REVIEW ARTICLE

Endoscopic management of benign tracheobronchial tumors

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ABSTRACT Even though benign tracheobronchial tumors are quite rare, they still can induce airway obstruction, result in suffocation, and need emergent management to remove the obstructing lesions and make the respiratory tracts unobstructed. Although the preferred therapy is surgery, it is still difficult to deal with the tumors in some cases, and the complications of surgery are common. Therefore, bronchoscopic managements, such as Nd: YAG laser, electrocautery, APC and Cryotherapy, are very important to treat benign tracheobronchial tumors and can cure most of them.

The efficacy of therapeutic endoscopy for the treatment of patients with benign airways obstruction has been established. However, in order to maximally eradicate the benign tumors with minimal damage to patients, the success of bronchoscopic managements for the treatment strongly depends on the diligent identification of the various factors, including the location, size, shape of tumor, and the age, status, cardio respiratory function of patients, and full comprehension of the limits and potential of each particular technique.

Because the advantages and disadvantages of above mentioned interventional methods, single method can not solve all clinical issues. Therefore, in order to remove benign tracheobronchial tumors completely, and reduce the incidence of recurrence as far as possible, many doctors combine several methods of them to treat complicated benign tracheobronchial tumors. This article reviews the core principles and techniques available to the bronchoscope managing benign tracheobronchial tumors.

KEY WORDS: Benign tracheobronchial tumors; bronchoscope; electrocautery; argon plasma coagulation; Nd: YAG laser, cryotherapy

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Introduction

Primary tracheobronchial tumors are tumors originating from trachea or bronchi and quite rare. Most published data are case reports, experiences from very small series, or retrospective studies (1-3). According to the SEER database of National Cancer Institute, there were 574 cases of primary tracheobronchial tumors between 1973 and 2004, and the incidence was about 2.6 patients per 100 000 peoples (4). However, primary benign tracheobronchial tumors are more seldom seen. Gaissert et al (5) reported 357 cases of primary tracheobronchial tumors that had been diagnosed and treated in Massachusetts general hospital in the last 40 years. Of the mentioned 360 tumors (3 patients had two different types of tumor), there were 326 malignant tumors (90.6%), 135 squamous cell carcinoma (37.5%), 135 adenoid cystic carcinoma (37.5%), 11 carcinoid tumor (3.1%), 14 sarcoma (3.9%), and 34 benign tumors (9.4%). Shah et al (6) reported 185 cases of benign tracheobronchial tumors that had been diagnosed and treated in single hospital from 1980 to 1991. They found that the most common tumors were papillary epithelioma (28.6%), hamartoma (24.3%), and amyloid tumor (11.4%).

Regardless of malignant or benign tumors, they all can obstruct the respiratory tract and threat the life of the patients. So, rapid management of airway obstruction and recovery of ventilation of respiratory tract is the chief purpose of therapy (7). For benign tracheobronchial tumors, the preferred therapy is surgery including sleeve resection (8). However, for the benign tumors locating in trachea, main bronchi, and eminence, surgery is difficult and bring great trauma to the patients (9). Therefore, bronchoscopic managements, such as neodymium-yttrium-aluminum-garnet laser (Nd: YAG) laser (10-11), electrocautery (12-13), argon plasma coagulation (APC) (14-15), and Cryotherapy (16-17), are very important to treat benign tracheobronchial tumors and can cure most of them. Because a few of them are prone to recurrent or change to malignancy,

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it is very important to repeat bronchoscopes to follow up and we must carefully practice interventional bronchoscope to avoid hampering possible surgery in future. According our experience and literature, the following conditions are considered as indications for endoscopic treatment: (i) tumors are strictly located in tracheobronchial lumen and don't exceed subsegmental bronchi; (ii) the basilar part of tumors is not wide, and do not across more than 3 bronchial cartilage rings; (iii) tumors with peduncular structure are more suitable; (iv) tumors have low probability of recurrence; (v) the patients' condition is not suitable for surgery (Table 1).

This article reviews the core techniques available to the bronchoscope managing benign tracheobronchial tumors, summarizes the advantages and disadvantages of each technique, and .discusses the combined use of these techniques.

