



# The role of bronchoscopy in the multidisciplinary approach to benign tracheal stenosis

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**Abstract:** Benign tracheal stenosis can cause dyspnea, wheezing, and cough mimicking other obstructive lung diseases which often leads to a delay in the diagnosis. Risk factors and etiologies for tracheal strictures include autoimmune diseases, infection, gastro-esophageal reflux disease (GERD), radiation injury and iatrogenic factors such as post-intubation and post-tracheostomy. Once suspected, tracheal strictures are diagnosed by performing a thorough evaluation involving clinical exam, laboratory workup, pulmonary function test, chest imaging and bronchoscopy. Bronchoscopy plays a pivotal role in the diagnosis of stenosis and along with the imaging and physiologic assessments leads to a proper description of the stenosis based on all parameters that matters for management. Surgical resection provides a definitive management in most patients with idiopathic or post intubation/tracheostomy stenosis, however, factors such as severe comorbidities, length and location of the stricture can preclude patients from undergoing curative surgery. Several bronchoscopic interventions including mechanical or laser assisted dilation, electrosurgery (ES), airway stenting and pharmacological treatment with mitomycin C (MMC) and intralesional steroid have been reported in the literature for management of patients who are not surgical candidates. Herein, we review the role of bronchoscopy and illustrate the importance of a multi-disciplinary team (MDT) approach comprising of interventional pulmonologists, thoracic surgeons and otorhinolaryngologists in the diagnosis and management of patients with benign tracheal stenosis.

**Keywords:** Tracheal stenosis; tracheal stricture; benign central airway obstruction (CAO); multi-disciplinary approach; bronchoscopy

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## Introduction

In this article, we will provide a brief overview of tracheal stenosis symptoms, risk factors, and management strategies. We will focus on the role of bronchoscopic evaluation and management, specifically highlighting essential components of the bronchoscopic evaluation of patients with tracheal stenosis pertinent to deciding whether to proceed with

endoscopic or open surgical treatment. Bronchoscopic evaluation of tracheal stenosis is critical to the assessment of the morphology, extent, and severity of stenosis, and is considered as the gold standard before pursuing any treatment options. We will describe and illustrate some of the fundamental therapeutic principles employed when addressing benign tracheal stenosis via bronchoscopy and summarize the relevant published data on such techniques.

**Table 1** Etiology of tracheal stenosis

Mechanism	Diagnosis
Local injury	Post-tracheostomy
	Post-intubation
	Trauma
	Airway Burn Injury
	Chemical Inhalation injury
	Radiation injury
Systemic disorders	Granulomatosis with polyangiitis
	Relapsing polychondritis
	Sarcoidosis
	Amyloidosis
	Inflammatory bowel disease
Infectious	Tuberculosis
	<i>Aspergillus</i>
	<i>Klebsiella rhinoscleromatis</i>
	<i>Staphylococcus Aureus</i>
	<i>Blastomycosis</i>
Miscellaneous	Tracheobronchopathia osteochondroplastica
	Broncholithiasis
	Idiopathic
	Post-transplant anastomotic stenosis
Idiopathic	No cause identified after a thorough work up and history

### Symptoms

Tracheal stenosis, a form of central airway obstruction (CAO), is frequently misdiagnosed as asthma or chronic obstructive pulmonary disease (COPD) (1). Patients with CAO share symptoms with other obstructive lung diseases and typically present with dyspnea, wheezing, cough, and even cough syncope. In cases of severe tracheal stenosis, patients can have stridor, dysphagia and dysphonia, especially for lesions involving the subglottis (2).

### Risk factors

Benign tracheal stenosis has varied etiologies including gastro-esophageal reflux disease (GERD), airway infection, radiation, inhalation or chemical injury, systemic

autoimmune disorders [granulomatosis with polyangiitis (GPA), sarcoidosis, relapsing polychondritis], and iatrogenic due to trauma from airway manipulation (endotracheal intubation or tracheostomy). A potential mechanism for the development of stenosis is an altered inflammatory response to injury, ischemia of the tracheal mucosa and excessive scar formation. Associated cartilage destruction leads to full thickness and/or concurrent tracheomalacia (*Table 1*) (1,3). Trauma due to endotracheal intubation or tracheostomy placement is the most common acquired cause of tracheal stenosis (4). Risk factors for post-intubation tracheal stenosis (PITS) include traumatic intubation, long duration of intubation (>14 days), prone positioning, and high cuff pressure in the endotracheal tube (ETT) cuff (>30 cmH<sub>2</sub>O), which is likely the main and the most frequent cause (5). Risk factors for post-tracheostomy tracheal stenosis (PTTS) include excessive force used during tracheostomy placement with cartilage fracture, regional ischemic necrosis, tracheostomy site infection, high tracheostomy site, and friction between the distal tracheostomy tube and the tracheal wall (6). Overall risk factors for both PITS and PTTS include previous radiation, obesity, GERD and diabetes (5,6). However, etiology for tracheal stenosis may remain undiagnosed in 18% of the cases (7).

### Overview of management strategies

Definitive management of tracheal stenosis includes bronchoscopic interventions and open surgery, the latter having the potential of being curative in selected cases. Because of high GERD prevalence and low risk profile, most patients are being prescribed anti-reflux medications. Oral corticosteroids, and antibiotics for tracheal stenosis are usually reserved for acute decompensations in the setting of airway edema and infection, respectively. In cases where the tracheal stricture results from underlying connective tissue disorder, systemic immunosuppressive therapy, and endoscopic interventions remain central to management (8). Bronchoscopic interventions involve laser-assisted mechanical dilation (LAMD), electrosurgery (ES) knife or needle, mechanical dilation with rigid bronchoscopy, endoscopic balloon dilation, intralesional steroid injection or mitomycin C (MMC) application, and in refractory or complex lesions, silicone stent insertion may be considered (9-17). Tracheal resection of hypertrophic stenotic tissues is the procedure of choice in most patients with benign idiopathic or post intubation/tracheostomy tracheal strictures, with laryngotracheal reconstruction reserved

for patients with laryngeal involvement (3). Surgery offers definitive treatment and has high success rates when performed by experienced operators (10,18-23). However, factors such as severe co-morbidities (obesity, diabetes), high subglottic stenosis (SGS), or tracheal stenosis with a long vertical extent (>4–6 cm) may preclude surgery. Furthermore, a definitive surgical intervention is typically deferred during the acute inflammatory phase and is considered once the stenosis has matured and inflammation has subsided. In these patients, bronchoscopic interventions are performed as a bridge to surgery or a long-term palliative solution (24-27). In addition, for patients with SGS, while cricotracheal resection (CTR) is more effective than endoscopic management with regards to recurrence, voice quality and vocal cord paralysis are more common with the surgical treatment, and endoscopic management with intralesional steroid injection remains a common practice (28).

