INTERVENTIONAL Pulmonology

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INTERVENTIONAL pulmonology is a new field within pulmonary medicine focused on the use of advanced bronchoscopic and pleuroscopic techniques for the treatment of a spectrum of thoracic disorders ranging from tracheobronchial stenosis to pleural effusions associated with malignant tumors.1,4

TECHNIQUES USED IN INTERVENTIONAL PULMONOLOGY

Rigid Bronchoscopic Debulking or Balloon Dilation

Therapeutic use of bronchoscopy began over 100 years ago with the development of rigid bronchoscopes. These instruments have beveled tips, which are ideal for coring through large tumors in the airways and for dilating strictures, and they have large internal diameters, which facilitate debridement of tumors, evacuation of clots, and ventilation.5 Despite advances in other adjunctive endoscopic techniques, rigid bronchoscopic recanalization remains the treatment of choice for life-threatening tracheobronchial obstruction (Fig. 1).

Balloon dilation has become an attractive alternative to dissection with a blunt rigid bronchoscope in less urgent cases of obstruction caused by malignant tumors. The technique is best used in combination with bronchoscopic laser therapy and placement of a tracheobronchial stent for the treatment of airway stenosis.6 Balloon bronchoplasty has also been used successfully to treat other disorders, including tuberculosis, fibrosing mediastinitis, and strictures associated with lung transplantation8 or prolonged intubation.6 It is less successful when used alone to treat stenosis accompanied by extrinsic airway compression and is contraindicated in patients with tracheobronchomalacia.6,8

Although in the majority of cases, balloon dilation is performed while the patient is under general anesthesia, treatment of certain airway lesions (e.g., short fibrotic strictures) can be accomplished with the use of a fiberoptic bronchoscope while the patient is under conscious sedation. Complications of balloon dilation of airway lesions include bronchospasm, chest pain, perforation of the airway, pneumothorax, and pneumomediastinum.6,8

Endobronchial Laser Therapy

Perhaps the most widely known technique in interventional pulmonology is laser bronchoscopy. Lasers produce a beam of monochromatic, coherent light that can induce tissue vaporization, coagulation, hemostasis, and necrosis. Although primarily useful in the ablation of endoluminal malignant tumors, bronchoscopic laser therapy is also beneficial for the treatment of other tracheobronchial disorders, including inflammatory strictures, obstructive granulation tissue, amyloidosis, and benign tumors such as hamartomas.10,12

In 1976, Laforet et al. reported on endobronchial laser ablation of an obstructive neoplasm.13 Since then, several types of lasers have become available for the management of tracheobronchial obstruction. The carbon dioxide laser, used mainly by otolaryngologists, allows shallow penetration of tissue (to a depth of 0.1 to 0.5 mm) and highly precise cutting, but it has minimal hemostatic properties and must be used through a rigid bronchoscope.11,14 It is ideal for the management of laryngeal lesions. Interventional pulmonologists primarily use the neodymium:yttrium–aluminum–garnet (Nd:YAG) laser, which provides deeper penetration of tissue (to a depth of 3 to 5 mm), superior photocoagulation, and improved hemostasis, but with less precision in cutting. Photocoagulation with an Nd:YAG laser can be performed through a rigid or flexible bronchoscope, but rigid bronchoscopy remains the preferred method for the treatment of patients who have respiratory distress due to severe tracheobronchial obstruction.

The use of a laser in the tracheobronchial tree requires careful consideration of the anatomical location and configuration of the lesion. If the lesion is in close proximity to the esophagus or the pulmonary artery, endobronchial laser therapy poses a risk of fistula formation. Use of laser therapy in a patient with tracheobronchial narrowing due to extrinsic compression may result in perforation of the airway. In addition, prolonged obstruction of the airway (for more than six weeks) may lead to refractory atelectasis or bronchiectasis, minimizing the benefits of endobronchial recanalization.
Although endobronchial laser therapy is generally safe and well tolerated, it may be complicated by cardiac arrhythmias,15 perforation of the airway, pneumothorax, hemorrhage, hypoxemia, or endobronchial fire (ignition of the bronchoscope or endotracheal tube).4,16-18 In rare cases, pulmonary edema or fatal pulmonary venous gas embolism has been reported.19-21 Patients with endotracheal tubes and those who require high concentrations of supplemental oxygen are at increased risk for endobronchial fire. Fortunately, the overall risk is less than 0.1 percent.11,22 The overall rate of mortality attributable to endoscopic laser therapy is quite low, not exceeding 0.3 to 0.5 percent in several large series.16,17,22,23

