Endobronchial Prostheses

13

Septimiu Dan Murgu and Sean Patrick Stoy

Abbreviations

6MWT	Six-minute walk test
BAO	Benign airway obstruction
BPF	Bronchopleural fistula
CAO	Central airway obstruction
CPAP	Continuous positive airway pressure
CT	Computed tomography
DATS	Dynamic A-shaped tracheal stenosis
EBUS	Endobronchial ultrasound
ECAC	Expiratory central airway collapse
EDAC	Excessive dynamic airway collapse
EPP	Equal pressure point
ERF	Esophagorespiratory fistulas
ETT	Endotracheal tube
FLS	Flow-limiting segment
HRQOL	Health-related quality of life
IOS	Impulse oscillometry
MAO	Malignant airway obstruction
MRC	Medical Research Council
P lat	Lateral airway pressure
PL	Intraluminal pressure
POTS	Postoperative tracheal stenosis
Ppl	Pleural pressure
QOL	Quality of life
R	Resistance
RP	Relapsing polychondritis
RRP	Recurrent respiratory papillomatosis
SEMS	Self-expandable metallic stents
TBM	Tracheobronchomalacia
TLC	Total lung capacity

Introduction

This chapter emphasizes on the indications, physiologic basis, and complications of airway stent insertion. Airway stents have been consistently shown to help patients suffering from benign and malignant central airway obstruction[1] and esophagorespiratory fistulas, by improving their airflow, quality of life, and potentially survival. The incidence rate of adverse events depends on patient-related factors and on specific stent-tissue interactions. Prior to inserting such a device, the bronchoscopist should determine the need and expected benefits of this procedure. A first step is to objectively classify the obstruction based on histology, mechanism of obstruction and dynamic features (Fig. 11.1). An objective assessment of the extent and severity of airway narrowing is necessary, as well as an accurate assessment of the impact of the airway narrowing on functional status (Fig. 13.1).

S.D. Murgu, MD, FCCP (✉) • S.P. Stoy, MD
The University of Chicago Medicine,
5841 S Maryland Ave, MC 6076,
Chicago, IL 60637, USA
e-mail: smurgu@medicine.bsd.uchicago.edu

[1]Central airway obstruction is defined in this chapter as any clinically significant narrowing of the airway from the subglottis to the lobar bronchi.

J.P. Díaz-Jimenez, A.N. Rodriguez (eds.), *Interventions in Pulmonary Medicine*,
https://doi.org/10.1007/978-3-319-58036-4_13

Classification of Central Airway Obstruction	
Qualitative Criteria	**Qualitative Criteria**
I. Histology Benign Malignant **II. Mechanism of obstruction** Extrinsic compression Intraluminal exophytic; infiltrative; stricture Mixed **III. Dynamic features** Fixed Dynamic	**I. Severity of airway narrowing** Normal; Mild: Moderate; Severe **II. Extent of airway narrowing** Normal; Mild: Moderate; Severe **III. Functional Impairment** Normal; Mild: Moderate; Severe

Fig. 13.1 Classification of central airway obstruction based on qualitative and quantitative criteria. Dynamic features refer to the phase of respiration during which there is flow limitation. In a fixed obstruction, there is limitation to flow both during inspiration and expiration, while in dynamic obstruction, only during a respiratory phase, as is the case with tracheomalacia. The quantitative criteria could be objectively assessed. For instance, based on physiologic data, for tracheal stenosis, the severity of airway narrowing can be quantified as mild (<50% narrowing), moderate (50–70%), and severe (>70%); the extent is the vertical length of the stenosis and, based on outcomes from bronchoscopic and open surgical interventions, can be quantified as mild (<1 cm), moderate (1–4 cm), and severe (>4 cm). Functional impairment can be objectively assessed using a variety of validated tools such as MRC dyspnea scale or WHO functional class

Historical Perspective

Since the beginning of documented airway stent insertion at the end of nineteenth century, tracheobronchial prostheses have been generally made of two types of materials: metal or rubber. As the understanding of airway physiology and its interaction with the prosthetic materials has advanced, the manufacturers take into consideration the biomechanical and biocompatibility characteristics, even though this information is not always available to the practicing bronchoscopist. Clinically used airway stents are currently made of polymers, alloy metallic mesh, or a combination of the two (aka hybrid stents). In general, the pure metallic stents have been abandoned because of severe complications.

The future may see the incorporation of treatment agents such as chemotherapeutic (i.e., mitomycin C, paclitaxel), radioactive agents or bioabsorbable stents [1]. In theory, stents made of bioabsorbable polymers may be ideal, especially in pediatric population, as they can support the airway wall and dissolve after the remodeling process is completed, thus providing temporary airway stiffness, sometimes necessary in infants with tracheobronchomalacia. Such stents have the advantage of potentially avoiding the need for repeated interventions under general anesthesia for removal or revision [2–4]. Only pilot human studies of bioabsorbable stents have been published to date [5, 6]. Bioabsorbable drug-eluting stents have the potential advantage of reducing the risk of stent-related complications, but they have only been studied in animal models of benign tracheal stenosis [1]. In animal models, novel bioabsorbable stents (made of polycaprolactone) with cisplatin elution have been developed to overcome some of the problems associated with chronic indwelling stents (tumor ingrowth, fracture, migration) [7]. The mechanical strength of these stents was shown to be comparable to the strength of Ultraflex SEMS and provided a steady release of cisplatin for >4 weeks in vitro. The in vivo study showed sustained cisplatin levels in rabbit trachea for >5 weeks with a minimum drug level in blood. Histologic examination showed an intact ciliated

epithelium and marked leukocyte infiltration in the submucosa of the stented area, findings suggesting potential use in malignant CAO. In a recent human study, six biodegradable polydioxanone tracheal stents were safely implanted in four patients with benign inoperable tracheal stenosis. The authors report that all patients had "some" benefit from treatment and suggested that further research is needed to fully assess the outcomes of this therapy [8]. Whether these stents will be incorporated into clinical practice remains to be determined.

