# Tracheobronchial Stenosis
## Causes and Advances in Management

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**KEYWORDS**

• Tracheobronchial stenosis • Systemic therapy • Bronchoscopy • Bioabsorbable stenting

**KEY POINTS**

- Tracheobronchial stenosis results from malignant and benign causes.
- Treatment includes systemic therapy in addition to endoscopic or surgical approaches.
- Balloons, heat therapy, and stenting are useful for stenosis involving the proximal airways. These therapies may provide immediate improvement in dyspnea.
- Surgical resection of limited benign and malignant stenosis has a high success rate and may provide long-lasting results.
- New surgical therapies, as well as developments in bioabsorbable stenting, hold promise for the future treatment of tracheobronchial symptomatic stenosis.

### INTRODUCTION

Airway stenosis may involve the glottis, subglottis (below the vocal cords but above the inferior cricoid), or tracheobronchial tree. It may be congenital or acquired, caused by benign or malignant diseases, focal or diffuse, and present with various symptoms. Patients with significant stenosis may present with dyspnea, wheezing, or stridor. Stridor occurs when the airway diameter in an adult diminishes to approximately 6 mm. Given that congenital and pediatric stenosis may often have different causes and require different treatments, this article focuses primarily on adult stenosis of the tracheobronchial tree.

### EVALUATION

Beyond the physical examination, evaluation often includes a combination of physiologic, radiographic, and endoscopic assessments. Pulmonary function tests may show a delay in reaching peak expiratory flow, a truncation of peak expiratory and peak inspiratory flow, and/or an abrupt decrease in expiratory flow at the end of expiration. There may be flattening of the inspiratory and expiratory phases in the presence of fixed upper airway obstruction. A chest radiograph may detect tracheal disease although multiplanar computed tomography (CT) is useful for characterization of disease extent, exact configuration, and for planning treatment. This airway CT is different from neck or chest CT scans with thinner cuts that allow for three-dimensional reconstruction. Often called virtual bronchoscopy, the three-dimensional external and internal airway images have a high sensitivity and specificity compared with rigid bronchoscopy.[1] For dynamic collapse, such as in tracheobronchomalacia, inspiratory and expiratory CT imaging may demonstrate the characteristic crescent changes seen with collapse of the posterior membrane.

Subsequent evaluation is typically done via endoscopy. Defining the injury and assessing the

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presence of active inflammation and edema are essential. Bronchoscopic biopsies may secure the pathologic diagnosis. Recent studies demonstrate that measuring lateral airway wall pressure on each side of the stenosis and plotting pressure-pressure curves can quantitatively assess the site of maximal obstruction and degree of stenosis. The investigators suggest these measurements estimate the need for additional procedures more than bronchoscopy alone and demonstrated that the cross-sectional area, dyspnea scale, pulmonary function tests, pressure difference, and angle of the pressure-pressure curve improved after interventional procedures.[2] An understanding of potential causes is also required to guide therapy.

## CAUSES AND PATHOGENESIS

Although dynamic obstruction, such as occurs with vocal cord dysfunction or tracheobronchomalacia, causes similar symptoms, this article focuses on stenosis that is fixed. Tracheobronchial stenosis may be predominantly intraluminal, such as postintubation tracheal stenosis, or from extrinsic compression, caused by a tumor. Glottic, subglottic, and high tracheal stenosis may require significantly different stabilization and treatment than carinal or bronchial stenosis. Furthermore, therapeutic approaches may be different depending on whether the disease is benign or malignant, and the extent of disease. The more common conditions causing tracheobronchial stenosis are listed in **Box 1** and shown in **Figs. 1** and **2**.

**Box 1**
**Common causes of tracheobronchial stenosis**

| *Cause of Tracheal or Bronchial Stenosis* |
|---|
| Focal inflammation |
| Tracheostomy |
| Intubation |
| Trauma |
| Burns |
| After transplant |
| Systemic inflammation |
| Wegener granulomatosis |
| Relapsing polychondritis |
| Sarcoidosis |
| Amyloidosis |
| Inflammatory bowel disease |
| Others |
| Infectious |
| Tuberculosis |
| *Aspergillus* |
| Others |
| Dynamic collapse |
| Focal malacia |
| Diffuse tracheobronchomalacia |
| Miscellaneous |
| Saber sheath trachea |
| Tracheobronchopathia osteochondroplastica |
| Broncholithiasis |
| Idiopathic |
| Malignancy |
| Adenoid cystic carcinoma |
| Squamous cell carcinoma |
| Lung cancer: non–small and small cell |
| Metastatic disease |