Table 1. Principles of endoscopic management of benign tracheobronchial tumors

1	Endoscopic management should not interfere with the possible surgical plan in future
2	Endoscopic management should have limited short and long term applications
3	Clinician should select the optimal endoscopic techniques according to the location, size, shape of tumors, and the age, status, cardio respiratory function of patients

Rigid bronchoscope or flexible bronchoscope

Rigid bronchoscope has been used for more than 100 years. From 1970s, because that its practice need general anesthesia and its poor visual scope in tracheobronchial, it has been replaced gradually by flexible bronchoscope. From 1980s, with the emergence of interventional bronchoscope, rigid bronchoscope has been applied by more and more doctors again. In Italy, the usage of rigid bronchoscope has achieved to 17.6% (18). Meanwhile, with the development of electronical technique, the blind zone of rigid bronchoscope has disappeared. Rigid bronchoscope can maintain the respiratory tract unobstructed, and has a lateral aperture, which can connect with breathing machine. So, it is also called ventilating bronchoscope (19-20). The value of rigid bronchoscope is that it can allow flexible bronchoscope, or other instruments to go straight through its lumen, which allows rigid bronchoscope complete almost all operations including stenting, laser ablation, argon plasma coagulation, foreign bodies removing and cryotherapy.

There several advantages of rigid bronchoscope. The first, rigid bronchoscope has several tunnels which can allow suction catheter, lasing fiber, or electrode reach target simultaneously. So we can execute suction and ablation simultaneously, and remain the visual field clean to make for practice. Because suction catheter is larger, we can rapidly remove the secretion and blood. The second, rigid bronchoscope has larger tunnel than flexible bronchoscope, which allow biopsy forceps to remove large tissue and flexible bronchoscope to permeate itself to reach target. The third, when performing thermal ablation, it is easier for flexible bronchoscope to be injured. The fourth, rigid bronchoscope can connect with ventilating machine in order to prove the patient's breathing, support enough oxygen, avoid asphyxia. Finally, the patients are submissive and not painful due to general anesthesia (Table 2).

Although rigid bronchoscope with general anesthesia is safe when experienced doctors performing it, the patients still face the risk induced from general anesthesia. Hanowell et al (21) reported 73 cases of Nd: YAG laser therapy with general anesthesia. In this paper, they reported the death of the patients was zero; total incidence of complications was 30.1%. The most common complications are hypotension (10.9%), ventricular ectopy (8.2%), hypertension (5.5%), and supraventricular tachycardias (5.5%). The incidence of heart block, myocardial infarct, and myocardial ischemia is 1.4% respectively. According our experience, the contraindication of rigid bronchoscope should be unstable angiocardiopathy, arrhythmia threatening life, acute respiratory failure combined intractable hypoxemia, head and neck malformation, and cervical cord diseases.

Although there is no blind zone for rigid bronchoscope due to modern optical techniques, it is still difficult for rigid bronchoscope to treat the tumors locating in the bronchi which form acute angle, or bronchi of superior lobe (Figure 1). In addition, sometimes rigid bronchoscope can not pass stenosis. In these conditions, we have to use flexible bronchoscope to reach the target, or pass through the stenosis to observe mucosa of distal bronchi and basilar part of tumors roundly. In modern time, the instruments of argon plasma coagulation, Nd: YAG laser and cryotherapy can be fitted into flexible bronchoscope. So, for the majority of cases, we can handle endobronchial tumors via flexible bronchoscope. But for some cases, we have to turn to rigid bronchoscope because that flexible bronchoscope can not control the respiratory tract, or perform artificial ventilation.

So, we must decide which bronchoscope is optimal according to the location, size, shape of tumor, and the age, status, cardio respiratory function of patients. Generally, for

Table 2. Comparison of rigid vs. flexible bronchoscope

	Advantages	Disadvantages
Rigid bronchoscope	1. has several tunnels allowing multiple operations to perform simultaneously	1. need general anesthesia
	2. has large tunnel allowing flexible bronchoscope to permeate itself to reach target	2. can not reach the tumors locating in the bronchi which form acute angle, or bronchi of superior lobe
	3. can connect with ventilating machine to make sure patients' breathing	3. can not pass sever stenosis
	4. The patients are submissive due to general anesthesia	
	5. can be used to stop bleeding in some cases	
Flexible bronchoscope	1. can reach some tumors which rigid bronchoscope can not reach	1. can not control airway
	2. can pass through sever stenosis	2. can not adopt some high power instruments
	3. can be performed under surface anesthesia	