As of this writing, the originally described problems of migration, granulation, mucus plugging, infection, and even airway perforation and fatal hemoptysis are still present after stent insertion [9]. Therefore, operators have to carefully review the indications and expected results before inserting airway stents.

Indications

Airway stents are generally used for symptomatic extrinsic airway compression with or without associated airway mucosal infiltration. Stents can also be used if there is still significant (generally considered more than 50%) narrowing after the endoluminal component of a purely exophytic or mixed type of obstruction has been treated using one or more bronchoscopic techniques[2] [10]. Various stents have been used as well for sealing malignant esophagorespiratory and bronchial stump fistulas. Stents are occasionally used to improve symptoms of severe tracheobronchomalacia or excessive dynamic airway collapse, in patients who are refractory to more conservative measures (i.e., continuous positive airway pressure) and are not candidates for an open surgical procedure (i.e., tracheobronchoplasty for diffuse disease or sleeve resection for focal disease) [11, 12]. Studies performed within the last 20 years have shown that airway stents improve lung function in patients with central airway obstruction. In this section, we will describe the indications of stent insertion based on the mechanism of obstruction.

Extrinsic Compression

Extrinsic compression from benign or malignant thyroid disease, primary lung tumors (Fig. 11.2), mediastinal masses, or massive intrathoracic lymphadenopathy is the most common indication for airway stent insertion. Rarely, vascular abnormalities such as aortic aneurysm, vascular sling, and double aortic arch may cause symptomatic airway obstruction and may require stent insertion for patients who do not undergo corrective surgery.

Intraluminal Obstruction

Stent insertion may be useful in selected cases of endoluminal exophytic benign central airway obstruction (CAO); this is the case of refractory endobronchial recurrent respiratory papillomatosis (RRP) when medical and other endobronchial therapies fail to restore airway patency. Case reports show that papilloma debulking and silicone stents can offer adequate control of symptoms [13]. However, histologically benign intraluminal obstruction necessitating stent insertion is mostly caused by strictures, either idiopathic or related to other disorders. The most common cause of benign strictures is post-intubation and post-tracheostomy stenosis (Fig. 13.2), but it is important to note that a variety of other conditions associated with strictures should be ruled out before making the diagnosis of idiopathic stenosis. This is relevant as the management strategies need to be individualized. Examples include granulomatosis with polyangiitis (GPA; formerly Wegener granulomatosis), amyloidosis, sarcoidosis, ulcerative colitis, post-tuberculosis, or *Klebsiella rhinoscleromatis* infection. For example, 12–23% of patients with GPA develop tracheobronchial stenosis. A recent multicenter retrospective study of 47 patients

[2]These include rigid or flexible bronchoscopic resection, laser, electrocautery, cryotherapy, photodynamic therapy, or brachytherapy and are described in detail in other chapters in this book.

