Outcomes of airway stenting for advanced lung cancer with central airway obstruction

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Abstract

Approximately 30% of lung cancer patients will develop central airway obstruction (CAO). Interventional therapeutic bronchoscopy including airway stenting (AS) providing immediate and effective palliation is therefore essential to improve quality of life (QoL). However, no report has demonstrated the survival benefit of AS. We retrospectively reviewed 65 patients with CAO due to lung cancer who underwent AS from June 1994 to May 2008. Seventy-nine stents were required. Silicon, metallic, or both stents were placed in 42 (60%), 19 (29%), or eight (11%) patients, respectively. Single stent was required in 53 (83%) patients, double in 10 (14%), and triple in two (3%). AS could provide acute relief of central airway and significant improvement was seen in 98% of patients. Fifty-nine patients with detailed observations were assessed further. Morbidity and mortality rates were 22% and 8%, respectively. AS resulted in 25.2% of one-year survival rate and 6.2 months of median survival time (MST). AS followed by adjuvant therapy provided a four-month increase in MST, although overall survival was not significantly changed. This study represents a single-institution experience. Although an aggressive strategy of AS is justified in order to improve symptoms and QoL, AS itself did not contribute to survival benefit.

Keywords: Airway stenting; Interventional therapeutic bronchoscopy; Central airway obstruction; Lung cancer

1. Introduction

Approximately 30% of patients with lung cancer will develop central airway obstruction (CAO) [1–3]. The gold standard treatment for airway obstruction is surgical resection and reconstruction. However, most patients with CAO due to lung cancer are poor surgical candidates on the basis of either physiological or oncological criteria. Interventional therapeutic bronchoscopy (ITB) providing immediate and gratifying palliation is therefore essential to improve the quality and length of life. ITB includes mechanical core-out of tumor, laser vaporization, photodynamic therapy, brachytherapy, cryotherapy, electrocautery and airway stenting (AS). In particular, AS can provide immediate, durable and stable airway patency resulting in reliable and prolonged relief of airway symptoms. Management of malignant airway disease requires comprehensive and accurate evaluation of resectability by general thoracic surgeons. Palliative therapy is reserved for unresectable patients. The optima management of these patients with CAO includes the use of radiotherapy, laser therapy, photodynamic therapy and AS. Therefore, in 1994, we established an airway interventional bronchoscopy program for the management of CAO in the Division of Thoracic Surgery at Tokyo Medical University. Over the past 15 years, we performed 361 ITBs for 283 patients with CAO due to benign or malignant disease. In the current study, we retrospectively reviewed all these patients and especially focused on 59 patients with CAO due to advanced lung cancer to perform a detailed analysis on the effectiveness of AS.

2. Patients and methods

2.1. Patients

Two hundred and eighty-three patients who underwent ITBs for CAO from June 1994 to May 2008 were retrospectively reviewed in this study with the approval of the Institutional Review Board. Access to patients’ medical records was approved by Tokyo Medical University and patients’ confidentiality was maintained.

2.2. Interventional therapeutic bronchoscopy

Indications of ITB included known unresectable malignant CAO, the development of lobar collapse during or after treatment, acute or subacute changes in respiratory status not otherwise explained, or evidence of endobronchial disease amenable to palliation. All ITBs were performed in a laser and fluoroscope-equipped operation room. Rigid and flexible bronchoscopy was performed in almost all patients.

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Details of airway preparation for AS by dilation or coring out a tumor have also been previously described [4–6]. Briefly, mechanical debulking using the tip of the rigid bronchoscope was first carried out followed by laser ablation or balloon dilation of the residual tumor using Nd:YAG laser (KTP/YAG Surgical Laser System, Laserscope, San Jose, CA, USA), argon plasma coagulation (APC300 and ICC200; ERBE, Tubingen, Germany) and microwave (Microwave; Altres, Tokyo, Japan) or balloon dilation (CRE fixed-wire balloon dilators, Boston Scientific, Natick, MA, USA).

2.3. Airway stenting

AS was considered in patients in whom it was impossible to restore more than 50% of the lumen even after airway dilation or who required repeated airway dilation [4]. Two-thirds of the stents used in this series were silicone rubber (Dumon, Novatech, Aubagne, France) with external studs. Y stents (Dumon, Novatech, Aubagne, France) were also surfaced with studs, but these were predominately held in place by their geometry at the carina. Self-expandable metallic stents, Ultraflex (Boston Scientific, Natick, MA, USA) and Spiral Z (Medico’s Hirata, Tokyo, Japan) were used when there was difficulty in stably placing a silicone stent, extreme extrinsic compression resulting in silicone stent migration, or inability to place a large enough silicone stent into the airway.

