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Survival Outcomes of Post–mastectomy Breast Cancer Patients Treated with Hypofractionated Radiation Treatment Compared to Conventional Fractionation –a Retrospective Cohort Study

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Abstract

Introduction: For post–mastectomy patients, radiation treatment with conventional fractionation with a treatment duration of five weeks was the frequently used regimen, whereas hypofractionated regimens are recently used in the adjuvant treatment, which has a shorter treatment time over three weeks. We determined to estimate the treatment outcome by survival analysis between these two fractionation schedules to determine if any difference exists between these two groups.

Methods: We retrospectively reviewed the data of 348 breast cancer patients who had received adjuvant radiation treatment to the breast from January 2010 to December 2013. After assessing the eligibility criteria, 317 patients had received post–mastectomy radiation treatment to the chest wall and axilla and followed up till December 2018. The conventional fractionation schedule consisted of 50 Gy in 25 fractions, 2 Gy per fraction over five weeks, whereas the hypofractionated schedule was 42.6 Gy in 16 fractions with 2.66 Gy per fraction, over 3.2 weeks. Survival outcomes using 5– year Overall survival and 5–year Disease–free survival between these two fractionations were estimated and compared between the conventional and hypofractionated radiation treatment.

Results: All patients were females with a median age of 50 [IQR 45 to 58] and a median follow–up of 60 months. Of the 317 patients, 194 (61%) received hypofractionated radiation and 123(39%) conventional fractionation. The Kaplan–Meier estimates of the 5– year survival rate were 81% (95% CI = 74.9 to 87.6%) for the hypofractionated group (n = 194) and 87.8% (95% CI = 81.5 to 94.6%) for the conventional fractionation

group (n = 123). The log–rank test revealed no evidence of a difference between the survival rates over time (p= 0.1). Restricted mean survival time in the hypofractionated group was 54.5 months, and in the conventional fractionation group was 57 months. Further investigation with cox proportional hazards regression analysis, which controlled for age, N stage, and T stage, showed that patients with conventional fractionation radiotherapy were 0.6 times less likely to die than those with hypofractionated radiation (95% CI for the hazard or risk ratio = 0.31 to 1.21; P = 0.2). However, there is no statistical evidence to say the reduction in mortality is different from null.

5–year disease–free survival for the hypofractionated group (n= 194) was 62.6% (55.7–70.2) whereas that for the conventional fractionation group (n=123) was 67.8% (59.8–76.8). However, there was no evidence to say any difference between the disease–free survival rates on the log–rank test (p=0.39). Restricted mean disease–free survival time in the hypofractionated group was 45.1 months compared to 46.9 months for the conventional fractionation group

Conclusion: In post–mastectomy breast cancer patients receiving radiation treatment, the survival outcome with conventional and hypofractionated radiation therapy is comparable.

Keywords: Post–mastectomy breast cancer, Conventional fractionation radiation therapy, Hypofractionated radiation therapy, 5–Year Disease–Free Survival, 5– Year Overall Survival

Introduction

Breast cancer is one of the most frequently diagnosed malignancies, accounting for 2.3 million cases in the GLOBOCAN 2020 database. It is the most significant cause of cancer death in females, accounting for 6.9 per cent of all cancer deaths. Numerous Asian countries are experiencing dramatic increases in both incidence and fatality rates⁽¹⁾. The World Health Organization (WHO) has recognized this issue, and its Global breast cancer initiative (GBCI) seeks to reduce breast cancer mortality by 2.5 per cent per year, resulting in a 40% reduction in breast cancer fatalities by 2040, averting 2.5 million lives⁽²⁾. Improving access to comprehensive treatment is a means for reducing breast cancer mortality and is a challenge for many Asian countries.

Breast cancer treatment is often comprehensive with various modalities, including surgery, chemotherapy, targeted therapy, radiation, and hormonal treatment. Radiation treatment plays a crucial role in the management of early as well as locally advanced breast cancer. The percentage of patients who will receive radiation treatment during their course of treatment is more than 80%, but a significant number of patients have not received the recommended radiation treatment⁽³⁾. Also observed is an undue delay in the initiation of radiation treatment which was associated with worse overall survival⁽⁴⁾.

