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ASSESSMENT OF CHANGES IN PULMONARY FUNCTION AFTER RADIATION IN LUNG CANCER PATIENTS – A PROSPECTIVE OBSERVATIONAL STUDY

Oncology

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ABSTRACT

Background: Randomized trials have found that treatment with chemotherapy & radiotherapy led to improved survival for inoperable locally advanced non small cell lung cancer patients (NSCLC). Sufficient data is not available in our developing country regarding changes on pulmonary function after radiotherapy in lung cancer. Despite newer technical developments of radiation therapy in treatment of NSCLC, radiation–induced lung toxicity (RILT) remains a crucial problem. Clinically assessed RILT scores have their limitations, and more objective measures such as pulmonary functions tests (PFTs) might help to improve treatment protocol.

Objectives: Assessment of pulmonary function with respect to FEV1, FVC, FEV1/FVC, PEFR, FEF25 – 75%.

Material & Methods : All biopsy proven 62 cases of Non small cell carcinoma of lung (NSCLC) were included. All patients received post chemotherapy conventional external radiation 60 Gy in 30 fractions for 6 weeks by Teletherapy Theratron 780e Cobalt60 machines. After clinical assessment, all patients were placed for Pulmonary function tests (FEV1, FVC, FEV1/FVC, PEFR, FEF25 – 75%) at baseline, 1 month, 3 month after completion of radiation. Spirometric analysis was done by electronic spirometer (HELIOS 702). Data analysis was done by SPSS software.

Results: 62 patients were included in this study. All lung function parameter did not shows significant changes after radiation, compared to baseline study. All p value show >0.05.

Conclusion: In my study, no statistically significant changes are found in the lung function parameters.

KEYWORDS

External radiation, lung function, spirometric analysis

INTRODUCTION:

Worldwide, nowadays lung cancer is the common cause of death in both men and women[1]. Approximately 70% to 80% of lung cancer cases are non-small-cell lung cancer (NSCLC). The prognosis of patients with advanced NSCLC is generally considered poor, with a median survival of 9–11 months and a 2-year survival around 20%-30%[2,3]. With the advancement of newer chemotherapy drugs, median survival is increased nowadays[4]. The median survival of patients with untreated advanced disease is reported to be 4–6 months[5]. In advanced disease, patients are placed for radical treatment with newer chemotherapy molecule and local radiation[6,7]. Pulmonary Function Test(PFT) are breathing tests to find out how well one breath move air in and out of the lungs and how well oxygen enters the body. Forced vital capacity (FVC) and forced expiratory volume in the first second (FEV_1) are considered essential parameters. It gives information about an existing pulmonary obstruction, loss of lung retraction etc.

Thoracic radiotherapy (RT) is associated with significant alterations in lung function as assessed by objective pulmonary function tests (PFTs) [8,9].

The potential side effects of radiation therapy for lung cancer is symptomatic radiation pneumonitis & radiation fibrosis [10]. Sufficient data is not available in our developing country regarding changes on pulmonary function after radiotherapy in lung cancer. Despite newer technical developments of radiation therapy in treatment of NSCLC, radiation–induced lung toxicity (RILT) remains a crucial problem. Clinically assessed RILT scores have their limitations, and more objective measures such as pulmonary functions tests (PFTs) might help to improve treatment protocol.

AIMS & OBJECTIVES :

Purpose of this study was assessment of pulmonary function with respect to FEV1, FVC, FEV1/FVC, PEFR, $FEF_{25-75\%}$. Depending on PFTs, future treatment strategy can be determined regarding radiation technique upgradation.

MATERIALS & METHODS :

All biopsy proven 62 cases of Non small cell carcinoma of lung (NSCLC) stage III attending the OPD of Radiotherapy, R G Medical College & NRS medical college, satisfying the specified Inclusion and Exclusion Criteria were included. Inclusion criteria was 1) age above 30 years and below 70 years, 2) Patients with stage IIIA, IIIB, (AJCC 7th edition) patients who received definitive chemotherapy, 3) ECOG performance status 0 or 1. 4) Baseline normal hematological, renal and hepatic profile. 5) Baseline normal cardiac and pulmonary function status. Exclusion criteria was 1) Metastatic lung cancer & stage I & II, 2) Patients underwent lung surgery, 3) Previous history of any malignancy. 4) Severe pulmonary or heart disease, 5) Neuropsychiastry illness.