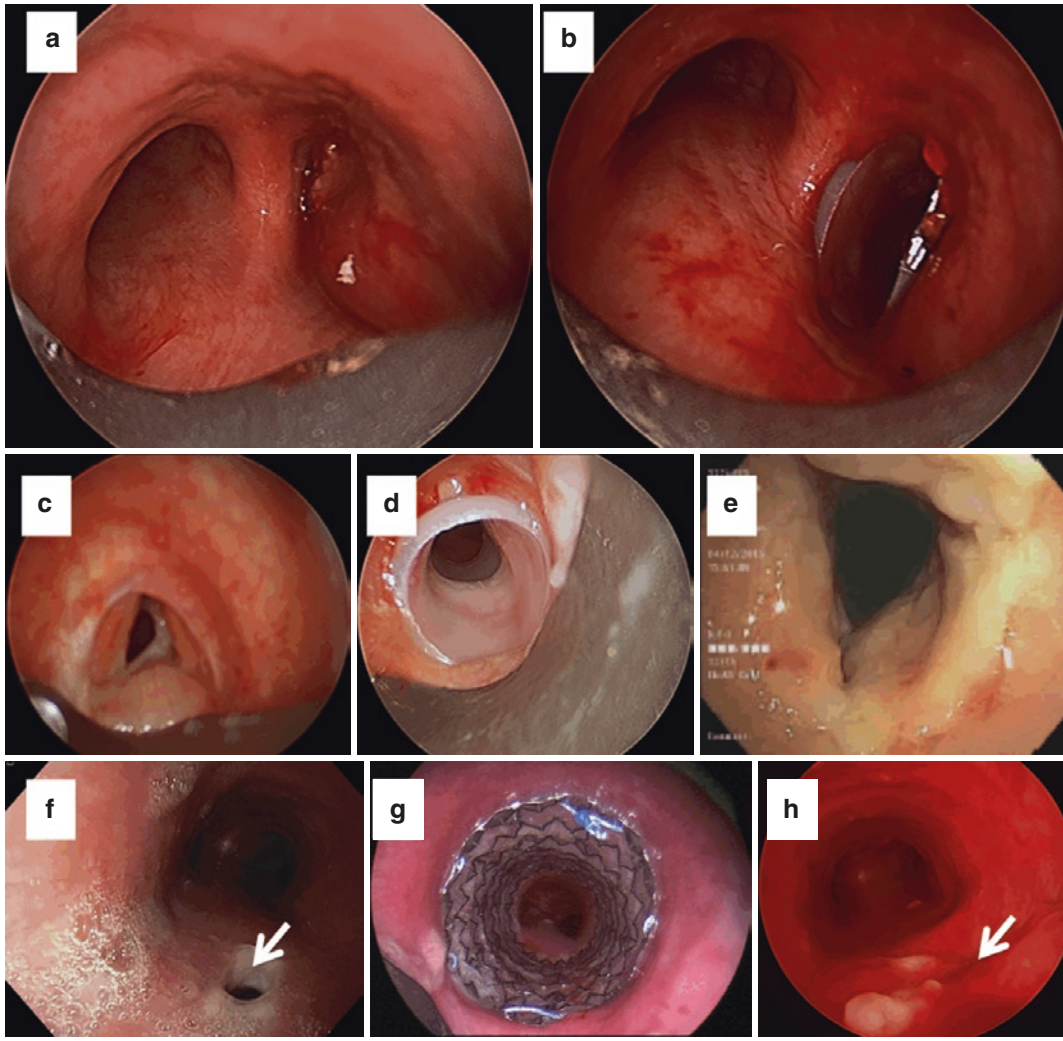

Fig. 13.2 Indications for airway stent insertion. Severe extrinsic compression of the right mainstem bronchus due to primary lung cancer, before (**a**) and after (**b**) silicone stent insertion. Severe, complex post-tracheostomy, triangular or A-shaped stenosis with malacia in a nonsurgical candidate before (**c**) and after (**d**) a 16 × 40 mm straight silicone stent was inserted. Follow-up bronchoscopy triggered by excessive coughing and inability to raise secretions demonstrated restored tracheal patency, but the stent migrated down to the main carina (**e**) and required removal. Benign gastro-tracheal fistula (**f**) after esophagectomy and gastric pull-up procedure. As repeat surgery was unsuccessful at closing the fistula, a fully covered SEMS was used (**g**). Four weeks later the stent was removed and, fortunately, the airway wall completely healed (**h**) without recurrence of the fistula during the follow-up

with GPA-associated tracheobronchial stenosis found that these patients benefit from a delay in any interventional procedures following the diagnosis, allowing for a "cooling off" period from the associated inflammation. It is also advisable to have patients on an increased dose of corticosteroids to >30 mg/day during the periprocedural period [14].

The remainder of this section will focus on the role of stent insertion for benign stenoses associated with intubation (PITS) and tracheostomy (PTTS). The incidence rate of benign tracheal stenosis following intubation has historically ranged from 0.6 to 19% and following tracheostomy from 6 to 65%. Fortuitously the advent of low-pressure cuffs has substantially decreased

these rates (by up to tenfold), yet still 1–5% of patients suffer from traumatic symptomatic PITS or PTTS, typically occurring 2–3 months following the event [15]. It remains to be determined whether the introduction of new mechanical ventilators with continuous endotracheal cuff pressure monitoring could further reduce the incidence of PITS. For post-intubation or post-tracheostomy strictures, stent placement should be considered only in inoperable patients; in addition, patients need to be symptomatic and the lumen of the airway below half of its normal after other interventional endoscopic techniques have been applied.

Benign airway obstruction can be classified in a variety of ways, and management techniques and success rates vary based on the type of stenosis. For example, a simple web-like stricture (extent less than 1 cm), which is dilated and does not recur, will not require a stent [16, 17]; a complex stricture, however, often has associated chondritis, and dilation alone (with or without laser assistance) is not usually successful, and a stent would be required to maintain airway patency [18]. Another way of classifying strictures uses the terms "structural" and "dynamic": a structural stenosis is a result of scarring and fixed constriction of the airway—this is the most common form. A dynamic stenosis is a form of focal, localized malacia with variability of obstruction dependent on the variability of transthoracic pressures during respiration. Another classification has been proposed to exist: that of a dynamic A-shaped tracheal stenosis (DATS) which is an amalgamated variation that combines both a structural stenosis from a fractured anterior cartilage ring with a dynamic stenosis from posterior malacia (Fig. 13.2). This results in a triangular "A-shaped" trachea on imaging. This is an important finding as the structural component is not the result of scaring/shrinkage of the trachea, and as such the management of DATS differs significantly from that of other structural forms of benign airway strictures. Specifically, patients with DATS do not benefit from dilation alone. At the same time, due to the dynamic component to the stenosis, patient experiences higher rates of stent migration than typical structural stenosis patients (Fig. 13.2) [15].

Silicone stent insertion performed using rigid bronchoscopy under general anesthesia is considered an acceptable alternative to surgery for inoperable patients with complex tracheal strictures. A 2016 retrospective study of 90 patients undergoing stenting for histologically benign airway obstruction showed that in patients with simple stenosis undergoing stenting, there was a 100% success rate with a single stent placed and mean stent duration of 5.6 months. On the other hand, patients with complex stenoses did not fare as well: 45% required multiple re-stenting procedures, 60% required stent repositioning, the stents remained in place for 12 months, and despite this the success rate was 70% at 1 year [17]. In an older study of 42 patients with complex stenoses, only 9 were surgical candidates, and 33 were treated with silicone stent insertion, with a success rate of 69% [19]. The success rate of bronchoscopic treatment once stents are removed (usually after at least 6 months) in cases of complex stenosis is reportedly low (17.6%) suggesting the need for long-term indwelling airway stent. A higher rate of airway stability after stent removal (46.8%, in 22 out of 47 patients) was described after stents remained in place for a longer period of time (mean of 11.6 months) [20], with almost 50% of patients (12/22) having their stents for more than 12 months. Predictors of success of bronchoscopic treatments are stenoses less than 1 cm in vertical extent and without associated malacia (i.e., chondritis). Lesion extent (i.e., height) and intubation-to-treatment latency have also been reported to independently predict the success of bronchoscopic intervention. In one study, 96% of patients with lesions <3 cm in height were successfully treated bronchoscopically, but the success rate decreased to 20% for lesions longer than 3 cm. Patients with stenosis present for more than 6 months since the original injury were also less likely to be successfully treated bronchoscopically [21], suggesting that the established fibrotic tissue counteracts the expansile force of the remaining cartilage [22]. In fact, knowing the integrity of the cartilage in post-intubation or post-tracheostomy stenoses is important in the treatment decision-making process. In complex post-intubation/tracheostomy