Postoperative radiation after breast-conserving surgery is indicated in most early breast cancer patients, reducing breast cancer recurrence to half and decreasing cancer death to one-sixth⁽⁵⁾. Further evidence of postoperative radiotherapy was obtained from a meta-analysis of 22 randomized trials showing that radiotherapy after mastectomy and axillary dissection will reduce the recurrence and breast cancer mortality in lymph node-positive diseases⁽⁶⁾.

The conventional fractionation with 2 Gy per fraction for post-mastectomy radiation therapy to the chest wall and lymph node is 50 Gy in 25 fractions over five weeks. Such a long fractionation schedule has several logistical issues in resource-limited countries and in many countries like India, where there is already a long waiting time for starting radiation treatment and higher costs associated with it⁽⁷⁾. It would be helpful if overall treatment time could be reduced without compromising the effectiveness. The conventional fractionation was designed based on earlier radiobiological data that the sensitiveness of breast cancer is lesser than that of early responding normal tissues with $\alpha\beta$ of 10 Gy. The trials

from the UK estimated the $\alpha\beta$ of breast cancer is 3.5 to 4.7 Gy, which is similar to that of the late responding normal tissues, and found out hypofractionation schedule is safe and effective⁽⁸⁾. The Ontario trial also stated that a hypofractionation schedule of 42.5 Gy in 16 fractions over 3.2 weeks is more convenient and acceptable⁽⁹⁾. The twenty-year follow-up results of the British Columbia trial, which assessed the benefit of radiation in post-mastectomy patients, also used a hypofractionated schedule with 37.5 Gy in 16 fractions found out that the use of radiation leads to improved survival outcomes⁽¹⁰⁾. Strong evidence for preferential use of hypofractionation in postmastectomy patients was limited even though widely practiced. However, a single institution phase 3 randomized controlled non-inferiority trial to test the efficacy of a 3-week hypofractionation schedule compared with a conventional 5-week schedule established the non-inferiority of the hypofractionated schedule⁽¹¹⁾. In the backdrop of this, we decided to analyze the data retrospectively of breast cancer patients who had received post-mastectomy radiation with either conventional or hypofractionation radiation to assess the survival to find any meaningful difference between these two fractionation schedules.

Methods

We retrospectively reviewed the medical data of 348 people who had received postmastectomy radiation in our institution from January 2010 to December 2013 and followed up till 2018. The study was approved by the Human Ethics Committee of the institution. We recorded the demographic and clinical profile, including age, sex, symptoms, menopausal status, side of the disease, ECOG performance status, comorbidities. Also recorded the Histopathology report, TNM status according to AJCC 7th edition, treatment details including the type of surgery, axillary dissection status, margin status, hormonal status, chemotherapy received, endocrine therapy, radiotherapy dose, and fractionation and type of recurrence. A previous study from Tehran compared and reported 5year OS rates of 100% for conventional and 95.2% for hypofractionated

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schedules⁽¹²⁾. Assuming similar 5year survival rates and power of 80% and 5% alpha error sample size of 320 patients is calculated. We included all eligible patients during the study period.

Females with histologically confirmed carcinoma of breast stage I to stage III who underwent a modified radical mastectomy (MRM), chemotherapy, radiation treatment with either the standard fractionation of 50 Gy in 25 fractions or hypofractionated schedule of 42.6 Gy in 16 fractions with a minimum of five years follow up period were included in the study. The surgical component consisted of managing the primary site, which had modified radical mastectomy and regional lymph node dissection, which consisted of axillary dissection and included minimum level I and level II lymph nodes in all patients. Inadequate Lymph node dissection was defined as those with < 10 lymph nodes retrieved. Excluded were those who underwent BCS, patients aged >70 years, histology other than carcinoma, and radiation dose fractionations other than the standard fractionation or the Hypofraction schedule. Patients with multiple primary sites of malignancies and patients who had received prior radiotherapy to the chest for other malignancies are excluded. Patients who developed locoregional recurrence, metastasis, second malignancies before initiation of radiation treatment are excluded from the analysis.