In a study of Nd:YAG laser therapy in approximately 1800 patients with endobronchial obstruction due to malignant tumors, recanalization rates exceeded 90 percent for tumors located in the trachea, main-stem bronchi, and right intermediate bronchus.4 The treatment was less successful in patients with peripheral lesions (recanalization rate, 50 to 70 percent) or with associated extrinsic airway compression. Serious complications, such as hemorrhage, pneumothorax, or cardiorespiratory failure, occurred in less than 3 percent of all patients.

Several retrospective case series have compared survival rates among patients undergoing laser therapy for advanced lung cancer with survival rates among historical controls.24,25 Laser therapy was associated with increased survival rates among patients with lung cancer who required emergency treatment to restore airway patency.24 In addition, Stanopoulos et al. reported successful weaning from mechanical ventilation after endoscopic laser debulking in 9 of 17 patients with advanced lung cancer (53 percent) who presented in respiratory failure.26 Colt and Harrell reported similar findings when laser therapy was combined with placement of an endobronchial stent.27

![Figure 1. Algorithm for the Management of Central-Airway Obstruction Due to a Malignant Tumor.](image-url)
Photocoagulation with an Nd:YAG laser is an invaluable treatment for patients with airway obstruction due to benign endoluminal tumors. In a study reported by Shah and colleagues, complete resection was achieved with a single laser treatment in 62 percent of patients with benign tumors. Other investigators have reported similar findings, with rates of complete resection ranging from 50 percent to 80 percent.

Endobronchial Brachytherapy

Endobronchial brachytherapy involves the bronchoscopic insertion of a thin, hollow catheter through a malignant obstruction under fluoroscopic guidance. A radioactive implant is then inserted into the catheter and left in position for a predetermined period (2 to 40 hours, depending on the dose rate).

In 1922, Yankauer reported the use of rigid bronchoscopic brachytherapy for the palliation of airway obstruction due to malignant tumors. Modern techniques, including the use of flexible bronchoscopes, polyethylene afterloading catheters, and iridium-192 implants, were first described in 1983. Since the development of techniques involving a high dose rate in the 1980s, endobronchial brachytherapy has become a particularly attractive option for outpatient treatment.

Relief of airway obstruction is the primary goal of endobronchial brachytherapy, although curative treatment may be attempted in conjunction with external-beam radiation in selected patients. Brachytherapy is safest and most effective for central airway lesions, although in one study, small peripheral tumors proved to be more responsive than bulkier central tumors. Among patients with obstruction due to malignant tumors, rates of recanalization range from 60 percent to 90 percent, with decreased dyspnea, cessation of hemoptysis, and relief of cough in most cases. Brachytherapy has also been used for the prevention and treatment of airway stenosis related to recurrent growth of granulation tissue in patients with lung transplants.

Endobronchial brachytherapy may require multiple treatments to be effective. It is generally used as an adjunct to either photocoagulation with an Nd:YAG laser or conventional external-beam irradiation in an effort to achieve both rapid and sustained recanalization in patients with obstruction due to malignant tumors. Brachytherapy may also be administered in conjunction with the placement of an endobronchial stent in patients with extrinsic compression of the airways due to malignant tumors.

Serious complications of brachytherapy include massive hemoptysis and fistula formation. Because of the risk of fatal hemorrhage, every effort should be made to rule out the involvement of central vessels before treatment is administered. The incidence of serious complications varies widely, with rates as low as 0 to 10 percent in some of the largest studies and as high as 30 to 42 percent in two small studies.

Photodynamic Therapy

Photodynamic therapy is currently approved by the Food and Drug Administration for the palliation of airway obstruction caused by malignant tumors as an alternative to surgery in selected patients with minimally invasive central lung cancer. Photodynamic therapy works on the principle that certain compounds, such as hematoporphyrin derivatives, function as photosensitizing agents, rendering malignant cells susceptible to damage from monochromatic light. The selective effect of photodynamic therapy on malignant cells is thought to be due to the greater up-
take and retention of photosensitizing agents in neoplastic cells than in normal cells. This effect appears to be most pronounced approximately 24 to 48 hours after infusion of the photosensitizing agent. For this reason, bronchoscopic treatment of target lesions is often performed one to two days after the agent has been injected. Subsequent bronchoscopy is often required to débride necrotic tissue.