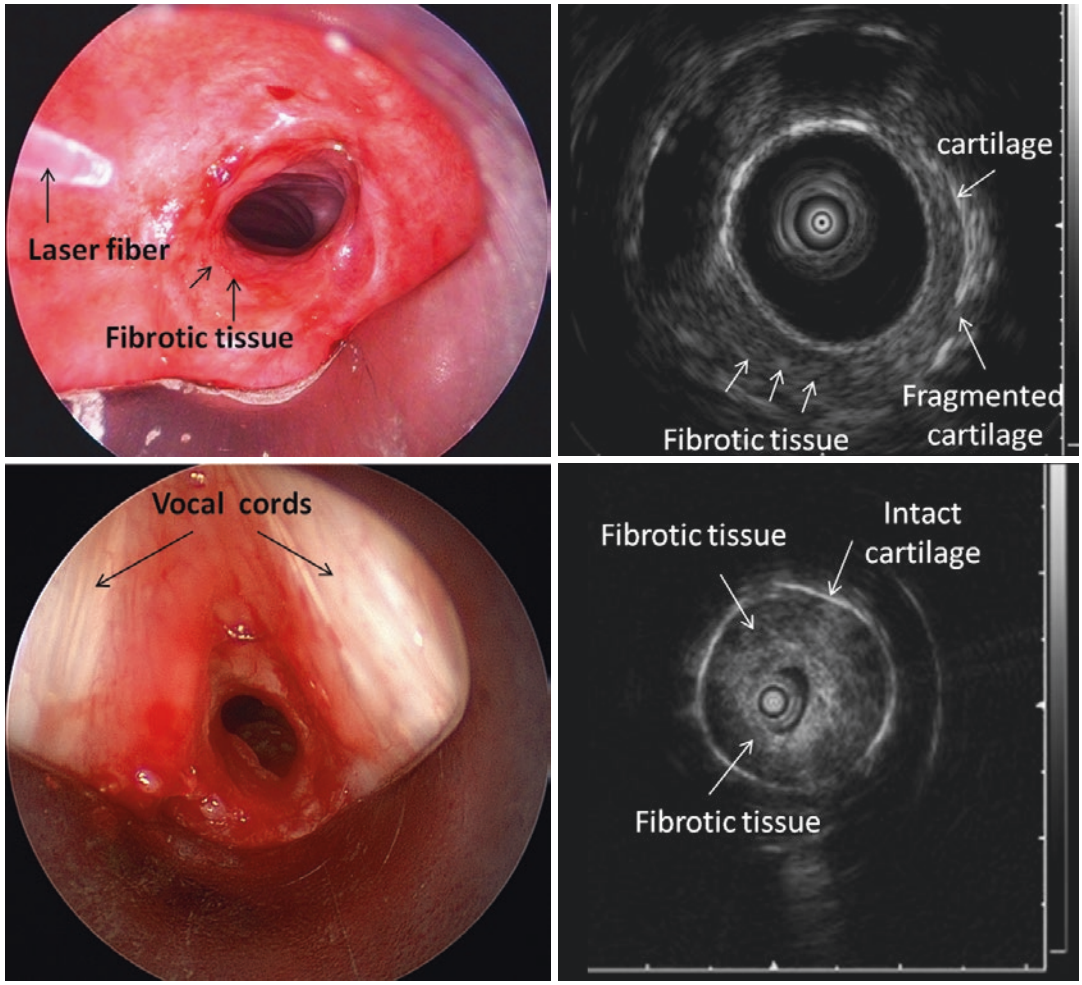

Fig. 13.3 Rigid bronchoscopic and sonographic view of laryngotracheal stenosis. In the *upper panel*, the circumferential post-intubation tracheal stenosis is noted, but on white-light imaging, the cartilage cannot be assessed. High-frequency endobronchial ultrasound (20 MHz probe) can identify the cartilage and its disruption. The knowledge that the cartilage is affected could impact management since simple laser-assisted mechanical dilation without stent insertion is unlikely to maintain airway patency in the long term. In the *lower panel*, idiopathic subglottic stenosis at the level of the cricoid is seen on white-light imaging, but the intact cricoid cartilage itself is only identified on high-frequency endobronchial ultrasound

stenosis, cartilage integrity or lack thereof is not always easily assessed on white-light bronchoscopy, mainly because of the overlying stenotic hypertrophic tissues [23] (Fig. 13.3). To assess the integrity of the cartilage, one may use high-frequency endobronchial ultrasound (20 MHz balloon-based radial probe) during the bronchoscopic intervention. The EBUS image using this system has a high resolution and allows visualization of the stenotic tissue and the cartilaginous structures and may be a surrogate of gross histology for tracheal stenosis; for instance, in idiopathic tracheal stenosis, the cartilage is known to be normal, but there is clear hypertrophy of the mucosa and submucosa as visualized by EBUS as well. On the other hand, in complex stenoses, there is partial or total destruction of cartilage histologically which can be identified by EBUS [23] (Fig. 13.3).

When used for benign stenosis, silicone stents are preferable and can be helpful for splinting post-intubation/tracheostomy stenoses and are

considered appropriate to palliate airway narrowing in nonsurgical candidates[3] [18, 24, 25]. Stent-related complications, however, are not uncommon in this disease and include migration, obstruction from secretions, infection, and significant granulation tissue formation at the proximal or distal extremities of the stent [9, 26].

Silicone T-tubes (Montgomery T-tubes) or tracheostomy tubes are sometimes used for benign tracheal strictures; they should be inserted through the area of stenosis, if possible, to conserve airway not involved by the stenosis lesion. For most patients who do not require mechanical ventilatory support, a silicone T-tube could provide symptomatic improvement [27]. These therapies are warranted in the few patients with critical stenoses who are neither candidates for surgery or indwelling airway stent insertion or who develop recurrence after such interventions [18]. T-tubes can also be used when tracheal resection and reconstruction or dilation techniques are either not available or have failed or as a solution for patients who had silicone stent placement complicated by frequent migrations [26]. In a large case series including 53 patients with complex tracheal stenoses (24 post-tracheostomy), silicone T-tube insertion was effective in 70% of patients with limited complications [28]. The sharper edge of the proximal aspect of the T-tube, in cases when it has to be cut, suboptimal tracheostomy tract (i.e., non-midline stoma), as well as its placement within 0.5 cm from the vocal cords are known risk factors for granulation tissue development[4] [28]. In addition, airway secretions may become dry and cause obstruction. Patients, families, and referring physicians probably benefit from instruction on how to care for and monitor T-tubes. Frequent bronchoscopies may be necessary to remove mucus plugs, with some investigators performing a 3–4 biweekly bronchoscopies, followed by once every 4 weeks once stent patency has been documented [28].

