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Central Airway Obstruction

Benign Strictures, Tracheobronchomalacia, and Malignancy-related Obstruction

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The purpose of this article is to provide an update on methods for palliating symptoms in patients with histologically benign and malignant central airway obstruction. We review the published literature within the past decade on postintubation, posttracheostomy, and TB- and transplant-related airway strictures; tracheobronchomalacia; and malignant airway obstruction. We review terminology, classification systems, and parameters that impact treatment decisions. The focus is on how airway stent insertion fits into the best algorithm of care. Several case series and cohort studies demonstrate that airway stents improve dyspnea, lung function, and quality of life in patients with airway obstruction. Airway stenting, however, is associated with high rates of adverse events and should be used only when curative open surgical interventions are not feasible or are contraindicated. CHEST 2016; 150(2):426-441

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In patients with central airway obstruction (CAO), clear definitions and classifications are relevant to determine treatment options, estimate prognosis and provide a common language for meaningful research. The syndrome of CAO generally is defined as occlusion of > 50% of the trachea, mainstem bronchi, bronchus intermedius, or a lobar bronchus. The first step in evaluating CAO is to classify the obstruction objectively on the basis of histologic findings, mechanism, and dynamic features. The extent and severity of airway narrowing and their impact on functional status should be assessed objectively[1] (Fig 1). Parameters that impact decision-making process regarding bronchoscopic dilation, stent insertion, and surgical resection in patients with CAO are reviewed herein. To guide this review, we performed a literature search described in e-Appendix 1.

Histologically Benign Airway Strictures

Benign strictures constitute the majority of benign forms of CAO and include airway

ABBREVIATIONS: CAO = central airway obstruction; CSA = cross-sectional area; ECAC = expiratory central airway collapse; EDAC = excessive dynamic airway collapse; LTS = laryngotracheal stenosis; NIPPV = noninvasive positive pressure ventilation; PEP = positive expiratory pressure; PITS = postintubation tracheal stenosis; PTTS = posttracheostomy tracheal stenosis; QOL = quality of life; SEMS = self-expandable metallic stents; TBM = tracheobronchomalacia

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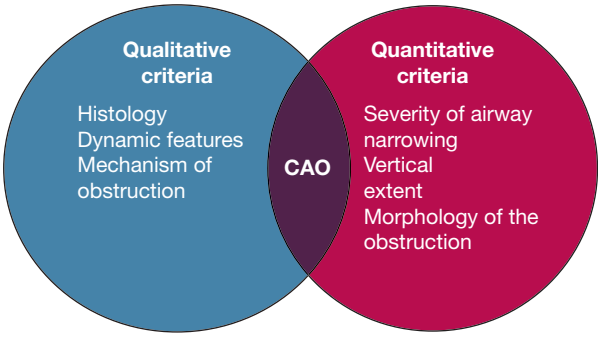

Figure 1 – *Quantitative and qualitative classification criteria for CAO. Histologic results are subclassified as benign or malignant; dynamic features, as fixed or variable (aka dynamic); and mechanism of obstruction, as exophytic endoluminal, strictures, extrinsic compression, and mixed obstruction. Quantitative criteria are based on objective assessments: severity of narrowing usually is defined as normal, mild (< 50% obstruction), moderate (51%-70%), or severe (71%-100%). Vertical extent, more pertinent to strictures requiring surgery or stent insertion, must be measured precisely. The airway morphology (ie, shape of the narrowing) must be documented objectively because it impacts flow, independent of the reduction in the cross-sectional area. CAO = central airway obstruction.*

stenosis mainly related to postintubation tracheal stenosis (PITS), posttracheostomy tracheal stenosis (PTTS), post-TB infection, and transplant-related and idiopathic stenoses. In this section, we describe classification systems and qualitative and quantitative parameters relevant to treatment and define physiologic rationales and outcomes of stent insertion for these entities.

Classification Systems

The purpose of classification systems is to provide a common language that enables storage and retrieval of data for clinical use, enhances the quality of care and management of health resources, and provides clinicians and researchers with an objective tool that can be used for designing meaningful outcome studies. The involvement of a multitude of specialties (eg, otolaryngologists, thoracic surgeons, and interventional bronchoscopists) in the management of laryngotracheal stenosis (LTS) has resulted in the development of several classification systems with different criteria (Table 1). None of these systems included all parameters relevant to treatment decisions likely because classification systems evolve over time as the understanding of a disease process improves. Several factors are taken into account for individualizing treatment and follow-up strategies in patients with LTS. These include severity of airway narrowing, extent, cause (origin), morphology (shape of stenosis), voice characteristics, swallowing, and overall functional impairment.[2-7] Parameters from existing classification systems pertinent to treatment are summarized in Table 2.

Extent, Morphology, and Cause

The vertical length, location of the stenotic airway, and presence of multifocal disease affect treatment options. Accurate measurements of the involved airway's length and precise location in relation to the vocal cords and main carina are relevant for determining suitability for open or bronchoscopic interventions. Multidetector CT often is used in the assessment of LTS and is more useful than spirometry for identifying the location, extent, severity, and morphology of airway narrowing but may be affected by the respiratory phase, presence of secretions, and intra- and interobserver variability.[8,9] Bronchoscopic optical coherence tomography and balloon-based radial probe endobronchial ultrasound allow cross-sectional imaging of the airway wall microlayers[10] but are not used routinely in clinical practice (Fig 2).

White light bronchoscopic evaluation remains the standard of practice for suspected CAO, allowing for quantitative measurements of stenosis and direct assessment of vertical extent and stricture complexity.[11] Stricture complexity is a predictor of outcome after bronchoscopic and surgical interventions. Simple strictures, defined as < 1 cm in vertical extent and without malacia, typically are treated with laser-assisted mechanical dilation, and stent insertion should be avoided because it can lead to further airway injury and potentially worsen resectable disease.[12] Inoperable complex strictures, however, often require stent insertion.

The morphology (shape) of the stricture can clarify the cause. Table 3 summarizes the terms used to describe the morphology of LTS and possible treatments for each group on the basis of morphology. Complex, circumferential stenosis most commonly occurs because of PITS, whereas triangular strictures are due to tracheostomy with cartilaginous injury.[13] A stricture's morphology impacts flow dynamics, symptom severity, and treatment options.