Treatment decisions and clinical course are dictated by the disease acuity, patient's co-morbidities, functional status, and importantly, the etiology, location, extent, morphology and degree of airway narrowing (1,29-34). A multi-disciplinary team (MDT) that involves the expertise and collaboration of otolaryngology, thoracic surgery, and interventional pulmonology helps facilitate the accurate and timely diagnosis of tracheal stenosis and enables evidence-based management (1). Whether the management is endoscopic or surgical will ultimately depend on stenosis and patient-related factors. Several of these factors are decided after thorough noninvasive and bronchoscopic evaluation.

### Evaluation of tracheal stenosis

A complete workup for tracheal stenosis involves evaluating the etiology, assessing the mechanism of injury, and classifying the stenosis based on factors that impact management. This includes a series of non-invasive testing such as pulmonary function tests, serologies, and chest and neck imaging. In addition, associated symptomology including vocal cord function, swallowing dysfunction, and overall functional status should be noted (3,34-36).

### Non-invasive evaluation of tracheal stenosis

Evaluation of tracheal stenosis starts with a thorough history and physical examination, which can help determine the etiology of the tracheal stenosis. Determining the

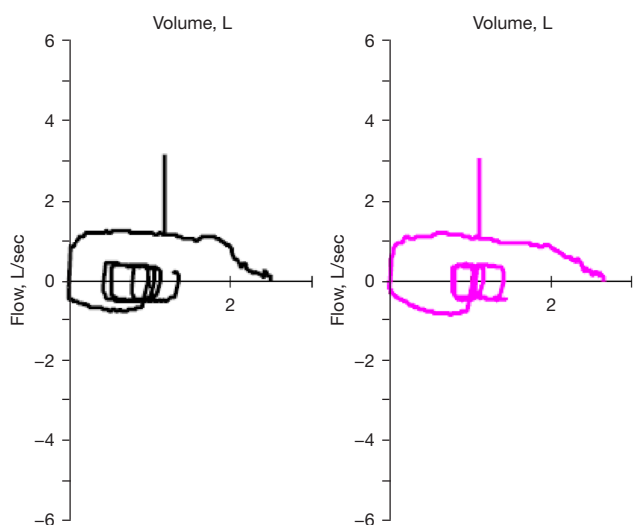
patient's functional status impacts treatment decisions. The patient's voice and ability to swallow should be assessed as tracheal stenosis, especially with laryngeal involvement, may present with dysphonia and dysphagia. A serologic evaluation to establish whether there is an underlying systemic autoimmune disorder should be obtained (1). In these regards, a study of 92 patients with non-traumatic laryngotracheal stenosis (LTS) found that 25% of cases were due to GPA, with 75% being idiopathic, with all other serologic testing being equivocal (37). Of note, anti-neutrophil cytoplasmic antibody (ANCA) are positive in approximately 60% of patients with limited GPA, so a negative ANCA does not rule out GPA, and biopsies are still needed in such cases (38). Establishing a firm etiology is essential as recurrence rate for patients with GPA is high after surgical interventions. In one small study, 9% failed laryngotracheal resection and reconstruction (LTRR) and required tracheostomy, 55% required dilations after LTRR and 18% developed lower airway stenosis (39). These data suggest that LTTR should not be first choice in patients with GPA-related LTS.

Spirometry can show the classic pattern of truncation of inspiratory and expiratory limbs on the flow volume loops; however, this pattern lacks sensitivity, and these findings can be appreciated only when the tracheal lumen is reduced to 6–8 mm (40). Furthermore, spirometry does not precisely localize strictures and is an insensitive test for mild to moderate narrowing and offers functional, not anatomical information (40,41) (*Figure 1*).

Computed tomography (CT) imaging of the neck and chest with or without 3D reconstruction can help determine the extent (length) of the tracheal stenosis and quantify the degree of airway narrowing (42,43). However, these findings are affected by the respiratory phase and the presence of secretions (40,44). Secretions can overestimate the degree of narrowing while a CT scan done at full inspiration can underestimate the degree of narrowing during tidal respiration. A dynamic CT neck and chest may help identify associated tracheomalacia or excessive dynamic airway collapse (*Figure 2*) (1).

### Bronchoscopic evaluation of tracheal stenosis

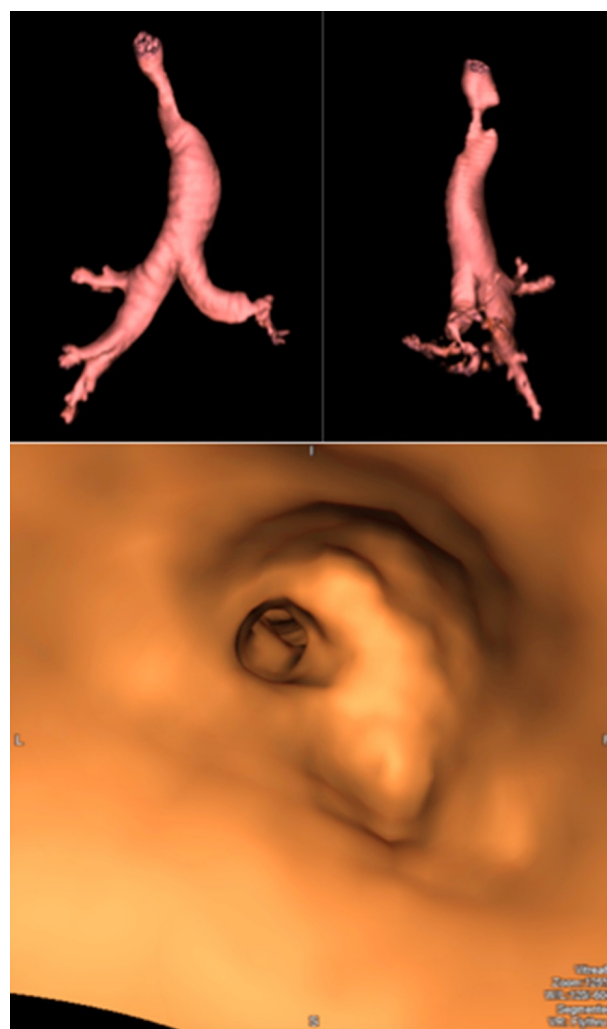
Direct airway visualization via bronchoscopy remains the diagnostic gold standard for the workup of tracheal stenosis and is essential for determining patient candidacy for endoscopic or surgical treatments. It allows simultaneous assessment of vocal cord function, and quantitative



**Figure 1** Flow volume loop demonstrating tracheal stenosis with flattened inspiratory and expiratory flow loop. The pattern was reproducible with repeated maneuvers.

measurement of the stenosis (length, location and degree of narrowing), determining the morphology (shape) of the narrowing, and identifying associated tracheomalacia (45). Endotracheal biopsies may help determine the etiology of the tracheal stenosis (1). Additionally, using the radial endobronchial ultrasound (r-EBUS) at 20 MHz frequency during bronchoscopy, may permit non-invasive bronchoscopic measurements of the tracheal diameter (46) and even assessment of the hypertrophic tissues and airway cartilage integrity (47).