## FOCAL BRONCHIAL DISEASES

Both malignant and benign diseases may cause focal narrowing of the tracheobronchial tree. Within the trachea, malignancy predominates. Primary tracheal malignancies include squamous cell carcinoma and adenoid cystic carcinoma, among others. Non–small cell lung cancer and small cell lung cancer are obvious causes of obstruction due either to extrinsic airway compression, intrinsic airway tumor, or a combination of both. When confined to the trachea or mainstem bronchi, surgical resection may be curative. Metastatic disease from a variety of conditions may cause obstruction from endobronchial deposits or massive adenopathy. Breast, colorectal, renal cell, and melanoma are the most common extrathoracic malignancies to metastasize to the lungs. When the disease is advanced, various endoscopic modalities may complement chemotherapy or radiation therapy. Typically, bronchoscopic management includes a combination of opening the airway (balloons), debulking the tumor (heat or cold therapy), and stabilizing the airway for the longer term (stenting). These treatment modalities are described later.

The most common causes of benign iatrogenic stenosis include intubation, tracheostomy, and lung transplant. Mucosal ischemia followed by granulation tissue and fibrosis often creates 1.5 to 2.5 cm of stenosis after intubation or tracheostomy with cuffed tubes.[3] With low-pressure cuffs and maintaining a pressure less than 30 mm Hg, the incidence after intubation has decreased to 1%, whereas after tracheostomy, stenosis

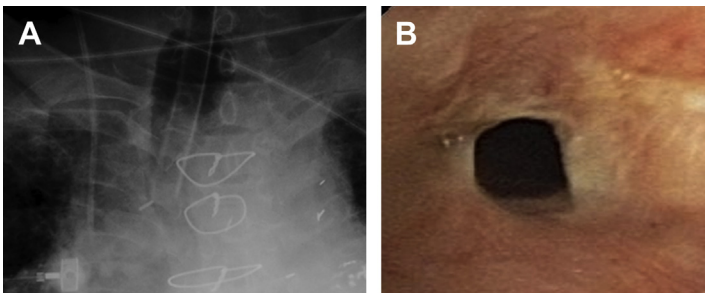


**Fig. 1.** Iatrogenic causes of benign tracheal stenosis. (*A*) Overinflation of the endotracheal tube may lead to mucosal ischemia and subsequent stenosis. Cuffed tracheostomy tubes pose a similar risk. Tracheal stenosis from these focal insults may look like that shown in (*B*).

approaches 10% to 15% and bronchial anastomotic stenosis after transplant occurs in up to 15%.[3]

A variable degree of stenosis has been reported in up to 90% of patients with tuberculosis.[3] Airway involvement from tuberculosis likely evolves in stages, from submucosal tubercules to ulceration and necrosis. Subsequent healing can lead to fibrosis, often with long segments of circumferential stenosis. Stenosis of the airways can also occur from adjacent lymphadenopathy. Prebronchoscopic sputum results are often negative despite active disease, and CT findings may be nonspecific.[4]

Aside from tuberculosis, other infectious organisms can cause tracheobronchial stenosis. *Klebsiella rhinoscleromatis* is an encapsulated gram-negative bacterium endemic in tropical and subtropical areas; it causes rhinoscleroma, a slowly progressive granulomatous disease. Nodules or

