A Retrospective Study of Patients Undergoing Palliative Radiotherapy for Airway Obstruction due to Lung Cancer

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Abstract. Background/Aim: In advanced stage lung cancer, bulky tumors can cause serious symptoms such as malignant airway obstruction (MAO). Prompt response to airway obstruction might be essential to improve quality of life and prolong life expectancy. Palliative external beam radiotherapy (EBRT) is a less invasive and highly safe treatment method that can alleviate symptoms and at the same time treat lung cancer. However, there are few reports on the results of palliative radiotherapy performed for improving airway obstruction and obstructive pneumonia. Therefore, this study retrospectively examined the effectiveness of palliative radiotherapy. Patients and Methods: We reviewed 38 lung cancer patients with MAO who underwent EBRT. Patients were treated with a median dose of 37.5 Gy (range=30-40 Gy) in 10-20 fractions. Whether a patient was a responder or non-responder was assessed by whether the bronchus that was obstructed before EBRT reopened or improvement of obstructive pneumonia was observed on follow-up chest X-ray or computed tomography after EBRT. Results: The median survival time was 135 days (range=31-469 days) for the responders to EBRT and 45 days (range=23-355 days) for non-responders; this difference was statistically significant (p=0.03). One-year overall survival rate was 18.5% and 0% for the responders to EBRT and non-responders, respectively. Conclusion: Palliative EBRT might be an important option for non-curative lung cancer patients with MAO.

Lung cancer is the fourth most common malignancy among men and the third most common among women in Japan (1) and is the most commonly diagnosed and leading cause of cancer-related deaths worldwide (2). Advances in diagnostic imaging have made it possible to detect lung cancer at an early stage, but the number of patients who are already at an advanced stage at diagnosis remains high (3). In such patients with advanced lung cancer, malignant airway obstruction (MAO) caused by a large tumor in the trachea can cause symptoms such as coughing, pain, bleeding from the airways, respiratory distress, as well as hoarseness and superior vena cava syndrome (4). Post-obstructive pneumonia, which affects about 7.6% of lung cancer patients, is defined as an infection in the lung parenchyma secondary to bronchial obstruction (5, 6). Response to treatment is slow and usually not curable with antibiotic therapy alone. Repeated infections and recurrences are common. About 10-15% of patients develop serious complications such as lung abscesses, empyema, hemorrhage, and fistula formation (7). Prompt response to airway obstruction is essential to improve quality of life (QOL) and prolong life expectancy. It is also expected that additional anticancer treatments, such as chemotherapy, can be indicated if the patient’s general condition improves.

However, lung cancer patients with MAO are often patients with advanced stage lung cancer, such as those with metastases or locally advanced disease, and often have poor performance status (PS). Thus, they are usually not candidates for chemotherapy or surgery. Interventional pulmonology is used to treat endobronchial lesions to relieve the obstruction, palliate symptoms, and treat the infection (5). However, many complications associated with the
procedure have been reported (8), therefore patients with a short prognosis are not indicated. Endobronchial brachytherapy is also used to relieve airway obstruction and is an effective treatment for MAO (9-12). However, this is a time-consuming therapy, and for effective and safe treatment, physician-patient cooperation is essential. Therefore, this treatment is not possible for patients who are unable to follow the physicians’ instructions, such as those with postural fluid retention. However, palliative external beam radiotherapy (EBRT) is a less invasive and highly safe treatment method that can alleviate symptoms and at the same time treat lung cancer. However, there are few reports on the results of palliative radiotherapy performed for the purpose of improving airway obstruction and obstructive pneumonia. Therefore, we retrospectively examined the effectiveness of palliative radiotherapy.

**Patients and Methods**

**Patient selection.** The present study was retrospective, with an opt-out consent method, and approved by the Ethics Committee of the Saitama Medical Center, Saitama Medical University (2021-109). The medical records of patients with lung cancer whose airway was obstructed or narrowed by a lung mass and who underwent EBRT for the tumor that obstructed the distal airway from January 2018 to December 2020 at Saitama Medical Center, Saitama Medical University were reviewed. The eligibility criteria were as follows: 1) lung cancer; 2) patients with airway obstruction that was complete, or part of the airway was obstructed, and those with post-obstructive atelectasis or pneumonia found on simple chest X-ray or computed tomography (CT); and 3) patients who underwent palliative EBRT for MAO. The presence of prior systemic treatment or resection due to lung cancer was not included in the selection criteria. A total of 48 patients underwent EBRT for airway obstruction; however, we selected 38 patients whose medical records, especially post-treatment imaging results, were available for use in the retrospective analysis. The excluded 10 patients had no follow-up image data to use in assessing treatment response.

