

REVIEW ARTICLE

TRACHEAL AND BRONCHIAL STENOSIS: ETIOLOGIES, BRONCHOSCOPIC INTERVENTIONS AND OUTCOMES

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ABSTRACT:

Tracheal stenosis is narrowing of the trachea by neoplastic or non-neoplastic processes. Symptoms develop when the narrowing impedes flow and increases resistance within the airways. Medications, such as bronchodilators, are unable to significantly improve the airflow in these circumstances due to the fixed anatomic defects and other modalities are required. Bronchoscopic interventions include the use of balloons, ablative treatment and stenting, among others, to increase the airway diameter and provide symptomatic relief. Surgical resection is indicated in some causes. This article will review causes and bronchoscopic treatment options for common causes of tracheobronchial stenosis.

INTRODUCTION:

Patients with significant stenosis may present with dyspnea, wheezing or stridor. Airway stenosis should be considered as a cause of above symptoms in the absence of significant parenchymal disease, evidence of pulmonary hypertension or pulmonary embolus. A chest X-ray may detect tracheal disease although multiplanar computed tomography (CT) is useful for characterization of disease extent, exact configuration, and for planning treatment. 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. Pulmonary function tests may show a flow limitation in the inspiratory and/or expiratory loops. Subsequent evaluation is typically done bronchoscopically.

Etiologies and Pathogenesis

It is helpful to distinguish between malignant and benign etiologies for tracheobronchial stenosis as well as to consider the level of aggressiveness based on the underlying disease and potential for cure. Furthermore, particularly for benign disease, it is important to consider whether the obstruction is dynamic (tracheobronchomalacia) or fixed. Finally, the level and extent of obstruction is crucial in the initial decision-making: Subglottic etiologies may require tracheostomy for treatment or airway stabilization. Short tracheal strictures are perhaps most amenable to bronchoscopic or surgical resection, whereas diffusely stenotic and distal airways may not be. In many cases, airway interventions are palliative and often coupled with additional systemic therapy when appropriate. The airway interventions may be very successful, yet without appropriate evaluation and expertise, may also create problems due to the technical challenges or complications of the treatment. Systemic approaches may include steroids for systemic inflammatory disorders, antibiotics for infectious causes, and chemotherapy or radiation for malignancy. It is when these fail or are not felt to be feasible that procedural efforts should be the mainstay. The more common conditions causing tracheobronchial stenosis are listed in Table I, shown in Figure II and many are described below.

Several malignant conditions may affect the tracheobronchial tree. Non-small and small cell lung cancers are obvious causes of obstruction due either to extrinsic airway compression, intrinsic airway tumor or a combination of both. Adenoid cystic carcinoma occurs within the large airways, and metastatic disease from a variety of conditions may cause obstruction from endobronchial deposits or massive adenopathy. It is not the goal of this paper to discuss comprehensive management. The procedures described below are useful for palliation of advanced malignancy or to improve a patient's functional status such that chemo- or radiation therapy can be provided.

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Typically the bronchoscopic management includes a combination of opening the airway (balloons), debulking tumor (heat or cold therapy), and stabilizing the airway for the longer term (stenting).

There are many benign causes of tracheal stenosis. Because “stenosis” typically means a fixed defect, care should be used when grouping focal or diffuse malacia into this category. Tracheobronchomalacia and excessive dynamic airway collapse create obstruction of the airways due to luminal narrowing that varies with inhalation and exhalation. It has been proposed that tracheomalacia involves cartilaginous weakening whereas excessive dynamic airway collapse is limited to laxity of the posterior membrane¹. Each condition has dynamic collapse rather than fixed stenosis and may improve with non-invasive ventilation (continuous positive airway pressure, or CPAP). Stenting with Y-shaped silicone stents may bridge patients to more definitive therapy with tracheobronchoplasty, a surgical intervention requiring specific expertise and a thorough evaluation. Excellent reviews are suggested for additional understanding^{2,3}.

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 – 2.5 cm of stenosis following intubation or tracheostomy with cuffed tubes⁴. An example is shown in Figure I. With low pressure cuffs, the incidence after intubation has decreased to 1% whereas post-tracheostomy stenosis approaches 10-15% and post-transplant bronchial anastomotic stenosis occurs in up to 15%⁴. A combination of multiplanar CT scanning with three dimensional reconstruction of images and bronchoscopic evaluation can determine the configuration of the stenosis (web-like versus complex or bottleneck), length of stenosis and the appearance of the airways around the stenotic areas. This can help guide therapeutic strategies.