2.4. Follow-up and assessment

Patients were extubated at the end of the procedure and usually discharged within a week after bronchoscopic assessment. Airway humidifications by an ultrasonic nebulizer and medication of tranilast, an antiallergic drug suppressing granulations were usually used during hospitalization and after discharge. Patients underwent bronchoscopy approximately every one to six months. Nearly 40% of patients were referred from other institutions and most patients had advanced and terminal disease, which limited the practicality of returning to our institute for follow-up care. Details of the stent procedure, availability and prognosis were obtained from the operative notes, medical records and office charts in our institutions or discussions, or a combination of these with the patients, their family, or referring physicians.

The survival curve was estimated using the Kaplan–Meier method. Differences between survival curves were computed with the log-rank test. A \( P < 0.05 \) was considered statistically significant (StatView 5.0 SAS Institute Inc, Cary, NC, USA).

3. Results

3.1. Airway stenting for advanced lung cancer

One hundred and ten ITBs were performed in 93 lung cancer patients with CAO in this period. Of these 93 patients, 65 (69%) patients required 79 airway stents during ITB. Silicon, metallic, or both types of stents were placed in 42 (60%), 19 (29%), or eight (11%) patients, respectively. The number of stents required in a patient was single in 53 (83%) patients, double in 10 (14%) patients, and triple in two (3%) patients. Fig. 1 shows the distribution and type of 79 stent placed in this series. Twenty-eight (36%), 17 (22%), 16 (21%), 14 (18%), and four (5%) stents were placed in the carina, left main bronchus, right main bronchus, trachea, and truncus intermedius, respectively. In airway obstruction at the carina position, we usually used silicon Y stents (82%), otherwise dynamic Y stents (18%). Silicon stents tend to be used in the right main bronchus, while metallic stents tend to be used in the left in this series.

Because 39% of patients in this series were referred from other institutions, the practicality of returning to our institute for follow-up care was limited. In addition, patients with low grade malignant tumor were excluded in the further analysis of prognosis. Therefore, 59 (90%) of 65 patients were then extracted for further analysis including survival, morbidity, and mortality. As shown in Table 1, there were 51 male and eight female patients, ranging in age from 42 to 91 years with a mean of 63.9 years. The histological classification was 30 squamous cell carcinoma, 20 adenocarcinoma, four large cell carcinoma, three small cell carcinoma and two unclassified carcinoma. The distribution of clinical staging or patient status at the time of AS demonstrated that most of patients were stage III/IV terminal cases, postoperative recurrence or refractory to their previous treatment.

AS were performed in 59 advanced lung cancer patients with CAO with no intraoperative death, however percutaneous cardiopulmonary support (PCPS) was initially prepared or required in five (8.5%) cases. AS has the ability to provide acute relief of central airway is remarkably
effective, and significant improvement can be seen in 98% of patients. However, severe complications from stenting occurred in 13 patients, including severe mucus retention requiring bronchoscopic toilet repeatedly \((n=9)\), idiopathic pneumothorax \((n=3)\), idiopathic pyothorax \((n=2)\), esophageal stenosis requiring balloon dilation \((n=1)\) and acute pulmonary distress required mechanical ventilation \((n=1)\). Five of 59 patients died within 30 days or could not be discharged after the stenting procedure due to operation-related, disease progression or refractory to adjuvant treatment of lung cancer. Therefore, AS related morbidity and mortality rate in this series was 22% and 8%, respectively. In addition, two outpatients had late death on 32 days or five months later because of airway perforation and hemoptysis.

Survival curve of this series was demonstrated in Fig. 1, which results in 25.2% of one-year survival rate and 6.2 months of median survival time (MST). As shown in Fig. 2, these patients in this series were classified by four groups according to the clinical course before and after AS. AS is a palliative procedure intended to improve symptoms of CAO. Forty-one percent of patients were able to receive adjuvant treatment including chemotherapy and/or radiotherapy after AS. Fig. 2b shows that while MST of patients with adjuvant treatment after AS was longer than those without, the difference was not statistically significant \((P=0.16)\).

4. Discussion

Both patients with benign or malignant airway obstruction suffer from disabling dyspnea, obstructive pneumonia and impending suffocation. ITB may provide immediate and gratifying palliation that can rescue the patients from imminent death and assure an improvement in quality of life (QoL). Of the 283 patients who underwent 361 ITBs in our cohort, 71% of which were for malignant disease the as same as previous reports. The leading cause of CAO requiring ITB is lung cancer (31%) followed by thyroid cancer (27%), and esophageal cancer (7%). As shown in Table 1, major histological types of lung cancer were squamous cell carcinoma and adenocarcinoma. Most of the patients have limited prognosis because of advanced stage disease or had been refractory to a conventional therapy.