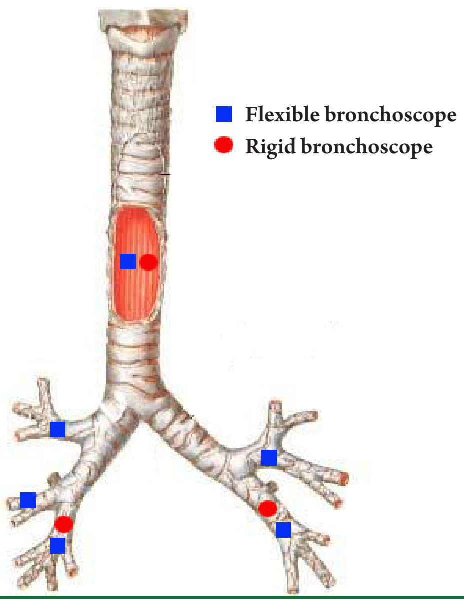

Figure. 1 The applicability of rigid or flexible bronchoscope.

those patients who have good status and cardio respiratory function, if their tumors are small and easy to remove, or the risk of perforation and hemorrhea is low, we use flexible bronchoscope. However, for those patients who have bad status and cardio respiratory function, if their tumors are large and difficult to remove (predicted operation time is more than 30 minutes), or the risk of perforation and hemorrhea is high, we use rigid bronchoscope. According our experience, we usually use the two kinds of bronchoscope simultaneously. We use rigid bronchoscope to control respiratory tract, remove secretion and blood, stop bleeding, treat tumors with cryotherapy or argon plasma coagulation, and use flexible bronchoscope to reach the target which rigid bronchoscope can not reach.

Electrocautery

From 1930s, electrocautery has been used in interventional bronchoscope. However, only until coil of electrocautery was improved by Hooper and Jackson (22), electrocautery was used extensively. Electrocautery remove tumors by its thermal effects which can degenerate protein, induce tissue coagulation necrosis. Electrocautery is suitable for tumors with peduncular structure. Coulter et al (23) treated 25 cases of benign tracheobronchial tumors with electrocautery. Of these tumors, there were 12 cases of granulation tissue, 6 cases of papillary epithelioma, 3 cases of hamartoma and lipoma respectively. Except for granulation tissue, all tumors were cured one time. The complications were hemorrhage (10.5%) and cough (2.6%). Electrocautery can be used in flexible or rigid bronchoscope. We can use snare to remove the stem of tumors. For those large tumors, or the tumors without stem, we can use electrocautery to fulgerize the tumors to the depth of 2-3mm (24), then use biopsy forceps to clear eschar and necrotic tissue, and then repeat those steps. If the removed tumor is too big to pass the tunnel, we can take it out with bronchoscope together, or let patients expectorate the lesion immediately. In addition, electrocautery can also be used to stop bleeding (Table 3).

The primary consideration of electrocautery is safety. Because tracheobronchial is adjacent to heart, arteriae aorta, and pulmonary artery, we must pay careful attention to this practice to avoid tracheobronchial injury, perforation, mediastinal

Table 3. Comparison of several endoscopic instruments

Methods	Anesthesia	Characteristic	
Electrocautery	General/Surface	1. Can be used to snare	1. Perforation and hemoptysis due to probe and eschar removement
		2. Contiguous technique	2. Airway fire
		3. Treatment depth is 2-3mm	
APC	General/Surface	1. Uncontiguous technique	1. Hypoxemia due to large oxygen consumption
		2. Treatment depth is 3-4mm	2. Airway fire
			3. Air embolism
Nd: YAG laser	General mostly	1. Uncontiguous technique	1. Perforation and hemoptysis due to high power or misoperation
		2. Treatment depth is deeper and is decided by power	2. Hypoxemia due to necrotic tissue and secretion
			3. Cough and atmospheric pollution due to smoke
			4. Reactive hyperplasia of granulation tissue
			5. Airway fire
			6. Air embolism
Cryotherapy	General/Surface	1. Contiguous technique	1. Repeated treatments due to superficial therapy and necrotic tissue
		2. Treatment depth is 2-3mm	2. The tip of bronchoscope could be freezed by probe
		3. Small effect on cartilaginous rings	3. Hemoptysis after freezing thawing
		4. Does not induce cicatricial constriction	

emphysema, and severe hemoptysis. Another consideration is that electrocautery may induce airway fire as a kind of thermal cautery, especially when oxygen concentration is higher than 40%. So, we should keep oxygen concentration lower than 40%, and igniting material away.

