Original Article

Comparison of Effects of Two Radiotherapy Techniques, Two Tangential / Single Anterior Supra-clavicular Field and Two Tangential / Two Anterior and Posterior Opposed Supra-clavicular Fields on Lung Volumes and Peripheral Oxygen Saturation

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Abstract

Background: Chest wall irradiation for early breast cancer affects forced vital capacity (FVC), forced expiratory volume in the first second of expiration (FEV1) and may change peripheral oxygen saturation (SpO2). In our institute chest wall is irradiated with a four field technique: two tangential and two oppositional anterior and posterior supraclavicular fields. Regional recurrence in this technique is less than 5 percent.

Materials and Methods: We conducted this study to compare changes in FEV1, FVC and SpO2 between standard three field and four fields technique. Materials and methods: We randomized 51 stage I and II breast cancer cases after modified radical mastectomy and completion of chemotherapy in two groups. In group I patients were treated with four field and in group II with three field technique using cobalt 60 teletherapy. Patients with a history of smoking, pulmonary disease, heart disease and any deformities in chest wall were excluded. Patients were stratified due to central lung distance (CLD), fields separation in tangential fields and filed borders defined in standard manner. Radiotherapy dose was 50.4 Gy in 28 fractions. Spirometry and pulse oxymetry was done before, one month after and three months after the completion of radiotherapy.

Results: FEV1, FVC and FEV1/FVC showed no significant difference between two groups one month and three months after radiotherapy. Also there was no significant difference in FEV1, FVC, FEV1/FVC one month after radiotherapy comparing with pre-radiotherapy values. There were significant differences in FEV1 and FVC reduction three months after radiotherapy in comparison with pre-radiotherapy values ($P<0.001$, $P<0.006$ respectively). SpO2 showed no significant difference between two groups and also in each group after one and three months.

Conclusion: Locoregional radiotherapy of chest wall and supraclavicular lymph nodes causes reduction in FEV1 and FVC three months after radiotherapy but there is no significant difference between three field and four fields techniques. We suggest this study be completed by using pulmonary function tests including spirometry and diffusion capacities.

Keywords: breast cancer, radiotherapy technique, lung volumes, pulse oximetry

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IJCP 2009; 2: 71-75

Introduction

Chest wall irradiation for early breast cancer increases locoregional control and overall survival [1-4] but it adversely affects forced vital capacity (FVC), forced expiratory volume in the first second of expiration (FEV1) [5] and may change peripheral oxygen saturation (SpO2). Different radiation techniques are used in different centers around the world depending on disease stage [2, 3]. Even in similar disease stages, different methods are used according to available facilities.

Until 5 years ago we were irradiated supra-clavicular region with two opposite antero-posterior and postero-anterior fields to mid-plane without any weighting for all patients who needed regional radiotherapy. Using two opposite fields to treat supra-clavicular and axillary nodes are not routine but is used in about 40% of cases in community practice[6] and is sometimes the preferred technique[7,8]. We had less than 5 percent of locoregional recurrence (unpublished data) using this technique. We irradiate supra-clavicular region by one anterior open field in most cases now. We conducted this study to compare effects of two radiotherapy techniques of supra-clavicular irradiation on FEV1, FVC and SpO2.

Methods

We performed a randomized clinical trial. Sample size was calculated as 25 patients in each group (α=5%, power=80%, clinical significance level=0.45 standard deviation=0.6%)

Women with stage II and III breast cancer (according to TNM staging system 2002) who had undergone modified radical mastectomy and were referred for complementary radiotherapy to Imam Hossein Hospital entered the study. Smokers (more than half pack-year), patients with chronic lung disease (including asthma, chronic bronchitis, known interstitial disease, etc) chronic cardiac disease, and anatomic abnormalities of the chest wall were not included.