Post-mastectomy breast cancer patients who required adjuvant external beam radiation treatment were included in the study. Patients with T3 or T4 disease, positive lymph nodes, and positive surgical margins received adjuvant radiation. Patients received radiation treatment to the chest wall, axilla, and supraclavicular lymph node regions. All patients were planned with 2D conventional techniques and treated in a cobalt teletherapy machine. Patients were treated supine with the affected site arm abducted 90° or more and head turned to the contralateral side. The superior border was kept at the head of the clavicle, and the inferior border was marked 2 cm below the inframammary line to include most of the chest wall. The medial border is kept at the midline, and the lateral border is kept at the midaxillary line or posteriorly, depending on the scar of the postoperative drain site. In all cases, special care was taken to cover all the mastectomy wound scars completely in the radiation field. Three field techniques were used in the treatment with two opposing tangential beams for the chest wall and axilla and a direct anterior supraclavicular field added to the upper border of the tangential field. The supraclavicular field used was placed 1 cm lateral to the midline covering the supraclavicular

nodes, its inferior border kept below the head of the clavicle matched to the tangential field. The medial border of the supraclavicular extends superiorly through the medial border of sternocleidomastoid to the cricothyroid groove. The lateral border of the supraclavicular field is a vertical line extended laterally to the third of the humeral head to include the axilla. The dose of conventional fractionation schedule used was 50 Gy in 25 fractions, dose per fraction being 2 Gy given five days a week. In contrast, the hypofractionated schedule was 42.6 Gy in 16 fractions with 2.66 Gy per fraction, five days a week treatment.

The chemotherapy schedule consists of anthracycline and taxanes or alternate regimens if any contraindications to these regimens. Trastuzumab was used in Her 2 neu receptor-positive patients for one year. Endocrine therapy with either Tamoxifen, Letrozole, or Anastrozole was used for a minimum of 5 years and extended after that depending on menopausal status, the toxicity of the drug, and high-risk disease features.

Overall survival was calculated from the date of initiation of radiation treatment to the date of death due to any cause or last follow-up date. Censoring of survival time was done at the last follow-up date for patients lost on follow-up and did not turn up for scheduled follow-up visits. The most updated patient status was obtained from follow-up visit outpatient records and inpatient records of admitted patients. DFS was calculated from the date of initiation of radiation treatment to the date of the first breast cancer-related event, which includes local, regional, and distant relapse or last follow-up and death.

Statistical analysis

We compared the overall and disease-free survival between the conventional fractionation and hypofractionation groups, using the log-rank test and Cox regression. Prognostic factors included in the model were a priori fixed based on literature review and availability of variables in the database. All results were summarized with 95% confidence intervals. All analyses were done with R statistical software version 4.⁽¹³⁾

Results

A total of 348 patients received adjuvant radiation for breast from January 2010 to December 2013. Among these patients, 333 were MRM patients who received adjuvant radiation treatment; 15 patients were excluded as they were BCS with adjuvant RT. Among the 333 post-mastectomy patients, 16 were excluded based on the

eligibility criteria. Those excluded were seven patients >70 years age; two patients had lung metastasis, two patients developed local recurrence before RT in the same breast, one patient developed Local recurrence before RT in the opposite breast, one patient had Malignant phyllodes, one patient had pure ductal carcinoma in-situ, one patient had carcinoma stomach, one patient was male breast cancer. The remaining 317 patients were followed up till December 2018. All patients were females with a median age of 50[IQR 45 to 58] and a median follow-up of 60 months. Most patients, 179 (56.5%), were Stage III breast cancer cases followed by stage II 134 (42.3%). One patient was Stage I breast cancer, and the composite Stage could not be assigned to 3 patients due to unknown tumour size or nodal status. The most common histology was invasive ductal carcinoma. There were 29(0.09%) missing observations, with grade contributing 24(0.07%). Three observations were missing in the composite Stage and two in the chemotherapy schedule. We excluded these observations from further analysis. Of the 317 patients, 194(61%) received hypofractionated radiation and 123(39%) conventional fractionation. Most of the patients were in the T2 Stage, followed by T3, T4, T1, and Tx. Most patients were in N1, followed by N0, N2, N3, Nx, respectively.