Argon plasma coagulation

Argon plasma coagulation is a new kind of uncontiguous electrocautery technique, which can produce uncontiguous current between probe and tissue by iodinating argon. The argon plasma beam reaches target not only along straight line, but also from lateral exits (25). The depth of treatment is about 3-4mm, and the tissue can be divided into three zones from surface to bottom: dehydration zone, coagulation zone, and inactivation zone. From naked eyes, three zones show as eschar. Meanwhile, Argon plasma coagulation has the effect of hemostasis. Because the depth of treatment is superficial, it is relatively safer in the aspect of perforation and severe hemoptysis (26).

However, if you continue to treat after the formation of eschar, the fever can not penetrate the eschar to treat deep issue. Therefore, in order to treat large tumor, we have to clear eschar after every electrocautery. The traditional instrument of clearing eschar is biopsy forceps. However, because the tissue cleared by biopsy forceps every time is small, it will prolong the operation time and increase the risk of bleeding when repeating clearance. In addition, as a kind of thermal cautery, the oxygen consumption is so big that it is easy for the patients to suffer from hypoxemia, which can result in interruption of operation and airway fire. According to Reddy's report (27), argon plasma coagulation also can induce air embolism, which is related to the velocity of air current. So, we recommend that we should lower down the velocity of air current as far as possible if we can complete our operations.

Nd: YAG laser

In 1982, Dumont (28) first used Nd: YAG laser to treat 111 cases of tracheobronchial diseases including 6 cases of benign tumors. The advantages of Nd: YAG laser include good directionality, gasificated lesions which don't obstruct respiratory tract, less hemorrhage, less secretion, and less injury to normal tracheobronchial. Cavaliere et al (29) treated 59 cases of benign tracheobronchial tumors with Nd: YAG laser. Of these tumors, there were 14 cases of hamartoma, 11 cases of papillary epithelioma, 7 cases of amyloid tumor, 4 cases of tracheopathia osteoplastica, polyp and hemangioma respectively, 1 case of plasmocytoma, neurilemmoma, chondroma, ndometriosis and lipoma respectively, 1 case o+f fibroma, myofibroma, fibrohistiocytoma, scleroma and syphilis respectively. Except for 1 case of amyloid tumor, tracheopathia osteoplastica, and papillary epithelioma respectively, all patients were cured completely. No recurrence was observed in the follow up of 1 to 3 years.

In the practice of Nd: YAG laser, we should pay attention to some points: First, we should clear the necrotic tissue and secretion immediately in order to avoid them obstructing respiratory tract and hypoxemia. Once hypoxemia happens, we should stop therapy immediately, increase oxygen concentration, and clear the necrotic tissue and secretion. If necessary, we can use rigid bronchoscope or mechanical ventilation to remain the respiratory tract unobstructed. Second, optical fibers should be paralleled with tracheobronchial in order to avoid hemorrhage resulted from irradiating the wall of tracheobronchial vertically. Upon hemorrhage happening, we should stop therapy immediately, use rigid bronchoscope to oppress, or sprinkle adrenalin hydrochloride or thrombin to stop blooding. Third, the power should be restricted under 40W to avoid perforation and hemorrhage (30-31,34). Fourth, Nd: YAG laser also may induce airway fire when oxygen concentration is higher than 40% (32). We can prevent airway fire by reducing oxygen concentration, prolonging the interval of two irradiations, lowering the power, keeping optical fiber 1cm longer than bronchoscope or more. Fifth, we should clear the fume produced by tissue gasification to avoid cough and atmospheric pollution. Finally, if pulmonary veins are perforated and contact with air, it will result in air embolism (33). Other rare complications include myocardial infarction, bradycardia and cardiac arrest.