All patients received post chemotherapy conventional external radiation 60 Gy in 30 fractions over a period of 6 weeks by Teletherapy Theratron 780e Cobalt60 machines. After clinical assessment, all patients were placed for Pulmonary function tests (FEV1, FVC, FEV1/FVC, PEFR, $FEF_{25-75\%}$) at baseline, 1 month, 3 month & 6 month after completion of radiation. Spirometric analysis was done by electronic spirometer (HELIOS 702) at Physiology department. Data analysis was done by SPSS software v 24 for Windows and the P value was considered significant if less than or equal to 0.05 for a 95% Confidence Interval. Before the test was performed, all patients were informed properly about the procedure and informed written consent was taken. Permission from Institutional Ethical Committee was taken for this study.

RESULTS:

62 patients were studied. Out of these, 48 patients were male & 14 were female. 50 patients are smoker & 12 non smoker. 3 patients have past history of pulmonary tuberculosis.

Patients characteristics are shown in table 1. Number of cases of squamous cell carcinoma & adenocarcinoma are almost same (table 2). 35 cases are seen in stage IIIA, & 27 cases in stage IIIB. All lung function parameter did not shows significant changes after radiation, compared to baseline study. All p value show >0.05 (table 3).

Table 1: Patients characteristics

Characteristics	No. of patients (%)
Age	
< 50 years	17 (27.4)
>50 years	45 (72.6)
Sex	
Male	48 (77.4)
Female	14 (22.6)
Smoking status	
Smoker	50 (80.6)
Non smoker	12 (19.4)

Tobacco habit		
Addiction	42	(67.7)
Non addiction	20	(32.3)
Tuberculosis		
Past history	03	(4.8)
No history	59	(95.2)
ECOG score		
PS 0	38	(61.3)
PS 1	24	(38.7)
Residential status		
Urban	28	(45.1)
Rural	34	(54.9)

Table 2 : Tumour Characteristics

Tumour Characteristics	No. of patient (%)
Histopathology	32 (51.6)
Squamous cell carcinoma	30 (48.4)
Adenocarcinoma	
Stage	35 (56.5)
IIIA	27 (43.5)
IIIB	
T1N2M0	09 (14.5)
T2N2M0	07 (11.3)
T3N2M0	07 (11.3)
T4N0M0	08 (12.9)
T4N1M0	04 (6.5)
T1N3M0	10 (16.1)
T2N3M0	12 (19.4)
T4N3M0	05 (8.0)
Left side tumour	28 (45.2)
Right side tumour	34 (54.8)

Table 2 : PFT parameters Variations in Mean values

PFT PARAMETERS	Baseline Pre RT (Mean) (a)	30 days after RT completion (Mean) (b)	90 days After RT Completion (Mean) (c)	p value b vs a	p value c vs a
FVC%	94.62	92.47	91.28	0.331	0.271
FEV1%	94.60	93.24	91.20	0.216	0.099
FEV1/FVC	78.47	78.25	78.07	0.90	0.83
FEF25-75%	91.87	88.69	88.36	0.139	0.109
PEFR	93.82	92.46	91.55	0.094	0.078

P value < 0.05 is significant. (RT means radiation therapy)

DISCUSSION :

In our study, we found that incidence of NSCLC is higher in male patient (77.4%) than female (22.6%). Age wise incidence is higher in elder patients (>50 years age). Smokers are affected more than non smokers (80.6% vs 19.4%). Among the patients, tobacco addicted was 67.7% and non addicted was 32.3%. Rural people have more preponderance in lung cancer than the urban (54.9% vs 45.1%). Past history of pulmonary tuberculosis was seen in 4.8% cases. Adenocarcinoma & Squamous cell carcinoma were seen in almost equal proportion (51.6% vs 48.4%). Tumours had the right lung predilection (54.8%) than the left (45.2%). ECOG score was 0 in 61.3% cases & score 1 in 38.7% cases.

Data analysis of lung parameters was done with SPSS software. FVC% in baseline , at 30 days & 90 days after RT completion are 94.62, 92.47 (p value 0.337) & 91.28 (p value 0.271) respectively. FEV1% in baseline, at 30 days & 90 days after RT completion are 94.60, 93.24 (p value 0.216) & 91.20 (p value 0.099) respectively. FEV1/FVC in baseline, at 30 days & 90 days after RT completion are 78.47, 78.25 (p value 0.90) & 78.07 (p value 0.83) respectively. $FEF_{25-75\%}$ in baseline, at 30 days & 90 days after RT completion are 91.87, 88.69 (p value 0.139) & 88.36 (p value 0.109) respectively. PEFR in baseline, at 30 days & 90 days after RT completion are 93.82, 92.46 (p value 0.094) & 91.55 (p value 0.078) respectively (table 3). P value < 0.05 is considered significant.