PTTS and PITS appear to be the most common histologically benign strictures,[13,14] followed by idiopathic and autoimmune causes (eg, granulomatosis with polyangiitis, sarcoidosis, ulcerative colitis). Strictures also can occur as a fibrotic sequel of endobronchial TB. Those following lung transplantation are thought to be secondary to tissue ischemia and altered inflammatory response. A thorough search for an underlying cause is warranted prior to labeling the stricture as idiopathic. This search is particularly relevant

TABLE 1] Common Classification Systems for Laryngotracheal Stenosis

Classification System Study/Year		Classification Criteria			Comments
Myer et al[15]/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[6]/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 on the basis of 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 et al[5]/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 et al[7]/2007	Airway status 1. No airway prosthesis 2. Intraluminal airway prosthesis (stent) 3. Tracheostomy or tracheostomy-tube dependent, patient voices 4. Tracheostomy dependent, patient does not voice 5. Death as a result 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."	Voice 1. No problems with voice 2. Some problems with my voice 3. Making voice is effortful and significant difficulties being heard or understood 4. Can only produce a weak voice or whisper 5. No voice	Swallowing 1. Eat and drink normally 2. Normal diet but with some difficulty swallowing 3. Significant swallowing difficulties 4. Serious problem swallowing (ie, diet consists almost entirely of liquidized foods) 5. Unable to swallow	Comprehensive system used by otorhinolaryngologists Does not include extent and severity criteria (ie, reduction in CSA) Designed for documenting functional outcomes of adult laryngotracheal stenosis

(Continued)

TABLE 1] *(Continued)*

Classification System Study/Year		Classification Criteria			Comments
		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."			
Freitag et al[2]/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[3]/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.

CSA = cross-sectional area.

TABLE 2] 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 cm, 1-4 cm, > 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

See Table 1 legend for expansion of abbreviation.

for treatment because idiopathic LTS is a distinct entity characterized by hypertrophy of the mucosa and submucosa with intact cartilaginous structures, for which stent insertion should not be used (Fig 2).

Flow Dynamics and Functional Impairment

The work of breathing in CAO depends on the pressure change along the stenotic airway and is affected mainly by the degree of obstruction and airflow velocity.

Although it is not entirely justified by physiologic or outcome studies, CAO is defined as occlusion of $> 50\%$ of the trachea, mainstem bronchi, bronchus intermedius, or a lobar bronchus.[16] In mild tracheal narrowing (ie, $\leq 50\%$ reduction in cross-sectional area [CSA]), pressure drop is similar to that which occurs through the normal glottic opening and, therefore, is unlikely to cause symptoms.[17] Moderate obstruction (51%-70% reduction in CSA) produces variable