Ideal candidates for photodynamic therapy include patients with airway obstruction due to malignant polypoid endobronchial masses, with minimal extrinsic airway compression, and patients with minimally invasive tumors of the central airways. Metastatic tumors have also been treated successfully with photodynamic therapy. In patients with bulky tumors, endobronchial photodynamic therapy may substantially reduce the obstruction, with objective increases in spirometric measurements and subjective improvements in dyspnea and the quality of life. Complications of photodynamic therapy include increased photosensitivity of the skin and hemoptysis resulting from extensive tumor necrosis.

**Tracheobronchial Stenting**

The medical term “stent” was first used to denote a device that supported the healing of gingival grafts, developed by the British dentist Charles R. Stent. The term has since been used to refer to any device designed to maintain the integrity of hollow tubular structures, such as the coronary arteries and the esophagus. Anecdotal reports of attempts to use stents in the tracheobronchial tree date back to 1915. The Montgomery T tube, designed in the 1960s, was the first reliable, dedicated airway stent. However, stent implantation in the lower trachea and bronchi did not become standard medical practice until Dumon’s 1990 report on the safety and ease of placement of a dedicated airway stent made of silicone. Unlike silicone stents, metal stents can be placed with the use of a flexible bronchoscope, and they are less likely to migrate and more likely to preserve normal mucociliary clearance. Metal stents remain fairly expensive, however, and if they are misplaced in the airway, rigid bronchoscopy is often required for their removal. In addition, mucosal inflammation and the formation of granulation tissue are common at the proximal and distal ends of metal stents, and endoscopic intervention may be required to restore airway patency.

Endobronchial stents have a critical role in a multimodal endoscopic approach to both benign and malignant stenoses of the airways. Stenosis due to locally advanced bronchogenic carcinoma, for example, can be treated with a combination of endoscopic laser therapy and stent implantation in order to prevent respiratory failure (Fig. 3 and 4). Stent placement can also be used to maintain airway patency after endobronchial brachytherapy or can be combined with laser therapy and balloon dilation in the endoscopic management of fibrotic strictures.
Most studies of the efficacy of endobronchial stent placement have had impressive results. Dumon and colleagues reported excellent clinical outcomes and few complications with the use of silicone stents in patients with extrinsic airway compression due to malignant tumors but a lower success rate among patients with tracheal stenosis caused by other disorders. The most common complications in this study were migration of the stent, formation of granulation tissue, and inspissation of secretions. Rates of success, broadly defined as symptomatic relief, in smaller studies have ranged between 78 percent and 98 percent. In two small studies of patients who had been intubated because of respiratory failure due to unresectable tracheobronchial and mediastinal disease, stent placement facilitated extubation in nearly all the patients.

The benefits of stent placement appear to persist in patients who survive for a period of several months or years after implantation. Long-term follow-up data, however, are limited to benign disease, since the mean follow-up period in patients with airway compression due to malignant tumors does not usually exceed three to four months. Some authors have reported poor long-term results with the use of metal stents in patients with fibroinflammatory stenosis due to nonmalignant disorders. In addition, there have been case reports of massive hemorrhage associated with the use of stents in patients with extrinsic compression attributable to aneurysmal dilatation or congenital malformations of the aorta.

**Pleuroscopy**

This procedure, also known as medical thoracoscopy, was described in Europe by Jacobeus, a pulmonologist who adapted a rigid cytoscope for insertion into the pleural cavity. Pleuroscopy was initially used for the diagnosis and management of tuberculous lung disease, but it was abandoned once effective antimycobacterial drugs became widely available. The recent emphasis on minimally invasive surgical techniques has led to a renewed interest in the procedure.

Pleuroscopy as performed by interventional pulmo-
nologists differs from video-assisted thoracic surgery, in that local anesthesia and conscious sedation are most often used in lieu of general anesthesia, a single thoracic puncture is made rather than multiple incisions, and the procedure can be safely performed in an ambulatory care setting. Although pleuroscopy is primarily used for the diagnosis and management of pleural disorders, it can also be used to perform lung biopsy and manage spontaneous pneumothorax. Mortality rates associated with pleuroscopy are extremely low, ranging from 0.01 percent to 0.24 percent. Complications of the procedure include bleeding, persistent pneumothorax, and intercostal nerve or vessel injury.