A variable degree of stenosis has been reported in up to 90% of patients with tuberculosis⁴. Airway involvement from TB likely evolves in stages, from submucosal tubercles 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 .

Aside from TB, other infectious organisms can cause trachea-bronchial stenosis. *Klebsiella rhinoscleromatis* is an encapsulated gram-negative bacterium endemic in tropical and subtropical areas. Nodules or masses that form in the granulomatous phase may cause partial obstruction (pseudoepitheliomatous hyperplasia) and the final sclerotic phase may result in fibrosis. Similarly, fungi, and particularly *Aspergillus*, may cause a tracheobronchitis in immunocompromised hosts, such as those with AIDS, underlying malignancy or post-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 death⁴.

Bronchial anthracofibrosis demonstrates characteristic bronchoscopic findings in the absence of known pneumoconiosis or smoking⁴. 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.

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.

Wegener's granulomatosis is characterized by necrotizing granulomatous vasculitis which may lead to subglottic, tracheal or bronchial stenosis. Granulomatous inflammation and vasculitis is seen in the mucosa and submucosa early in the disease, whereas fibrosis ensues later. Bronchoscopy may demonstrate ulcerative tracheobronchitis, inflammatory or non-inflammatory stenosis⁵. Steroids and immunosuppressant therapy is the mainstay but bronchoscopy intervention may be required.

Bronchial involvement is more common than tracheal involvement in sarcoidosis. Bronchial wall thickening due to 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. Interventional techniques may be required for steroid-refractory cases.

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 below^{4, 5}.

Tracheobronchopathia osteochondroplastica spares the posterior membrane and typically appear as submucosal nodules extending into the tracheobronchial lumen. Histologically these are submucosal osteocartilaginous growths that leave the mucosal surface intact⁵. Treatment options for severe airway compromise includes surgical or laser resection, radiation or stent placement.

Broncholithiasis typically results from calcification of a lymph node due to prior 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, it may cause compression of the airways. Interventional or surgical approaches may be necessary depending on the compromise of the airways.

Rare causes of airway stenosis include inflammatory bowel disease in which either ulcerative colitis or Crohn's disease may produce airway inflammation. As with the aforementioned conditions, airway interventions may be required if systemic therapy is insufficient.

Bronchoscopic Interventions for Airway Stenosis

As mentioned above, the therapeutic options for airway stenosis depend on the etiology of the obstruction. Focal and limited stenosis may be amenable to surgical approaches. The techniques for surgery are beyond the scope of this paper. In general, however, they may include resection with end-to-end re-anastomosis, pericardial patch or rib cartilage tracheoplasty, autografts, homografts and slide tracheoplasty⁶.

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 repeated procedures are necessary. This section will focus 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. Balloons and dilators may also be used. Compliant balloons, such as the Fogarty, may be best for fleshy or necrotic intraluminal tumor that easily compresses. More rigid balloons, such as the CRE (controlled radial expansion; 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 with water or saline. Care must be taken so as not to tear the airways or rupture them by using too large of balloon or careless dilation. Metal dilators may also be used; common bile duct dilators, for example, have been described to dilate tracheal stenosis through an existing tracheostomy⁷.

Combination techniques are frequently used. For example, heat therapy may be essential for some types of stenosis. Circumferential web-like stenosis may benefit from incisions with an electrocautery knife (Figure 3). Imagining the face of a clock, three small incisions (at 9 o'clock, 12 o'clock and 3 o'clock) can be made with the knife such that the balloon will expand evenly and dilate the airway with targeted rather than sporadic and uncontrolled mucosal tearing. The initial slits may be made 1-3 mm in depth prior to inflation of the balloon. As a case in point, tight tracheal stenosis may require starting with a 6, 7, 8 mm CRE balloon and using serial dilation. The next balloon would be the 8, 9, 10 mm, then 10-11-12; 12-13.5-15; 15-16.5-18 and finally the 18-19-20 mm balloons. Several companies make balloons and their efficacy is likely similar; this author does not prefer one more than another. The length of the balloon should be noted. The balloons typically used for esophageal dilation are longer than balloons with dedicated airway use, although the former may be used in the airways if they are not placed too distally.