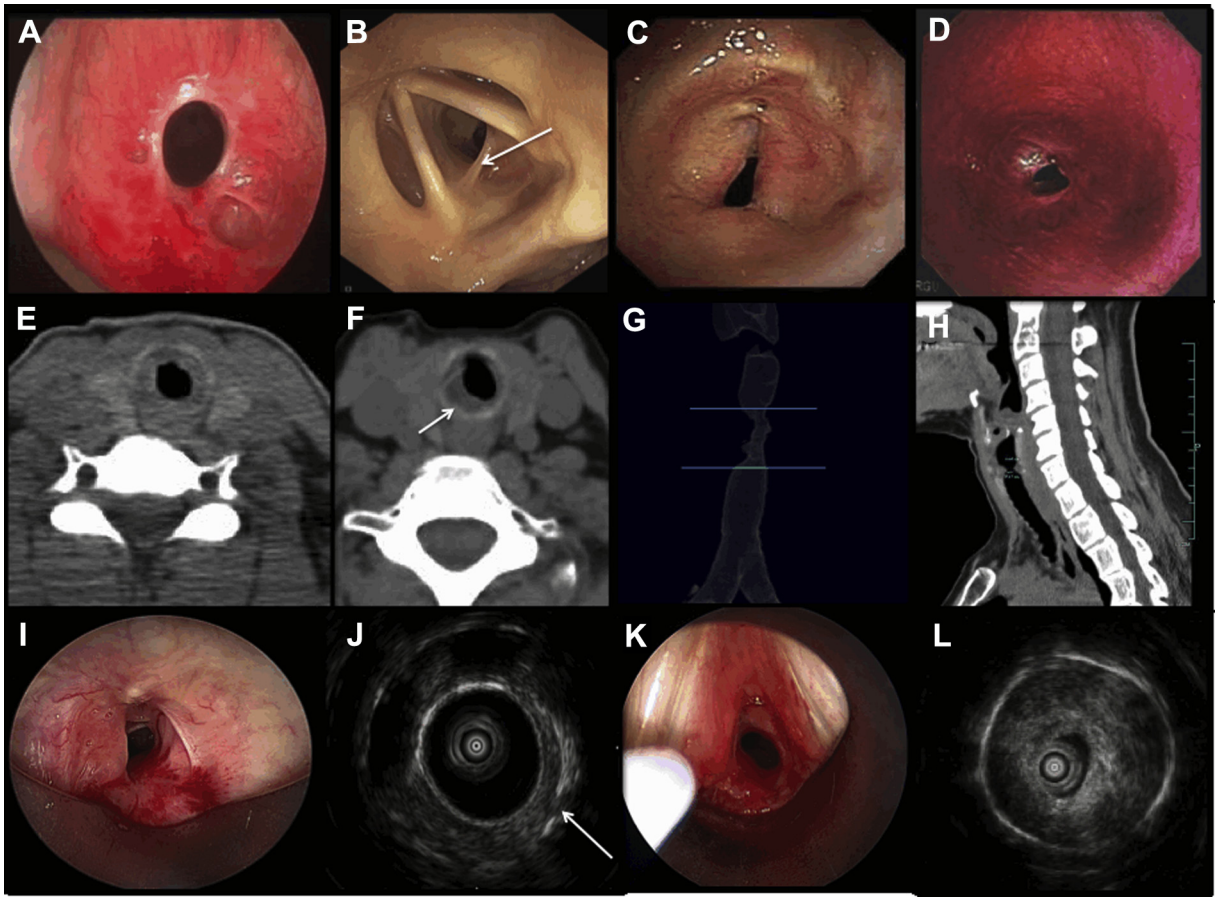

Figure 2 – *Morphologic types of benign tracheal strictures at bronchoscopy, CT, and balloon-based radial probe endobronchial ultrasound (EBUS). A, Elliptical idiopathic subglottic stricture. B, Eccentric subglottic stricture from granulomatosis with polyangiitis (arrow points to the stenotic tissue). C, Triangular (pseudoglottic) stricture after tracheostomy. D, Circumferential postintubation, simple (ie, weblike) stricture. E, Circumferential stricture (axial plane). F, Eccentric stricture (axial plane; arrow points to the hypertrophic stenotic tissue). G, Complex postintubation stenosis at three-dimensional reconstruction CT. H, Simple (< 1 cm in vertical extent), idiopathic stricture measured on sagittal CT image. I, Postintubation stenosis with hypertrophic stenotic tissues covering the cartilage. J, In the same patient, balloon-based radial probe EBUS reveals the calcified and fractured tracheal cartilage (arrow). K, Idiopathic subglottic stricture with hypertrophic stenotic tissues covering the cartilage. L, In the same patient, balloon-based radial probe EBUS reveals the intact cricoid cartilage (hyperechoic circular line).*

symptoms with significant pressure drops occurring at higher flow rates (eg, during exercise). Sedentary patients, however, usually remain asymptomatic at this stage. Severe stenosis (> 71% reduction in CSA) results in significant pressure drop even at a low flow rate, causing symptoms at rest or with mild exertion, and may warrant prompt intervention. An objective assessment of the degree of airway narrowing and functional status, therefore, is warranted.[1] Specifically in patients with LTS, the Medical Research Council dyspnea scale had a high interobserver correlation in a variety of respiratory diseases and correlated with spirometry and response to therapy.[18]

Patients with LTS, however, may have symptoms other than dyspnea, so a more global assessment of functional impairment is warranted in addition to assessment of dyspnea and flow limitation. Spirometry and flow volume loops may detect airflow limitation and can be used to monitor physiologic changes following interventions. The classic pattern of truncation of inspiratory and expiratory limbs on the flow volume loop, however, lacks sensitivity and usually is seen when the tracheal lumen already is reduced to 6 to 8 mm. In addition, spirometry does not identify the precise location, extent, or morphology of the airway narrowing.[8] Patients with subglottic stenosis also may develop dysphagia and dysphonia. Thus, voice and swallowing assessments complete a comprehensive LTS evaluation (Table 2).

Stent Insertion for Benign Airway Strictures

Surgical resection of hypertrophic stenotic tissues is the procedure of choice in the majority of patients with benign tracheal strictures. Severe comorbidities, stricture

TABLE 3] Morphological Classification of LTS With Possible Treatment Strategies

Morphology	Similar Terms in the Literature	Cause	Comments	Possible Treatments
Circumferential	Concentric	Cuff-related injury from the endotracheal or tracheostomy tubes Autoimmune disorders	Simple (one ring, less than 1 cm in the vertical extent) or complex (with chondritis, longer than 1 cm)	Surgical resection is the preferred curative intent treatment. Laser-assisted mechanical dilation for simple LTS Silicone stent insertion for complex LTS
Triangular	A shaped, lambdoid, pseudoglottic, stomal, posttracheostomy	Tracheal wall injury after tracheostomy: chondritis and subsequent focal malacia	For the same reduction in the CSA, this morphological type of LTS is associated with less impact on flow dynamics than is circumferential stenosis.	Surgical resection Silicone stent insertion
Eccentric	Oval, elliptical	Often after intubation or after thermal injury (inappropriate use of laser, electrocautery)	When after intubation, it is often a complex stenosis, common finding in cuff-related injury with cartilaginous damage	Surgical resection Laser-assisted mechanical dilation Silicone stent insertion
Complex stenosis	Scar stenosis, circumferential cicatricial stenosis, hourglass-like contraction, tapered	Most commonly after intubation and tracheostomy with cartilaginous injury	Long segments $>$ 1 cm or with tracheal wall injury or associated malacia (chondritis)	Surgical resection Silicone stent insertion in patients who are not surgical candidates
Simple stenosis	Weblike, membranous, abrupt	Mucosal ischemia following endotracheal intubation No associated chondritis	Short-segment concentric stenosis, $<$ 1 cm in vertical length	Often responds to laser-assisted mechanical dilation High success rate with tracheal sleeve resection

LTS = laryngotracheal stenosis. See Table 1 legend for expansion of other abbreviations.

location (eg, high subglottic), or long vertical extent (> 4-6 cm), however, may preclude open surgical intervention. Novel techniques, including tracheal implantation of a cartilage graft,[19] transplantation with an aortic allograft,[20] and transplantation of a tissue-engineered cadaveric airway by using colonization with the recipient's stem cells,[21] have been proposed as alternatives to tracheal sleeve resection or laryngotracheal reconstruction, but more evidence is necessary prior to implementing these techniques in practice.[22]

In patients who are not surgical candidates and in selected patients awaiting surgery, dilation with or without silicone stent placement remains at times the only alternative that may impact quality of life (QOL) significantly.[23] We suggest that the decision to insert a stent in patients with LTS should follow multidisciplinary discussions including specialists from thoracic and head and neck surgery. Self-expandable metallic stents (SEMS) arguably provide ease of placement by means of flexible bronchoscopy with or without fluoroscopy. In a public health notification in 2005, however, the US Food and Drug Administration recommended against the use of SEMS (available on the market at that time) for histologically benign airway strictures because of reported extensive granulation tissue formation and stent fracture, with associated risks for airway perforation and hemorrhage.[24,25]

Airway Stents for PITS and PTTS

In addition to potential bridging to surgery, silicone stents can be used as a definitive long-term palliative treatment of selected, inoperable, histologically benign strictures.[26-29] Retrospective case series or cohort studies (N = 28) constitute the published literature on PITTS and PTTS for the past 10 years (e-Table 1). These data suggest that practitioners use a multitude of stent types and that the initial success rate is high. This finding is offset, however, by the recurrence of stenosis after stent removal or complication rates. The exact timing for stent removal and optimal stent insertion selection criteria remain unknown. Predictors of success of stent insertion include stenoses < 1 cm in vertical extent and stenoses without associated malacia (eg, chondritis). It appears, however, that there is inadequate airway patency in > 50% of patients after stent removal at 7 to 32 months after stent insertion. The success rate of bronchoscopic treatment once stents are removed (usually after at least 6 months) in cases of complex stenoses is low (17.6%), suggesting the need for long-term indwelling airway stents. A higher rate (46.8%) was described after stents remained in place for a longer time (mean of 11.6 months), with almost 50% of patients having indwelling airway stents for more than 12 months (e-Table 1). These data suggest that in patients with complex PITS and PTTS and indwelling airway stents, the timing of cartilage regeneration without recurrence of stenosis is not always known.