If a tracheostomy tube is present during bronchoscopic evaluation, it should be removed to allow for complete airway inspection. If the patient is intubated, the endotracheal tube should be retracted as proximally as possible. In patients with high tracheal strictures, the use of a laryngeal mask airway (LMA) should be considered if patients require general anesthesia, but ideally, bronchoscopy should be performed with moderate sedation so patients cooperate with various speech and breathing maneuvers (2). However, in patients with suspected severe tracheal stenosis, the ideal choice of anesthesia for bronchoscopy (moderate anesthesia *vs.* general anesthesia) for airway evaluation should be selected after carefully assessing symptoms and pre-bronchoscopy imaging, when available. It is also essential to consider local expertise and availability of equipment for managing potential airway emergencies.



**Figure 2** 3D reconstruction of the CT scan of the neck and chest in a patient with complex benign airway stenosis. Reprinted from (1), © 2021, with permission from Elsevier. CT, computed tomography.

Several classification systems are available for grading laryngo-tracheal stenosis, mostly from otolaryngology literature. These include the Cotton-Myer scale, which grades the severity based on degree of airway narrowing (35), the Lano system, which grades the stenosis based on the number of locations involved (32), and the McCaffrey system, which grades the stenosis based on location and vertical extent of the stenosis (33). Bronchoscopic evaluation should be objective and assess the degree of narrowing, length of the stricture, morphology (circumferential, elliptical, crescent, triangular), complexity (with or without malacia), and precise location of the stricture in relation to the vocal cords, cricoid, and main carina

(1,3,29,30,34-36,48). Different classification systems are as listed in *Table 2*.

### *Extent and location*

The extent, or vertical length of tracheal stenosis, is important to measure, as it determines whether surgical resection can be considered. While surgical resection is considered a definitive treatment for strictures that are 1–4 cm in length, endoscopic techniques are usually used for lesions that are <1 cm or >4 cm, although there are reports of longer tracheal segments (6 cm) being successfully resected (3). Some operators prefer to use the ratio of the stenotic segment extent to the length of the trachea as a criterion for surgical selection (i.e., stenosis involving >40% of tracheal length having high risk of complications). Lesions shorter than 1 cm tend to be simple, without cartilage involvement and often respond to mechanical dilation with or without using laser or ES for performing radial incisions. Lesions longer than 4–6 cm may not be amenable to tracheal resection after discussions with expert tracheal surgeons due to risks for tension and anastomotic complications. Therefore, precise measurement of the extent of tracheal stenosis is essential during bronchoscopic evaluation. One can measure the vertical length of the stenosis by placing the tip of the bronchoscope adjacent to the most distal aspect of the stenosis while pinching the bronchoscope at the proximal end of the endotracheal tube/nostril/teeth level (depending on the insertion route). The bronchoscope is then retracted proximally until the tip of the scope is adjacent to the proximal end of the stenosis. The distance between where the scope is pinched and the proximal end of the endotracheal tube/nostril/teeth level is the length of the stenosis. Of course, the extent can be measured on the CT as well, but inflammation or small fibrotic bands may be missed by the CT. When describing tracheal stenosis in bronchoscopy reports, it is essential to

note its exact location in relation to the vocal cords, cricoid, and main carina. In particular, the distance should be measured between the distal edge of the stenosis to the main carina and between the proximal edge of the stenosis to the vocal cords (for lesions involving subglottis) or cricoid (for tracheal lesions only). Whether the stenosis involves the cricoid cartilage, and the subglottic larynx should be clearly noted, as surgical treatments depend on whether the subglottis or glottis are involved. The distribution of the stenosis and whether there is multifocal disease should also be identified (3).

### *Severity of airway narrowing*

The severity of airway narrowing affects symptoms, especially dyspnea and is relevant to treatment decisions in patients with tracheal stenosis (32,33,35). Pressure drop along the stenosis, which affects the patient's work of breathing, is primarily determined by the percentage reduction in airway caliber [i.e., cross-sectional area (CSA)] rather than the absolute decrease in the airway diameter (49). A physiologically abnormal obstruction is defined as a narrowing of the airway by >50%, as glottic opening results in a similar degree of pressure drop as a 50% tracheal stenosis (1,49).

When measuring the severity of airway narrowing, the bronchoscopist should measure and compare the CSA of the stenosis to a normal segment of the trachea {see below Eq. [1]}. Tracheal stenosis is categorized as mild (<50% reduction), moderate (51–70% reduction), or severe (71–100% reduction) based on the degree of airway narrowing and its impact on airflow limitation (see *Table 2*: Cotton-Myer's classification). A study showed that even experienced bronchoscopist often misclassify the degree of airway narrowing when using still bronchoscopic images to subjectively assess strictures of benign etiology, when compared to using CSA that were objectively analyzed using morphometric bronchoscopy (48).

$$\text{Airway narrowing severity} = \frac{\text{CSA of normal tracheal segment} - \text{CSA of stenotic tracheal segment}}{\text{CSA of normal tracheal segment}} \quad [1]$$



**Table 2** Classification systems for laryngotracheal stenosis

Classification system study/year	Classification criteria	Comments
Myer <i>et al.</i> /1994	Grade 1: 0–50% obstruction Grade 2: 51–70% obstruction Grade 3: 71–99% obstruction Grade 4: no detectable lumen	Based only on the degree of reduction in airway CSA
McCaffrey/1992	Stage I: lesions are confined to the subglottis or trachea and <1 cm long Stage II: lesions are isolated to the subglottis and >1 cm long  Stage III: subglottic/tracheal lesions not involving the glottis Stage IV: lesions involve the glottis	Based only on the vertical extent Predicts tracheal decannulation based on anatomic location and extent of stenosis 90% of stages I and II, 70% of stage III, and 40% of stage IV patients undergo decannulation successfully
Lano <i>et al.</i> /1998	Stage I: one subsite involved  Stage II: two subsites involved  Stage III: three subsites involved	Based on subsites involved (glottis, subglottis, trachea) Correlation between this staging and likelihood for successful decannulation Stage I: 94%, stage II: 78%, stage III: 20%
Nouraei <i>et al.</i> /2007	Airway status  No airway prosthesis  Intraluminal airway prosthesis (stent) Tracheostomy or tracheostomy-tube dependent, patient voices Tracheostomy dependent, patient does not voice Death because of a direct complication of airway disease  Dyspnea Grade 1: "I only get breathless with strenuous exercise" Grade 2: "I get short of breath when hurrying on level ground or walking up a slight hill" Grade 3: "On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace" Grade 4: "I stop for breath after walking about 100 yards or after a few minutes on level ground" Grade 5: "I am too breathless to leave the house or I am breathless when dressing"  Voice No problems with voice Some problems with my voice Making voice is effortful and significant difficulties being heard or understood Can only produce a weak voice or whisper No voice  Swallowing Eat and drink normally Normal diet but with some difficulty swallowing Significant swallowing difficulties Serious problem swallowing (i.e., diet consists almost entirely of liquidized foods) Unable to swallow	Comprehensive system used by otorhinolaryngologists Does not include extent and severity criteria (i.e., reduction in CSA) Designed for documenting functional outcomes of adult laryngotracheal stenosis

