RESEARCH ARTICLE

Effects of Definitive Chemoradiotherapy on Respiratory Function Tests and Quality of Life Scores During Treatment of Lung Cancer

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Abstract

Background: Chemoradiotherapy is an important treatment modality for lung cancers. The aim of this study was to investigate alterations in, as well as the interrelationship between, lung function and quality of life of patients receiving chemoradiotherapy due to locally advanced non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) limited to the thorax. Materials and Methods: The study included patients receiving definitive chemoradiotherapy for lung carcinoma. The respiratory function of the patients was assessed by measuring forced expiratory volume in 1 s per unit (FEV1) and forced expiratory volume in 1s per unit of vital capacity (FEV1/VC) before, in the middle of and after treatment. During the study, EORTC QLQ C30 and LC13 questionnaires developed by the Committee of the European Organization for Research and Treatment of Cancer (EORTC) were employed to evaluate the quality of life on the same day as respiratory function tests (RFT). Findings: The study included 23 patients in total: 19 (82.6%) diagnosed with NSCLC and 4 (17.4%) with SCLC. The average percentage FEV1 was 55.6±21.8% in the pre-treatment period, 56.2±19.2% in the middle of treatment and 60.4±22% at the end of treatment. The improvement in functional scores, symptom scores and general health scores during treatment was not statistically significant (P= 0.568, P= 0.734, P= 0.680, P=0.757 respectively). Conclusions: Although this study showed an improvement in respiratory function and quality of life of patients during treatment with thoracic chemoradiotherapy, no statistically significant results were obtained. While evaluating the effectiveness of treatments for lung carcinoma, the effects of treatment on respiratory function and quality of life should be considered.

Keywords: Lung carcinoma - chemoradiotherapy - respiratory function - quality of life

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Introduction

As the most frequent, common and important cause of cancer-related deaths, lung carcinoma results in more than one million deaths annually. Due to late diagnosis and high relapse rates, the 5-year survival rate is approximately 10%. As the prevalence of smoking is increasing in developed countries, lung carcinoma will be an important health problem in the future as well (Parkin et al., 2002; Sauter et al., 2008; MacKinnon et al., 2010; Panda et al., 2013; Amoori et al., 2014)

Lung carcinoma has two basic histological types: small cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC). Small cell lung carcinoma accounts for 13%, and non-small cell lung carcinoma accounts for 86% of lung cancers (Dong et al., 2009; Goldstraw, 2012). Sixty percent of these patients receive radiotherapy (Tyldesley et al., 2001). Curative surgery, radiotherapy and chemotherapy combinations can be used for patients with Stage 1-3 non-small cell lung carcinoma (NSCLC). Concurrent or subsequent definitive chemoradiotherapy can be used for patients with unresectable locally advanced NSCLC (Rowell and O'Rourke, 2004). Surgical treatment of SCLC is limited. Chemoradiotherapy is applied to a radiotherapy port for limited stage cancers, while chemotherapy can be applied alone for a generalized form of cancer (Ha et al., 2013; Wang et al., 2014).

Lung carcinoma affects regional ventilation and/or perfusion as a result of atelectasis or pressure on large vessels, caused by bronchial obstruction. Thoracic radiotherapy (RT) can improve ventilation-perfusion by reducing tumor size, but also causes a reduction in pulmonary function as a result of lung damage (Borst et al., 2005; Yuan et al., 2012).

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The the importance of quality of life has been emphasized for numerous chronic diseases. The World Health Organization (WHO) defines quality of life as "individuals' perception of their position in life in the context of the culture and value systems in which they live", which can simply be expressed as an individual response in daily life to the physical, mental and social effects of disorders affecting individual satisfaction in given life conditions (Orley and Kuyken, 1993). Quality of life and pulmonary parameters are important outcome measure during treatment of lung cancer (Mohan et al., 2008)

The aim of this study was to investigate the alterations in, as well as the interrelationship between, lung function and quality of life of patients receiving chemoradiotherapy due to locally advanced NSCLC and SCLC limited to the thorax.