Airway Stents for Posttransplantation-related Bronchial Strictures

Bronchial strictures and anastomotic complications after initial single lung transplantations were reported to be as high as 80%.[29] Improvements in surgical techniques, immunosuppression, and perioperative management led to a decrease in the incidence to 5% to 30%.[30,31] Stent insertion for transplant-related bronchial strictures was evaluated in 11 studies during the past 10 years, and the majority addressed the role of SEMS (e-Table 2). However, for bronchus intermedius strictures, one series suggested that the use of covered SEMS may not offer a therapeutic advantage over balloon dilation alone.[32] Silicone stent insertion after dilation may offer a less traumatic alternative to insertion of SEMS.[31] No direct comparison studies evaluated SEMS and silicone stents in this patient population. We believe that stent choice often is affected by local expertise and practice. Biodegradable stents may be a safe and effective alternative to SEMS in these patients and may obviate the need for permanent stenting.[33] Long-term outcome profiles of these devices remains to be defined further.

Airway Stents for Post-TB-related Stenosis

Endobronchial TB can manifest with diffuse endobronchial granulation, ulcerations, or a pseudomembranous pattern that, once healed, can cause fibrostenotic strictures.[34-36] We believe that the published data support the use of bronchoscopic interventions in patients with inoperable post-TB strictures, but the majority of patients require long-term stenting (> 12 months) to maintain airway patency[35,36] (e-Table 3).

Expiratory Central Airway Collapse

Expiratory central airway collapse (ECAC) includes tracheobronchomalacia (TBM) and excessive dynamic airway collapse (EDAC).[37] Issues related to terminology, classification systems, airflow dynamics, and management are discussed in this section.

Nomenclature, Classification Systems, and Physiology

Paired inspiratory-dynamic expiratory CT or bronchoscopy may demonstrate > 50% reduction in the CSA of the trachea and mainstem bronchi, a process traditionally considered pathologic and called *TBM*, *tracheobronchial collapse*, *expiratory tracheobronchial collapse*, *expiratory tracheobronchial stenosis*, *tracheobronchial dyskinesia*, or *EDAC*.[37] Several classification systems have been proposed, with the most recent one increasingly applied in the study of these entities (Table 4).[38-47] A certain degree of dynamic airway compression, characterized by invagination of the posterior membrane and narrowing of the airway CSA, represents a normal physiologic process (Fig 3). When this process is exaggerated, as an isolated finding in some healthy individuals during cough and forced expiration or more commonly in patients with obstructive airway disease (eg, asthma, COPD) or morbid obesity, the accepted current terminology is *EDAC* (Fig 3).[37-40] EDAC usually does not represent a true central airway disorder, and, in general, no invasive treatments are warranted. TBM, however, is an abnormality of the central airway and results from weakness of the tracheal or mainstem bronchial walls caused by softening or destruction of the supporting cartilaginous rings (Fig 3). Tracheoplasty or stent insertion is required in severe cases of TBM.[48-50] TBM and EDAC are diagnosed by means of paired inspiratory-dynamic expiratory chest CT or dynamic (aka functional) bronchoscopy (Fig 4).[51-54] These methods are complementary and have high inter- and intraobserver agreement.[55] Case series and reports continue to mislabel the expected EDAC seen in asthma, COPD, and obesity as a pathologic tracheobronchial process (ie, TBM).[56,57]

Impact on Flow Limitation: EDAC in COPD, Asthma, and Obesity

EDAC found at bronchoscopy or CT in patients with symptoms should trigger workup for the real cause of flow limitation. A 2014 study showed that EDAC is seen in 22% of patients with COPD when assessed by means of dynamic chest CT, even when defined as forced expiratory collapse > 80%.[58] This finding does not mean, however, that EDAC is flow limiting; this study and others showed no significant correlation between end-expiratory or

TABLE 4] Classification Systems Used for ECAC

Study/Year	Criteria	Comments
Rayl[41]/1965	Extent: based on location of airways involved: type I, proximal; type II, mediastinal; and type III, intrapulmonary	Central airway collapse: assessed during coughing on cinebronchography
Johnson et al[42]/1973	Severity: Four degrees of airway narrowing	TM: > 50% collapse during coughing on fluoroscopy
Feist et al[43]/1975	Cause: congenital and acquired	TM: > 50% collapse during coughing on fluoroscopy
Jokinen et al[44]/1977	Severity: mild (< 50%), moderate (50%-75%), severe (100%) Extent: TM, TBM, BM	TBM: expiratory reduction of > 50% in the anteroposterior diameter of the airways First classification based on bronchoscopic findings
Mair and Parsons[45]/1992	Cause: congenital, extrinsic compression, acquired Severity: mild (< 70%), moderate (70%-90%), severe (> 90%) airway narrowing	Described for pediatric TBM Empirical severity score
Masaoka et al[46]/1996	Cause and extent criteria only Pediatric, adult, and secondary	TBM: > 80% collapse during expiration Based on bronchoscopic estimations and frontal and lateral radiographs to estimate the narrowing
Murgu and Colt[47]/2007	Functional status (WHO 1-4) Extent (normal, focal, multifocal, and diffuse) Morphology: EDAC and TBM crescent, saber sheath, and circumferential Cause: idiopathic or secondary Severity: normal (0%-50%), mild (50%-75%), moderate (75%-100%), severe (100%) complete collapse	ECAC includes TBM and EDAC EDAC: defined as > 50% reduction in CSA during expiration because of bulging of the posterior membrane TBM: defined as collapse of the cartilaginous structures Based on bronchoscopic evaluation

BM = bronchomalacia; ECAC = expiratory central airway collapse; EDAC = excessive dynamic airway collapse; TBM = tracheobronchomalacia; TM = tracheomalacia; WHO = World Health Organization. See Table 1 legend for expansion of other abbreviations.