ITB including mechanical core-out of tumor, laser vaporization, photodynamic therapy, brachytherapy, cryotherapy, and electrocautery is itself effective for some patients with intrinsic and extrinsic compression of the tumor; however, results are not always sustainable. AS is a palliative procedure intended to provide durable and stable improvement of CAO by keeping airway patency. Therefore, 65 patients with advanced lung cancer in our series required 79 airway stents. There is no report which addressed a detail of distribution and type of stent placed in advanced lung cancer cases. In our series, silicon, metallic, or both types of stents were placed in 42 (60%), 19 (29%), and eight (11%) patients, respectively. Fig. 1 shows that 36%, 22%, 21%, 18%, and 5% of all stents were placed in the carina, left main bronchus, right main bronchus, trachea, and trunchus intermedius, respectively. At the carina position, we usually used silicon Y stents (82%), otherwise we used dynamic Y stents (18%). Silicon stents tend to be used in right main bronchus, while metallic stents tend to be used in left in this series. The development of self-expanding nitinol stents are reported to have improved complications previously reported and have advantages including

<table>
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<tr>
<th>Table 1. Demographics of 59 advanced lung cancer patients undergoing airway stenting</th>
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<tr>
<td>Mean age (range), years</td>
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<td>Male/female</td>
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<tr>
<td>Performance status</td>
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<td>Unknown</td>
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<tr>
<td>Histology</td>
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<td>Adenocarcinoma</td>
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<td>Squamous cell carcinoma</td>
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<td>Large cell carcinoma</td>
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<td>Undifferented carcinoma</td>
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<td>Clinical stage or status</td>
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<td>III/IV</td>
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<tr>
<td>Postoperation</td>
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<tr>
<td>Refractory to treatment</td>
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<tr>
<td>Severe complications</td>
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<td>Severe mucus</td>
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<td>Idiopathic pneumothorax</td>
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<td>Idiopathic pyothorax</td>
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<td>Esophageal stenosis</td>
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<td>Acute pulmonary distress</td>
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<td>Operation-related or hospital death</td>
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Fig. 2. (a) Survival curve of all this series, (b) survival comparison of patients with airway stenting followed by adjuvant treatment or not.
less migration, dynamic expansion, and simple insertion [7, 8]. Recently, self-expanding nitinol stents with a thin silicon cover have also become available, which are designed to prevent or inhibit tissue ingrowth through the body of the stent. In general, uncovered metallic stents are used in patients with predominantly extraluminal compression, while silicone-covered metallic stents may be favored in patients with intraluminal tumors.

There are several reports detailing the results of AS for malignant CAO [5, 8–14]. Although significant improvement of symptoms was clearly reported, no report could demonstrate the survival benefit for malignant disease. We understand that it is difficult to assess the true survival effect of AS, because most patients in our series are referred from outside and are usually managed in a tertiary referral center with limited follow-up data. MST was 6.2 months, and one-year survival was only 25.2% in our series (Fig. 3a), this would not be unexpected in this population of patients with advanced stage or refractory to conventional therapy. AS can provide effect acute relief to improve the symptoms of airway obstruction and to facilitate therapy. Only when it employs an additional therapy and yields an anti-tumor effect could it theoretically provide a survival benefit. Forty-one percent of patients in our series received some form of adjuvant treatment, while 59% of patients had exhausted all therapies and had received no additional therapy (Fig. 4). Some added but not statistically significant survival benefit of AS was documented in those patients who did receive adjuvant therapy. The combination treatment of AS followed by adjuvant treatment provided a four-month increase in median survival, although overall survival was not changed (Fig. 3b). Our criteria of adjuvant therapy following AS is based on patients with advanced stage and a refractory status that extended their survival by at least three months. According to the American Society of Clinical Oncology Clinical Practice Guideline [15], a platinum-based two-drug combination of cytotoxic drugs is recommended for patients with a performance status of 0 or 1 and a single cytotoxic drug is sufficient for patients with performance status of 2.

This study represents a single-institutional experience. Particularly, we focused on advanced lung cancer patients who underwent AS and demonstrate the possibility of survival benefit of AS followed by adjuvant therapy. Although an aggressive strategy of AS is justified in order to improve the symptoms of airway obstruction and to improve QoL in patients with malignant CAO, AS itself does not contribute a survival benefit. Therefore, it is important that AS plays a crucial role as a bridge to surgery and it is necessary for the development of effective adjuvant therapy.

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References