Patients were assigned to two radiotherapy groups through simple randomization(using computer-generated random numbers).In one group, patients received two tangential and single anterior supra-clavicular field radiotherapy and in the other group radiotherapy was carried out using two tangential and two anterior and posterior opposed supra-clavicular fields. Patients were positioned for radiotherapy by placing a wedge under the trunk such that the upper chest was parallel with the horizon, the arm on the side of treatment was perpendicular to body, and the hand was placed on occiput. Tangential fields with standard borders (medial border, 1-1.5 cm lateral to midline; lateral border, midaxillary line; inferior border, 1.5-2 cm below the breast fold on the opposite side; and superior border, first or second intercostals space) and the supra-clavicular field (superior border, cricothyroid membrane; inferior border, superior border of the tangential field; lateral border, anterior axillary fold; and medial border, midline) were drawn for the patients.

A tangential field simulator radiography was taken and the central lung distance (CLD=the distance between the posterior border of the tangential field and the posterior border of anterior thorax in the center of tangential field) was determined. Patients were treated five days a week with a 60cobalt radiotherapy unit, a daily dose of 180Gy and a total dose of 5040 Gy.

The technician who performed spirometry was blinded to irradiation techniques used.

Patients with metastasis requiring new chemotherapy regimens and those who did not return as scheduled and had an interruption of longer than two weeks for spirometry were excluded from the study.

Spirometry was done immediately before radiotherapy and after the completion of radiotherapy at the end of the first and third months. A trained technician using a Fukudon-Sangyo spirometer (model: Spiro-Analyzer st-250) measured FEV1, FVC and FEV1/FVC. Patients were fully instructed about the procedure before testing.

Additionally, peripheral oxygen saturation was measured for all patients on the same day of spirometry. On each occasion, saturation was measured at rest and repeated after six minutes walking. One trained technician measured oxygen saturation by an Oxy Pulse machine.

We analyzed data using SPSS v.11 software. To test the relationship among variables we compared mean (95% confidence interval), standard deviation, standard error and frequency percentage using X2 test.

To compare the means of two groups based on results of Kolmogronov-Smornov and

Leven's test, Student T test and Mann_whiitney U test were used.

The ethical regulations dictated in the act provided by Ministry of Health were strictly observed.

Results

In a general view 63 patients met the inclusion criteria. At the end of the follow-up period 12 patients were excluded and 51 patients were analyzed, out of whom 25 were in the three-field group and 26 were in the four-field group. Mean age was 44.76 (CI= 41.10-48.42) and 47.42 (43.22-50.62) years in the three-field and four-field groups respectively. The difference was not statistically significant.

Forty percent of patients in the three-field group and 34.6% in the four-field group had right breast involvement. Once more, the difference was not statistically significant.

Mean CLD was 2.41 Cm (CI: 2.19-2.63) in the three-field group and 2.36 Cm (CI: 2.18-2.54) in the four-field group.

All patients received Cyclophosphamide chemotherapy. About 20.8% of the patients in the three-field group and 33.3% in the four-field group received Taxanes; and the difference was not statistically significant. In all patients of the three-field group and in 97.1% of patients of the four-field group, the time between initiation of radiotherapy and the last session of chemotherapy was less than one month.

difference in pretreatment values of FEV1, FVC, and FEV1 / FVC ruled out the possible confounding effect of initial (pretreatment) pulmonary volumes on the post-treatment comparison of these volumes between the groups.

In table 1, mean and standard deviation of FEV1, FVC, and FEV1 / FVC at the end of the first and third months post-radiotherapy are compared between the two groups. As shown, these values do not differ between the three-field and four-field group.