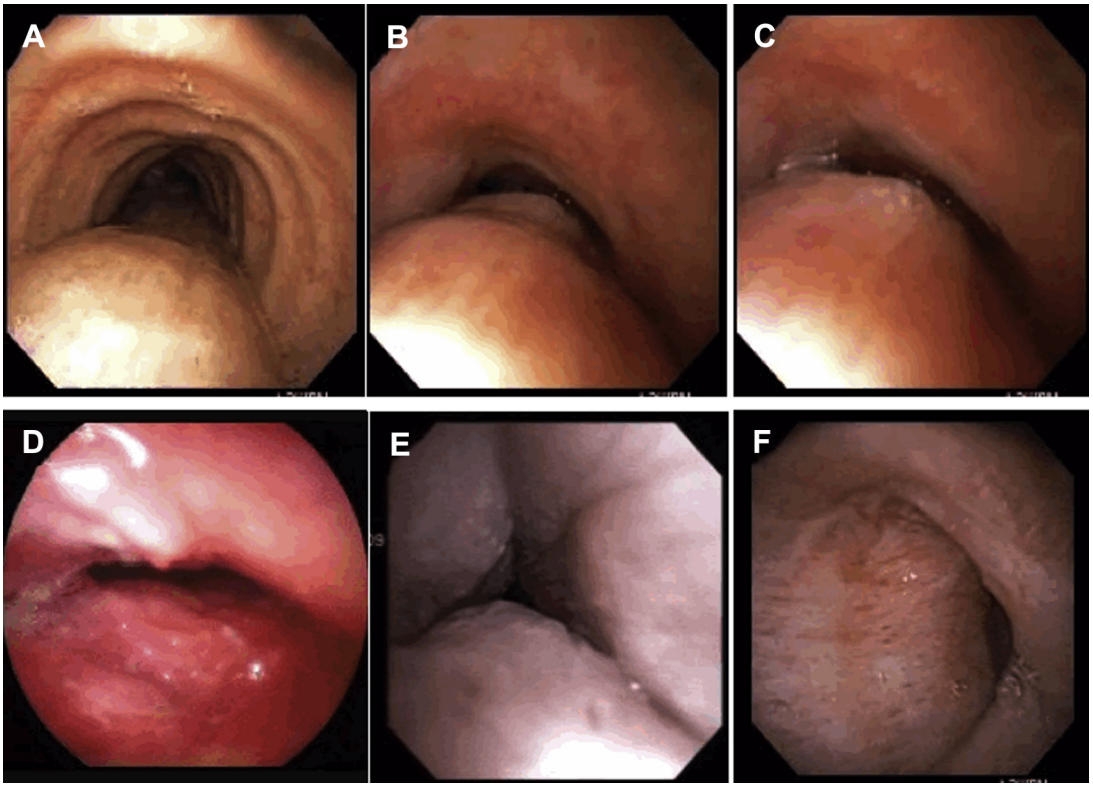

Figure 3 – *Morphological types of expiratory central airway collapse. A, Normal, physiologic dynamic airway compression (DAC). B, Excessive dynamic airway collapse (EDAC; the airway cross-sectional area [CSA] is reduced by > 50% during forced expiration). C, Severe EDAC; the airway CSA is reduced by 100% during coughing (the posterior membrane contacts the anterior cartilaginous wall). In DAC and EDAC, the cartilaginous wall is intact. D, Crescent type of tracheomalacia in which the anterior wall is flattened. E, Circumferential type of tracheomalacia in relapsing polychondritis, characterized by collapse of the entire cartilaginous ring and airway wall edema. F, Severe (100% closure) saber sheath type of tracheomalacia due to collapse of the lateral walls during expiration in a patient with posttracheostomy stricture.*

dynamic expiratory collapse and percent predicted FEV_1.[58,59] Flow limitation theories explain these findings. During maximal forced expiration, with development of highly negative transmural pressure in the airway segment downstream (ie, mouthward) from the site of flow limitation (choke point) (Fig 5), even healthy individuals can demonstrate substantial intrathoracic tracheobronchial narrowing. This process is exaggerated in COPD, asthma, and morbid obesity (Fig 3).[60,61] COPD and morbid obesity influence several aspects of airway flow leading to EDAC (Fig 5). Expiratory collapse is associated significantly with BMI, with worse tracheal collapse among patients who are morbidly obese.[39,60] Studies also suggest that the prevalence of both TBM and EDAC is related directly to age, sex (female), and asthma severity, with EDAC being much more frequent than TBM in all patients with asthma.[40]

Although EDAC, defined as > 70% reduction in CSA during expiration because of bulging of the posterior membrane, was found in 17% of patients in another study, there was no correlation between the degree of obstruction and the results from pulmonary function tests, supporting the current understanding that EDAC is a CT or bronchoscopy imaging finding localized downstream from the choke points and, thus, not responsible for flow limitation.[39,62] Healthy people may have EDAC without any effects on expiratory flow. EDAC was seen in 78% of healthy subjects with normal pulmonary function test results, with some healthy individuals having 80% to 90% CSA reduction.[63] The likely preferred method for clarifying flow limitation in EDAC requires intraluminal airway pressure measurements across the collapsing airway.[64] Old physiologic studies using airway pressure measurements show no pressure drop along the collapsible airway in EDAC.[62] A systematic evaluation of patients with severe EDAC (71%-100% collapse), however, has not yet been performed. Such a study potentially could clarify the true physiologic impact of EDAC and assist in patient selection for membranous tracheoplasty or stent insertion.

Stent Insertion for ECAC

Published studies on stent insertion for TBM and EDAC are case series, and some included stents that may not be

