Lung Cancer

Laser Therapy and Airway Stenting for Central-Type Lung Cancer

JMAJ 46(12): 547–553, 2003

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Abstract: Endoscopic procedures such as laser therapy and airway stenting are attracting attention as therapeutic methods for the treatment or preservation of pulmonary functions in inoperable cases. Among types of lung cancer, the best candidates for photodynamic therapy (PDT) using low-power laser and photosensitizer are cases with central-type early stage lung cancer, and complete remission (CR) can be expected. CR was achieved in 86.4% of cases with endoscopic early-stage lung cancer treated with PDT. High-power laser therapy for advanced lung cancer is performed for the purpose of palliative opening of tracheobronchial lesions presenting stenosis and obstruction due to tumors. This procedure was effective in 81.0% of cases with obstructive advanced lung cancer treated with Nd-YAG laser vaporization. If re-stenosis after the reopening of bronchial lumen is a problem, airway stenting is effective for maintenance of bronchial lumen, producing dramatic improvement of dyspnea immediately after stenting. These various endoscopic procedures are minimally invasive methods based on the respect for and improvement of the patients' QOL.

Key words: Central-type lung cancer; Laser therapy; Photodynamic therapy (PDT); Airway stenting

Introduction

Lung cancer has a tendency to develop preferentially in aged people as well as other types of cancer. Although the development of diagnostic techniques has gradually improved the detection of early-stage lung cancer, many of the newly detected cases still have inoperable...
advanced cancer, and some cases of early-stage cancer are inoperable because of cardiopulmonary dysfunction due to high age. Endoscopic procedures such as laser therapy and airway stenting intended for the treatment or preservation of pulmonary functions in these inoperable cases are considered very important.

**Low-Power Laser Therapy for Early-Stage Lung Cancer**

Photodynamic therapy (PDT) for cancer using a combination of low-power laser irradiation and tumor selective photosensitizer was first applied clinically by Dougherty et al. in 1978 to the skin metastasis of breast cancer. Since then, we have been studying the clinical application of the world’s first endoscopic PDT in cooperation with them. In Japan, PDT using a tumor selective photosensitizer Photofrin and excimer dye laser was covered by the national health insurance system in April 1996. Thereafter, the combination of Photofrin and YAG-OPO laser was included. The mechanism of the action of this PDT is considered to involve singlet oxygen, which is generated through photochemical reactions and causes degenerative necrosis of tumor cells.

1. **Indications**

The best candidates for PDT are cases with central-type lung cancer in the early stage. While the therapy is intended for complete remission (CR), this currently requires satisfaction of the following endoscopic conditions: (1) the peripheral margin of the lesion can be identified; (2) the lesion is located in a position that can be irradiated with laser easily; (3) the lesion is superficial with a major diameter of 1.0 cm or less; and (4) histological type is early superficial squamous cell carcinoma.

2. **Therapeutic results of PDT**

Laser irradiation is performed endoscopically 48 to 78 hours after the intravenous administration of 2.0 mg/kg of Photofrin (Fig. 1). The irradiation energy is 100 to 200 J/cm², and energy levels in this range do not cause any heat degeneration or other adverse effect. The technique is referred to as “low-power” because of this fact. The duration of irradiation is usually 10 to 20 minutes.

CR was achieved in 165 out of 191 lesions (86.4%) of endoscopic early-stage lung cancer. The analysis of treatment results according to various factors is summarized in Table 1. Recurrence after CR was observed in 21 lesions (11.0%). Reasons hindering CR included the difficulty in identifying the peripheral margin of the lesion, infiltration of the lesion beyond bronchial cartilage, and the difficulty of laser irradiation due to the tangential orientation of the lesion to the laser beam direction. Recently, techniques such as fluorescence bronchoscopy and endobronchial ultrasonography are used for objective evaluation of the extent and depth of the lesion. The 5-year survival rate was 94.2% excluding deaths of other diseases and 68.3% including deaths of other diseases. Figure 2 presents a case treated with PDT.