S.Margaritora and co-workers [11] performed a study that shows an impairment of respiratory function is evident in the immediate postoperative setting in patients with non–small cell lung cancer receiving induction chemoradiotherapy. In the long-term period, a general recovery in diffusing capacity of the lung for carbon monoxide was found, whereas an improvement of forced expiratory volume in 1 second, vital capacity, total lung capacity, and residual volume was detected in the younger.

Guerra et.al [12] investigated the effect of modern radiation techniques IMRT, 3DCRT with proton beam on PFTs in NSCLC patients. DLCO is reduced in majority of patients after radiation. On multivariate analysis, pre-treatment DLCO, GTV, lung and heart dosimetric data and total radiation dose were associated with post treatment DLCO decline.

Gopal R et.al, [13] performed a study that shows that the addition of chemotherapy to RT significantly exacerbates the post-RT decrease in TLC and DLCO. The greatest decrease in DLCO occurs in patients treated with concurrent chemoradiation.

Miller et al. [14] reported that by 1 year, the median FEV1 and forced vital capacity were similar as baseline and the median DLCO was 90% of baseline.

Regarding radiation, Borst GR et al, [15] evaluated the changes in pulmonary function after high-dose radiotherapy (RT) for non-small-cell lung cancer in patients with a long-term disease-free survival. PFTs were measured in 34 patients with inoperable non-small-cell lung cancer before RT and at 3 and 18 months of follow-up. Thirteen of these patients had a pulmonary function test (PFT) 36 months after RT. Changes were expressed as relative to the pre-RT value. The authors also evaluated the impact of chronic obstructive pulmonary disease, radiation pneumonitis, mean lung dose, and PFT results before RT on the changes in pulmonary function. At 3, 18, and 36 months, a significant decrease was observed for the T(lcoc) (carbon monoxide transfer factor corrected for hemoglobin)(9.5%, 14.6%, and 22.0%, respectively) and the alveolar volume (5.8%, 6.6%, and 15.8%, respectively). The decrease in FEV(1) was significant at 18 and 36 months (8.8% and 13.4%, respectively).

Anne G.H. Niezink et al. [16] proved that pulmonary function declines after RT, especially after (chemo)radiation using 3DCRT, IMRT, or volumetric modulated arc therapy (VMAT), and to a lesser degree after SABR. Declines of FEV1 seem to be considerably less pronounced than declines of DLCO. Lung DVH parameters do not seem to predict post−treatment pulmonary function changes for patients irradiated with SABR, but in non−stereotactic treatment, decreasing lung function depends on lung DVH parameters, especially on MLD and V20. Only one study found lung DVH parameters as risk factors using multivariable analysis, but, overall, there is a severe lack of appropriate multifactorial models predicting post−radiotherapy lung function based on clinical factors combined with DVH parameters.

Radiation pneumonitis (RP) is one of the major dose-limiting toxicities in patients receiving radiotherapy for lung cancer. Higher radiation doses will improve local control rate but also increase the incidence of treatment related toxicity [17].

Radiation pneumonitis is the most common toxicity after radiotherapy for thoracic tumors and can have substantial influence on the morbidity and mortality of patients with lung cancer. Therefore, it is essential to find out the predictive factors for the development of RP to reduce the incidence of RP. Many studies reported that radiation dose and irradiated lung volumes are closely associated with the risk of RP leading to significant changes in PFT. Several Dose volume parameters have been proposed as predictive factors for RP but still there is no consensus about which parameters are ideal for predicting the RP [18,19,20].

In our study, external radiation was given in Cobalt 60 machine. There are much advancement nowadays regarding newer technique of external RT (3D CRT, IMRT, IGRT etc.) which can provide high dose radiation in target volume with less normal tissue damage.

In our study, long term observation could not be done due to shortage of time. Follow up PFT at 6 month, 9 month, 12 month would be more informative. More number of cases is required for acurate interpretation & outcome.

CONCLUSION :

In this study. All the lung function parameters were carefully observed. After a meticulous analysis, no significant changes in lung function was detected. As this is single institutional study, more number of

patients & multi institutional data and long duration follow up are required to achieve the conclusion.

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