

Endoscopic Treatment of Bronchial Carcinoids in Comparison to Surgical Resection: A Retrospective Study

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Background: Surgery is the gold standard of lung carcinoid treatment. However, bronchoscopic treatment may provide a complete cure in selected patients. The aim of the study was to review the results of laser treatment of bronchial carcinoids and to compare the outcome after laser resection against the outcome after surgical resection.

Methods: Seventy-three patients, 29 men and 44 women, median age 53 years (range, 23 to 78 y), with bronchial carcinoids were treated by surgical resection (n = 48) or endobronchial ablation (n = 25). Bronchoscopic treatment was also performed in 5 of 48 surgical patients as a part of the surgical treatment strategy.

Results: Among 25 patients treated endoscopically, 16 were successfully treated with laser, whereas 9 were operated subsequently. One major complication was registered, as an inadvertent ventilation caused a non-fatal fire of the bronchoscope during Nd:YAG laser procedure. Forty-eight patients underwent surgical resection. Most of the patients underwent lobectomy and bilobectomy (30 and 5 patients, respectively). Four of the patients were dead by the end of the study, 1 was treated with laser, and 3 treated with surgical resection. The overall survival was 94.5% in the surgical group and 94.4% in the group treated with endoscopic ablation ($P = 0.9$). None of the 69 survivors had any sign of recurrence on computed tomographic scans and bronchoscopy by the end of the study.

Conclusions: This is a retrospective study and no randomization has been performed. However, the results add evidence to the view that transbronchial laser treatment may be offered as a safe, stand-alone procedure in the treatment of typical carcinoid tumor in the central airways.

Key Words: carcinoid, interventional bronchoscopy, lung resection

Bronchial carcinoids are neuroendocrine tumors that account for <1% of all primary lung neoplasms.¹ Carcinoids are classified into typical and atypical, with atypical tumors having a more aggressive behavior and a worse prognosis.² Even though carcinoids are considered to be malignant, they only cause metastases into regional lymph nodes in 10% to 15% of cases and distant metastases in 15% of cases, most likely to the liver, bones, adrenal gland, or brain.^{3,4}

Surgery is considered to be the gold standard of treatment, with a survival rate after surgical resection as high as 95% after 5 years.⁵ Endobronchial intervention by laser ablation has been used as palliative treatment in inoperable patients, or to reduce tumor volume before surgery.⁶ Cavaliere et al⁷ demonstrated that laser ablation of polypoid bronchial carcinoids could eradicate the tumors, and that most of the patients had no relapse. Another study showed that in some cases of lung surgery after initial laser treatment, no carcinoid tissue was found in the resected material.⁸ After successful treatment, other authors have suggested that bronchoscopic treatment may be an option for total cure in some patients with endobronchial carcinoids.^{9,10} However, there is still a need for documentation confirming that the laser ablation technique for removing carcinoids is comparable to thoracic surgery regarding the survival rate and relapse-free period.

The aim of the present study was to review the results after using endobronchial laser ablation for the treatment of bronchial carcinoids at our institution. No randomization was performed, but the outcome for the group treated with laser ablation was compared with the group that underwent surgical resection.

PATIENTS AND METHODS

Between 2002 and 2010, 73 patients (29 men and 44 women), with a median age of 53 years

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(range, 23 to 78 y) and bronchial carcinoids, were treated by surgical resection (n = 48) or endobronchial ablation (n = 25) in our institution (Table 1). They were all included in a retrospective cohort study.

The criteria for laser ablation with curative intent were (1) presumably a typical type of tumor histology; (2) polypoid growth of the tumor; and (3) the absence of obvious distal metastases. Because of technical reasons, tumors localized distally to the subsegmental level were not treated with laser ablation as it is difficult to perform intraluminal procedures in the smaller bronchi. Patients who did not fulfill the criteria were treated with surgical lung resection. Bronchoscopic treatment was also performed in 5 of 48 surgical resection patients as a part of the surgical treatment strategy. Preoperative bronchoscopic treatment enabled a better assessment of the tumors and restored airways in patients with preoperative obstructive pneumonia. Among the 73 tumors, 46 were located on the right side and 27 were located on the left side of the bronchial tree (Fig. 1).

Data

Sex, age, treatment modality, complications, and dates of intervention in all patients were consecutively registered in the clinical database of the department. Additional data such as histology of the tumors, TNM staging, and information regarding the postoperative period were retrospectively collected from the medical charts. Two groups were compared: patients who only underwent bronchoscopic treatment with curative intent and patients who underwent surgical resection. The median age of patients in the 2 groups were 37 years (range, 23 to 74 y) and 59 years (range, 23 to 78 y), respectively.