Materials and Methods

Patient selection

This study included patients with locally advanced NSCLC and patients with SCLC limited to the thorax, who were followed-up at Antalya Education and Research Hospital, in the Medical Oncology and Radiation Oncology clinics between 2011 and 2012, and were histopathologically confirmed and staged via imaging methods. The performance score for the study was assessed according to the scoring system of the Eastern Cooperative Oncology Group (ECOG). This study included patients with an ECOG between 0 and 2, objectively measured disease, sufficient bone marrow reserves, and normal hepatic and renal function. Patients with an ECOG score ≥3 and/or whose treatment was initiated in another clinic and continued in our clinic were excluded. The patient files were analyzed retrospectively and information on age, gender, disease stage and treatment was obtained.

Radiotherapy

For each patient, a PET-CT fusion was implemented on computed-tomography (CT) images acquired by T-Bar while the patient was supine. The tumor tissues and lymph node stations involved were contoured in accordance with PET-CT and current planning CT data, and then GTV (gross tumor volume), CTV (clinical target volume) according to tumor localization, and PTV (planning target volume) were established. Using a linear accelerator of 6/18 MV photon energy and a fraction dose of 2 Gy/day, a total of 66 Gy or 60 Gy external RT was administered to patients with NSCLC or SCLC respectively. All patients continued to the treatment unremittingly.

Chemotherapy

Chemotherapy was planned in accordance with patient age and ECOG scoring system. Two different chemotherapy protocols were administered: ***i)*** Protocol 1: Cisplatin 50/3 g/m^2/day, on day 1, 8, 29 and 36, concurrent with radiotherapy; etoposide 50 mg/m^2/day between days 1-5 and 29-33.

Hydration and polyantiemetic treatments were used to manage the side effects of this protocol. The biochemical follow-up was conducted by weekly hemograms. *ii)* Protocol 2: Carboplatin concurrent with radiotherapy, out of 2 AUC (area under the concentration versus time curve [AUC] 2.0, Calvert formula)/weekly.

This treatment protocol was primarily administered to patients aged 70 years or older.

Respiratory function tests (RFT) and quality of life assessments

The respiratory functions of patients included in this study were assessed by measuring forced expiratory volume in 1 s per unit (FEV1) and forced expiratory volume in 1 s per unit of vital capacity (FEV1/VC), before, in the middle and at the end of treatment. During the study, EORTC QLQ C30 and LC13 questionnaires developed by the Committee of the European Organization for Research and Treatment of Cancer (EORTC) to evaluate the quality of life with cancer were used on the same day as RFT.

Statistical analyses

Statistical analyses were performed using SPSS software version 15. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests) to determine whether or not they were normally distributed. Descriptive analyses were presented using means and standard deviations for normally distributed variables, and medians and interquartile range (IQR) for the non-normally distributed and ordinal variables. The effect of treatment on the change in RFT over time was investigated using repeated measures analysis of variance. The Greenhouse-Geisser correction was used when the sphericity assumption was violated. The functional scores, symptom scores, general health scores, and social function scores measured by EORTC QLQ C30 were assessed using the Friedman test, due to the abnormal distribution of data. An overall 5% type-I error level was used to infer statistical significance.

Results

The study included 23 patients in total: 19 patients (82.6%) diagnosed with NSCLC and four patients (17.4%) diagnosed with SCLC. Out of the patients with NSCLC, 12 (52.2%) had squamous cell carcinoma and seven (30.4%) had adenocarcinoma. The average age of patients was 64.6±7.7 (range 41-78). All patients with SCLC were at the limited stage, while 13 (56.5%) patients with NSCLC were at stage 3A and five were at stage 3B. One patient was a stage 4 patient with metastasectomy.

A history of respiratory disease was noted in three patients (13%) and a history of cardiac disease in two (8.7%). The average percentage of FEV1 was 55.6±21.8 before treatment, 56.2±19.2 in the middle of treatment and 60.4±22 at the end of treatment. The improvement in respiratory function was assessed by repeated measures analysis of variance. The effects of treatment on respiratory function tests were not significant (P=0.603).