The median age was 50 years(IQR 45–58) in the hypofractionated group and 49[IQR 43 to 57] in the conventional fractionation radiotherapy group. Both groups were comparable across the two groups except for Stage and schedule (Table 1).

For our patients with cancer, the Kaplan–Meier estimates of the 5–year survival rate after treatment were 81%% (95% CI = 74.9 to 87.6%) for the hypofractionated group (n = 194) and 87.8% (95% CI = 81.5 to 94.6%) for the conventional fractionation group (n = 123) (Figure 1). The log–rank test revealed no evidence to say there is a difference between the survival rates over time (p= 0.1). Median survival time could not be assessed. Restricted mean survival time in the hypofractionated group was 54.5 months and in the conventional fractionation group 57 months. Further investigation with cox proportional hazards regression analysis, which controlled for age, N stage, and T stage, showed that patients with conventional fractionation radiotherapy were 0.6 times less likely to die than those with hypofractionated radiation (95% CI for the hazard or risk ratio = 0.31 to 1.21; P = 0.2). However, there is no statistical evidence to say the reduction in mortality is different from null. Proportional hazard assumptions were met in global and individual tests for the model.

Characteristics	Hypofractionation RT(n=194)	Conventional RT(n=123)
Age (median [IQR])	50.00 [45.00, 58.00]	49.00 [43.50, 57.00]
Left side (%)	95 (49.0)	67 (54.5)
Adjuvant chemotherapy		
(%)	122 (62.9)	86 (69.9)
T Stage (%)		
T1	9 (4.6)	8 (6.5)
T2	80 (41.2)	56 (45.5)
T3	58 (29.9)	35 (28.5)
T4	46 (23.7)	24 (19.5)
TX	1 (0.5)	0 (0.0)
N stage (%)		
N0	53 (27.3)	43 (35.0)
N1	59 (30.4)	43 (35.0)
N2	57 (29.4)	24 (19.5)
N3	23 (11.9)	12 (9.8)
NX	2 (1.0)	1 (0.8)
Inadequate axillary dissection (%)		
	95 (49.0)	75 (61.0)
ER (%)		
Positive	73 (37.6)	46 (37.4)
Negative	106 (54.6)	72 (58.5)
Unknown	15 (7.7)	5 (4.1)
PR (%)		
Positive	75 (38.7)	47 (38.2)
Negative	104 (53.6)	71 (57.7)
Unknown	15 (7.7)	5 (4.1)
Grade (%)		
1	6 (3.3)	4 (3.6)
2	144 (78.7)	85 (77.3)
3	33 (18.0)	21 (19.1)
Premenopausal (%)	96 (49.5)	59 (48.0)
Positive margin (%)	40 (20.6)	27 (22.0)
Comorbidity (%)	84 (43.3)	49 (39.8)
Composite Stage (%)		
I	0 (0.0)	1 (0.8)
II	74 (38.5)	60 (49.2)
III	118 (61.5)	61 (50.0)
Chemotherapy schedule (%)		
Anthracycline &Taxane	65 (33.9)	16 (13.0)
Anthracycline\ taxane	122 (63.5)	99 (80.5)
Others	5 (2.6)	8 (6.5)

Table 1. Baseline and treatment characteristics of population
RT= Radiation Therapy
ER= Estrogen Receptor
PR= Progesterone Receptor

Characteristic	DFS			OS		
	HR ¹	95% CI ¹	p-value	HR ¹	95% CI ¹	p-value
Hypo-fractionated RT	0.81	0.44, 1.47	0.5	0.98	0.65, 1.47	>0.9
Age	0.99	0.96, 1.03	0.7	0.98	0.96, 1.00	0.11
T Stage						
2	0.66	0.21, 2.05	0.5	1.67	0.59, 4.75	0.3
3	0.70	0.22, 2.20	0.5	1.96	0.68, 5.60	0.2
4	1.66	0.55, 4.99	0.4	4.08	1.44, 11.5	0.008
N Stage						
1	1.76	0.77, 4.02	0.2	2.71	1.46, 5.03	0.002
2	2.09	0.88, 4.93	0.093	3.48	1.85, 6.55	<0.001
3	3.01	1.10, 8.25	0.032	4.84	2.33, 10.0	<0.001

Table 2. The multivariable-adjusted hazard ratios for DFS and OS

¹HR=Hazard Ratio

¹CI =Confidence Interval

DFS=Disease-Free Survival. OS=Overall Survival.