**Radiotherapy.** An Optima CT 660 Pro Advance scanner (GE Healthcare, Bloomington, IL, USA) was used to obtain CT images for radiotherapy planning. Radiotherapy treatment plan was created using Eclipse (Varian Medical Systems, Palo Alto, CA, USA) software. The radiation oncologists established gross tumor volume (GTV) as the whole or part of the intrapulmonary mass that was thought to be causing the airway obstruction. Since the treatment was for palliative purposes, GTV was limited to the responsible lesion as much as possible. Subsequently, the clinical target volume and planning target volume were contoured with appropriate margin, considering the patient’s condition. Three-dimensional conventional radiotherapy plans were created and used to prescribe a median dose of 37.5 Gy (range=30-40 Gy) in 10-20 fractions. Radiotherapy dose prescription protocols are summarized in Table I.

**Evaluation of the effect of radiotherapy and statistical analysis.** The effectiveness of EBRT was evaluated through changes in radiographic findings and/or clinical course assessed by radiation oncologists and medical oncologists. The chest X-ray or CT before EBRT was compared with that after EBRT. Whether a patient was a responder or non-responder was assessed by whether the bronchus, which was obstructed by the pulmonary mass prior to EBRT, was found to be reopened on follow-up chest X-ray or CT after EBRT. The overall survival (OS) duration was defined as the period from the beginning of radiotherapy to the date of death from any cause. We divided the patients into two groups according to their histology, small-cell carcinoma and non-small-cell carcinoma and compared them.

Kaplan-Meier method and Generalized Wilcoxon test were used for survival curves. Fisher exact test was used to assess the significance of the association between tumor histology and response to EBRT. All analyses were performed using the program BellCurve for Excel, and a p-value <0.05 was considered statistically significant.

**Results**

**Patient characteristics.** Patient characteristics are shown in Table I. Thirty-eight patients were enrolled in this study. The median age was 72.0 years (range=45-87 years) and most of them were over 65 years old (81.6%). Their Eastern Cooperative Oncology Group (ECOG) PS were 0-2 (34 patients) and 3-4 (4 patients). Their clinical stages based on the new TNM (tumor, nodes, and metastases) classification,
8th edition, were 2 (1 patient), 3 (15 patients), and 4 (22 patients). Eighteen patients had obstructive pneumonia.

**Treatment outcomes.** The OS curve for all patients is shown in Figure 1. The overall median survival time was 112 days (range=23-469 days). During the follow-up period, 36 (94.7%) deaths were confirmed. The median survival time was 135 days (range=31-469 days) for the responders to EBRT and 45 days (range=23-355 days) for non-responders; this difference was statistically significant ($p=0.03$) (Figure 2). One-year OS rate was 18.5% for the responders to EBRT and 0% for non-responders.

The median survival time was 81 days (range=25-375 days) for patients with small-cell lung cancer and 136 days (range=23-469 days) for patients with non-small-cell lung cancer, and there was no significant difference between the two groups ($p=0.29$).

The effect of palliative EBRT on a patient with airway obstruction due to lung cancer that compressed the left main bronchus is shown in Figure 3. Palliative EBRT resulted in patency of the bronchus and improvement of the left atelectasis.

**Discussion**

MAO usually occurs during a terminal condition and has a poor prognosis. Pneumonia secondary to MAO is usually polymicrobial and difficult to cure with antibiotics alone (7). Choi et al. analyzed 75 patients with lung cancer with MAO and reported that the median survival time was 3.4 months, and one-year OS rate was 15.9% (13). Lee et al. analyzed 95 patients and reported that the median survival time was 124 days, and one-year OS rate was 9.9% (14). Nihei et al. reported that the median survival time was 114 days, based on a review of 24 patients (15). In this study, the median survival time was 112 days, one-year OS rate was 15.7%, and 36 (94.7%) deaths were confirmed during the follow-up period.

Although the expected prognosis is poor, the symptoms associated with MAO decrease QOL and require treatment. There are several treatment options for MAO, including an interventional pulmonology technique or endobronchial brachytherapy (5, 9, 10).

Zaric et al. analyzed 48 cases and reported that QOL and overall health was found to be statistically significantly improved ($p<0.0001$) by neodymium yttrium-aluminium-garnet laser resection according to The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (16). Kashiwabara et al. reported that transbronchial microwave ablation (MWA) was effective for malignant central airway obstruction by comparing OS between patients treated by transbronchial interventions of NWA and those of stenting (17). However, the interventional pulmonology technique requires a lot of experience and high skills, and many complications associated with the procedure have been reported. Hayashi et al. analyzed 93 cases and reported that the median survival time was 6.2 months, and one-year OS rate was 25.2% after interventional pulmonology, and suggested that stenting is indicated only for patients with a prognosis of 3 months or longer (8).