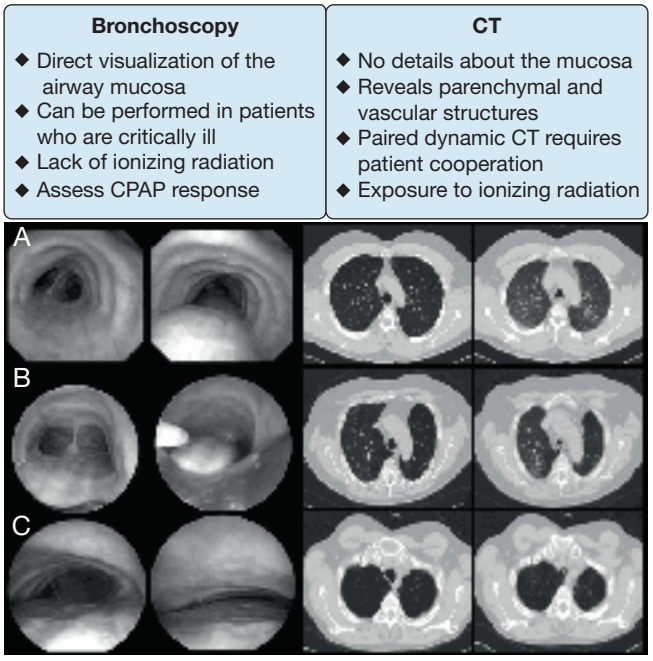

Figure 4 – *Dynamic bronchoscopy and correlating paired inspiratory-dynamic expiratory CT images in normal DAC (A), EDAC (B), and crescent type of tracheomalacia (TM) (C). In DAC and EDAC, the cartilage remains intact and of similar morphology during expiration as noted at bronchoscopy and CT (A and B), whereas in TM there is evident flattening of the anterior cartilaginous wall (C). See Figure 3 legend for expansion of abbreviations.*

currently available on the market. On the basis of the current understanding of airflow physiology in these patients, we believe that stent insertion should be reserved for patients with severe TBM not responding to the treatment of the underlying disorder and noninvasive positive pressure ventilation (NIPPV). TBM due to relapsing polychondritis is one such disease for which one or more stents are often necessary because of a diffuse lack of airway cartilaginous support (Fig 6). For EDAC, NIPPV can be offered with nocturnal and intermittent application during the day, with pressure settings determined during bronchoscopic titration (Fig 6).[65-67]

QOL and functional status are improved in the short term in 70% and dyspnea in 90% of patients after silicone stent insertion for ECAC. The FEV_1, however, does not seem to improve after stent insertion or membranous tracheoplasty.[48,50] Almost 10% of these patients may have bronchoscopy-related complications.[48] Stent-related adverse events in these disorders are also common and include obstruction from mucous plugging and migration and require multiple bronchoscopies.[50] Case series also report on improved airway patency and symptoms without immediate major complications after the use of SEMS for TBM, but stent-related complications, including stent fracture, can occur and require removal.[68] On the basis of the limited available evidence, for patients with severe, diffuse, and symptomatic TBM, we suggest that silicone stent insertion be used to improve dyspnea and QOL. In some centers, silicone stents are used as a bridge to membranous tracheoplasty or as a definitive therapy in patients who are not surgical candidates. Future algorithms should include airway pressure measurements to determine whether the collapsing segment is flow limiting as an alternative to a proposed stent trial.[62] For patients with TBM, on the basis of the 2005 Food and Drug Administration warning, the previously studied metallic stents cannot be recommended for improving dyspnea or QOL. Newer models of SEMS with different biomechanical properties may be safer but will require further study.

Intermittent NIPPV for EDAC and TBM

Application of positive airway pressure may serve as a pneumatic stent[67] because the intraluminal pressure is increased, thus improving airway stiffness and expiratory flow. Airflow also may be improved simply because lung volumes are higher during positive pressure ventilation.[69] CPAP improved dyspnea, cough, and secretion management in selected patients with TBM. The pressure necessary to maintain airway patency can be determined by performing bronchoscopy assisted by NIPPV.[66] NIPPV has been used in adults