COMMON CLINICAL APPLICATIONS

Endoluminal Airway Obstruction

Endoluminal obstruction of the tracheobronchial tree may result from various benign and malignant processes. The most common cause of endobronchial obstruction is advanced bronchogenic carcinoma. In patients with inoperable tumors of the central airways, restoration of airway patency may provide palliation and may even prolong life, particularly in the case of impending respiratory failure.

Signs and symptoms of central airway obstruction vary but often include wheezing, cough, stridor, hoarseness, hemoptysis, and chest pain. A careful pre-treatment evaluation should be performed to distinguish symptoms attributable to focal tracheobronchial lesions from those related to underlying diffuse airflow obstruction, parenchymal lung disease, or both. Mild-to-moderate tracheal stenosis, for example, may contribute only marginally to the degree of dyspnea experienced by a patient with severe chronic obstructive lung disease. Although pulmonary-function testing and thoracic imaging techniques such as computed tomography (CT) and magnetic resonance imaging may be useful in the evaluation of a patient

Figure 4. Chest Radiographs of a 66-Year-Old Woman with Severe Dyspnea and Hemoptysis and a History of Endometrial Carcinoma. Complete atelectasis of the right lung was noted, with an ipsilateral shift of the trachea and mediastinum and a bulging mass in the region of the right main bronchus (Panel A, magnified area, arrow). Diagnostic bronchoscopy showed a fungating tumor emanating from the orifice of the right main bronchus and extending into the distal trachea. Nd:YAG–laser photocoagulation was performed, with debulking of the endobronchial tumor and insertion of a metal stent (Wallstent) in the right main bronchus (Panel B, long arrow). A metastatic focus is visible in the inferolateral aspect of the right lower lobe (short arrow).
with suspected obstruction of the central airway, bronchoscopy, either rigid or flexible, remains the diagnostic gold standard.\textsuperscript{1}

The bronchoscopic approach to the management of endoluminal obstruction depends on the location of the lesion, the presence or absence of associated extrinsic compression, and the degree of clinical urgency (Fig. 1). Rigid-bronchoscopic debulking, with adjunctive laser therapy or electrocautery, is recommended when airway recanalization must be performed on an emergency basis. If endobronchial obstruction is accompanied by marked extrinsic compression, the placement of a stent may be beneficial.

The complexity of a lesion is equally important in determining the best approach to resection. Tracheal webs, for example, are often managed by laser resection alone, whereas complex fibrotic strictures may warrant the combination of rigid-bronchoscopic or balloon dilation, laser resection, and stent placement (Fig. 3 and 4). For focal tracheal stenoses in low-risk patients, surgical resection and primary reanastomosis should remain the first-line therapy.\textsuperscript{104}

**Extrinsic Airway Compression**

Extrinsic airway compression usually results from malignant involvement of structures adjacent to the central airways, such as mediastinal lymph nodes or the esophagus, but it may be associated with a benign process, such as fibrosing mediastinitis,\textsuperscript{105} tuberculosis,\textsuperscript{106} aneurysmal dilatation of the aorta,\textsuperscript{76} or sarcoidosis.\textsuperscript{107} The clinical signs and symptoms of extrinsic airway compression often mimic those of endobronchial obstruction. The diagnosis is established on the basis of bronchoscopic evidence of marked narrowing of the airway in the absence of an endobronchial mass. Chest CT has an important adjunctive role in identifying anatomical structures external to the narrowed lumen.

Therapeutic options in the management of extrinsic airway compression are limited. Ablative endoscopic approaches such as laser therapy, cryotherapy, photodynamic therapy, and electrocautery are contraindicated because of the risk of airway perforation. Although some patients with malignant disease may benefit from endobronchial brachytherapy, tracheobronchial stent placement is the palliative treatment of choice for patients with symptomatic extrinsic airway compression.

