Cancer Biol Ther 2002;1:18-21.
7. Rajkumar T, Soumittra N, Nancy NK, Swaminathan R, Sridevi V, Shanta V, *et al.* BRCA1, BRCA2 and CHEK2 (1100 del C) germline mutations in hereditary breast and ovarian cancer families in South India. Asian Pac J Cancer Prev 2003;4:203-8.
8. Valarmathi MT, Sawhney M, Deo SS, Shukla NK, Das SN. Novel germline mutations in the BRCA1 and BRCA2 genes in Indian breast and breast-ovarian cancer families. Hum Mutat 2004;23:205.
9. Mittra I, Mishra GA, Singh S, Aranke S, Notani P, Badwe R, *et al.* A cluster randomized, controlled trial of breast and cervix cancer screening in Mumbai, India: Methodology and interim results after three rounds of screening. Int J Cancer 2010;126:976-84.
10. Sankaranarayanan R, Ramadas K, Thara S, Muwonge R, Prabhakar J, Augustine P, *et al.* Clinical breast examination: Preliminary results from a cluster randomized controlled trial in India. J Natl Cancer Inst 2011;103:1476-80.
11. van Maaren MC, de Munck L, de Bock GH, Jobsen JJ, van Dalen T, Linn SC, *et al.* 10 year survival after breast-conserving surgery plus radiotherapy compared with mastectomy in early breast cancer in the Netherlands: A population-based study. Lancet Oncol 2016;17:1158-70.
12. Parmar V, Hawaldar R, Nair NS, Shet T, Vanmali V, Desai S, *et al.* Sentinel node biopsy versus low axillary sampling in women with clinically node negative operable breast cancer. Breast 2013;22:1081-6.
13. Somashekhar SP, Zaveri Shabber S, Udupa Venkatesh K, Venkatachala K, Parameswaran RV, Vasan Thirumalai MM, *et al.* Sentinel lymphnode biopsy in early breast cancer using methylene blue dye and radioactive sulphur colloid – A single institution Indian experience. Indian J Surg 2008;70:111-9.
14. Dinshaw KA, Budrukkar AN, Chinoy RF, Sarin R, Badwe R, Hawaldar R, *et al.* Profile of prognostic factors in 1022 Indian women with early-stage breast cancer treated with breast-conserving therapy. Int J Radiat Oncol Biol Phys 2005;63:1132-41.
15. Rangarajan B, Shet T, Wadasadawala T, Nair NS, Sairam RM, Hingmire SS, *et al.* Breast cancer: An overview of published Indian data. South Asian J Cancer 2016;5:86-92.
16. Ghosh J, Gupta S, Desai S, Shet T, Radhakrishnan S, Suryavanshi P, *et al.* Estrogen, progesterone and HER2 receptor expression in breast tumors of patients, and their usage of HER2-targeted therapy, in a tertiary care centre in India. Indian J Cancer 2011;48:391-6.
17. Manjunath S, Prabhu JS, Kaluve R. Estrogen receptor negative breast cancer in India : Do we really have higher burden of this subtype Indian J Surg Oncol 2011;2:122-5.
18. Wong NS, Anderson BO, Khoo KS, Ang PT, Yip CH, Lu YS, *et al.* Management of HER2-positive breast cancer in Asia: Consensus statement from the Asian oncology summit 2009. Lancet Oncol 2009;10:1077-85.
19. Sandhu GS, Erqou S, Patterson H, Mathew A. Prevalence of triple-negative breast cancer in India: Systematic review and meta-analysis. J Glob Oncol 2016;2:412-21.
20. Trivers KF, Lund MJ, Porter PL, Liff JM, Flagg EW, Coates RJ, *et al.* The epidemiology of triple-negative breast cancer, including race. Cancer Causes Control 2009;20:1071-82.
21. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, *et al.* Race, breast cancer subtypes, and survival in the Carolina breast cancer study. JAMA 2006;295:2492-502.
22. Gogia A, Raina V, Deo SV, Shukla NK, Mohanti BK. Triple-negative breast cancer: An institutional analysis. Indian J Cancer 2014;51:163-6.
23. Agarwal G, Nanda G, Lal P, Mishra A, Agarwal A, Agrawal V, *et al.* Outcomes of triple-negative breast cancers (TNBC) compared with non-TNBC: Does the survival vary for all stages? World J Surg 2016;40:1362-72.
24. Badwe R, Hawaldar R, Parmar V, Nadkarni M, Shet T, Desai S, *et al.* Single-injection depot progesterone before surgery and survival in women with operable breast cancer: A randomized controlled trial. J Clin Oncol 2011;29:2845-51.
25. EBCTCG (Early Breast Cancer Trialists' Collaborative Group); McGale P, Taylor C, Correa C, Cutter D, Duane F, *et al.* Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: Meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet 2014;383:2127-35.
26. START Trialists' Group; Bentzen SM, Agrawal RK, Aird EG, Barrett JM, Barrett-Lee PJ, *et al.* The UK standardisation of breast radiotherapy (START) trial a of radiotherapy hypofractionation for treatment of early breast cancer: A randomised trial. Lancet Oncol 2008;9:331-41.
27. Whelan T, MacKenzie R, Julian J, Levine M, Shelley W, Grimard L, *et al.* Randomized trial of breast irradiation schedules after lumpectomy for women with lymph node-negative breast cancer. J Natl Cancer Inst 2002;94:1143-50.