5-year disease-free survival for the hypofractionated group(n= 194) was 62.6%(55.7–70.2) whereas that for the conventional fractionation group(n=123) was 67.8%(59.8–76.8). However, there was no evidence to say any difference between the disease-free survival rates on the log-rank test(p=0.39). Median disease-free survival could not be assessed. Restricted mean disease-free survival time in the hypofractionated group was 45.1 months compared to 46.9 for the conventional fractionation group. We further analyzed the data with cox proportional hazards regression analysis with age, composite Stage, and T stage controlled for, showing those with hypofractionated radiotherapy had a hazard ratio of 0.98 compared to the normal group (95% CI for the hazard ratio was 0.65 to 1.47). All assumptions were met in the global and individual tests for the model (Table 2).

Discussion

In our study, the use of hypofractionated radiotherapy with a larger dose per fraction after mastectomy does not affect survival adversely when compared to the standard conventional fractionation of 50 Gy in 25 fractions over five weeks. The hypofractionated schedule will be completed in 3.2 weeks and takes fewer days than the

standard fractions schedule, which takes a long five weeks to complete treatment. The number of days saved also means the dose per fraction is saved, effectively utilizing limited resources with minimum wastage. Shorter treatment duration has long-standing implications in breast cancer treatment in countries where the number of radiotherapy facilities is inadequate and centres lagging in the initiation of radiation treatment to patients with long waiting times. The delay in initiation of radiation treatment is proven to adversely affect outcomes among breast cancer patients in multiple studies^(14, 15). The standard fractionation took 35 days to complete the treatment, whereas the hypofractionated schedule took only 22 days to complete the treatment. Completing treatment within a shorter time has several advantages, including patient convenience with shorter hospital visits, increased turnover of patients treated, and judicious use of resources considering the increasing number of patients who will require radiation treatment from each centre.

The use of hypofractionation in post-mastectomy breast cancer is extrapolated from the results of the hypofractionation trials, which included mainly early breast cancers where the majority underwent breast conservation surgery followed by adjuvant radiation treatment. Extrapolating the results to more advanced disease patients and postmastectomy patients has a robust radiobiological rationale based on the estimated lower α/β values similar to the surrounding late reacting normal tissues. Therefore, a hypofractionation schedule utilizing a higher dose per fraction is justified, keeping the total dose lower while maintaining comparable radiobiological effectiveness for the late reacting tissues. A hypofractionation program for post-mastectomy patients is supported mainly by retrospective studies^(16–19). The Ontario trial used a fractionation schedule of 42.5 Gy with 2.66 Gy per fraction in 16 fractions which mostly treated early breast cancers after breast conservation surgery with a conventional or hypofractionated plan to the whole breast with no difference in overall survival or disease-free survival between the two groups⁽⁹⁾. Our study also used the fractionation schedule of 42.6 in 16 fractions over 22 days. Most of the patients have high T2 and T3 disease, Stage II and Stage III disease, mainly locally advanced breast cancers with a few early breast cancers and high-risk features where locoregional therapy to the chest wall and regional lymph nodes is given after primary surgery.