**Tracheobronchomalacia**

Diffuse or focal tracheobronchomalacia is perhaps the most challenging disorder encountered by the interventional pulmonologist. Cartilaginous tracheobronchomalacia, as seen in patients with post-intubation injury or relapsing polychondritis,\textsuperscript{108} reflects a loss of the structural integrity of the trachea or mainstem bronchi due to destruction of the airway’s cartilaginous rings. Membranous, or crescentic, tracheobronchomalacia is manifested by airway collapse during exhalation as a result of laxity of the membranous portion of the trachea and main bronchi and is usually seen in patients with long-standing chronic obstructive pulmonary disease.\textsuperscript{109} Focal tracheobronchomalacia may be a complication of long-standing intubation\textsuperscript{108} or an anastomotic complication after lung transplantation.\textsuperscript{110} Tracheobronchomalacia is best diagnosed on the basis of fiberoptic bronchoscopy, with the patient breathing spontaneously, although dynamic CT scanning, with images obtained on inspiration and expiration, is often helpful.

The endoscopic treatment of choice for patients with diffuse tracheobronchomalacia is the insertion of a silicone or expandable metal stent. This intervention is more likely to be successful in patients with the cartilaginous type of tracheobronchomalacia than in those with the membranous type. For many patients with focal tracheobronchomalacia, surgery is the best therapeutic option. An alternative treatment for selected patients with diffuse tracheobronchomalacia is the pneumatic stent afforded by noninvasive ventilatory techniques such as nasal continuous positive airway pressure.\textsuperscript{111,112}

**Pleural Effusions Due to Malignant Tumors**

Large, symptomatic pleural effusions resulting from primary or secondary malignant processes affect substantial numbers of patients with primary breast or lung cancer at some point during the course of their illness.\textsuperscript{3} Such patients often present with dyspnea and chest pain. Although thoracentesis can confirm the underlying diagnosis and temporarily alleviate dyspnea, repeated thoracentesis does not provide long-term control of respiratory symptoms. In fact, pleural effusions due to malignant tumors recur an average of four or five days after thoracentesis.\textsuperscript{113} Similarly, tube thoracostomy alone is ineffective for the long-term control of malignant effusions.\textsuperscript{114}

The interventional pulmonologist can offer several therapeutic options to patients with symptomatic, recurrent pleural effusions. Patients who have complete lung reexpansion after thoracentesis but in whom pleural fluid reaccumulates rapidly may be good candidates for tube thoracostomy, followed by chemical pleurodesis with doxycycline, bleomycin, or talc slurry.\textsuperscript{115-117} Pleurodesis with talc slurry has proved effective in preventing the reaccumulation of pleural fluid in 72 percent to 95 percent of cases.\textsuperscript{115,118,120} Alternatively, patients may opt for outpatient pleurodesis with the insertion of a small-caliber chest tube outfitted with a one-way valve, which allows for drainage at home.\textsuperscript{121} Semipermanent, implantable pleural catheters such as the Pleurx catheter (Denver Biomedical, Golden, Colo.) can induce sufficient pleural irritation by themselves to achieve pleurodesis in approximately 46 percent of patients.\textsuperscript{122} Alternatively, pleuroscopy may be performed. This
procedure is the gold standard in the diagnosis of pleur- 
el effusions caused by malignant disorders, with a 
sensitivity of more than 90 percent.123,124 as compared 
with 60 to 80 percent for large-volume thoracentesis 
and closed pleural biopsy.22 Talc pleurodesis with the 
use of pleuroscopy, which can be performed during a 
brief hospital stay, with minimal side effects, provides 
effective control of pleural effusions due to malignant 
conditions in 71 to 100 percent of patients.125-127 
Pleuroscopic talc poudrage may be unsuccessful in 
achieving pleurodesis in patients with lung parenchy-
ma that cannot reexpand because of bulky pleural 
disease, long-standing exudative effusions, or a large, 
obstructive endobronchial mass.128,129 Patients with 
complex effusions and multiple adhesions may benefit 
from traditional video-assisted thoracic surgery.

CONCLUSIONS

In the past decade, tremendous technical advances 
have been made in thoracic endoscopy and the adjuc-
tive use of lasers, stents, and electrocautery probes. 
Although primarily palliative, interventional pulmo-
nology may soon provide definitive alternatives to 
surgery for conditions such as early-stage lung cancer 
and benign endobronchial tumors. Advances in molecular 
biology and immunology will undoubtedly lead to fur-
ther progress in this new discipline. Ultimately, 
interventional pulmonologists may use bronchoscopic 
and pleuroscopic techniques to administer gene ther-
apy or immunotherapy, or both, for the treatment and 
prevention of disorders as diverse as cystic fibrosis and 
lung cancer.

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