



HYPOFRACTIONATED POSTMASTECTOMY RADIATION THERAPY IS SAFE AND EFFECTIVE: OUR INSTITUTIONAL EXPERIENCE.

Oncology

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ABSTRACT

Retrospective analysis of 60 post mastectomy breast cancer patients receiving hypofractionated radiotherapy 39 Gy / 13 fractions, 2.3 weeks at 3 Gy/fraction was done. Assessment was done for quality of life, local relapse, loco-regional relapse, distant relapse, acute and late radiation toxicities.

Results: Maximum number of patients was in age group 40-49 years, postmenopausal, invasive ductal carcinoma grade 2 and higher BMI. The locoregional relapse was 6.7% and distant relapse was 18.3%. Quality of life of patient was improved due to less overall treatment time, less hospital stay, less economical burden and acceptable toxicity.

Conclusion: The hypofractionated radiotherapy in mastectomy breast cancer patients can be safely, effectively and feasibly given utilizing its radiobiological effect.

KEYWORDS

Hypofractionated Radiotherapy, Breast Cancer, Quality of life.

INTRODUCTION:

Adjuvant irradiation constitutes an important component in the post operative treatment of breast cancer, reaching as far as 25-30% of work load in radiotherapy department. Some approaches to reduce delays and optimize available resources include accelerated schedules of daily doses slightly superior to standard ones. The conventional regimen is 50 Gy/25 fractions several trials had utilized altered fractionations ranging from 2.5 Gy in 16 fractions to 3 Gy in 13 fractions(1).

Radiobiological basis of hypofractionation: Hypofractionated schedules are potentially attractive in treatment of breast cancer(2). From radiobiological point of view, the linear quadratic model suggests that when α/β ratio of tumor is the same or less than that of the critical normal tissue, then a larger dose per fraction (hypofractionation) with a modest decrease in total dose, may be equally or potentially more effective than conventional fractionation(3). An estimate of 4gray for α/β value has been already reported for the fractionation sensitivity of breast cancer. The low estimated α/β ratio for breast cancer means that it is probably as sensitive to fraction size as is dose limiting normal tissue and hypofractionation for breast cancers may actually be advantageous. Thus, breast cancer seems a promising field for hypofractionated schedules of radiation.

MATERIALS AND METHODS:

60 post mastectomy breast cancer patients aged between 20-80 yrs with good Karnofsky performance scale ($\geq 70\%$) with stage T1-3N0-1M0 (biopsy proven) who underwent modified radical mastectomy followed by chemotherapy and radiotherapy after 3 weeks interval were selected. Patient with KPS ≤ 70 , co-morbid condition like uncontrolled hypertension, diabetes mellitus, cardiac disease, connective tissue disorders, inoperable cases, pregnant women and with distant metastasis were excluded. The fractionation regimen given to the patient was hypofractionation schedule of 39Gy/13 fractions /3.3 weeks (3 Gy/fraction). The acute and late radiation toxicities as per the RTOG criteria related to skin, subcutaneous tissue, esophagus, lung, arm edema and shoulder joint movement restrictions from grade 0 to grade 3 were assessed(4). All the patients completed the planned treatment in time and none discontinued. After completion of radiation, hormonal therapy was started as per receptor study. First follow up was done after 1 month and then for 3 monthly in first year and 6 monthly in 2 years. Total follow up period was 2 years in which loco-regional control, distant metastasis, late radiation toxicity and quality of life assessment was done.

TABLE 1: Demographic and clinical characteristics of patients

A) Age

Age (years)	Percentage (%)
20-29	1.67
30-39	10.00
40-49	35.00
50-59	18.33
60-69	26.66
70-79	6.66
80	1.67

B) Menopausal status

Status	Percentage (%)
Pre menopausal	35
Post menopausal	65

C) BMI:

BMI	Percentage (%)
18.5-24.9	18.33
25-29.9	25.00
>30	56.67

D) Histological type

Type	Percentage (%)
Invasive ductal	95.00
Invasive lobular	1.67
Mixed ductal/lobular	0.00
Others - Papillary adenoca (1) Medullary ca (1)	3.33

E) Pathological Node status

Status	Percentage (%)
Positive	56.66
Negative	30
Not known(no axillary surgery)	6.66
Not known(missing data)	6.66

F) Tumour size (cm)

Size	Percentage (%)
<2 cm	20.00
2-5 cm	63.33
>5 cm	16.67

G) Tumor grade

Grade	Percentage (%)
1	26.67
2	45.00
3	18.33
Not known	10.00

H) Adjuvant therapy:

Therapy	Percentage (%)
None	0
Chemotherapy & no hormonal therapy	66.67
Chemotherapy & hormonal therapy	33.33

I) Lymphatic treatment (Axilla)

Treatment	Percentage (%)
Surgery & no radiotherapy	5.00
Radiotherapy & no surgery	13.33
Surgery & radiotherapy	81.67

J) Receptor study

Study	Positive(%)	Negative(%)	Not known(%)
ER	20.00	66.67	13.33
PR	15.00	71.67	13.33
HER-2 new	21.67	38.33	40.00

TABLE 2: Radiation toxicity

Site	Grade	Acute toxicity (%)	Chronic toxicity (%)
Skin	0	0	8.33
	1	41.67	36.67
	2	50	50
	3	8.33	5
S.C tissue	0	0	8.33
	1	53.33	50
	2	41.67	38.33
	3	5	3.33
Esophagus	0	68.33	71.67
	1	25	25
	2	6.67	3.33
	3	0	0
Lung	0	83.33	66.67
	1	13.33	16.67
	2	3.33	11.67
	3	0	5
Shoulder restrictions	0	75	63.33
	1	16.67	25
	2	6.67	66.7
	3	1.66	5
Arm edema	0	91.67	68.33
	1	5	16.67
	2	3.33	8.33
	3	1.66	6.67

TABLE 3: Survival analysis of relapse and mortality

Relapse and mortality	Percentage (%)
Local relapse	8.33
Local regional relapse	6.67
Distant relapse	18.33
Any breast cancer related event	33.33
All cause mortality	11.67
IHD	5.00
Symptomatic rib#	0.00
Symptomatic lung fibrosis	8.33

DISCUSSION AND RESULT:

The breast cancer is as sensitive to fraction size as the normal tissues. Various combined trials like START TRIAL A(2) & B(5) present mounting evidence that hypo fractionation is a safe and effective

approach to breast cancer radiotherapy. 60 post mastectomy female breast cancer patients were included in the study. Maximum patient were in age group 40-49 years, post menopausal, with higher BMI. The invasive ductal type of breast carcinoma was predominant (95%) with 56.7% patients having positive pathological nodal status, 38% patients having tumor size between 2-5cm and 45% patients with tumor grade 2. Acute and chronic radiation toxicities were tolerable. During radiotherapy, on weekly follow-up, maximum patients were subjected to grade 2 skin reactions (50%), Grade 1 subcutaneous tissues reactions were seen in 53.3% of patients. No acute adverse reactions were observed in esophagus and lung in maximum patients (68.3% and 83.3% respectively). Only 8.3% patients were having arm edema and 25% patients were having shoulder movement restrictions. Mean overall treatment time was 22.5 days.

For chronic radiation toxicity, 50% patients were having grade 2 skin reactions and 50% patients were having grade 2 subcutaneous tissue reactions. 71.7% patients were having grade 0 reaction in esophagus and 66.7% patients were having grade 0 reaction in lung. Only 5% patients were having grade 3 shoulder movement restrictions and only 6.7% patients were having grade 3 arm edema.

In two years follow up study; local relapse was in 8.3% patients, loco-regional relapse in 6.7% patients and distant relapse in 18.3% patients. Overall mortality was in 11.6% patients.

CONCLUSION:

The principal end points specified in the protocol were local, loco-regional relapse, normal tissue effects and quality of life with health economic consequences. Various randomized trials that compared hypofractionated radiation therapy with conventional radiation therapy also demonstrated no difference in late radiation mortality or local recurrence. A shorten fractionation schedule will lessen the burden of treatment for women and will have important quality of life benefits with respect to convenience and less time away from home and work(6,7). The toxicities were also well tolerable.

A median follow up of 2 years is too short to allow assessment of all the potential late normal tissue effects. Follow up of all women within the trial is continuing in order to assess the long term effects of the fractionation schedules. However the RMH/GOC pilot data (median follow up of 10years) showed that the relative effects of different fractionation schedules remain unchanged over time(8,9).

In conclusion, our data are consistent with the hypothesis that breast cancer shows similar responsiveness to the fraction size as the late responding normal tissues of the breast, as indicated by the α/β estimates. A prospective phase II trial on hypofractionation post mastectomy radiation therapy is safe and effective was done by Atif J. Khan et al published in journal of clinical oncology in June 2017(10).

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