**Table 2** (continued)

Table 2 (continued)

Classification system study/year	Classification criteria	Comments
Freitag et al./2007	Type Structural Type 1: exophytic or intraluminal Type 2: extrinsic Type 3: distortion Type 4: scar or stricture Dynamic or functional Type 1: damaged cartilage or malacia Type 2: floppy membrane Degree of stenosis Code 0: no stenosis Code 1: <25% Code 2: 26–50% Code 3: 51–75% Code 4: 76–90% Code 5: 91–100% Location: I: upper one-third of the trachea II: middle one-third of the trachea III: lower one-third of the trachea IV: right main bronchus V: left main bronchus	Designed for grading tracheal stenosis from pulmonologists' perspective The degree of severity criterion is not justified physiologically The structural types are not mutually exclusive
Ghorbani et al./2012	Diameter of stricture Score 0: stenosis rate between 0% and 25% Score 1: stenosis rate between 26% and 50% Score 2: stenosis rate between 51% and 75% Score 3: stenosis rate between 76% and 90% Score 4: stenosis rate 91% or higher Type of stenosis Score 1: granulation tissue Score 2: granulation tissue, fibrosis, and inflammation Score 3: fibrosis Score 4: malacia Clinical symptoms Score 1: dyspnea only during intense activity Score 2: dyspnea during normal activity but physical examination results are normal Score 3: long inhalation and exhalation but with no stridor or retraction Score 4: stridor and retraction	The degree of severity criterion is not justified physiologically Terminology for types of stenosis is composed of pathophysiologic processes

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As mentioned, for mild stenosis (<50% reduction in CSA), the pressure gradient which develops across the stenosis is of similar magnitude as seen with a normal glottis opening. Therefore, patients with mild stenosis

are typically asymptomatic, even with exertion (49,50). Significant pressure drop occurs at higher flow rates for moderate stenosis (51–70% reduction in CSA). Thus, these patients typically experience symptoms during exertion.

For severe stenosis (71–100% reduction in CSA), there is a significant pressure gradient across the stenosis, even at low flow rates, leading to symptoms with mild exertion or even at rest (1,49,51). Thus, being precise in the assessment of airway narrowing severity is key in attributing symptoms to the actual stenosis itself. This is important as patients with tracheal stenosis may have comorbidities that also cause dyspnea.

### *Morphology (shape of stenosis)*

Broadly, a stenotic area can be classified as simple or complex based not only on the extent but whether the cartilage is involved and if there is associated malacia. A simple stricture is defined as less than 1 cm in vertical extent and without malacia. A complex stricture is defined as longer than 1 cm in vertical extent or with associated malacia or full thickness tracheal wall injury. This classification for PITS is important as simple stenosis often responds to LAMD and stent insertion is avoided to limit further airway injury and potentially worsen a resectable disease. The associated chondritis predicts poor results and failure of endoscopic treatment (52). Idiopathic lesions, especially SGS, are characterized by hypertrophy of the mucosa and submucosa with intact cartilaginous wall and a stent insertion should not be performed in these cases. Thus, a thorough evaluation of stenosis complexity bronchoscopically, with a CT scan and EBUS should be performed. With the use of EBUS intra-operatively, a bronchoscopist can visualize hypertrophic tissue thickness and cartilage structure to determine integrity. Cartilage destruction determines the complexity of stenosis and could predict poor response to dilation alone. The location and thickness of stenotic tissues can also guide treatment strategies including choosing optimal site for laser or electrocautery radial incisions, or intralesional steroid injections.

In addition, the shape of the airway lumen at the stenotic level affects flow dynamics and symptoms. In a computer modeling study of tracheal stenosis lesion, morphology impacted flow velocity and the pressure drop across the stenosis, with triangular stenosis causing less pressure drop than elliptical ones for the same CSA (51). Morphology seems to also affect outcomes of endoscopic procedures. The completely circumferential strictures were shown to lead to poorer outcomes because they require more interventions when compared with eccentric lesions (52). Thus, describing the shape of the stenosis as well as associated malacia are important factors for treatment decisions and outcomes,

and these factors can be assessed during a bronchoscopic evaluation under moderate sedation.

### **Bronchoscopic management of tracheal stenosis**

The choice of intervention is generally dictated by all these factors reviewed above as well as operability, patient's quality of life, and availability of technology or treatment modality (3). A multi-disciplinary airway team approach that includes otolaryngology, thoracic surgery, and interventional pulmonology is essential in determining treatment timing and modality. Parameters from classification systems pertinent to treatment are summarized in *Table 3*. Surgical resection of the stenotic area is the procedure of choice for most patients with benign tracheal stenosis, especially if complex in nature and not due to a systemic inflammatory disorder (e.g., GPA). However, co-morbidities such as diabetes, prior tracheostomy, prolonged steroid usage, high subglottic location, length of the lesion (>4–6 cm) can be prohibitive for resection. Mechanical dilation, laser therapy, ES, stent placement and adjuvant local pharmacologic therapy such as steroid injections and mitomycin application can be considered (53). Herein we describe and review the evidence for the endoscopic therapeutic options and their outcomes.

### *LAMD*

The laser cutting effects on tissues can be safely and effectively used in the endoscopic management of tracheal stenosis. Tissue vaporization (cutting) or photocoagulation are determined by power density, absorption, scattering, and delivery system. Power density depends on power setting, distance from the fiber to the target tissue and exposure time. Absorption and scattering make the difference between cutting and coagulation. For example, the CO<sub>2</sub> laser has an infrared wavelength of 10,600 nm and is an excellent cutting tool due to its high absorption and low scattering. It is widely preferred in otolaryngology for treating SGS.