Self-expandable metallic stents (SEMS) have been associated with significant complications and are to be avoided, if possible, in benign disorders. Immediate symptomatic improvement is reported and expected, but the long-term complications are common and may be life threatening [29].

Self-expandable silicone stents, contrary to metal stents, have the advantage of being easily removable. They are, however, placed under rigid bronchoscopy or suspension laryngoscopy. Some of these silicone stents have been studied in benign airway obstruction including tracheal stenosis and malacia [30]. While immediate symptom palliation was established in most cases, the incidence of complications was high (75%) with stent migration occurring in 69% of cases [30, 31].

Postoperative Tracheobronchial Stenosis

A variant of histologically benign tracheal stenosis, postoperative tracheal stenosis (POTS) is a challenging problem following tracheal resection. Despite improved recognition and surgical techniques, the rate of POTS is 2–9% following tracheal resection. The majority patients with POTS are not candidates for further surgical management due to a combination high general surgical risk, poor lung function, and technical difficulties associated with previously resected tracheal segments. As such, bronchoscopic intervention is considered a therapeutic option. In a single-center retrospective review, 30 patients with POTS managed by bronchoscopic intervention were studied. Interventions included dilations (balloon or bouginage), YAG laser, and stenting (63% underwent silicone stents, no metallic stents were used). The majority (97%) achieved improvement in dyspnea within 24-h post-procedure. Stents were successfully removed in 37% of patients. Average stent duration in those amenable to removal was 7 months; 16% of those with stents removed developed tracheobronchomalacia [32].

[3] Coexistent diseases: coronary heart disease, severe cardiac or respiratory insufficiency or poor general condition.

[4] Granulation tissue formation at the proximal end of the T-tube has also been described, and it is believed that chronic airway irritation incites infection and promotes or aggravates granulation tissue formation.

Mixed Obstruction: Malignant Central Airway Obstruction

Malignant central airway obstruction (CAO) is a frequent complication of primary lung cancer and other cancers, which metastasize to the chest (especially breast, colon, melanoma, and renal cell cancers). Malignant CAO can be intrinsic (endobronchial/intraluminal), extrinsic, or a mixed obstruction, which has features of both intrinsic and extrinsic obstructive patterns. The most common form of malignant CAO is a mixed obstruction [33]. In a series of 172 patients who underwent stent insertion for malignant CAO at a tertiary cancer institution, 62.5% of the stents were placed for mixed disease, while only 16.4% and 14.8% were placed for extrinsic compression and intraluminal obstruction, respectively [9]. In general, the management principles for malignant intraluminal obstruction are the same as those for benign disease: if there is still obstruction after recanalization with various ablative techniques, if extrinsic compromise is present, or if there is a loss of airway structure (i.e., severe malacia due to cartilage invasion and destruction by tumor), a stent is placed to maintain airway patency.

Management of malignant CAO often requires a combination of multiple different management modalities. The choice of technique and method is operator dependent and is contingent not only on the etiology of the obstruction but also operator familiarity and preference. To study the impact of procedural volume and choice of technique in bronchoscopic management of malignant CAO, a large multicenter retrospective review of bronchoscopic management of patients with malignant CAO was undertaken from the American College of Chest Physicians (CHEST) Quality Improvement Registry, Evaluation, and Education (AQuIRE) registry. Overall the study found that despite significant inter-institutional differences in procedural preferences and volumes, there was no impactful difference in technical success and that one specific therapeutic modality could not be recommended over another [33].

Interventional treatment of malignant CAO is considered to be primarily palliative as once cancer progresses to the point of CAO, it is almost invariably incurable. As such endoscopic interventions focus predominantly on attempting to improve quality of remaining life. Relieving the CAO due to malignant disease has been proposed to prevent post-obstructive pneumonia, sepsis, and septic shock, allow extubation, change in level of care, permit initiation of systemic therapy, and potentially improve survival. There is evidence that bronchoscopic therapies often provide acute relief of the obstruction, improve quality of life, and serve as a therapeutic bridge until systemic treatments become effective [34–36]. Prospective studies show that bronchoscopic intervention for malignant CAO is associated with improvement in the six-minute walk test (6MWT), spirometry, and dyspnea [37]. In addition, studies show that airway stent insertion resulted in significant palliation of symptoms in patients with malignant CAO as evaluated by Medical Research Council (MRC) dyspnea scale and performance status [38].

In the AQuIRE registry mentioned above, bronchoscopic interventions were associated with a significant decrease in dyspnea (decrease in Borg score by 0.9 ± 2.2). Specifically, 48% reported clinically significant improvement in dyspnea, 43% reported no change, and 9% had worsened dyspnea. Of particular relevance, dyspnea improved proportionally to the pre-procedure severity of dyspnea: the more dyspneic prior to procedure, the more improvement in dyspnea after the intervention. Another notable finding was that those with lobar (as opposed to more central) obstruction were less likely to have much improvement in dyspnea. Bronchoscopic interventions were also associated with a significant increase in health-related quality of life (HRQOL). Overall 42% had a significant improvement of HRQOL, 33% remained unchanged, and 25% reported worsened HRQOL. Again, as with the predictors of dyspnea relief, a higher baseline Borg (i.e., worse baseline dyspnea) predicted a more pronounced improvement in HRQOL, while those with lobar obstruction were found to have less improvement in HRQOL [33]. While airway patency was improved in >90% of patients, less than half improved their HRQOL scores. These findings

suggest that we need better prediction models for who will improve dyspnea and HRQOL after such interventions. Despite the focus on palliation and improved quality of life with these procedures, a significant post-procedural survival advantage was also apparent in those without severe performance limitations prior to their procedures when compared with historical controls [38].