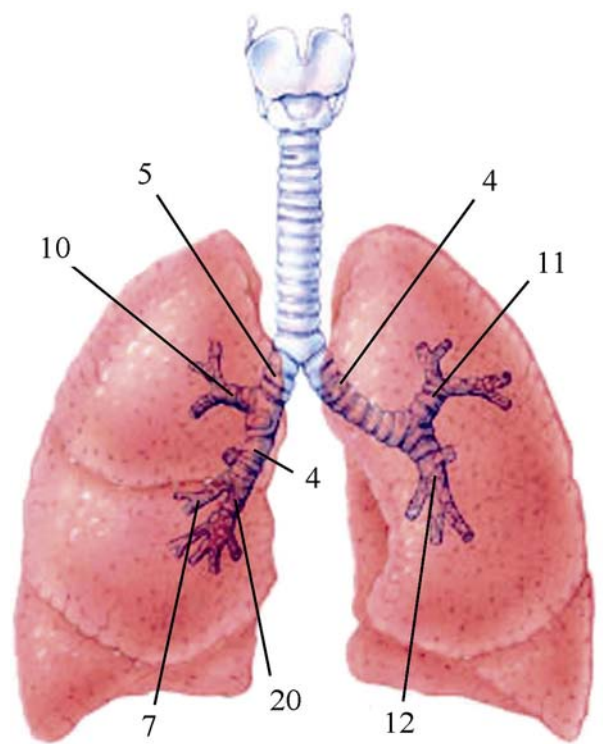


FIGURE 1. Localization of carcinoid tumors in 73 patients treated for bronchial carcinoids. *a+*

Interventional Bronchoscopy

Bronchoscopic procedures were performed by interventional pulmonologists in an operating room setting. Most procedures were performed with a flexible bronchoscope through the endobronchial tube. Lesions were treated using a Nd:YAG laser set to 40 to 45 W and a second laser treatment after a 1-second interval to avoid overheating and combustion of the tumor. In patients with large tumor masses, a rigid bronchoscope with rigid forceps was used for tumor

TABLE 1. Demographic and Clinical Characteristics of 73 Patients Treated for Bronchial Carcinoid

	Total	Curative Laser Only	Surgery		
			Total Surgery	Surgery Without Preoperative Laser	Surgery With Preoperative Laser
N	73	25	48	43	5
Median age (range)	53 (23-78)	37 (23-74)	59 (24-78)	61 (24-78)	53 (24-77)
Sex, male/female	29/44	12/13	17/31	16/27	1/4
Typical carcinoids	62	25	37	34	3
Atypical carcinoids	11	0	11	9	2
Symptomatic/asymptomatic	57/16	22/3	35/13	30/13	5/0
Lobectomy	35	5	30	27	3
Wedge resection	7	0	7	7	0
Segmentectomy	3	0	3	3	0
Bilobectomy	8	3	5	4	1
Pulmectomy	4	1	3	2	1

debulking. Balloon dilatation was used as a part of the postprocedural stenosis treatment.

Anesthesia

The procedures were performed under total intravenous anesthesia using propofol and remifentanyl for the induction and maintenance of anesthesia. Neuromuscular blockade was induced using 0.15 mg/kg cisatracurium, and was continued by 0.2 mg/kg/h if needed. Respiration was maintained at a rate of 10 to 15/min with a peak pressure of < 30 mm Hg. The proportion of oxygen in the anesthetic gas mix was 0.3 to 0.9 without using the laser and 0.35 ± 0.05 during laser ablation. All of the patients were ventilated using a closed circuit connected to the ventilator.

Surgical Treatment

Surgical resection was performed through a lateral thoracotomy. In most cases, lobectomy, wedge resection, or segmentectomy were performed. In some patients, bilobectomy or pneumonectomy were required (Table 1). All resected specimens were sent for histologic examination.

Statistics

We compared survival rates between the patients who were treated with endobronchial laser ablation with curative intent and the patients who underwent surgical treatment. The end-of-study date was set at March 1, 2011. The SPSS program for Windows (version 16.0; SPSS Inc., Chicago, IL) was used for statistical analysis. A *P*-value of < 0.05 was considered as statistically significant. The study was approved by The Regional Committee for Research Ethics.

RESULTS

The median length of the symptomatic period at the time of diagnosis was 6 months. Symptoms were present in 57 of the patients (77%). The most common signs on admission to the hospital were coughing (productive or not) in 25 cases (34%), dyspnea in 18 (25%), recurrent pneumonia in 25 (34%), chest pain in 8 (11%), and hemoptysis in 12 (16%). One of the patients had carcinoid syndrome. Sixteen patients were asymptomatic (22%) (Table 2).