3. **Complications and precautions**

The generation of necrotic substances during several days after PDT may cause obstructive pneumonia due to airway obstruction, and these substances must be removed bronchoscopically. The only major side effect of Photo-
**Table 1** Results of PDT for Early-Stage Lung Cancer by Endoscopic Diagnosis (The 1st Department of Surgery, Tokyo Medical University)

<table>
<thead>
<tr>
<th>Endoscopic diagnosis</th>
<th>No. of lesions</th>
<th>CR (rate)</th>
<th>PR</th>
<th>Recurrence after CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodular</td>
<td>31</td>
<td>28 (90.3%)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Hypertrophic</td>
<td>149</td>
<td>128 (85.9%)</td>
<td>21</td>
<td>19</td>
</tr>
<tr>
<td>Polyp</td>
<td>11</td>
<td>9 (81.8%)</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

**Identification of peripheral**

- **Possible**
  - 145
  - 134 (92.4%) (98.1%)*
  - 11
  - 20

- **Impossible**
  - 46
  - 31 (67.4%)
  - 15
  - 1

**Tumor size (cm)**

<table>
<thead>
<tr>
<th>Diameter (cm)</th>
<th>No. of lesions</th>
<th>CR (rate)</th>
<th>PR</th>
<th>Recurrence after CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.5</td>
<td>58</td>
<td>55 (94.8%)</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>0.5 ≤ &lt;1.0</td>
<td>78</td>
<td>74 (94.9%)</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>1.0 ≤ &lt;2.0</td>
<td>31</td>
<td>25 (80.6%)</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>2.0 ≤</td>
<td>24</td>
<td>11 (45.8%)</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>191</td>
<td>165 (86.4%)</td>
<td>26</td>
<td>21</td>
</tr>
</tbody>
</table>

*1 cm or less in diameter. CR: complete remission, PR: partial remission.

Fig. 2 A case in complete remission after PDT

A male, 77-year-old patient with nodular-type early-stage lung cancer in left B10 bifurcation. The patient was diagnosed as squamous cell carcinoma (carcinoma in situ) based on biopsy. Endoscopy performed 2 months after PDT revealed complete disappearance of tumor, and biopsy indicated CR.
frin is photosensitivity of the skin (sunburn). To prevent this effect, patients should avoid being exposed to direct sun light for about 2 weeks after dosing. Even if patients develop sunburn, it resolves with time in many cases.

**High-Power Laser Therapy for Advanced Lung Cancer**

The purpose of this therapy is to cauterize and vaporize tumors endoscopically using the high energy of the laser beam. Therefore, this procedure is indicated for tracheobronchial lesions developing stenosis or obstruction due to tumors.

### 1. Laser systems for vaporization

Nd-YAG (neodymium-yttrium-aluminum-garnet) laser system at the wavelength of 1,064 nm is used commonly. The Nd-YAG laser light is poorly absorbed by hemoglobin and water compared to the CO₂ laser, while it has high penetration into tissues. KTP/YAG laser and diode laser systems have also been developed recently. The KTP/YAG laser is a complex laser oscillation system that can switch freely between KTP laser (532 nm) suitable for incision and vaporization and Nd-YAG laser suitable for coagulation and hemostasis.

The diode laser has advantages of small size and stable output characteristics, and is maintenance-free. A small portable unit can operate with domestic 100-V power source, facilitating bedside treatment for patients that cannot be transported to the endoscopy room.

### 2. Indications

High-power laser vaporization of tumors is used in the role of local adjuvant therapy for radiotherapy, chemotherapy, and airway stenting. The main targets are tumors occurring in large airway in the range from the trachea to the entries to segmental bronchi. It is also indicated for emergency life-saving treatment in cases with serious ventilatory insufficiency due to tracheobronchial obstruction presenting a risk of asphyxia. Palliative indications include atelectasis and obstructive pneumonia due to advanced cancer, preparation for stenting, and hemostasis for the bleeding from tumors.

### 3. Complications and precautions

The process of tumor vaporization can damage surrounding normal tissues. Because of the risk of bronchial perforation, it is crucial to set the laser energy as low as 10 to 20 W to vaporize the margin of tumor. In particular, greatest care should be taken in irradiating a tumor where the peripheral bronchus is not identified. Considerable experience is required before performing accurate irradiation to lesions responding to the breathing and cough reflex of the patient.

Because the most dangerous complication is massive bleeding from blood vessel perforation, the operating physician must be fully acquainted with the anatomic location of blood vessels. Equipment for intubation, oxygen administration, etc. must always be provided at hand, so that it can be used when hemorrhage is not controlled by hemostatic irradiation and infusion of vasoconstrictors. Massive aspiration of the soot and smoke generated from the laser vaporization of tumors may cause serious respiratory insufficiency in the patient.