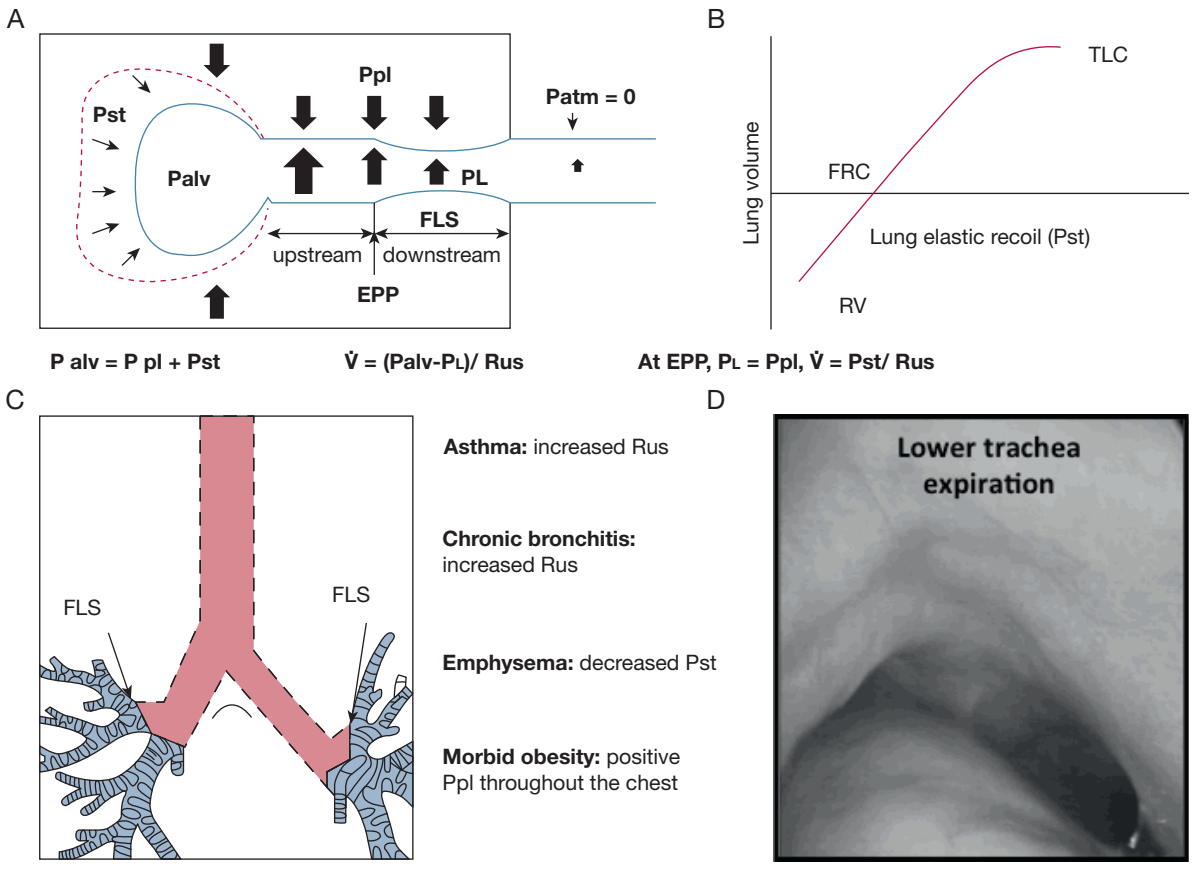

Figure 5 – *EPP theory for expiratory flow limitation and physiologic relevance of EDAC. A, The Palv causes air to flow during expiration and is approximately equal to the Pst plus the Ppl: Palv = Ppl + Pst. During forced expiration, the PL eventually becomes equal to the Ppl at the EPP. In the upstream segment (in an alveolar direction from the EPP), the Ptm (Ptm = PL − Ppl) is positive but in the downstream segment (mouthward from the EPP) is negative within the intrathoracic airways. At a given lung volume, driving pressure upstream from the EPP would be equal to Pst, and downstream from the EPP, airways would be compressed during expiration. This region of compression of intraluminal caliber is referred to as an* FLS *or* choke point. *In emphysema, for instance, the reduced Pst and increased resistance of the upstream segment result in decreased transluminal pressure and consequent increased airway collapse; in morbid obesity, the reduced Pst from restriction and increased pleural pressures also result in EDAC. B, As lung volume decreases from TLC toward RV, the Pst)decreases as well, and Ppl increases during forced expiration. C, The EPP migrates upstream during expiration, resulting in a lengthening of the increasingly narrow downstream segment (note compressed trachea and mainstem bronchi). This increases airway resistance and prevents further increases in expiratory airflow, causing the EPP to become fixed when airflow becomes constant. FLSs move peripherally during exhalation to the lobar and segmental and at most subsegmental bronchi. D, Bronchoscopic image captured in the lower trachea showing EDAC in a patient with morbid obesity and emphysema. EPP = equal pressure point; FLS = flow-limiting segment; FRC = functional residual capacity; Palv = alveolar pressure; Patm = atmospheric pressure; PL = intraluminal pressure; Ppl = pleural pressure; Pst = elastic recoil pressure of the lungs; Ptm = transmural pressure; Rus = resistance of the upstream segment; RV = residual volume; TLC = total lung capacity; V̇ = flow. See Figure 3 legend for expansion of other abbreviations.*

with TBM from relapsing polychondritis and TBM from long-standing compression by a large goiter or thyroid cancer and in patients with tracheomalacia after thyroidectomy. Noninvasive positive expiratory pressure (PEP) also improves expiratory flow and cough efficiency in patients with ECAC.[70] PEP increases flow during cough spirometry and may provide a useful adjunct to chest physiotherapy. High PEP levels (eg, 20 cm H_2O), however, may worsen expiratory flow.[70] Future studies are warranted to investigate bronchoscopic NIPPV or other forms of noninvasive PEP titration to document improvements of ECAC on imaging and airflow.

Malignant CAO

Malignant CAO can be palliated and, therefore, requires prompt recognition and intervention.[71] It is seen most commonly in patients with locally advanced lung cancer, although airway metastases may occur, mostly from thyroid, breast, or colon cancer; melanoma; or renal carcinoma. In patients with lung cancer for which surgery is considered curative, resection is the preferred management of CAO. In all other patients, the goal of CAO management is to restore airway patency to improve symptoms or prevent postobstructive pneumonia. Airway patency can be achieved with multiple modalities, including laser therapy, contact

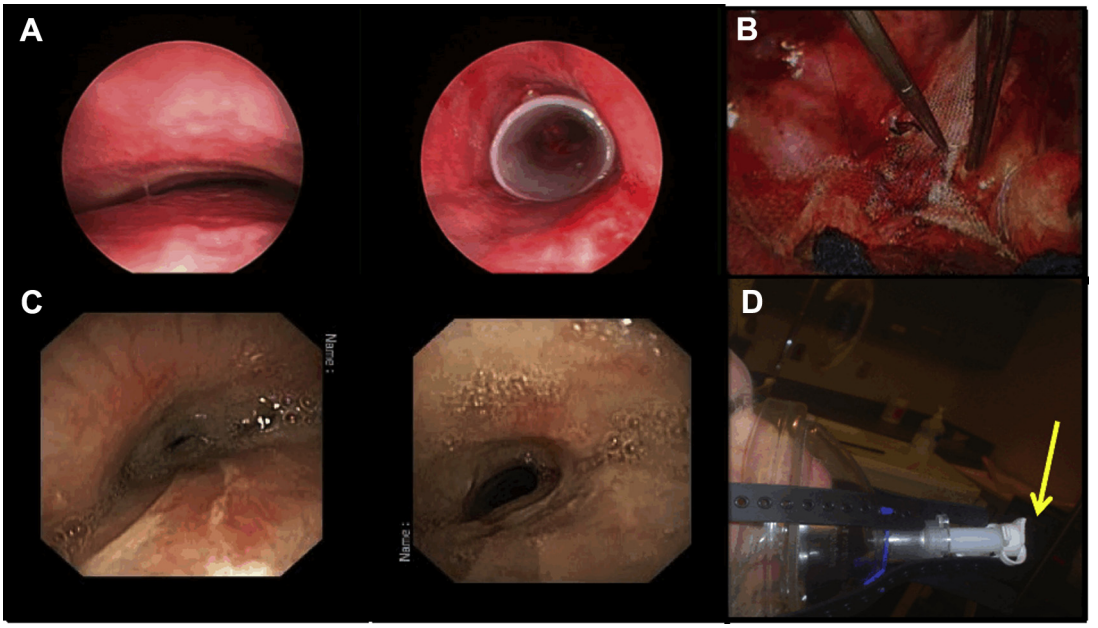

Figure 6 – *Treatment options for EDAC and tracheobronchomalacia. A, Crescent type tracheomalacia before (left) and after (right) straight studded silicone placement. B, Mesh suturing during membranous tracheoplasty. C, Bronchoscopy on CPAP for a patient with left main bronchomalacia. During tidal expiration, on CPAP 0 cm H_2O, there is near complete closure of the airway (left). During tidal expiration, on CPAP of 10 cm H_2O, the airway lumen patency is maintained (right). D, A full-face mask is secured to the patient's face with elastic straps, and a dual-axis swivel adapter (yellow arrow) is attached to the mask and connected to the ventilator. See Figure 3 legend for expansion of abbreviations.*

electrocautery, argon plasma coagulation, cryotherapy, photodynamic therapy, brachytherapy, and airway stenting.[72] The approach to malignant CAO is variable among clinicians and institutions. It also seems unlikely that one method of endobronchial debulking is superior to another. The decision to place an airway stent, however, has important consequences for the patient and health-care use. Appropriate patient and stent selection criteria are summarized in this section.