Twenty-five patients were treated with Nd:YAG laser ablation. A total of 29 procedures were performed. Twenty-one patients received only 1 procedure, whereas Nd:YAG laser ablation was used more than once in 4 patients. Among the 25 patients treated with the laser with curative intent, 16 did not require surgical

TABLE 2. Symptoms at the Time of Bronchial Carcinoid Diagnosis in 73 Patients Treated for Bronchial Carcinoid

	No. (%)
Recurrent pneumonia	25 (34)
Cough	25 (34)
Hemoptysis	12 (16)
Dyspnea	18 (25)
Pain	8 (11)
Weight loss	3 (4)
Night sweating	7 (10)
Carcinoid syndrome	1 (1)
Asymptomatic	16 (22)

treatment as the carcinoid was successfully eradicated. Five of the patients underwent lobectomy after bronchoscopic ablation with curative intent, as it was not possible to eradicate the rest of the tumor with the laser.

One major complication was registered. Inadvertent ventilation with 100% oxygen caused a nonfatal fire in the flexible bronchoscope during Nd:YAG laser treatment. Postprocedural stenosis was registered in 2 patients and successfully treated with balloon dilatation. No significant bleeding was registered during the procedures. Neither preoperative nor postoperative mortality occurred.

Among the total number of 73 patients, 48 underwent surgical resection. We performed wedge resection in 7 patients, segment resection in 3 patients, and pulmetomy in 3 patients. Most of the patients underwent lobectomy and bilobectomy (30 and 5 patients, respectively; Table 1). Bronchoscopic treatment was also performed in 5 of 48 surgical resection patients as a part of the surgical treatment strategy. No tumor tissue was found in the resection material after initial bronchoscopic treatment in 3 of the patients who were operated on. No significant complications were registered during the postoperative period.

The median follow-up period was 3 years (range, 0.5 to 8 y). All patients were followed up with bronchoscopy and thorax computed tomographic scans yearly for 5 years postoperatively. At the end of the observation period, 4 of the patients had died, 1 had been treated with laser ablation alone, and 3 had been treated with surgical resection alone. Overall, survival by the end of the study was 94.5% in the surgical group and 94.4% in the group treated with endoscopic ablation (*P* = 0.9). Survival in patients with typical and atypical carcinoids were 96.7% and 81.8%, respectively; *P* = 0.05. None of the 69 survivors, either in the interventional

bronchoscopy group or in the surgical treatment group, had any sign of recurrence on computed tomographic scans and bronchoscopy by the end of the study.

DISCUSSION

A tendency for polypoid growth, central localization, a low rate of local and distant metastases, and a high survival rate in the patients with carcinoid tumors suggest that bronchoscopic treatment is an effective initial treatment option in a subset of patients (Fig. 2). Laser ablation alone was effective in 64% of the patients in our study. This shows that the risk of recurrence after laser ablation is rather low and indicates that bronchoscopic intervention in many cases can be a useful and curative modality in the treatment of bronchial carcinoids. The survival rate of patients treated with laser ablation alone was comparable to that of patients treated with surgery. However, the fact that as much as 36% of the patients required supplemental surgical treatment raises some important concerns, such as the suitability of selection criteria for interventional bronchoscopy treatment.

This study supports previous experience where selected patients with an intraluminal typical bronchial carcinoid were treated bronchoscopically. The patient selection is extremely important. Several authors have proposed selection criteria for radical laser treatment.^{11–13} The most important of these could be a distinction between intraluminal and extraluminal carcinoid tumors for the selection of patients. Good bronchoscopic accessibility, typical carcinoids, and no signs of

extraluminal extension and metastases, could also favor more reliable results of radical treatment.¹² A rather high rate of subsequent lung resections in the present study proves that patient selection for bronchoscopic treatment may be quite challenging.

It might not always be possible to make a definitive histologic diagnosis based on the pre-operative biopsies from tumors, but whenever the analysis shows a presumably typical histology, laser ablation can be chosen as a treatment option. A definitive histologic classification is sometimes only possible after complete surgical resection. Atypical carcinoids have a much more aggressive behavior with higher metastases and lower survival rates.^{14,15} In the present study, the difference in survival between patients with typical and atypical carcinoids was also shown to be significant. These patients should only be treated with surgical resection.