Concerning survival outcome in postmastectomy hypofractionated radiation treatment, our results contrast a study from Taiwan that reported a higher 5-year overall

than the conventional schedule (73.0% and 62.7%), respectively. Still, there was no significant difference in the 5-year disease-free survival, concluding that hypofractionated radiation therapy has similar efficacy as conventional radiation treatment ($p=0.048$)⁽¹⁶⁾. Our survival rates are comparable to a study from China which prospectively examined the efficacy and safety of the hypofractionation with conventional fractionation in postmastectomy breast cancer patients, which had similar 5-year OS (86% for conventional vs 84% for hypofractionated) and 5-year DFS (70% vs 74%) with no meaningful difference between the two groups⁽¹¹⁾. Yet another study from Thailand that retrospectively analyzed their data reported that their 5-year OS and 5-year DFS were higher in the conventional fractionation group than the hypofractionated group, which was not statistically significant ($p=0.396$ and $p=0.385$, respectively)⁽²⁰⁾. We also obtained similar results with the higher outcome in conventional fractionation, both 5-year OS (81% vs 87.8%) and 5-year DFS (62.6% vs 67.8%) for the hypofractionated and conventional fractionation schedule, respectively, with no meaningful difference between the schedules. The lower survival rates observed in the hypofractionated radiation schedule could be due to the higher percentage of Stage III patients in that schedule compared to conventional fractionation (61.5% vs 50%, respectively).

In our study, there is a uniform proportion of patients with right and left-sided cancers in both hypofractionated

received chemotherapy either as neoadjuvant or adjuvant treatment. The lower percentage of patients undergoing neoadjuvant chemotherapy is probably due to the preference of surgeons to opt for primary surgery, which is a modified radical mastectomy in primarily operable disease. Irrespective of the timing of chemotherapy to surgery, whether neoadjuvant or adjuvant, breast cancer-related mortality is similar to either of the approaches⁽²¹⁾. Only very few breast conservations surgery was done in our study, probably due to the patient choice and the non-availability of surgical expertise for breast conservation and reconstructive procedures. In our study, all the patients underwent axillary dissection as evaluation of axilla was necessary for diagnostic and therapeutic benefit since sentinel lymph node sampling was not being done during that period. For adequate assessment of the axilla, a minimum number of 10 lymph nodes are to be dissected⁽²²⁾. In our study, most of the patients have inadequate lymph node dissection. In node-negative patients, when ten or more lymph nodes are removed, there is improvement in overall survival. Similarly, retrieving more than 20 lymph nodes in node-positive patients is associated with improved overall survival^(22,23). The probable reason for inadequate dissection in our study could be the surgeon's technical expertise and experience in breast surgery, the concerns for lymphedema, and the advanced age of the patients.

In our study with adjuvant radiation with either the hypofractionated or standard fractionation, no difference in survival inadequate axillary dissection is unlikely to influence the survival rates. Similarly, a study that tried to evaluate the optimal axillary surgical management of node-positive axilla did not find an improvement in survival with more than ten lymph nodes dissected⁽²⁴⁾. More than half of the people had an inadequate axillary dissection in our study, and they were distributed in both treatment groups with significant differences. But we could not find any survival difference as far as inadequate axillary dissection is concerned. The surgical expertise in accurately picking up the enlarged and at-risk lymph nodes at the time of surgery, even though the total number of lymph nodes retrieved is low. For patients with positive margins, boost irradiation was not planned, localization of exact area based on the orientation of specimen where boost has to be given would have been tricky, and also the practice of boost radiation to chest wall varies widely in recent times with more active chemotherapy regimens which have a favourable effect on locoregional control and survival rates⁽²⁵⁾.

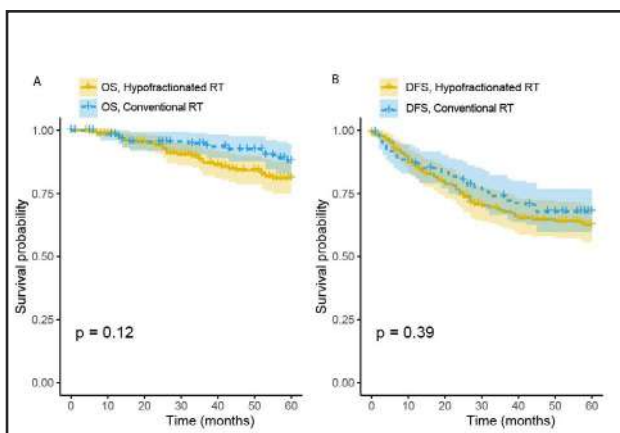


Figure 1. Kaplan–Meier curves of 5-year OS (A) and 5-year DFS (B) with hypofractionated radiotherapy and Conventional radiotherapy in breast cancers

and standard fractionated radiation regimes; as such, any adverse effect, even if it had occurred, would have been equally distributed in both treatment schedules. Also, the hypofractionated schedule consists of a lower total dose than the conventional fractionation the equivalent dose in