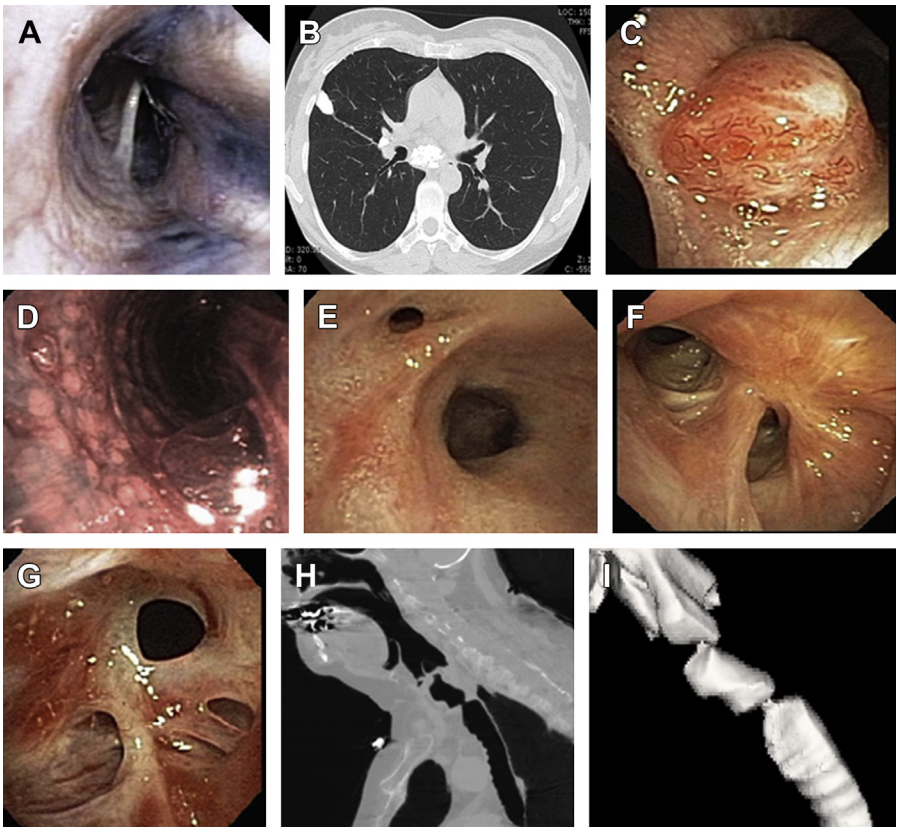


**Fig. 2.** Examples of benign tracheobronchial stenosis. (*A*) Anthracosis. (*B*) Broncholithiasis, as shown on CT scanning. (*C*) Endoscopic image of the adjacent mucosal reaction. (*D*) Tuberculosis with submucosal granulomas. (*E*) Bronchial stenosis caused by Wegener granulomatosis. (*F*) Posttransplant bronchial stenosis. (*G*) Complex webbed stenosis of unknown cause. (*H*) Sagittal and (*I*) three-dimensional reconstruction of focal benign tracheal stenosis.

masses that form in the granulomatous phase may cause partial obstruction (pseudoepitheliomatous hyperplasia) and the final sclerotic phase may result in fibrosis. Biopsy or cultures assist in establishing the diagnosis.[4] Fungi, particularly *Aspergillus*, may cause tracheobronchitis in immunocompromised hosts, such as those with AIDS, underlying malignancy, or after transplant. Epithelial ulceration and submucosal inflammation occurs and may lead to strictures, whereas deeper bronchial wall necrosis may lead to bronchial or bronchovascular rupture and death.[3]

Bronchial anthracofibrosis demonstrates characteristic bronchoscopic findings in the absence of known pneumoconiosis or smoking.[3] It is hypothesized that the black pigments are derived from anthracotic material in the adjacent lymph nodes, with possible perforation of the nodes or penetration of carbon particles into the mucosa. Healing with a fibrotic response may lead to bronchial narrowing or obstruction. A CT scan may demonstrate mediastinal and hilar lymphadenopathy and endoscopy may reveal smooth bronchial narrowing. Atelectasis may accompany these findings. Biopsy should be performed to exclude malignancy.[4]

Tracheobronchopathia osteochondroplastica spares the posterior membrane and typically appears as submucosal nodules extending into the tracheobronchial lumen. Histologically, these are submucosal osteocartilaginous growths that leave the mucosal surface intact.[5] Treatment options for severe airway compromise include surgical or laser resection, radiation, or stent placement.

Broncholithiasis typically results from calcification of a lymph node caused by previous infection with organisms such as *Tuberculosis* or *Histoplasmosis*. The lymph node may erode into the airway in which case the patient may cough up calcified material. Alternatively, the lymph node may cause compression of the airways. Interventional or surgical approaches may be necessary depending on the compromise of the airways.

Idiopathic tracheal stenosis occurs almost exclusively in middle-aged women. A weblike or complex stenosis develops mostly in the area of the cricoid. Although endoscopic therapy is efficacious, late recurrences are frequent and the disease requires ongoing follow-up.[4]

## SYSTEMIC DISEASES

Relapsing polychondritis is associated with recurrent inflammation of cartilaginous structures of the nose, external ear, peripheral joints, and airways. Up to 50% of patients may develop airway involvement, often starting at the larynx or subglottic space and progressing to involve more of the tracheobronchial tree. An inflammatory infiltrate develops in the cartilage and perichondrial tissue. The ensuing airway inflammation may lead to airway strictures, whereas collapse of the cartilaginous support may also lead to tracheobronchomalacia. The diagnosis may be made by meeting specific clinical criteria, whereas a chest CT may demonstrate attenuation of the airway walls (classic smooth thickening of anterior and lateral walls with characteristic sparing of the posterior membrane). Cartilaginous destruction may lead to the need for tracheobronchial stenting.[4]