Table 1: *Pretreatment, one-month post treatment and three-month post treatment values of FEV_1, FVC, and FEV_1 / FVC in breast cancer patients treated with three or four field radiotherapy*

Parameter	Three-field group (n=25)		Four-field group (n=26)		Significance Level
	Mean	SD	Mean	SD	
Pretreatment FEV_1	1.84	0.36	1.87	0.37	NS
Pretreatment FVC	1.96	0.4	2.04	0.42	NS
Pretreatment FEV_1/FVC	0.94	0.04	0.92	0.05	NS
1-month post treatment FEV_1	1.76	0.42	1.85	0.41	NS
1-month post treatment FVC	1.87	0.47	2.09	0.7	NS
1-month post treatment FEV_1/FVC	0.94	0.05	0.91	0.1	NS
3-month post treatment FEV_1	1.71	0.39	1.77	0.36	NS
3-month post treatment FVC	1.84	0.4	1.93	0.45	NS
3-month post treatment FEV_1/FVC	0.92	0.06	0.92	0.06	NS

SD= Standard Deviation
NS= Not significant

Table 2: *Comparison of pretreatment FEV1, FVC, and FEV1 / FVC values with values obtained one month and three months after radiotherapy in all patients (n=51)*

Parameter	Pretreatment		1-month post treatment		3-month post treatment		a	B
	Mean	SD	Mean	SD	Mean	SD		
FEV_1	1.86	0.36	1.81	0.41	1.74	0.37	NS	0.001
FVC	2.00	0.41	1.98	0.60	1.89	0.43	NS	0.006
FEV_1/FVC	0.93	0.05	0.92	0.08	o.92	0.06	NS	NS

SD= Standard Deviation; NS= Not significant
a= Significance level before and one month after treatment
b= Significance level before and three months after treatment

Mean pre- radiotherapy FEV1 value was 1.84 liters (1.70-1.98) in the three-field group and 1.87 liters (1.73-2.01) in the four-field group. Mean FVC value was 1.96 liters (1.80-2.12) and 2.04 liters (1.88-2.20) in the three-field and four-field group, respectively. Mean FEV1 / FVC value in the three-field and four-field groups was 0.94 (0.93-0.95) and 0.92 (0.93-0.94), respectively. No statistically significant difference was observed in any of these three pulmonary function values. A lack of significant

Pre and post radiotherapy values of FEV1, FVC, and FEV1 / FVC were compared two by two in all patients regardless of number of fields used for radiotherapy which is shown in table 2. An important point in this table is that the values of FEV1, FVC, and FEV1 / FVC and oxygen saturation before radiotherapy were not significantly different from their values one month after radiotherapy. Whereas

Table 3: *Comparison of resting and exertional peripheral oxygen saturation before treatment, one month after treatment and three months after treatment in three-field and four-field groups*

Parameter	Three-field group		Four-field group		Significance level
	Mean	SD	Mean	SD	
Pretreatment Spo_2	95.66	0.72	96.15	0.83	NS
Spo_2 one month after treatment	95.90	1.29	96.36	0.68	NS
Spo_2 three month after treatment	96.17	1.28	96.31	0.99	NS
Exertional Spo_2 before treatment	96.20	1.14	96.52	0.69	NS
Exertional Spo_2 one month after treatment	96.65	1.89	96.05	1.22	NS
Exertional Spo_2 three month after treatment	95.76	1.95	95.95	1.17	NS

SD= Standard Deviation; Spo_2= Peripheral Oxygen Saturation; NS= Not Significant

FEV1, FVC values three months after radiotherapy decrease significantly compared to their pretreatment levels ($p<0.001$ and $p<0.006$ respectively).

Mean oxygen saturation was 95.66% (95.30-96.02) and 96.15% (95.77-96.53) in the three-field and four-field group, respectively. Moreover, pretreatment oxygen saturation after exercise was 96.2% (95.6-96.8) in the three-field group and 96.52% (96.49-96.55) in the four-field group. None of the above-mentioned differences was statistically significant.

Table 3 shows peripheral oxygen saturation one and three months after radiotherapy in resting and post-exercise states. No statistically significant difference is noted.