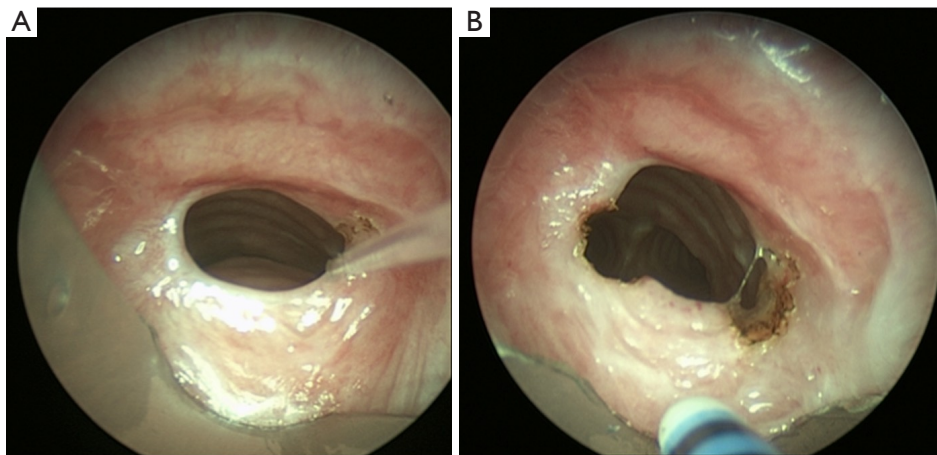
Laser bronchoscopy can be done both via flexible and rigid bronchoscopy and each modality carries its own advantages and disadvantages (54). At our institution, we mainly use rigid bronchoscopy to perform endoscopic laser treatments. For tracheal stenosis, we apply mucosal sparing technique, which involves two to three radial incisions by laser followed by gentle dilation with the rigid bronchoscope or by an inflatable endoscopic balloon (17). Laser treatments should not be circumferentially applied



**Table 3** Classification criteria that impact management for benign airway strictures

Criteria	Description
Functional class	Modified World Health Organization functional classification
1	Asymptomatic: ordinary physical activity does not cause symptoms
2	Symptomatic on exertion: there is no discomfort at rest, but normal physical activity causes increased symptoms
3	Symptomatic with daily activity: there is no discomfort at rest, but less than ordinary activity causes increased symptoms
4	Symptomatic at rest: symptoms may be present at rest and are increased by almost any physical activity
Extent	Location and distribution of the stenotic airway segment
Vertical length	(<1, 1–4, >4 cm)
Location	Glottic, subglottic, tracheal, or tracheobronchial
Morphology	Describes the shape of the airway lumen
Simple	Short-segment concentric stenosis, <1 cm in vertical length, without malacia
Complex	Long segments, >1 cm, with tracheal wall injury or associated malacia
Pseudoglottic	Refers to triangular stenosis
Eccentric	Refers to uneven distribution of the hypertrophic stenotic tissues
Circumferential	Refers to concentric (360°) distribution of the hypertrophic stenotic tissues
Voice quality	Describes presence of phonation-related symptoms
1	No problems related to voice
2	Some problems related to voice, needing repetition, closer proximity, or modulation
3	Significant problems related to being heard, needing significant augmentation
4	Problems with whispering
5	No voice
Origin	Describes the underlying cause responsible for the airway abnormality
Idiopathic	No underlying cause identified
Secondary	Secondary to known underlying processes or previous airway injury
Severity	Describes the degree of reduction in CSA
1	Normal: no reduction in CSA compared with normal airway caliber
2	Mild: reduction in CSA <50%
3	Moderate: reduction in CSA 51–70%
4	Severe: reduction in CSA $\geq$ 71%
Swallowing function	Describes the degree of swallowing impairment
1	No issues
2	Pain with swallowing, able to swallow liquids and solids
3	Pain with swallowing, able to swallow liquids only
4	Unable to swallow liquids or solids

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**Figure 3** Simple tracheal stenosis treated with laser and EC. (A) Simple web like tracheal stenosis with the use of laser. (B) Simple web like tracheal stenosis with electrocautery knife assisted radial incision at 4 o'clock and 8 o'clock position. Reprinted from (1), © 2021, with permission from Elsevier. EC, electrocautery.

**Table 4** Different laser characteristics

Type of laser used in airway	Wave length (nm)	Coagulation	Cutting precision	Vaporization	Absorption	Depth of penetration (mm)
Nd:YAG	1,064	++	+	+++	Proteins of any opaque tissue	5–15
Nd:YAP	1,340	+++	++	+	Water	3
Ho:YAG	2,100	+	+++	++	Water	0.5
KTP	532	+	++	++	Hemoglobin	1
CO <sub>2</sub>	10,600	+	+++	+++	Water	0.1
Thulium	2,000	+++	+++	+	Water	<1
Diode	1,318	++	++	+	Water	3–5
Argon	516	+++	+	+	Hemoglobin	1

Reprinted with permission of the American Thoracic Society, Miller *et al.*, 2013. Annals of American Thoracic Society. Copyright © 2022 American Thoracic Society. All rights reserved. +, low efficacy; ++, medium efficacy; +++, high efficacy. Nd:YAG, neodymium-doped yttrium aluminium garnet; Nd:YAP, neodymium-doped yttrium aluminium perovskite; Ho:YAG, holmium-doped yttrium aluminium garnet; KTP, potassium titanyl phosphate; CO<sub>2</sub>, carbon dioxide.

to the lesion as these risks inducing further stenosis due to secondary retraction and scarring of the mucosa. The incisions should be precise and without collateral thermal damage, which are best obtained with the CO<sub>2</sub> or potassium titanyl phosphate (KTP) lasers (*Figure 3A*). Characteristics of lasers used in bronchoscopy are reviewed in *Table 4* (55).

The best outcomes with laser therapy are noted in simple, web-like stenosis which can be potentially cured

when combined with mechanical dilation. In PITS, the cure rate ranges from 60% to 95% after two to three treatment sessions (17,56,57). One study including 167 post-intubation and 34 post-tracheostomy stenoses, showed that 96% of cases with simple stenosis had a full resolution with endoscopic therapy alone when compared to 79% of cases with complex stenosis (58). In another study with long-term follow-up in 98 patients with a benign tracheal

obstruction from various causes treated with laser therapy, only 60% showed complete resolution without needing another treatment modality (59). Literature on post infectious strictures is limited with the outcomes depending on associated chondritis (malacia). One retrospective study of post-tuberculosis airway stenosis showed that malacia and prior bronchoscopic laser-assisted resection were associated with less favorable outcomes, including symptom recurrence (60). In tracheal stenosis secondary to systemic inflammatory diseases (e.g., GPA), laser therapy has been used in a combined approach with systemic therapy (61).