Wegener granulomatosis is characterized by necrotizing granulomatous vasculitis, which may lead to subglottic, tracheal, or bronchial stenosis. It has been reported that 10% to 20% of patients with Wegener granulomatosis develop laryngotracheostenosis.[6] Granulomatous inflammation and vasculitis are seen in the mucosa and submucosa early in the disease, whereas fibrosis ensues later. Bronchoscopy may demonstrate ulcerative tracheobronchitis, inflammatory stenosis, or noninflammatory stenosis.[5] Steroids and immunosuppressant therapy are the mainstay but bronchoscopic intervention may be required. Surgery may also be required, including laryngotracheal reconstruction, albeit with increased risk of postprocedural repeated dilation.[6]

Bronchial involvement is more common than tracheal involvement in sarcoidosis. Bronchial wall thickening caused by granulomas and peribronchial interstitial fibrous tissue may result in smooth or irregular luminal narrowing. Lobar or segmental bronchial obstruction may occur from airway wall fibrosis, granulomatous inflammation, or lymph node compression. As with the inflammatory diseases described earlier, when systemic therapy fails to control disease, bronchoscopic interventions may be required.

Tracheobronchial amyloidosis may be present as an isolated manifestation with tracheal deposition of amyloid, or in conjunction with systemic amyloidosis. Pathologically, the amyloid is deposited in proximity to the tracheal gland acini and the blood vessel walls. The glands eventually atrophy and the amyloid produces irregular plaques and nodules in the mucosa. On occasion, masses may appear (amyloidomas) that may be radiographically difficult to distinguish from neoplasms. Biopsies are diagnostic, and Congo Red staining may highlight the amyloid. Radiation therapy may sometimes be required in addition to the interventional techniques described later.[3,5]

Rare causes of airway stenosis include inflammatory bowel disease; either ulcerative colitis or Crohn disease may produce airway inflammation.

Airway disease may present as ulcerative tracheitis and tracheobronchitis, bronchiectasis, and small airway disease such as obliterative bronchiolitis.[4] As with the aforementioned conditions, airway interventions may be required if systemic therapy is insufficient.

## VENTILATORY STRATEGIES BEFORE INTERVENTIONS FOR AIRWAY STENOSIS

Flexible and rigid bronchoscopy are performed to evaluate and treat airway stenosis. Whereas the flexible scope can be inserted in an unventilated patient, via a laryngeal mask airway or through the endotracheal tube, it contributes to obstruction because of its size. The rigid bronchoscope requires general anesthesia but allows ventilation through its side port. Intravenous short-acting agents such as remifentanil and propofol may be combined with narcotics, neuromuscular blockers, or inhaled agents during induction and throughout the procedure while maintaining strict airway control. With mid tracheal lesions, a decrease in respiratory rate or exhalational times may be necessary to minimize inspiratory pressures.

Many anesthesiologists use jet ventilation at low (20 breaths/min) or high (150 breaths/min) frequency. This may be performed with a catheter through the rigid bronchoscope, a laryngoscope, and a small (eg, 5.0 mm) endotracheal tube, or even via a transcricothyroid membrane catheter.[7] A series of 44 patients with severe upper airway obstruction demonstrated successful ventilation after transtracheal catheters placed under local anesthesia via the cricothyroid membrane or below the first or second trachea rings. Although minor complications occurred infrequently, they did not experience the major pressure-related problems reported elsewhere (pneumothorax, massive surgical emphysema, pneumomediastinum, and cardiovascular instability). The anesthesiologists adjusted the driving pressure or frequency when higher pressures were observed.[8] Other techniques include high-frequency positive pressure ventilation, high-frequency oscillatory ventilation, or cardiopulmonary bypass if adequate oxygenation cannot be maintained.

## BRONCHOSCOPIC INTERVENTIONS FOR AIRWAY STENOSIS

As mentioned earlier, the therapeutic options for airway stenosis depend on the cause of the obstruction. Patients with systemic diseases and clinically significant airway stenosis, benign yet inoperable disease, or advanced malignancy may require bronchoscopic interventions. Various bronchoscopic techniques are possible to relieve the obstruction. Although these procedures are expected to have an immediate impact when the appropriate patient is selected, long-term follow-up is essential to monitor the response to treatment and determine whether repeat procedures are necessary. This section focuses on airway balloons, heat modalities, and bronchial stenting to provide immediate relief for significant stenosis.