Enlarged mediastinal lymph nodes can also be a contraindication for radical laser treatment.⁴ However, lymph nodes can be enlarged because of causes other than malignancy. To clarify this, endobronchial ultrasound-guided needle aspiration can be performed. Bronchoscopic eradication could be an initial stage of treatment in many cases of potentially resectable intraluminal typical carcinoids, but such an approach could also have a certain risk of subsequent recurrence. Surgical resection remains the treatment of choice in patients with bronchial carcinoids. Survival after surgical treatment has been shown to be excellent and complications are rare.¹⁶

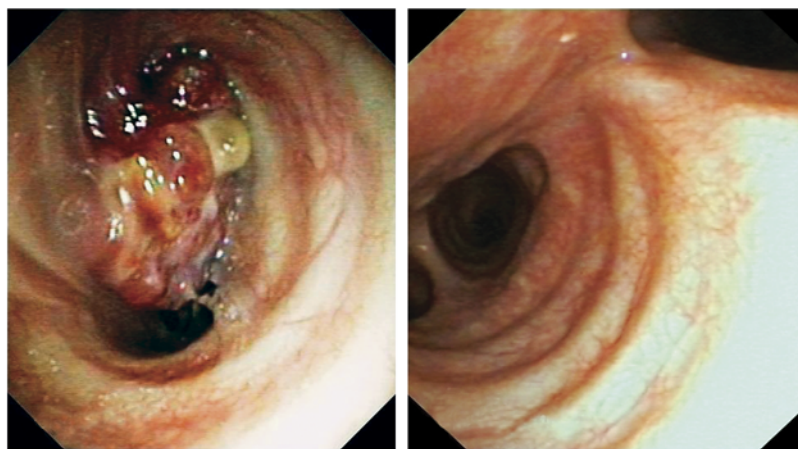


FIGURE 2. An example of successful bronchoscopic laser eradication of an endobronchial carcinoid. The picture to the left was taken during the first procedure, whereas the picture to the right was taken 1 year after the first control bronchoscopy procedure. **a+**

We encountered more difficulties in treating the carcinoids at the segmental level, where the distal tumor margin was not visible to the bronchoscopist. Therefore, it was not surprising that the laser treatment did not result in complete tumor eradication in 2 of these patients, or that subsequent surgery was required. Patients with unclear tumor margins may therefore be less suitable candidates for bronchoscopic treatment.

A study by Sutedja et al⁸ first showed that some patients had no signs of carcinoid tumors after laser resection. In the present study, 33% of the patients subsequently operated on for carcinoids showed no tumor tissue in the resected lung; although this number is rather small, this fact in itself illustrates the difficulty in selecting patients for bronchoscopic treatment.

Carcinoids develop slowly, and yearly follow-up of these patients can be advised. Because of the slow growth and subsequently delayed manifestation of a recurrent tumor, a follow-up period longer than 5 years may be required. However, no sound recommendation for the follow-up time required to detect any recurrence can be given on the basis of the present study.

The most frequent complications of interventional bronchoscopy are hypoxia, hemorrhage, and pneumothorax.¹⁷ Hypoxia is usually caused by the low oxygen concentrations (< 35%) used to avoid burning injury during laser ablation and most frequently occurs in patients with serious respiratory failure, but this complication is usually well handled by good levels of cooperation within the operation team.¹⁸ Serious complications were rare in our study (1.4%). One patient suffered endobronchial combustion as inadvertent ventilation with 100% oxygen caused a fire in the flexible bronchoscope during Nd:YAG laser treatment. This patient later had repeated laser and balloon dilatation procedures to treat bronchial stenosis and scarring, leading to recurrent episodes of airway infection. In the first few months after the procedure, this patient developed a serious airway obstruction, but after laser and dilatation procedures, the patient improved significantly, and forced expiratory volume in 1 second increased to 70% of the predicted level, and the airway infection subsided.

In one of the largest existing studies on interventional bronchoscopy, performed by Cavaliere et al,⁷ it was clearly shown that complications of interventional bronchoscopy are rare: only 10 of 1000 patients in their study suffered serious hemorrhages. The numbers can differ from study

to study, depending on the experience of physicians and the study population. However, this type of treatment has generally been proven to be safe and efficient.^{19,20}

In a similar study by Bini et al,³ 39% of the patients were asymptomatic upon presentation. In the present study, 22% of the patients had no symptoms. Some of the patients were treated with bronchodilators as the symptoms of airway obstruction raised a suspicion of asthma. Some other studies also reported that some patients had been treated for asthma for up to 4 years before carcinoid tumors were diagnosed.⁹ This fact calls for caution from both lung physicians and general practitioners.

Limitations of the Study

The conclusions are based on a single-center experience. Randomization was not possible in the present study. Carcinoids in the surgical resection group seem to involve the more distal airways or parenchyma than those in the laser treatment group and the 2 subsets of patients seem to be not exactly the same. Even though this was a retrospective study and no randomization was performed, the results provide evidence to show that transbronchial laser treatment can be offered as a safe, stand-alone procedure for the treatment of typical carcinoid tumors in central airways.

CONCLUSIONS

Laser ablation is a valuable tool for the treatment of bronchial carcinoids in carefully selected patients. The survival rate of patients treated with laser ablation alone seems to be comparable to the survival rate of patients treated with surgical resection. In addition, no carcinoid tumor recurrences were revealed. Bronchoscopic laser treatment is safe, with a low complication rate.

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