### *Electrosurgical management*

ES is available in monopolar and bipolar devices. In monopolar electrodes, current flows from the generator through the active electrode, into the tissue, through the patient, the dispersive electrode (grounding pad) and returns to the generator. In bipolar devices, the active and return electrodes are located at the target tissue site, typically within the instrument tip such as the forceps and current is limited to the tissue grasped (62). Monopolar ES is used for endoscopic cutting of fibrotic tissues in tracheal stenosis. Different types of monopolar electrodes are available (including blunt probe, knife, forceps and wire snare loops), but achieving contact of the probe with the mucosa at the site of treatment is necessary for this technique to be effective. Of note, argon plasma coagulation (APC) is a noncontact technique that utilizes ionized argon gas (plasma) to conduct monopolar electrical current to the nearest tissue. The temperature generated will determine the effect produced: coagulation (60–80 °C), desiccation (>100 °C), carbonization (>200 °C) and vaporization (>300 °C) but due to its diffuse tissue effects, APC should not be used for treatment of benign tracheal stenosis (63). ES knife or needle, in a contact mode, is the preferred ES modality for cutting through fibrotic tissues (*Figure 3B*). The depth of treatment from ES and histological effect can be assessed by visual feedback, unlike in laser therapy, where a tissue effect could go beyond the visual surface (64). ES is cheaper than laser and available in most hospitals.

In a study of 22 patients with benign tracheal stenosis, use of ES knife showed improvement in lung function and symptoms in 100% of the patients. Mean symptom free time was ~6 months and less than 50% of patients required second intervention (65). In a retrospective review of 15 patients with benign tracheal stenosis, ES was used in combination with rigid bronchoscopy and stent placement (80%) that showed a success

rate of 87% with stent removed later in 55% patients (66). As demonstrated in another retrospective series, ES has advantages when combined with balloon dilation. A case series that included 43 patients with benign tracheal stenosis noted that an integrated approach of ES needle knife combined with balloon dilatation decreased the proportion of restenosis requiring treatment from 82% to 47% at 6 months and had a lower stenosis degree after treatment (67). The above studies highlight the additional value of combining ES along with other strategies such as dilation and potentially stent placement in improving symptoms.

### **Adjuvant pharmacologic management**

A few pharmacologic options have been consistently used and reported in the literature for managing laryngotracheal stenoses, mainly involving intralesional steroid injection and MMC application. Wound healing and maturation are complex processes and these therapies are aimed at the inflammatory and proliferative phase of healing, respectively. The goal of these therapies is to suppress the propagation of inflammation and to modify the natural history of injury and wound formation (68).

### *MMC*

MMC is an antimicrobial agent that carries additional antimetabolite and antiproliferative properties. It works as an alkylating agent inhibiting DNA synthesis and suppressing RNA and protein synthesis at higher concentrations. In airway pathology, it works as an inhibitor of fibroblast proliferation in wound healing processes. Topical MMC has been studied as adjuvant therapy in benign airway stenosis (69), in conjunction with endoscopic treatments such as radial incision with laser and dilation with MMC, and dilation alone with MMC. A meta-analysis of 15 studies with 387 patients showed that 70% of patients remained symptom-free after one year since the intervention (70). This analysis also showed that in studies that compared endoscopic treatment with and without MMC, a symptom-free period >1 year was four times higher in patients receiving MMC. A randomized, double-blind, placebo-controlled trial with 26 patients with mixed benign etiologies showed a relapse rate of 7%, 36% and 69% at the 1-, 3- and 5-year mark with two applications compared to 33%, 58% and 70% with one application of MMC, respectively. The study showed that the recurrence rate is similar in these groups at the 5-year mark; however, a dual application strategy delays the recurrence of symptomatic restenosis (11).

### **Steroid injection**

Steroids are efficacious in the early inflammatory stage of injury mediated by prostaglandins, tumor growth factors, and interleukin-1 (71). Intralesional steroid injections have been shown to inhibit stricture formation by interfering with collagen synthesis, fibrosis, and chronic scarring. It has also been suggested that triamcinolone prevents the cross-linking of collagen that results in scar contracture so that if the scar is stretched and corticosteroid is injected into it, contracture will presumably not occur and causes a decrease in the fibrotic healing process (72).

Considering the etiology of injury/stenosis is essential and etiologies such as autoimmune diseases with active inflammation are known to benefit the most from intralesional steroid therapy. For example, a study evaluating effect of intralesional steroids in a total of 45 patients with autoimmune, idiopathic and traumatic etiology showed that 75% (9/12) of patients with autoimmune etiology achieved airway patency at 2 years; 3 patients who did not achieve benefit in the auto-immune group were noted to have long-term symptoms (7–18 months) and had tracheostomy at presentation (12). For SGS, endoscopic management with intra-lesion injection of steroids had a lower recurrence rate when compared with dilation alone and remains a preferred initial modality for managing SGS (28).

### **Airway stenting**

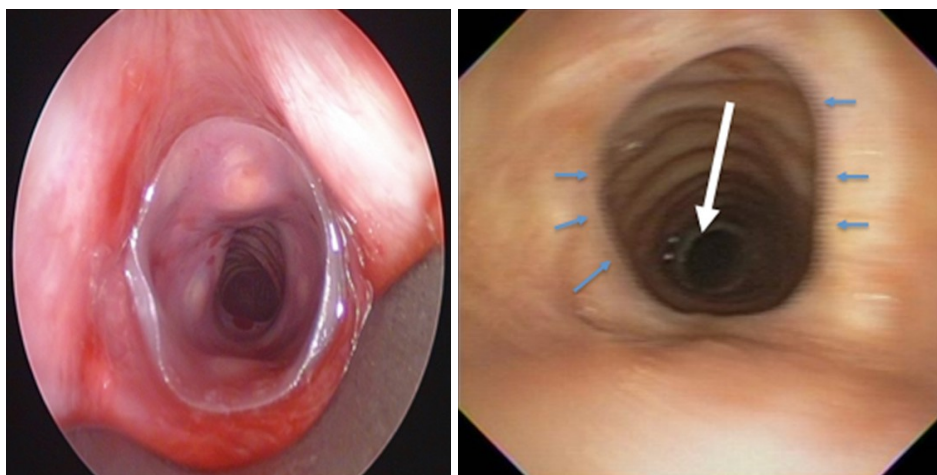
In patients who are non-operative candidates (either due to lesion characteristics or comorbidities) or in patients with recurrent stenosis after endoscopic or surgical treatment, an airway stent placement should be considered for symptom palliation. In 2005, given the high number of complications reported with metallic stents, the Food and Drug Administration (FDA) published an advisory on their use in benign airway lesions. In addition, FDA noted that patients with benign airway stenosis have a greater risk of severe complications than those with malignant disorders since the metallic tracheal stent is left in place longer (73). Hence, silicone stents are the preferred type in benign airway stenosis and could be considered a long-term option for palliation in non-surgical candidates. A 7-year follow-up study after placement of Dumon silicone stents in 263 patients who underwent 419 silicone stent placements for benign tracheal stenosis showed that of the 117 patients in whom the stent was removed, no recurrence was noted in 64 (25% of all cases). The mean duration of stent placement in this study was 1.2 years (74).