Airway dilation may be accomplished through rigid and flexible bronchoscopy. The rigid bronchoscope may core through areas of stenosis with the shear mechanics of the rigid scope providing dilation. A metal bougie dilator provides a similar effect. When this is not possible, balloon expansion may be useful. The benefits of balloons include the avoidance of surgery and other sophisticated techniques or equipment. Compliant balloons, such as the angioplasty balloon catheter (Fogarty), may be best for a fleshy or necrotic intraluminal tumor that easily compresses. More rigid balloons, such as the controlled radial expansion (CRE) balloon (Boston Scientific) may be used to dilate tight areas of stenosis. These balloons expand from 6 mm to 20 mm (using different balloon catheters) while being manually inflated. Care must be taken to avoid tearing the airways or rupturing them by using too large a balloon or careless dilation. In a recent study, patients demonstrated a subjective improvement in symptoms as well as 1-month sustained improvement in pulmonary function tests. However, for those who required more than 1 procedure, most required stenting. Combining their results with a literature review encompassing 340 patients and 554 balloon dilation procedures, the processes most amenable to balloon dilation were those with fixed stenosis; those with active inflammation, calcification, carcinoma, or in whom the surrounding cartilage was destroyed (malacia) were less responsive.[9]

Ablative techniques are frequently used to reestablish airway patency. These include heat and cold therapies. Circumferential weblike stenosis may benefit from incisions with an electrocautery knife (**Fig. 3**). Imagining the face of a clock, 3 small incisions (at 9 o'clock, 12 o'clock, and 3 o'clock) can be made with the knife and subsequent balloon dilation performed. The knife creates 1- to 2-mm incisions generating weak points such that the balloon will dilate the airway with targeted rather than sporadic and uncontrolled mucosal tearing. Recent analysis of the reusable electrode knife in the cut mode demonstrated improved symptoms, improved pulmonary function tests, and less fibrin production than laser therapy in a similar group of patients. Less than half of the

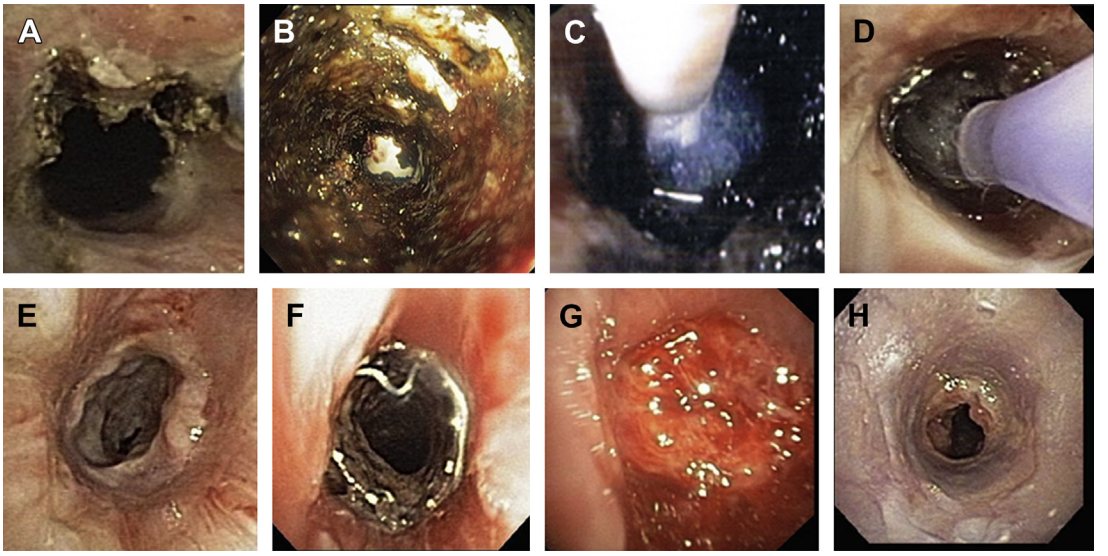


**Fig. 3.** Treatment options for tracheal stenosis. (*A*) Electrosurgical knife applied at the 3 o'clock position. (*B*) Results of cautery to reopen suprastomal stenosis. (*C*) Angioplasty balloon dilation. (*D*) The more rigid CRE balloon dilation. (*E*) Inflammatory tracheal stenosis. (*F*) This unique stenosis was treated with a hybrid stent before surgical resection. (*G*) Complete stenosis of the subglottic space. (*H*) Silicone stent after reestablishing patency.

patients in this small analysis required repeat intervention for weblike stenosis.[10]

Additional heat modalities used for treatment of tracheobronchial stenosis include electrocautery, argon plasma coagulation (APC) and laser therapy. These techniques are discussed elsewhere in this issue on interventional pulmonology and thus discussion here is kept brief. With cautery, an electric current is used to generate heat. Several devices may be used to apply this current, including the knife, a probe, and snare/cutting loop. Unlike the knife described earlier, the probe is blunt. The user sets the wattage (eg, 20–40 W) and depth of penetration; these combined with the time of topical impact determine the depth of mucosal destruction. In contrast, APC uses an argon gas charged with an electric current to achieve thermal tissue destruction. The argon gas flows flexibly around angles such that APC is suitable for bronchial segments that take off at acute angles to major airways. APC is a noncontact mode of thermal coagulation and as such, helps clear blood and mucus while performing superficial coagulation. Cerebral gas embolism has been reported as a unique complication of this procedure. Both electrocautery and APC offer advantages of ease and lower cost compared with laser therapy.[11]