Detailed discussion of ablative therapies can be found in the paper titled "endobronchial ablative therapies" by Dr. Seaman and Dr. Musani in this journal. Briefly, heat modalities include the electrocautery probe, argon plasma coagulator (APC) or laser therapy. With cautery, an electric current is used to generate heat. Several devices may be used to apply this current, including a probe, knife, and snare. Unlike the knife described above, the probe is blunt. The user sets the wattage (20-40 W, for example) 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 most common type of lasers used in the airways are the Nd-YAG (neodymium:yttrium aluminum garnet) and carbon dioxide (CO₂) lasers. The Nd-YAG provides tissue vaporization and coagulation. It has deeper thermal energy than the CO₂ laser and may penetrate up to 10 mm⁸. The CO₂ laser has more precise cutting abilities. The development of the flexible fiber CO₂ delivery system allows for the flexible bronchoscope to be used to ablate and cut with this laser. This contrasts with the typical microscope-mounted CO₂ laser that requires general anesthesia. The laser is typically in pulse mode at 5-10 Watts delivered to 2-3 wedges separated by tissue so as to avoid circumferential mucosal denuding. Post-operative dexamethasone may be given to minimize upper airway edema when this ablation is performed high in the airway⁹.

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 felt to impede the inflammatory response^{10, 11}.

Contact and spray cryotherapy have been described. Contact cryotherapy uses a probe in which 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 latter¹². Further studies are needed to document the efficacy and safety of spray cryotherapy.

Detailed discussion on airway stents can be found in Dr. Breen's paper on "Airway Stenting" in this journal. I will touch upon this topic here for the sake of complete discussion of options available for the treatment of airways stenosis. Airway stenting may be used either temporarily or chronically. Several different types of stents exist (Table 2; Figure IV), although metal stents received a black box FDA warning in the United States for benign disease in part due to their predisposition to form granulation tissue. As such, for benign conditions, silicone stents are preferred. The advantage to metal stents is that they typically can be placed with the flexible bronchoscope. Although fluoroscopy may be required, an alternative is to pass a small bronchoscope alongside the stent prior to its deployment to visualize the distal and proximal ends and to watch deployment. Stents may be tubular (silicone or metal), a Y-configuration that covers portions of the trachea and mainstem bronchi (silicone), an hourglass configuration with wider ends and a narrower center (silicone) or may be customized. The metal stents may be completely covered, partially covered, or uncovered.

There is no perfect stent. 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 that has a stent placed requires appropriate follow-up. This may be clinically, radiographically, endoscopically or preferably, a combination. The bronchoscopist that places the stent should know how to remove it. Although rigid bronchoscopy is not required, it is an important skill to have, particularly when complications arise. 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 success of silicone stent placement with subsequent removal for stenosis associated with 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 12.5 months in those patient's whose stenosis was successfully treated by the temporary silicone stent¹³. A patient with relapsing polychondritis and a silicone stent for 16 years has been recently described¹⁴.

The next generation of stents may be biodegradable. A polydioxanone stent has been described in adults post-transplant as well as in children¹⁵. These stents have been tolerated by the mucosa, maintain strength for 6 weeks and completely dissolve in 15 weeks. Bioabsorbable drug-eluting stents are being developed¹⁶. Transplantation of the tracheobronchial airway with a stem-cell-seeded bioartificial nanocomposite has recently been described¹⁷. These exciting developments may revolutionize the approach to tracheal stenosis over the next decade.

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 used¹⁸. Improvements that result from airway interventions in malignant disease likely deserve distinction from interventions for benign disease due to systemic effects of cancer. A few studies have investigated quality of life and dyspnea following airway interventions for cancer. Amjadi and colleagues used the validated European Organisation 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 above, 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 due to impact from symptoms such as pain from metastases and other factors that are not influenced by airway therapy¹⁹. 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 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 6-month survival was 46%²⁰.

SUMMARY

Tracheobronchial stenosis results from malignant and benign etiologies. 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 as well as improvement in quality of life. The next generation of airway interventions holds promise for further improvements in the treatment of these debilitating conditions.