Discussion

Gross et al classified pulmonary complications of radiotherapy as either acute or chronic(9). Acute complications are seen 6 to 12 weeks after radiotherapy and represent a kind of pneumonitis. Chronic complications, on the other hand, develop 6 to 12 months after radiotherapy as pulmonary fibrosis [3, 9, 10].

We did not observe any significant difference in lung volume and capacity (FEV1, FVC, and FEV1 / FVC) and peripheral oxygen saturation, one and three months after radiotherapy with either three or four field techniques, in patients with stage II and III breast cancer. Pre- radiotherapy comparison of spirometric findings also failed to show any significant difference between the two groups; a fact that precludes the possibility of a confounding effect of initial pulmonary volumes. Therefore, it is feasible to compare post- radiotherapy values independently between two groups.

When all 51 patients are considered, no difference is noted between FEV1, FVC, and FEV1 / FVC values before radiotherapy and one month after it; however, FEV1 and FVC, but not FEV1 / FVC, are dramatically reduced three months after radiotherapy compared to their basal levels. Peripheral oxygen saturation did not change significantly one or three months after treatment.

These findings are in line with those by Lund et al who measured FEV1and FVC one week and three months after radiotherapy in 25patients with breast carcinoma and reported no change after one week but a decrease after three months[11]. He also measured Transfer Factor of Lung for Carbon Monoxide (TLCO) and total lung capacity (TLC) and found no difference one and three months after radiotherapy [11].

Another factor to be considered is the effect of chemotherapy on pulmonary function. Chemotherapy has been shown, in some studies, to cause impaired PFT results in radiotherapy patients. Chemotherapy can acutely increase DLCO [4,12] and may confound the results of PFT one month after radiotherapy.

It is to be noticed that although FEV1 and FVC are reduced three months after treatment but the FEV1 / FVC ratio remains constant which suggests a restrictive pathology. Nevertheless, definitive diagnosis of restrictive lung disease requires measurement of vital capacity. Likewise in the study by Lund et al parallel reduction in both vital capacity and FEV1 demonstrated a restrictive rather than obstructive pathology [11].

The more the volume of lung exposed to radiotherapy the higher is the rate of pulmonary complications [10,13]. Lind studied the impact of the number of radiotherapy fields. The results showed that increased radiotherapy fields for individual lymph node regions (including supra-clavicular and internal mammary regions) was associated with an increased rate of pulmonary complications. For instance, when a separate field was compared for the internal mamillary region to the tangential and supra-clavicular fields pulmonary complication rate increased. This is due to more lung volume exposed to radiation [14]. Still, in our study in spite of the fact that the number of supraclavicular fields was different between two groups, since the area being radiated was the same pulmonary complications were almost identical and did not show significant differences. However, complications did arise in both groups.

A review of the literature shows that there has been more interest in the severity and incidence of pulmonary complications of breast cancer related radiotherapy rather than comparison of these complications in various methods of such treatment [2,3,15]. Therefore, we focused on the comparison of pulmonary complications in two different radiotherapy methods.

Our study is limited in some ways. Firstly, we were not able to measure DLCO, residual volume and total lung capacity nonetheless, peripheral oxygen saturation can be an index of DLCO. Secondly, due to lack of three dimensional treatment planning system at that time we did not draw a dose-volume histogram and therefore accurate determination of the volume of lung in the supra-clavicular field was not possible. These limitations should be answered in future studies. Treating deep seated regional lymph nodes in supra-clavicular area needs IMRT or additional posterior field as shown by XIAOCHUN [7]

Based on the results it could be concluded that despite a decrease in pulmonary volumes, especially at the end of the third month, no difference was observed in the severity of pulmonary complications between three-field and four-field groups. Therefore, radiotherapy with an anterior supra-clavicular field or two anterior and posterior supra-clavicular fields does not alter the complication profile. Moreover, in some breast cancers with more extensive involvement of lymph nodes, radiotherapy with two anterior and posterior supra-clavicular fields may more confidently treat deep lymph nodes[7,8].

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