The decision to place an airway stent following opening of a narrowed airway is based on its ability to prevent airway reocclusion. This strategy must be balanced with the long-term complications associated with an airway foreign body (ie, stent). Published literature on the outcomes and complications of airway stenting is composed mostly of small case series, cohort studies, and case reports. A summary of the original research articles published between 2005 and 2015 on stent insertion for malignant CAO is provided in e-Table 4.

Several larger-scale cohort and registry studies have provided more insight into the risks and benefits associated with airway stenting and other bronchoscopic interventions for malignant CAO.[73-77] Therapeutic bronchoscopy was successful in reopening of the airway in nearly all patients, and there were few related procedural complications, but the overall stent-related complication rate varied between 23% and 34% (Table 5). Nearly all of these complications required bronchoscopic intervention for secretion removal, granulation tissue ablation, or stent removal or replacement. There has been an increased appreciation regarding the development of stent-associated respiratory infections. A systematic review showed that 93 of the 501 patients (19%) with airway stents developed a respiratory tract infection.[78] In one study of 72 patients undergoing therapeutic bronchoscopy for malignant CAO, 23 patients (32%) developed a lower respiratory tract infection,[79] which resulted in significant morbidity and mortality, with six patients dying within 14 days of the infection. In another study of 172 patients with stents for malignant CAO, the development of a lower respiratory infection was associated the development of granulation tissue and worsened survival.[80]

Significant heterogeneity regarding patient population, types of airway stents, and consistency in the reporting of complications has limited the generalizability of study findings. A multicenter national registry of patients with malignant CAO sought to characterize the risks and benefits of therapeutic bronchoscopy better.[16,81] Technical success was achieved in 93% of patients, and airway stents were placed in 36.4% of the procedures. Death within 30 days of the procedure occurred in 119

TABLE 5] Frequency of Complications Following Airway Stent Placement

Parameter	Breitenbucher et al[73]/2008	Chhajed et al[74]/2010	Saji et al[75]/2010	Chung et al[76]/2011	Serrano et al[77]/2013	Ost et al[80]/2012
No. of Patients	60	130	59	149	86	172
Malignant	60	130	59	77	12	172
Benign	0	0	0	72	74	0
Stents placed	62	108	NR	211	123	195
Types of stent						
Metallic	62	46	NR	211	123	118
Silicone	0	43	NR	0	0	46
Hybrid	0	19	NR	0	0	31
Complications						
Overall	14 (23.3%)	37 (34.3%)	13 (22.0%)	69 (32.7%)	23 (26.7%)	NR
Mucous plugging	5 (8.3%)	8 (7.4%)	6 (10.2%)	…	NR	48 (24.6%)
Granulation	3 (5.0%)	3 (2.8%)	NR	32 (15.2%)	13 (17.5%)	38 (19.5%)
Tumor restenosis	3 (5.0%)	21 (19.4%)	NR	…	1 (8.3%)	25 (12.8%)
Stent migration	3 (5.0%)	5 (4.6%)	NR	16 (7.6%)	NR	27 (13.9%)
Stent fracture	NR	NR	NR	20 (9.5%)	5 (5.8%)	4 (2.1%)
Infection	NR	NR	NR	NR	2 (2.3%)	73 (37.4%)

NR = not reported.

patients (14.8%). The placement of a stent increased the odds of death within 30 days by 4.92, with Y stents carrying a greater risk than straight stents. The proximate cause of death in patients with stents was not available, but given that the overall procedure-related complication rate was low (3.9%), it seems that other longer-term events must be responsible. Despite the high technical success rate, clinically significant improvements in dyspnea and health-related QOL were seen in only 48% and 42% of patients, respectively. Patients with greater baseline dyspnea had the greatest improvements in dyspnea score and health-related QOL, and those with lobar obstruction (rather than tracheal, mainstem, or bronchus intermedius obstruction) had the least improvement.

This finding suggests the need for a better understanding of which patients and airway obstruction parameters warrant bronchoscopic interventions. Randomized controlled trials comparing different stents in malignant CAO, however, have not been performed to date. Confounding indications (ie, patients who undergo stenting may have a higher baseline disease burden or limited therapeutic options) cannot be ruled out as an explanation for the worsened outcomes in patients with stents. Given the findings from several studies, it seems wise to avoid stent placement if airway patency can be restored with ablative techniques alone.

Conclusions

The histological type, mechanisms of obstruction, extent, location, morphology, degree of airway narrowing, and patient functional status are factors that determine the need for open surgical or bronchoscopic interventions in patients with CAO. We believe that the original articles published in the past decade support the use of airway stents in the following specific circumstances:

1. For patients with inoperable, symptomatic complex PITS and PTTS, and post-TB stenosis, silicone stent insertion may improve dyspnea, and stent removal should be considered 6 to 12 months after insertion. For patients with symptomatic benign strictures, the studied SEMS did not improve dyspnea or QOL long term, and for patients with high tracheal stenosis or subglottic stenosis, SEMS should be avoided.
2. For patients with severe, diffuse, and symptomatic crescent type TBM, silicone stent insertion may be considered to improve dyspnea and QOL as a bridge to membranous tracheoplasty or as a definitive therapy in patients who are not surgical candidates. For EDAC, physiologic studies do not support the use of invasive airway stabilization. In selected patients with TBM and EDAC, NIPPV may be a feasible beneficial alternative, and metallic stents should be avoided because of high complication rates.

3. For patients with symptomatic posttransplant anastomotic bronchial stenosis or malacia, stent insertion improved lung function and dyspnea, but it should be reserved for patients who have symptoms and in whom bronchoscopic dilation has failed.
4. For patients with malignant CAO and moderate to severe symptoms, bronchoscopic interventions, including stent insertion, improved dyspnea, lung function, and QOL, although a better understanding of patient selection is necessary to achieve better outcomes more reliably.

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Additional information: The e-Appendix and e-Tables can be found in the Supplemental Materials section of the online article.

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