Disclaimer and Financial Disclosures: None

Common Causes of Tracheal or Bronchial Stenosis	
Infectious Tuberculosis Aspergillus Others Systemic inflammation Wegener's Granulomatosis Relapsing Polychondritis Sarcoidosis Amyloidosis Inflammatory Bowel Disease Others Focal inflammation Tracheostomy Intubation Trauma Burns Post-transplant Others	Dynamic collapse Focal malacia Diffuse TBM* Miscellaneous Saber sheath trachea TBO** Broncholithiasis Idiopathic Malignancy Small cell lung cancer Non-small cell lung cancer Adenoid cystic carcinoma Metastatic disease

Table I. Common causes of trachea-bronchial stenosis.

* *Tracheobronchomalacia*

** *Tracheobronchopathia osteochondroplastica*

Stent	Type of Stent	Type of Bronchoscopy	Comment
Ultraflex	Expandable metal	Flexible	Covered (except 1.5 cm at each end) or uncovered; Granulation tissue forms at uncovered areas
AERO	Expandable metal	Flexible	Covered
Wallstent	Expandable metal	Flexible	May be difficult to remove
Dumon	Nonexpandable silicone	Rigid	May require mucolytics (mucus plugging)
Hood	Nonexpandable silicone	Rigid	May require mucolytics
Polyflex	Expandable silicone	Rigid	Stent migration common

Table II. Common types of airway stents that can be placed in the trachea or proximal bronchi.



Figure I. Iatrogenic causes of benign tracheal stenosis. Overinflation of the endotracheal tube may lead to mucosal ischemia and subsequent stenosis. Cuffed tracheostomy tubes pose a similar risk. Tracheal stenosis may look like that shown in b.