In addition, high power Nd: YAG laser can induce reactive hyperplasia of granulation tissue, so it is not suitable for treating tuberculosis. And extensive irradiation can induce severe edema so that aggravate obstruction.

Brutinel (34) reported 116 cases of airway obstruction with Nd: YAG laser. Among the 176 times therapy, hemorrhage happened 10 times, and 3 cases died from asphyxia induced by hemorrhage. Fever happened 7 times, and prolonged mechanical ventilation happened 7 times. Airway obstruction and pneumothorax happened 2 times respectively. Of the 116 patients, 9 patients suffered from benign tracheobronchial tumors. After 1 year follow up, one patient died and the 1 year survival rate was 86%. All the 3 patients who died from hemorrhage were practiced with the condition of more than 90 W. After the death of these patients, the author restricted the power to 50W and there were no more deaths.

Cryotherapy

Cryotherapy can freeze the tumor and make necrosis of tumor by inducing liquid CO_2 to the tissue along the probe (35). Because the probe is muticous, and the depth of perforation is only 3mm, so it can not insert to the deep part of tumor (36). Therefore, cryotherapy is only suitable for superficial tumor, especially for those colloid tumor and sledged blood. The methods of cryotherapy include freezing cutting and freezing thawing. Freezing cutting means we use cryotherapy to freeze the tumor to an icefall, and then clear it with biopsy forceps. Freezing thawing means we freeze the tumor and let it thaw and fall off naturally. The advantages of cryotherapy include hat it does not induce hypoxemia, lower risk of perforation, no risk of air fire and fume, and small effect on cartilaginous rings. After cryotherapy, the necrotic tissue falls off gradually. Meanwhile, the peripheral mucosa grows to cover the lesion, so cryotherapy dose not induce cicatricial constriction (37).

One of the disadvantages is the superficial therapy, which means we have to repeat cryotherapy to treat large tumor. Another disadvantage is that the necrotic tissue will not fall off immediately, and we have to perform another bronchoscope to clear the necrotic tissue. Tchakaroff et al (38) reported two disadvantages of cryotherapy. The first is the tip of bronchoscope sometimes could be freezed by probe. The second is that it is prone to bleed after freezing thawing and cryotherapy had not the function of haemostasis.

Cryotherapy combined with argon plasma coagulation

Because the advantages and disadvantages of above mentioned interventional methods, single method can not solve all clinical issues. Therefore, in order to remove benign tracheobronchial tumors completely, and reduce the incidence of recurrence as far as possible, many doctors combine several methods of them to treat complicated benign tracheobronchial tumors.

It is reported that cryotherapy combined with argon plasma coagulation can rapidly remove large tracheobronchial tumors, shorten operation time, and prevent severe hemorrhage (39-40). The reason maybe that: (i) after cryotherapy, immediate argon plasma coagulation can reduce the risk of hemorrhage and shorten operation time; (ii) after argon plasma coagulation, freezing cutting can remove the necrotic tissue more conveniently than biopsy forceps. Usually, 2-3 times freezing cutting can remove eschar completely, which can also shorten operation time; (iii) after argon plasma coagulation, risk of hemorrhage when performing cryotherapy is reduced; (iv) we can repeat these steps until a large tumor is completely removed.

Nd: YAG laser or electrocautery combined with argon plasma coagulation

Nd: YAG laser or electrocautery combined with argon plasma coagulation can rapidly remove tumor with lower risk of perforation and severe hemorrhage (41-42). For large tumors, we can use electrocautery to remove tumor, then Nd: YAG laser to make the gasification of the residual tumor, finally argon plasma coagulation to treat basilar part of tumor to prevent recurrence. Because the superficial treatment depth, it is effective to avoid perforation and severe hemorrhage.

Conclusion

Benign tracheobronchial tumors are quite rare, and the preferred therapy is surgery. But many bronchoscopic treatments are very effective and the risk of recurrence or malignant change is very low, especially when several .treatments such as Nd: YAG laser, electrocautery, cryotherapy and argon plasma coagulation, are combined to treat tumors. This article introduced several bronchoscopic treatments and their combination with each other. To achieve the aim of radical cure and reduce the risk of recurrence as far as possible, we believe that we should evaluate each method including bronchoscopic treatments and surgery, and select the most suitable methods for out patients and make use of them synthetically.

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