The presence of stridor (reflecting critical CAO) prior to intervention was found to be a poor prognostic indicator for survival in patients undergoing bronchoscopic intervention for malignant CAO: those without stridor had a 1-year and 2-year survival of 35.5% and 31%, respectively, while those with stridor had a 1-year and 2-year survival of 12.5% and 0%, respectively. Patients requiring stent placement for malignant CAO as opposed to dilation ± other non-stenting interventions had significantly lower 1- and 2-year survivals [39]. It is not clear whether lower survival rates are because of the stenting or just because patients requiring stents had more severe/extensive airway obstruction.

Subsequent chemotherapy and/or radiotherapy has been shown to increase disease-free survival during the first year after restoration of airway patency [34, 40]. A retrospective single-center study of 48 patients with malignant CAO who underwent bronchoscopic intervention reviewed the effects of chemotherapy following bronchoscopic interventions. The patients who received post-procedural palliative chemotherapy had a median survival of 6 months with a 1-year and 2-year survival of 35% and 31%, respectively. Those patients who received no post-procedural chemotherapy had a median survival of 2.5 months with a 1-year and 2-year survival of 18% on 14%, respectively [39]. In addition, it appears that airway stent insertion followed by adjuvant therapy may improve survival of treatment-naive patients with severe symptomatic airway obstruction caused by advanced lung cancer. In one study, while the performance status and dyspnea scales improved in both treatment-naive and terminal-stage lung cancer, the median survival time and 1-year survival rate after stent insertion were 1.6 months and 5.1%, respectively, in the terminal-stage group and 5.6 months and 25.0%, respectively, in the treatment-naive group [41].

Lung cancer patients who develop respiratory failure due to CAO have particularly poor prognoses: only 25% are successfully liberated from the ventilator, and 40–70% die in the hospital. In addition to the quality of life issues, ventilated patients are often not considered candidates for additional oncologic treatment. Furthermore, patients with malignant CAO are given low priority for ICU level admission in the Society of Critical Care Medicine ICU admission recommendations [42], as they are considered to have low probability of reversibility and survival. A small single-center retrospective study addressed this assumption of lack of reversibility. Twelve patients with non-small cell lung cancer with associated CAO resulting in respiratory failure requiring mechanical ventilation who were not candidates for surgical procedures were managed with bronchoscopic intervention and various combinations of mechanical debulking, laser resection, and airway stenting: 66% underwent stenting. The majority (83%) was successfully liberated from mechanical ventilation, and the post-procedural median survival was 313 days. As such bronchoscopic intervention should be considered for lung cancer patients with respiratory failure due to CAO [43].

Stump Fistulas

A less common indication for stent insertion is to cover large stump fistulas after lobectomy or more commonly, after pneumonectomy [44]. In general, management strategies for bronchopleural fistula (BPF) depend on the underlying histology (malignant versus benign), size, time to fistula formation postsurgery, and health status of the patient. Surgery is the treatment of choice of this condition, but bronchoscopic techniques have been advocated as an option when surgery is not possible or has to be postponed [45]. Surgical repair is not a good option for patients requiring mechanical ventilatory support because postoperative mechanical ventilation is associated with a high failure rate due to persistent barotrauma on

the repaired stump [45]. As a general rule, when stents are used for this indication, a large stent must be used to seal the stump fistula as tight as possible in order to prevent aspiration pneumonia and empyema and allow satisfactory single-lung ventilation when the patient requires mechanical ventilation. Stent selection would depend on the size and location of the fistula, as well as on the physical properties of the stent and the operator's ability to manage potential stent-related complications. Several case reports and case series of endobronchial stent insertion for isolated fistulas have been published [46]. The effect of case selection is difficult to assess from the limited literature on this topic.

Esophagorespiratory Fistulas

Tracheoesophageal or broncho-esophageal fistulas can be covered by airway stents. While these fistulas can be congenital, the majority are acquired either after esophagectomy, after intubation, or in the setting of malignancy. Benign esophagorespiratory fistulas (ERFs) are not expected to improve after stent insertion, and, in fact, it should only be considered as a palliative intervention if there are no operative modalities (Fig. 13.2) [47].

Malignant ERF is common in esophageal cancer, having a 5–15% occurrence, and occurs rarely in bronchogenic carcinoma (~1%). Once developed, the prognosis is poor, with a poor QOL and 3–4 month survival. Although surgical resection and reconstruction has the greatest potential benefit, it comes at a high cost of complications and prolonged hospitalized recovery. Alternatively, gastro/jejunostomy tube feeding is a strategy utilized to minimize effect of malignant ERF, but this may not be accepted by patients and has the potential to further reduce quality of remaining life [48]. Palliation for malignant ERF is usually achieved with endoscopic placement of esophageal, airway, or parallel (dual) stent insertion (in the esophagus and airway). Dual stent insertion appears to work better than a single prosthesis. Particular attention should be paid to airway compression or erosion caused by placement of esophageal stents; if there is concern for significant tracheobronchial obstruction, operators should consider placement of an airway stent prior to the esophageal one (Fig. 13.4).

The choice of tracheal stent used for ERF closure should take into consideration the size and location of the fistula. The Freitag classification system [49] was developed to systematically define the location and severity of central airway stenosis, but this system can be used to define the location of an ERF: Location I, upper third of trachea; II, middle third or trachea; III, lower third of trachea; IV, carina; V, right mainstem; VI, bronchus intermedius; VII, left mainstem; and VIII, left distal bronchus. Using this system and by defining a small fistula as one that is <1 cm in size, a single center developed an algorithm for stent choice in ERF stenting: an I-shaped stent for small fistulas in Locations I, II, and VIII; an L-shaped stent for small fistula in Locations V, VI, VII; and a Y-stent for any fistulas in Locations III or IV or large fistulas in Locations II, V, and VII. This approach resulted in complete fistula closure in 72% of patients and clinically beneficial partial closure in the remaining patients [48].