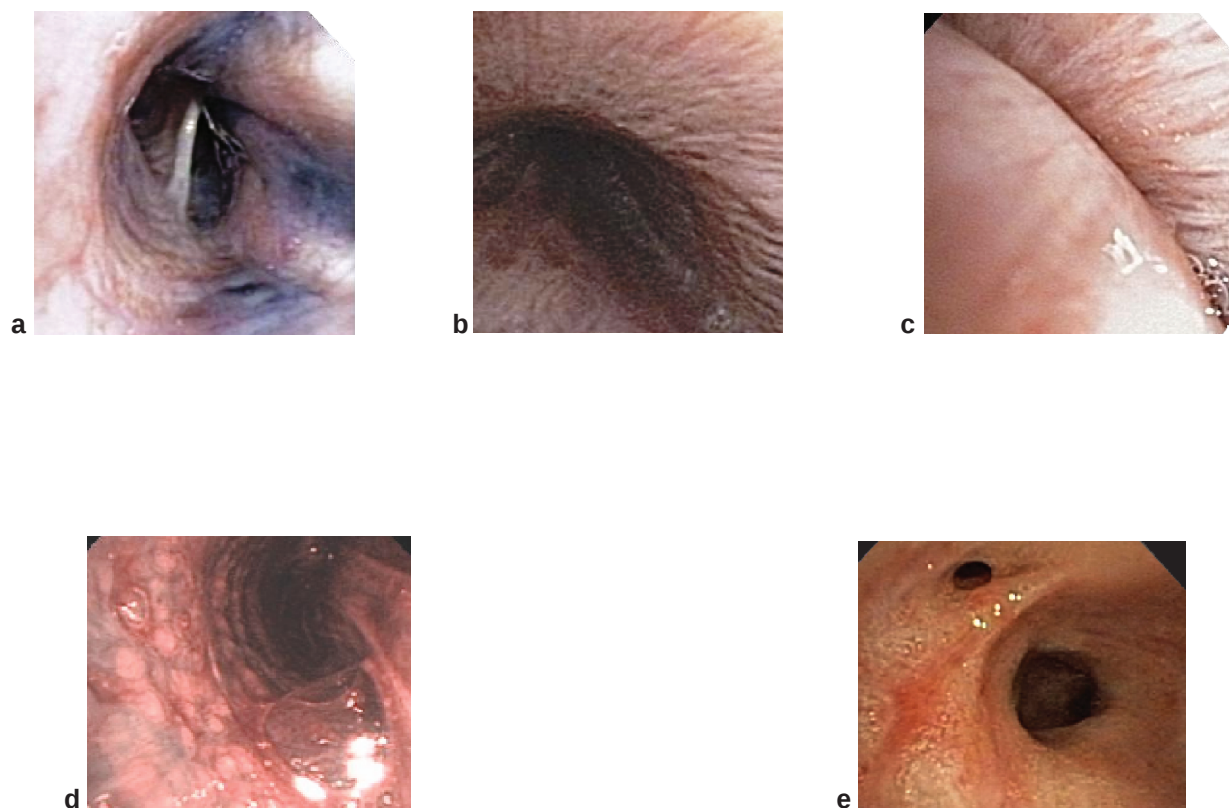


Figure II. Non-focal causes of stenosis may include (a) anthracosis and (b,c) dynamic airway collapse. (b) The left mainstem is open with inhalation but (c) shows complete collapse with exhalation. (d) Tuberculosis with submucosal granulomas. (e) Bronchial stenosis due to Wegener's granulomatosis.

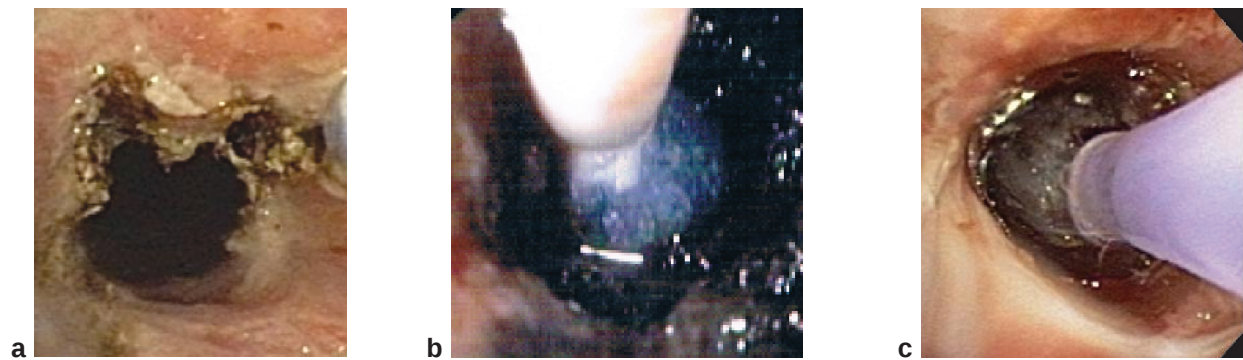


Figure III. Endobronchial techniques to relieve stenosis include the electrocautery probe, (a) electrocautery knife, laser therapy, and balloon bronchoplasty. The (b) fogarty balloon is much more compliant than the (c) CRE balloon and thus the latter is better for tight stenosis.

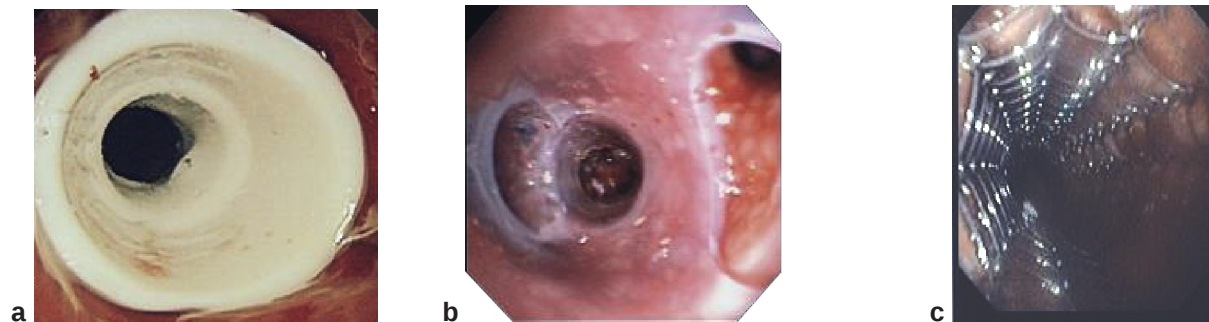


Figure IV There are various types of stents. Silicone stents may be tubular, (a) hourglass, or (b) Y-shaped but configured according to the specific needs. A (c) metal stent should be avoided in benign stenosis due to the potential for excessive granulation.

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