Even though various chemotherapy drugs and schedules are available for breast cancer patients, anthracyclines and taxanes are commonly used. The vast majority of the patients in our study have received anthracycline and taxane-containing regimens, either sequential or lone regimens. Although there is a significant difference in the chemotherapy schedule between the two fractionation schedules, the difference in survival rates could not be observed between chemotherapy regimens or fractionation schedules. The benefit of adding taxanes to anthracyclines with improvement in overall survival in breast cancer patients is seen especially in node-positive disease with lesser use in studies with or without lymph node-positive patients and node-negative patients⁽²⁶⁾. Our data also contained patients with lymph node-positive and negative disease, and this may be the reason which failed to show any difference in survival rates.

In our study, irrespective of the difference in fractionation of radiation treatment in the post-mastectomy patient, the survival does not differ. Even though the idea of hypofractionation is extrapolated from whole breast radiation treatment, the results of our study prove that it can safely be administered in post-mastectomy patients. Even though we have used a single hypofractionation schedule, this may not be the optimal fractionation schedule. The study results justify the use of post-mastectomy hypofractionated radiation therapy and open the way for other different moderate programs of hypofractionation. Larger prospective randomized control trials are required to examine the results of this study.

The clinical applicability of this post-mastectomy hypofractionated schedule in a busy radiation oncology department decreases waiting time for initiation of treatment in a busy department. It provides logistical advantages due to lesser treatment days. The results show that a hypofractionated schedule in post-mastectomy patients is a good alternative and should be considered as a viable option.

Limitations: An inherent drawback is the study's retrospective nature and inadequate lymph node assessment in the majority of the patients. We did record acute and late toxicity data but could not be analyzed due to the non-availability of all toxicities and their grading for most patients. Data on the dose received by the normal and critical structures were unavailable. A radiation boost to the chest wall in patients with positive margins was not considered. Long-term follow-up of the patients

could have been done. We hope these limitations will be addressed in future studies.

Strength: In our study majority of the patients were locally advanced and high-risk breast cancers, which is a growing concern in transitioning countries like India. Very few studies are available on postmastectomy hypofractionated radiation treatment. To the best of our knowledge, this study represents one of the largest studies from India, which compared two fractionation schedules in postmastectomy breast cancer patients. The study results add to the growing evidence that hypofractionated radiation treatment can be used safely in postmastectomy patients without compromising the outcome. The results support the hypothesis that hypofractionated radiation treatment is not different from standard fractionation.

Conclusion

Hypofractionated and standard fractionation schedules effectively treat postmastectomy breast cancer patients. There is no difference in survival between the two different fractionation. With shorter treatment days hypofractionation scheme is an attractive option in a limited-resource setting. Prospective trials with an assessment of toxicities are needed to examine the optimal hypofractionation schedule.

Author contribution statement:

CR and SSM conceived the idea for this study. CR contributed to the design of the study. SSM undertook the acquisition of data. IY and SSM did the statistical analysis of the data. CR and IY interpreted the data. CR drafted the work. SSM and IY revised the draft critically for intellectual content. CR, SSM, IY approved the final version to be published and agreed to be accountable for all aspects of the work.

Statement of conflict of Interest:

The authors declare no conflict of interest.

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Abbreviations:

OS – Overall Survival
DFS – Disease-Free Survival
IQR – Interquartile Range
CI – Confidence Interval

ECOG– European Co–operative Oncology Group

AJCC– American Joint Committee on Cancer

MRM– Modified Radical Mastectomy

BCS– Breast Conservation Surgery

RT– Radiotherapy

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