A dedicated fistula stent, the DJ cufflink-shaped prosthesis, was designed exclusively for closure of malignant ERF secondary to esophageal or lung cancer. It can be sized to the fistula diameter to occlude the abnormal communication [50, 51]. Insertion of silicone Y-stents was shown to improve symptoms, reduce infections, and improve the quality of life in patients with malignant ERF. Mean survival of these patients, however, remains dismal and is in the range of 2 months [52]. A conservative palliative approach including only symptomatic control but no palliative interventions (i.e., stent insertion) is not unreasonable especially since interventions in this frail population could be harmful. Without treatment, however, survival may be limited to only a few days [53]. On the other hand, a recent prospective study of 112 patients with malignant ERF, airway stents were inserted in 65 (58%) patients, esophageal stents in 37 (33%) patients, and both airway and esophageal stents in 10 (9%) patients. Contrary to previous data, the authors found an overall mean survival of 236.6 days

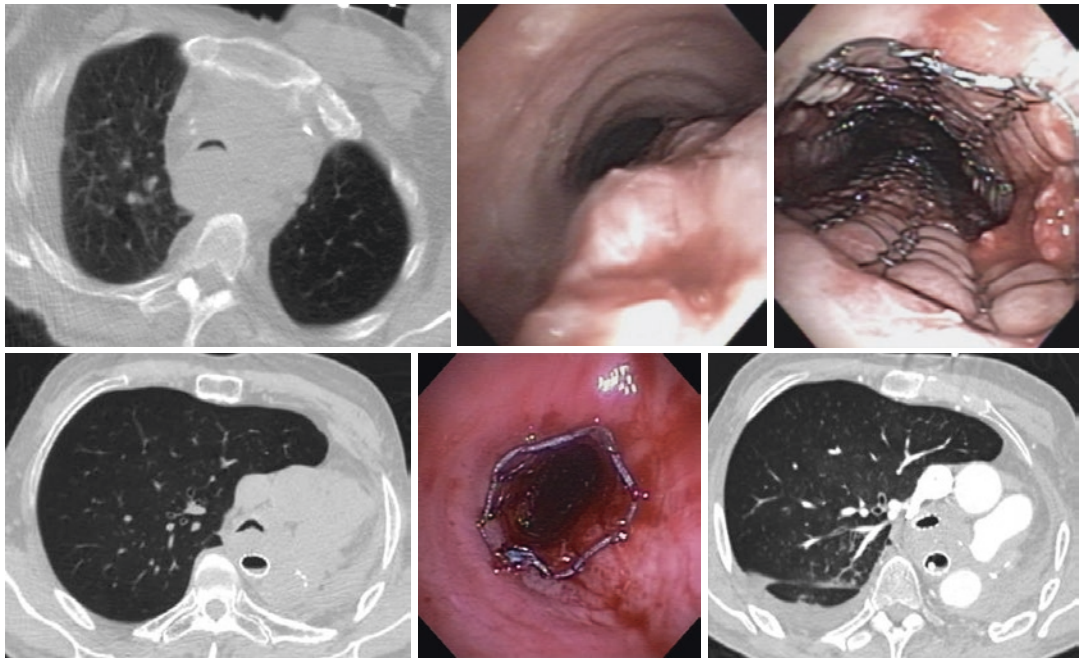

Fig. 13.4 Airway stents in obstruction caused by esophageal tumors. In the *upper panel*, chest computed tomography (CT) shows severe tracheal narrowing from a mediastinal mass, known to be esophageal carcinoma. Bronchoscopy confirmed the CT findings, and a partially covered metallic stent was placed to palliate the airway obstruction prior to esophageal stent insertion for dysphagia. In the *lower panel*, severe tracheal and right mainstem obstruction occurred after the insertion of an esophageal stent and resulted in respiratory failure in this patient with poor lung function from his previous pneumonectomy. A partially covered metallic stent was inserted from the lower trachea to the mainstem bronchus, palliating the obstruction and allowing liberation from mechanical ventilation

(airway stent 219.1 days, esophageal stent 262.8 days, and combined airway-esophageal stent 252.9 days). Since a few patients are operable, currently airway and/or esophageal stent insertion is mainly used with a palliative intent to improve the quality of life (QOL) in patients with malignant ERF [54].

Expiratory Central Airway Collapse

Airway stent insertion has been used to improve cough, secretions, and QOL in patients with expiratory central airway collapse (ECAC) [11, 12]. There are, however, different morphologic types of ECAC, for some of which stent insertion is not physiologically justifiable. Excessive dynamic airway collapse (EDAC) is due to bulging of the posterior membrane within the airway lumen during exhalation that narrows the lumen by 50% or more, and the cartilage is intact in this process. Tracheobronchomalacia (TBM), on the other hand, refers to softening of the airway cartilaginous structures [55]. The decision to insert an airway stent in these processes is complicated by at least two factors: (1) the lack of standardized definitions and cutoff values to define abnormal airway narrowing and (2) the lack of clear understanding if these entities are truly responsible for airflow limitation. In fact, the limit between normal and abnormal narrowing of the central airways has not been physiologically established, and different investigators propose different cutoff values. In addition, there is no standardized way to measure the narrowing in terms of location or respiratory maneuver (Table 13.1) [55]. To illustrate this lack of consensus, a study found that almost 80% of normal individuals met the currently accepted 50% narrowing during forced exhalation criterion [56]. In an attempt to provide a common language for these patients with ECAC, a classification system was proposed

Table 13.1 Summary of classification systems for expiratory airway collapse

First author/year	Parameters	Comments
Rayl/1965	*Extent*: proximal, mediastinal, and intrapulmonary airways	Collapse during cough on cine-bronchography
Johnson/1973	*Severity*: four degrees and focal type	TM: more than 50% collapse during coughing on fluoroscopy
Feist/1975	*Etiology*: congenital and acquired	TM: more than 50% collapse during coughing on fluoroscopy
Jokinen/1977	*Severity*: mild, moderate, severe	First classification based on bronchoscopic findings
	Extent: TM, TBM, BM	
Mair/1992	*Etiology*: congenital, extrinsic compression, acquired	Described for pediatric TBM
	Severity: mild, moderate, severe	Empirical severity score
Masaoka/1996	*Etiology* and *extent* criteria	TBM: >80% collapse during expiration
	Pediatric, adult, and secondary	
Murgu/2007	*Functional class*	Stratification criteria (Functional class, extent and severity are objectively assessed)
	Extent	Morphology includes EDAC and three forms of TBM[a]
	Morphology	Origin: idiopathic or secondary
	Origin (Etiology)	
	Severity	