### **Stents in post-intubation and post tracheostomy tracheal stenosis**

Most studies reporting on stenting combine PTTS and PITS when describing outcomes, however, these entities have different mechanism of injury, characteristics of stenosis, and treatment-related outcomes. A study of 117 patients with PITS and 88 patients with PTTS showed that the success rate without surgery was higher in the PITS than in the PTTS group (76.9% vs. 63.6%,  $P < 0.05$ ). Additionally, successful airway stent or tracheostomy removal was achieved in 46.2% of patients in the PITS and in 33.0% of the PTTS group ( $P = 0.06$ ) (75). This is likely due to the complex nature of PTTS, with associated malacia due to chondritis. In addition, the outcomes of bronchoscopic interventions depend on the precise location of PTTS, with one study of 99 PTTS patients showing that silicone stents were required more in stomal-type stenosis compared to cuff-related or tip stenosis (76% vs. 55%,  $P = 0.031$ ). It was also noted that cuff type stenosis had a higher success rate with respect to removal of tracheostomy tube compared to the other types of PTTS (71% vs. 45%,  $P = 0.012$ ) (76). This is relevant for the bronchoscopist as describing the exact location of PTTS becomes relevant for predicting outcomes.

In a study focused on PITS, among 60 complex stenosis patients, 47 patients (78%) required stent placement. Of these, 47% had their stent removed after one year and did not require further therapy. This study's mean duration of stenting was  $11.6 \pm 4.6$  months (16). Another study focusing on PITS showed a similar period of stent placement of 12 months in 59 patients, of whom 22 (40%) had the stent removed and required no further intervention (25).

Thus, airway stents, when necessary, do not have to be a life-long intervention and based on the above data, they can be removed after a period of approximately 12 months or if a patient were to become a surgical candidate. Indeed, in some instances, airway remodeling can occur, resulting in the removal of stents and no stenosis recurrence. Based on the available literature, a stent removal should be attempted to evaluate airway patency as regeneration of the tracheal cartilage is possible and patency may be restored (*Figure 4*). While the optimal time frame for a trial of stent removal is unknown, a higher rate of success (46.8%) was described when stents remained in place for a longer time (mean of ~12 months) (16). A recent study of 128 subjects with complex tracheal stenosis secondary to PITS and PTTS treated with protocolized duration for silicone airway stenting showed that restenosis at 1 year after stent removal was seen



**Figure 4** Patent airway due to remodeling after long term indwelling silicone airway stenting. Approximately 1 year after insertion, stent has migrated down to the main carina (white arrow). The airway cartilage re-modelled at the level of the stricture and there was only minimal airway narrowing (blue arrows), not requiring intervention. Reprinted from (1), © 2021, with permission from Elsevier.

in 58% of the patients, with no difference between PITS and PTTS. In this study, the stent was removed after 6 months during the first 8 years and after 4 months during the next 8 years (77). Based on the available data, it appears that for a successful removal of the stent with lower risk of restenosis, stents should be in place for a minimum of 12 months.

#### **Stenting in post-infectious stenoses**

A wide variety of infectious etiologies result in airway stenosis such as tuberculosis, fungal (*Aspergillus*, *Blastomycosis*), viral (SARS-COV2) or bacterial tracheitis (*Klebsiella rhinoscleromatis* or *Staphylococcus aureus* tracheitis). In tuberculosis-endemic areas, airway complications are frequently encountered and seen in up to 20% of patients. A retrospective series of 71 patients with stent placement for stenosis secondary to endobronchial tuberculosis showed successful removal in 56% patients with a median duration of 12.5 months for stent placement; 38% of patients required permanent stent placement (78). In another retrospective series, 75 of 80 (94%) required airway stenting to maintain patency. There was an immediate improvement in lung function and symptoms in 88% post-stenting. Stent was successfully removed in 72% of patients after a median of 14 months with recurrence noted in 9% of patients requiring repeat stent placement (79). Granulation tissue (76%) and migration (70%) were the commonest complications in this group (80). Based on these data, we suggest that for complex post-tuberculosis (post-TB) strictures, stents should be in place for a minimum period of 12 months for eventual successful

removal with decreased restenosis rates.

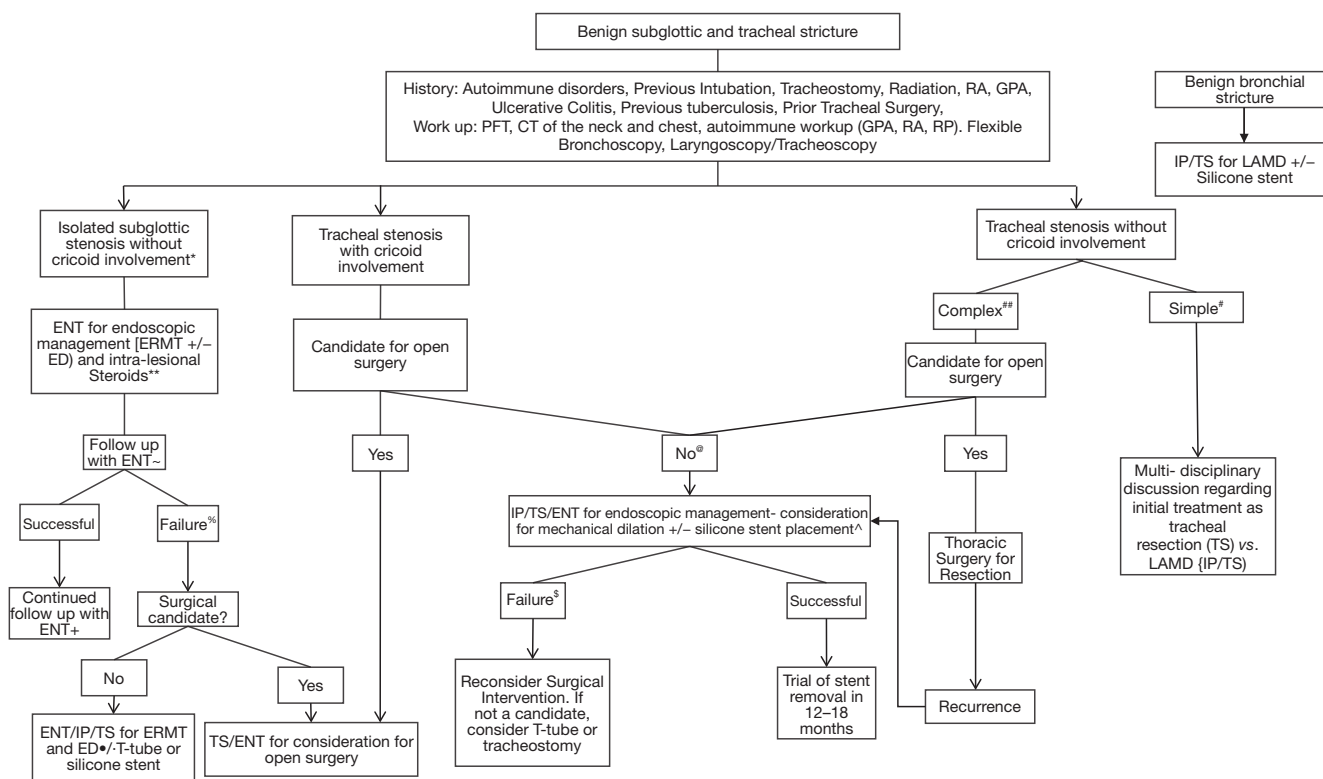
#### **Use of self-expanding metallic stents in benign tracheal stenosis**