The most common type of lasers used in the airways are the neodymium–yttrium-aluminum-garnet (Nd-YAG) and carbon dioxide ($CO_2$) lasers. The Nd-YAG provides tissue vaporization and coagulation. It has deeper thermal energy than the $CO_2$ laser and may penetrate up to 10 mm.[12] The $CO_2$ laser has more precise cutting abilities. The development of the flexible fiber $CO_2$ delivery system allows for the flexible bronchoscope to be used to ablate and cut with this laser. This contrasts with the typical microscope-mounted $CO_2$ laser, which requires general anesthesia. The laser is typically in pulse mode at 5 to 10 W delivered to 2 to 3 wedges separated by tissue to avoid circumferential mucosal denuding. Postoperative dexamethasone may be given to minimize upper airway edema when this ablation is performed high in the airway.[13] All heat therapies require that a patient receive less than 40% inspired oxygen to avoid airway fires during the procedure.

Mitomycin C may be an adjunct to radial incisions made with laser or cautery. Pledgets of cotton soaked in mitomycin C are topically applied to the areas of stenosis. This is believed to impede the inflammatory response.[14,15] A prospective, randomized, double-blind placebo-controlled trial of 26 patients with laryngotracheal stenosis of various causes suggested that 2 applications 3 to 4 weeks apart delayed but did not prevent the recurrence of stenosis in benign disease.[15] A retrospective analysis of 67 procedures in 36 patients also demonstrated a longer symptom-free interval than when endoscopy was used without mitomycin C.[16] To our knowledge, there is no Cochrane review or

meta-analysis of the effects of mitomycin C and thus its use requires further investigation before claiming efficacy.

In contrast to heat and medical therapies, contact and spray cryotherapy have been described. Contact cryotherapy uses a probe whereby extreme cold is alternated with internal body temperature to create a freeze-thaw cycle. Its efficacy is debatable as results have been variable. Spray cryotherapy uses a 7-French catheter and nitrogen as a base cryogen. Approximately 25 W (J/s) of energy is transferred, similar to laser therapy, but there is no risk of airway fire with the latter. Early results with spray cryotherapy are encouraging but further studies are needed to document its efficacy and safety.[17]

Airway stenting is an important strategy for managing various types of tracheobronchial obstruction. Stents are also discussed in other articles in this issue. Airway stenting may be used either temporarily or chronically. Several different types of stents exist (see **Fig. 3**), although metal stents have a US Food and Drug Administration black box warning for benign disease in part because of their predisposition to form granulation tissue. For benign conditions, silicone stents are preferred. These stents may be tubular, a Y-configuration that covers portions of the trachea and mainstem bronchi, an hourglass configuration with wider ends and a narrower center, or may be customized. On the other hand, metal stents are tubular. The advantage of metal stents is that, unlike silicone stents, they can be placed with the flexible bronchoscope. The metal stents may be completely covered, partially covered, or uncovered. Metal stents are more expensive than silicone stents. Both are susceptible to migration, granulation tissue formation, mucus plugging, and other complications.

Practice management varies, but any patient who has a stent placed requires appropriate follow-up. The duration a stent should remain in place is not known and likely depends on the clinical scenario. Patients with malignant stenosis often die with the stent in place; benign stenosis may require long-term placement. Factors predicting the ability to remove stents in tuberculosis included the lack of complete lobar atelectasis and performing stent placement within 1 month of the development of any atelectasis. Stents were left in place for 12.5 months in those patients whose stenosis was successfully treated by the temporary silicone stent.[18] A patient with relapsing polychondritis and a silicone stent for 16 years has been described recently.[19] Thus, the exact duration of stent placement varies according to each patient.