It is clinically proven that endobronchial brachytherapy is effective for patients with a significant endobronchial tumor.
that causes symptoms of obstructive pneumonia. Celebioglu et al. analyzed 95 patients and reported that the symptoms (dyspnea, cough, hemoptysis, and pneumonia) and bronchial obstruction index improved significantly (12). However, only a limited number of hospitals can provide endobronchial brachytherapy. Especially in Japan, the treatment used to be available, but to the best of our knowledge, there are few facilities that offer it today. One reason for this is that

Figure 3. Images from a lung cancer patient who underwent palliative radiotherapy for malignant airway obstruction. A) Pre-treatment chest x-ray and computed tomography (CT) images; B) Treatment planning images; C) Post-treatment chest x-ray and CT images. Prior to radiotherapy, the left main bronchus was compressed by lung cancer (indicated by arrow in Figure 3A), leading to extensive atelectasis in the left lung. Radiotherapy resulted in patency of the left main bronchus and improvement of the left atelectasis.
endobronchial brachytherapy is a labor- and time-intensive procedure. The patient is expected to cooperate with the physician and remain still for long periods of time for effective and safe treatment, which is a difficult request for a patient with a poor general condition.

Palliative EBRT has some advantages over these treatments. The irradiation technique we used in this study is conventional three-dimensional conformal radiotherapy that can be performed with a general-purpose radiotherapy device. It can be performed in many facilities where radiotherapy is performed, though some of the high-precision radiotherapies that have been developed in recent years can only be provided by a limited number or devices and facilities. Time to treatment is short and palliative EBRT can be performed in patients with a poor respiratory condition or hemoptysis who are expected to start treatment as soon as possible. Treatment time is also short and can, thus, be performed in patients who have difficulty in maintaining the same position for a long time. Furthermore, EBRT is less invasive and has a lower risk of fatal complications. Because radiotherapy has a therapeutic effect on lung cancer, even when the purpose of EBRT is palliation, it may be a bridge toward more aggressive therapy.

As for palliative EBRT for MAO, Lee et al. suggested that EBRT can be a good treatment option for bronchial obstruction; the response rate was 78.9%, and patients who responded to EBRT had significantly higher survival than those who did not respond to EBRT (14). Nihei et al. also reported that responders to EBRT had a higher survival time than non-responders to EBRT (median, 192 days vs. 43 days, respectively) and the difference was statistically significant (15). Choi et al. reported that one-year OS rate was 33.1% in the responding group and 0% in the non-responding group, and the difference was statistically significant (13). In this study, we analyzed the effects of palliative EBRT performed to improve airway obstruction and obstructive pneumonia in 38 patients with lung cancer with MAO. A median dose of 37.5 Gy was applied and responders to EBRT had significantly higher survival time (median survival time; 135 days vs. 45 days) and higher one-year OS rate (one-year OS rate: 18.5% and 0%) than non-responders to EBRT. These results are comparable to previous reports. From a pathological point of view, there was no significant difference between patients with small-cell lung cancer and those with non-small-cell lung cancer in this study. It is generally believed that small-cell lung cancer is more sensitive to radiotherapy than non-small-cell lung cancer, but since the patients included in this study had a short expected life expectancy, we assume that no difference in OS by pathology was observed.

There are some limitations to this study. First, the number of cases was small. Second, because of its retrospective nature, items not listed in the chart (for example, ECOG PS) could not be evaluated. In addition, it is difficult to follow up on the therapeutic effect of patients and the patients who had no follow-up image data regarding treatment response were excluded, which could have caused selection bias. In order to solve these problems, prospective observational studies including QOL evaluation are required. We retrospectively examined the effectiveness of palliative radiotherapy performed in patients with lung cancer for the purpose of improving airway obstruction and obstructive pneumonia and revealed that the OS rate was significantly higher in the responders to EBRT compared to that in non-responders. We believe that palliative EBRT might be an important option for lung cancer patients with MAO. Further research such as a prospective observational study is required.

Conflicts of Interest

The Authors have no financial relationships to disclose in relation to this study.

Authors’ Contributions

T.T. and T.Y. developed the concept. N.U., T.T., T.Y. and S.U. researched the data. N.U. wrote the manuscript. T.T., T.Y. and S.U. contributed to the discussion of the manuscript. N.U., T.T., T.Y., F.M., S.K., M.S., R.S., S.U., T.H., S.H. and M.S. had full access to all the data in the study and reviewed the manuscript.

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