### 4. Therapeutic results

Nd-YAG laser vaporization was performed in 177 cases of obstructive advanced lung cancer at the 1st Department of Surgery, Tokyo Medical University. The result was considered effective if tumor diameter or obstruction was reduced by 50% or more, and ineffective if the reduction was less than 50%. Overall, 143 of 177 cases (81%) were evaluated as effective. As seen from the location occupied by tumors, the percentage of effective results was 93% (64/69) for lesions in the trachea or main bronchi and 73% (79/108) for lesions in lobar or segmental bronchi. Complications included massive hemorrhage in 10 cases (6%) and bronchial perforation in 4 cases (2.3%).
Stenting for Central Airway Obstruction

While Nd-YAG laser vaporization is effective as a palliative treatment for obstructive tracheobronchial lesions, re-stenosis occurring after the reopening of bronchial lumen presents a problem. In addition, this method is ineffective for stenosis by extrinsic compression due to outward tumor advancement beyond the tracheobronchial wall. Stenting is effective for maintaining airway in such cases. Dramatic improvement of dyspnea can be achieved immediately after stent insertion.

1. Various types of stents

**Dumon Stent**: This stent is made of silicone and has studs on the surface to prevent migration. Because barium is encapsulated in silicone, the stent can be identified under X-ray fluoroscopy. A Y-shaped stent is used for stenosis around the tracheal bifurcation. It is not affected by the problem of tumor ingrowth, is effective also for infiltrative stenosis, and can be removed. Figure 3 shows a case of Dumon stent insertion.

**SEMS (self-expandable metallic stent)**: SEMS is the general term for a metallic stent that expands by the action of its own resilience (Z-stent, Ultraflex, and Wallstent). SEMS can be inserted easily via a flexible bronchoscope. The small volume before expansion means that the stent does not require elaborate pretreatment and can be inserted safely into highly stenotic sites. For this reason, it is often used for the purpose of emergency airway reopening.
Dynamic Stent: This is a composite Y-shaped stent made of silicone and metal. A horseshoe shaped stainless steel pieces are used in place of tracheal cartilage. The membranous portion is made solely of silicone to allow physiological movement of the stent. This mechanism was developed for the purpose of facilitating expectoration by coughing. This stent is used for long stenosis of the trachea and stenosis around the tracheal bifurcation.

2. Indications

Good candidates for airway stenting are cases with dyspnea showing no response to other therapies, 50% or more stenosis in central airway, preserved pulmonary function and blood flow in the peripheral area with stenosis, and a prognosis of 3 months or longer survival. Indications for malignant disease include (1) maintenance of bronchial lumen after dilation for infiltrative airway stenosis and obstructive lesions; (2) tracheobronchial malacia due to repeated laser vaporization; (3) stenosis by extrinsic compression of trachea and bronchi due to mediastinal lymph node metastasis, lymphoma, and mediastinal tumors; and (4) closing of esophagotracheal/bronchial fistula.

3. Therapeutic results

Colt and Dumon inserted 502 airway stents in 286 cases, and reported that mean duration of stent placement in cases with benign lesions was 14.2 months compared with 3.3 months in cases with malignant lesions. Becker inserted 165 various types of stents in 95 cases, and reported a 2-year survival rate of 50% in cases of stenosis that developed after response to treatment, as well as records of patients who survived for 5 years without recurrence. Bolliger et al. studied 31 cases of malignant disease and obtained a mean survival time of 4 to 6 months. This survival exceeding 3 months suggested the efficacy of this technique. Improvement of dyspnea in 86 to 100% of cases has also been documented in many reports.

According to the report of Diaz-Jimenez, complications of airway stenting using Dumon stents included migration and displacement in 17.5%, granulation in 6.3%, and symptomatic retention of secretion in 6.3%. Using Wallstent, Bolliger and Monier reported that they observed deviation and displacement in 12 to 15%, granulation in 15%, symptomatic retention of secretion in 19 to 38%, and re-stenosis in 36%.11,12

Conclusion

PDT is considered a very effective minimally invasive treatment for central-type early-stage lung cancer. At present, efforts are continuing for the development of novel photosensitizers that can be used for PDT with better accumulation to tumors, reduced side effect (sunburn), and longer excitation wavelengths improving tissue transmission. A chlorine-based agent called ME2906 (NPe6) is considered as the most promising second-generation photosensitizer after Photofrin. Compact diode laser system for PDT has also been developed in response to this newly development of photosensitizer with long excitation wavelength. It is certain that PDT using novel photosensitizers and diode laser systems will be in the main stream of clinical practice.13

High power laser vaporization and airway stenting are performed as local therapies for central airway stenosis caused by advanced cancer, and these procedures offer dramatic improvement of dyspneic symptoms. These various endoscopic procedures are considered new therapeutic methods based on the respect for and improvement of the patients’ QOL.

REFERENCES