## RESULTS OF AIRWAY INTERVENTIONS

For idiopathic tracheal stenosis, initial success is high, but recurrence is typical. In a retrospective study of 23 patients with idiopathic stenosis treated at 9 institutions, the stenosis recurred in 30% of patients at 6 months, 59% at 2 years, and 87% at 5 years. A combination of therapies was frequently used.[20] Improvements that result from airway interventions in malignant disease likely deserve distinction from interventions for benign disease because of the systemic effects of cancer. A few studies have investigated quality of life and dyspnea after airway interventions for cancer. Amjadi and colleagues[21] used the validated European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and included 20 patients over 6 months. Using a combination of the therapies described earlier, more than 80% of airway caliber was restored in 80% of patients and 85% of patients demonstrated an improvement of dyspnea scores at 24 hours that extended to 30 days. Quality-of-life response was variable, likely because of the impact of symptoms such as pain from metastases and other factors that are not influenced by airway therapy. A separate retrospective cohort study of 37 patients with high-grade symptomatic central airway obstruction evaluated exercise capacity, lung function, and quality of life. More than 90% of patients had restoration of airway patency (>50% of airway restored). Statistically significant improvements in the 6-minute walk test were noted up to 180 days. Dyspnea scores, resting Borg, forced expiratory volume in 1 second, and forced vital capacity were improved at day 30. An improvement in quality of life was seen in 43% of patients. The median survival was 166 days and the 6-month survival rate was 46%.[22]

## FUTURE ENDOBRONCHIAL THERAPY

Biodegradable airway stents are under investigation and have been placed in humans. Polydioxanone is a semicrystalline biodegradable polymer that has some shape memory and degrades over time by random hydrolysis. The degradation time has not been exactly defined. Four children received 11 polydioxanone tracheal stents and 3 of the 4 are alive and in good clinical condition 12 months after the first stents were placed. It was difficult to predict the amount of radial force needed to maintain an airway without causing granulation tissue or creating risks for erosion, and to predict the rate of degradation.[23] Twenty biodegradable stents have been placed

in 6 patients after lung transplant who developed bronchial stenosis at the anastomosis. These stents were also made of polydioxanone; 5 of the 6 patients were alive and intervention free up to 44 months after the first stent was placed.[24] Various ongoing studies in animal models of this and other materials (polycaprolactone[25]) may lead to clinically applicable biodegradable airway stents in the future.

## SURGICAL MANAGEMENT

Surgery is possible for localized malignancy as well as benign stenosis that affects less than half of the trachea. The aforementioned interventional procedures may play an important preoperative role to establish airway patency and enhance safety and ease of perioperative ventilation. Other preoperative interventions include aggressive treatment of gastroesophageal reflux, evaluating for the presence of aspiration, and preoperative treatment of patients colonized with methicillin-resistant *Staphylococcus aureus*.

The location of stenosis may dictate the type of surgical procedure performed. The main types of therapeutic procedures for subglottic stenosis include laryngotracheal resection and anastomosis, laryngoplasty without segmental resection and with or without bone or cartilage grafting, or endoscopic procedures. The Cotton-Meyer grading scale describes the degree of stenosis and resection is accomplished using a single-stage laryngotracheal reconstruction (LTR) or double-stage LTR procedure. Cricotracheal resection may be performed when the larynx is spared.[26] Pearson described the technique of anterolateral cricoid cartilage resection and primary thyrotracheal anastomosis with preservation of the recurrent laryngeal nerve in 1975. Grillow subsequently described the use of a flap of posterior membranous trachea in cases of circumferential subglottic stenosis.[27] A recent meta-analysis demonstrated that laryngotracheal resection was more effective than the other 2 techniques, especially in the absence of glottic involvement. The random-effect pooled success rate of LTR was greater than 95%, that of laryngoplasty was 76%, and that of endoscopy highly variable (40%–82%). The investigators concluded that laryngoplasty is suitable for resection of long segments or subglottic stenosis with glottis involvement. Patients with less than 1 cm of stenosis and without framework destruction may be reasonable candidates for endoscopic management as a first modality, with surgery reserved for failure.[28]

Significant advances in tracheal surgery occurred in the 1950s and refinements in the techniques led to resection of longer segments. The main principles of resection include meticulous dissection to preserve the blood supply of the trachea and recurrent laryngeal nerves, as well as avoidance of excessive anastomotic tension. As with laryngotracheal involvement, the types of tracheal surgery depend on the location of the stenosis. Cotton and Fearon introduced the costal cartilage augmentation procedure in 1976 that has become known as LTR and other open techniques have been adopted, including the anterior cricoid split, tracheal resection with end-to-end reanastomosis, and slide tracheoplasty.[1]

In slide tracheoplasty, a long stenotic segment is divided transversely at its midpoint and the upper and lower stenotic segments divided longitudinally, anteriorly, and posteriorly. The splayed upper and lower segments are then slid together to produce a trachea with quadrupled cross-sectional area.[29]