The average functional score was 69.4 before treatment, 73.5 in the middle of treatment and 78.3 at the end of treatment. The effects of treatment on functional

tests were not statistically significant (P=0.568). The average symptom score was 29.2 before treatment, 29.1 in the middle of treatment and 29 at the end of treatment. There was no significant change in symptom score after treatment (P=0.734). The average general health score was 55.7 before treatment, 57.5 in the middle of treatment and 59 at the end of treatment. The effects of treatment on general health score were not significant (P=0.680). The average social function score was 69.5 before treatment, 72.7 in the middle of treatment and 77.5 at the end of treatment. The effects of treatment on social function scores were not significant (P=0.757).

Discussion

In this study, there were no significant changes in respiratory function scores during chemoradiotherapy. Unlike in this study, Marks et al. assessed the pulmonary symptoms due to radiotherapy, as well as radiographic changes and subclinical changes in pulmonary function tests in 184 patients receiving radiotherapy to the thorax, and the relatively low pre-radiotherapy RFT values were observed to have a tendency to decline after radiotherapy in most of the patients with pulmonary symptoms (Marks et al., 2012). Similar results were demonstrated by Ming et al. in a prospective study in which pre- and post-radiotherapy lung perfusion examinations (SPECT) and respiratory function tests (RFT), as well as changes in the lung function of 53 patients who received radiotherapy after being diagnosed with lung cancer, breast cancer and lymphoma were assessed (Fan et al., 2001). Gopal et al. assessed the effects of thoracic radiotherapy and different chemotherapy combinations by RFT performed before and after radiotherapy, and demonstrated that respiratory function deteriorated with treatment (Gopal et al., 2003). In these studies, respiratory function was assessed using pre- and post-treatment controls. In our study, although there was a tendency towards improvement of respiratory function during treatment, this tendency was not statistically significant.

In the long term, thoracic radiotherapy worsens the outcome of respiratory function tests. A study by Borst et al. (2005) demonstrated that pulmonary function was significantly reduced 3 months after radiotherapy and that a significant reduction in FEV1 occurred within 18-36 months. The reduction in pulmonary function is associated with the average lung dosage, and a greater reduction in RFT was observed in patients with chronic obstructive pulmonary disease.

Yuan et al. (2012) investigated global and local pulmonary function disorders during radiotherapy through assessments performed before and in week 3 of treatment in 56 patients receiving thoracic radiotherapy. Although the reduction in degree of dyspnea determined by common terminology criteria for adverse event version 3 was statistically significant in week 3 of radiotherapy (p=0.01), no statistically significant change was observed during the remainder of the treatment period (p>0.05). Similar to our study, no statistically significant changes in RFT parameters were demonstrated during radiotherapy.

As an indicator of the physical, psychological and social health of an individual, the quality of life is affected by lung cancer, as in all chronic diseases. Tests that assess the quality of life enable measurement of the extent to which the disease affects the daily life, health and happiness of the patient. For individuals with chronic respiratory diseases, the quality of life is assessed in order to determine the differences between a better and a worse level of health, and to enable an understanding of the benefit of treatment during treatment alterations. Therefore, quality of life scores are beneficial for the assessment of treatment received. In addition, this measurement reflects the difference between the desired and current life style. Our study found that functional scores, symptom scores, general health scores, and social function scores measured by EORTC QLQ C30 did not change with chemotherapy.

A prospective study by Lagendijk et al. (2001) assessed the changes in pre- and post-treatment quality of life by EORTC QLQ-C30 and QLQ-LC13 in 164 patients with NSCLC who received a radical treatment (60 Gy). A gradual decrease was demonstrated in functional scores and general health scores, in particular between months 6-12 after the completion of radiotherapy.

Pijls-Johannesma et al. (2009) assessed the quality of life of 57 patients with NSCLC and SCLC who received high-dose accelerated hyperfractionation radiotherapy or combined chemoradiotherapy. This study showed that the general quality of life decreased after radiotherapy and returned to its basic level at month 3, after which it remained stable.

Ozturk et al. (2009) investigated the changes in respiratory function, as well as quality of life scores, due to treatment in 28 patients with NSCLC who received radical or post-operative radiotherapy. As in our study, no changes in functional scores, general health scores or social function scores were noted. They demonstrated that treatment improves the symptom scores.

Although there was an improvement in respiratory function and quality of life during treatment with thoracic chemoradiotherapy in our study, no statistically significant results were achieved. The effects of treatment on respiratory function and quality of life of patient should be considered to assess the effectiveness of treatments received due to lung cancers.

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