Recently, a third generation of metallic stents which are fully covered and self-expandable are being considered in patients with benign tracheal stenosis. A study of 30 patients with 40 stents showed a clinical success rate of 40% (no additional interventions after elective stent removal) but 50% of the stents had to be removed secondary to stent related complications after a median 77 days (81). Another study of 19 patients with fully covered self expandable metallic stent (SEMS) for benign tracheal stenosis had stents removed in all patients secondary to complications at a median of 3 months (82). Based on the available limited studies on long term efficacy and safety, fully covered SEMS should not be considered as the first choice of stent in management of inoperable benign tracheal stenosis but are an option in scenarios where a rigid bronchoscopy cannot be performed for inserting silicone stents. These patients should be closely followed up for potential complications.

#### **Multi-disciplinary management of tracheal stenosis**

Patients with tracheal stenoses of all types benefit from a collaboration within a multidisciplinary team of physicians with expertise in different endoscopic and surgical





**Figure 5** A multi-disciplinary management algorithm in patients with benign airway strictures mechanical dilation: LAMD or cold knife assisted mechanical dilation. ERMT (PPI, ICS and TMP/SMX). ED, ENT, IP, TS. All patients with airway stent will follow the stent protocol defined below. Stent follow-up protocol: flexible bronchoscopy with moderate sedation 4–6 weeks post stent placement. Follow up bronchoscopy every 2–3 months or based on clinical symptoms. 0.9% normal saline nebulizer 5–10 mL three times a day. Stent card & stent education. \*, this algorithm applies only to iSGS. For patients with connective tissue disorders, first treatment option will be endoscopic management due to high recurrence rate post-surgical resection; \*\*, endoscopic management depending on severity of symptoms. Patient will undergo radial incision with or without mechanical dilation; ~, outpatient follow up with ENT including outpatient laryngoscopy and in-office injection of intralesional steroids; %, failure defined as patients requiring more than 3 interventions over 2–3 years with symptomatic recurrence and >50% stenotic index, despite office-based intralesional corticosteroid injection; ^, consider use of office based intralesional steroid injection to maintain patency and reduce time to re-intervention; #, complex: longer than 1 cm in length, with or without chondritis; #, simple: less than 1 cm in length, without chondritis; @, factors affecting surgical candidacy include multiple comorbidities, prolonged steroid use, stricture location, or long vertical extent (>4–6 cm); ^, stent follow up protocol—flexible bronchoscopy in 6–8 weeks post stent placement, followed up by flexible bronchoscopy every 2–3 months or as needed based on the symptoms. Normal saline (0.9%) nebulization three times a day. Stent card and education; ^, failure defined as repeated procedures including recurrent stent migration, followed by symptomatic recurrence of stenosis. Reprinted from (1), © 2021, with permission from Elsevier. RA, rheumatoid arthritis; GPA, granulomatosis with polyangitis; PFT, pulmonary function test; CT, computed tomography; RP, relapsing polychondritis; IP, interventional pulmonology; TS, thoracic surgery; LAMD, laser assisted mechanical dilation; ENT, ear, nose & throat surgery; ERMT, endoscopic resection (+/- wedge approach) with adjuvant medical therapy; ED, endoscopic dilation; PPI, proton pump inhibitors; ICS, inhaled corticosteroids; TMP/SMX, trimethoprim/sulfamethoxazole; iSGS, idiopathic subglottic stenosis.

techniques. At a minimum, this team should involve otolaryngologists, thoracic surgeons, and interventional pulmonologists. In multidisciplinary airway meetings and clinics, the team discusses and considers different methods for management of tracheal diseases including

conservative medical management alone, endoscopic incisions and dilation, stenting, and open surgical resection. Algorithms of multidisciplinary care, based on lesion location, etiology, extent and patient operability have been proposed and used in practice (Figure 5). At our



institution, multidisciplinary management of complex airway cases includes regular conferences to discuss patients and review imaging, laryngoscopy, and bronchoscopy videos. This is often followed by shared clinics for further evaluation and joint procedures in the operating room. Notably, collaborative management in the operating room is also frequently utilized for both airway assessment and therapeutic management. In some cases, airway patency must be restored emergently via rigid bronchoscopy, but an evaluation by a surgeon can be performed simultaneously, especially for patients who are known to have a complex stenosis and are otherwise surgical candidates. Other times, the otolaryngologists manage the subglottic disease while the interventional pulmonologists address the tracheal component. Another function of the multidisciplinary complex airway care team is to manage patients who develop short or long-term tracheostomy-related adverse events, including but not limited to stomal strictures, SGS, stenosis/granulation distal to the tracheostomy and tracheoesophageal fistulas. For inpatients, allied healthcare providers (nurses, physician assistants, or respiratory therapists) with specialized training in tracheostomy management should be involved for consistent follow up and early detection of any tracheostomy-related issues and to assure an optimal post procedure management (downsizing the tracheostomy tube, capping trials, and decannulation). Speech and language pathologists are integral members helping patients to resume speech and swallowing function. Studies have described the approach to implementation of tracheostomy specialists and have demonstrated improved outcomes with fewer complications and critical incidents. Tracheostomy specialists can also help to educate other staff members in tracheostomy management. Since the beginning of COVID-19 pandemic, there has been even more of a need for careful tracheostomy management from multidisciplinary specialized care teams (83,84).

## Conclusions

Benign tracheal stenosis requires a comprehensive evaluation and multidisciplinary management. Short of true airway emergencies, we recommend an inspection bronchoscopy prior to any intervention to assess lesion characteristics that impact decision regarding endoscopic or surgical management. For inoperable patients, there are several bronchoscopic techniques including laser, electro-surgical, mechanical dilation, stenting, as well as local application of mitomycin or intralesional steroid injection. We recommend

a multidisciplinary approach integrating thoracic surgery, otolaryngology, and interventional pulmonology to ensure optimal and timely care for patients with tracheal stenosis.

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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