Tracheal resection with reanastamosis is seen as a procedure of choice given its high success rate (71%–95%) and minimal morbidity.[30] It can be accomplished using a neck collar incision for high stenosis or median sternotomy for mid to lower tracheal stenosis. After dissection from the surrounding tissue, reanastomosis may be end-to-end tracheal, cricotracheal, or thyrotracheal, depending on the location of the stenosis. Securing sutures between the skin of the chin and anterior chest may maintain neck flexion to avoid excess tension at the anastomosis during the early preoperative period.[31] Early extubation, avoidance of systemic corticosteroids, and use of absorbable submucosal sutures may limit complications.[30] Pericardial patches, rib grafting, and other techniques have also been described to facilitate resection. Over 40 years and 503 patients with postintubation stenosis, results were good in 87.5% of patients. All benign and 70% of malignant tumors were resectable. Recent perioperative mortality was 3% and anastomotic complications occurred in 15%. Multivariate analysis demonstrated that length of resection, diabetes, redo resections, laryngeal involvement, pediatric age, and presence of tracheostomy were important prognostic factors for complications.[32]

Further distally into the airways, carinal resections are feasible although complicated. Typically, either a median sternotomy or right thoracotomy is performed and the neocarina is fashioned from the 2 divided main bronchi. The longer bronchus is usually anastomosed end to end with the trachea and the shorter bronchus attached to the sidewall

of the longer bronchus with end-to-end anastomosis. Bronchial resections for malignant or benign stenosis are also performed. A bronchial sleeve resection begins with bronchotomy of the proximal airway followed by anastomosis with the lower airways. The diseased segment is removed, tension-free anastomosis is attempted, and occasional pedicled pleura or pericardium can be used between the bronchial anastomosis and vasculature.[33]

## FUTURISTIC SURGICAL APPROACHES

Autografts, allografts, bioengineered tracheal platforms, and tracheal transplants may become more prominent in the future. The innate complexity and compromising blood supply of the trachea make a single tissue graft of the trachea rarely sufficient to achieve adequate function. Autografts include a patient's own tissue to reconstruct the airways; for example, resection of bronchi and replacement in the trachea, or muscle flaps to bridge defects resulting from tracheobronchial reconstruction. The grafts must have rigidity, epithelium, and adequate vascular supply.

Seguin and colleagues[34] demonstrated that functional tissue could be regenerated in sheep after replacement of the trachea with a cryopreserved aortic allograft. The use of cryopreserved specimens would offer advantages for use in tissue banks, for permanent storage, and by limiting the need for immunosuppression. It has been shown that respiratory epithelial cells and cartilage can regenerate in animal models of aortic allografts and that the allograft progressively transforms into a structure resembling tracheal tissue. Airway stenting was mandatory in pigs to prevent collapse of the initially compliant graft, and the investigators concluded that long-term stenting was necessary to provide stability as the neotrachea formed.[35] Tracheal replacement using bioabsorbable scaffolds[36] have been described. These studies are still mostly limited to animals.

Composite tissue grafts may include costal cartilage for support, mucosal grafts (buccal, palate) for epithelium, and pedicled flaps or free tissue transfer flaps for blood supply. Prosthetic scaffolds, such as a mesh, have been combined with free tissue flaps in advanced efforts to reconstruct the airway. An overview of unique surgical approaches to tracheal reconstruction is recommended.[37] A tissue-engineered tracheal allograft has been described, using a cadaveric trachea decellularized and with human leukocyte antigens removed, and with autologous bronchial epithelial cells harvested, cultured, and implanted on the internal surface of the trachea. Bone marrow–derived mesenchymal stem cells were harvested and differentiated toward chondrogenesis and implanted on the external surface of the tracheal graft. Although it revascularized well, there are concerns about the dependability of neovascularization of free grafts.[37]

Tracheal transplant is a challenge because of the vascular supply of the trachea, constant movement of the trachea, and constant exposure to bacteria. Only a few reports of tracheal transplant exist. The current concepts of tracheal transplantation include vascularization, growth of epithelium, and use of a chimeric product that includes donor tissue (cartilage, respiratory mucosa) and recipient tissue (membranous trachea, forearm fascia, forearm skin, and buccal mucosa). In this approach, the donor trachea is implanted in the forearm and allowed to vascularize, then epithelialized with recipient mucosal graft, and ultimately transposed into the trachea. Immunosuppressants are gradually withdrawn to allow anastomotic repopulation of recipient blood vessels and respiratory epithelium, and the recipient buccal mucosa and recipient forearm blood vessels preserve the airway lumen in the mid portion. This fascinating work is well worth reading.[38]

## SUMMARY

Tracheobronchial stenosis results from malignant and benign causes. Treatment includes systemic therapy in addition to endoscopic or surgical approaches. Balloons, heat therapy, and stenting are useful for stenosis involving the proximal airways. These therapies may provide immediate improvement in dyspnea. Surgical resection of limited benign and malignant stenosis has a high success rate and may provide long-lasting results. New surgical therapies, as well as developments in bioabsorbable stenting, hold promise for the future treatment of tracheobronchial symptomatic stenosis.

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