TM tracheomalacia, *TBM* tracheobronchomalacia, *BM* bronchomalacia, *EDAC* excessive dynamic airway collapse
[a]There are three morphologic types of TBM: crescent type, when the anterior wall is collapsing; saber-sheath type, when the lateral walls are collapsing; and circumferential or mixed type, when the anterior and the lateral walls are collapsing, as is seen with relapsing polychondritis

based on objective quantifiable criteria, which can be applied before and after stent insertion (Table 13.1) [55].

Studies show that in the short term (up to 10–14 days), airway stabilization with silicone stents in patients with expiratory central airway collapse (malacia and EDAC) improves symptoms, quality of life, and functional status [11, 12]. QOL and functional status scores improved in 70% of patients, and dyspnea scores improved in 91% of patients after stent insertion [12]. Stent-related complications in this case series included obstruction from mucus plugging and migration, and almost 10% of patients (5/52 patients) had complications related to the bronchoscopic procedure itself. Because the dynamic features of expiratory central airway collapse continuously alter the shape of the central airways as well as the surface contact between a stent and the airway wall, stent-related complications may occur more frequently in dynamic forms of airway obstruction than in fixed benign obstruction. Although not life threatening, these stent-related adverse events required multiple repeat bronchoscopies [11]. In another series of patients with mostly TBM, adverse effects from silicone stent insertion were very common, however, with a total of 26 stent-related adverse events noted in 10 of 12 patients (83%), a median of 29 days after intervention [11]. TBM due to relapsing polychondritis (RP) is one disease for which stent insertion is often necessary due to a diffuse lack of airway cartilaginous support. Both self-expandable metallic stents and silicone stents have been used in patients with malacia from RP [57, 58]. Sometimes, more than one stent may be required if symptoms persist after stent insertion, presumably because of distally migrated choke points [58]. Because airway stents are not the best solution for this disease, a more conservative approach such as continuous positive airway pressure (CPAP) may be safer. CPAP may indeed be considered a "pneumatic stent." The excessive airway narrowing in ECAC and the resulting turbulent flow result in increased airway resistance. This requires greater trans-

pulmonary pressures to maintain expiratory airflow and will increase the work of breathing and result in dyspnea. Thus, noninvasive positive-pressure ventilation such as CPAP decreases pulmonary resistance and can be used to maintain airway patency, facilitate secretion drainage, and improve expiratory flow. Small studies showed that nasal CPAP improves spirometry values, sputum production, atelectasis, and exercise tolerance, but its long-term efficiency has not been clearly demonstrated [59]. As of this writing, however, the limited published evidence suggests that QOL and functional status are improved in patients with ECAC undergoing stent insertion, but the lung function as measured by FEV_1 has not been consistently reported to improve after stent insertion or other forms of central airway stabilization (i.e., membranous tracheoplasty) [12]. These facts raise questions about the physiologic basis for stent insertion for both fixed and dynamic forms of CAO.

Physiologic Rationale for Airway Stent Insertion

In general, for symptomatic patients with fixed tracheal obstruction, a stent is inserted to improve the lumen to less than 50% obstruction; for symptomatic patients with dynamic obstruction, stents are meant to stabilize the airway at the collapsible segment responsible for flow limitation (aka choke point).

For tracheal stenosis, symptoms depend on the amount of pressure drop along the stenosis; this depends on the degree of the obstruction but also on the flow velocity through the airway narrowing. This flow dependence of symptoms explains why different patients with similar degree of airway narrowing have different clinical presentation, depending on their level of activity. These facts highlight the need to individualize treatment based not just on degree of narrowing as assessed by radiographic or bronchoscopic imaging but also on the stenosis impact on functional status. In fact, functional status and dyspnea scales may be more relevant than static lung function measurements, which were shown to weakly correlate with the MRC dyspnea scales in laryngotracheal stenosis [60]. In addition to functional status, a classification system for tracheal stenosis should include the extent, morphology, and severity of airway narrowing, factors that impact the decision to insert an airway stent. To quantify the severity of airway narrowing, the cutoff values used in the available systems are 50% and 70% to define moderate and severe stenosis, respectively [61]. These values seem to be justified by physiologic studies in which the investigators found that the effect of the glottis narrowing was noted to be of the same order as that of the 50% stenosis; these data suggests that a 50% or less narrowing may not even be clinically detected or require treatment; however, a significant pressure drop is seen at 75, 85, and 90% stenosis, pressure drop which correlates with significant work of breathing [62]. Based on these physiologic data, therefore, one could classify stenosis as mild, when less the 50% narrowing; moderate, from 50 to 70%; and severely narrowed when more than 70% of the lumen is occluded, justifying the practice of improving the airway lumen to less than 50% narrowing, with stent insertion, if necessary.

For expiratory central airway collapse, it is still not clear what degree of airway collapse is physiologically significant; furthermore, as of this writing, there are no accepted noninvasive physiologic tests to predict response to stent insertion. However, when patients have clear inability to raise secretions and recurrent pneumonia or even respiratory failure, then a stent is inserted regardless of the cause of collapse. From flow dynamics standpoint, the clinically relevant question in this process is whether stent insertion improves the expiratory flow. Physiologists proposed a theory to explain expiratory flow limitation, theory which is useful to understand the role of stent insertion in patients with dynamic CAO such as malacia or EDAC. Physiologic studies showed that once expiratory flow becomes limited at a given lung volume, there would be a region within the intrathoracic airway where intrabronchial and extra-bronchial pressures become equal (equal pressure point, EPP) (Fig. 13.5) [63]. At a given lung volume, driving pressure upstream

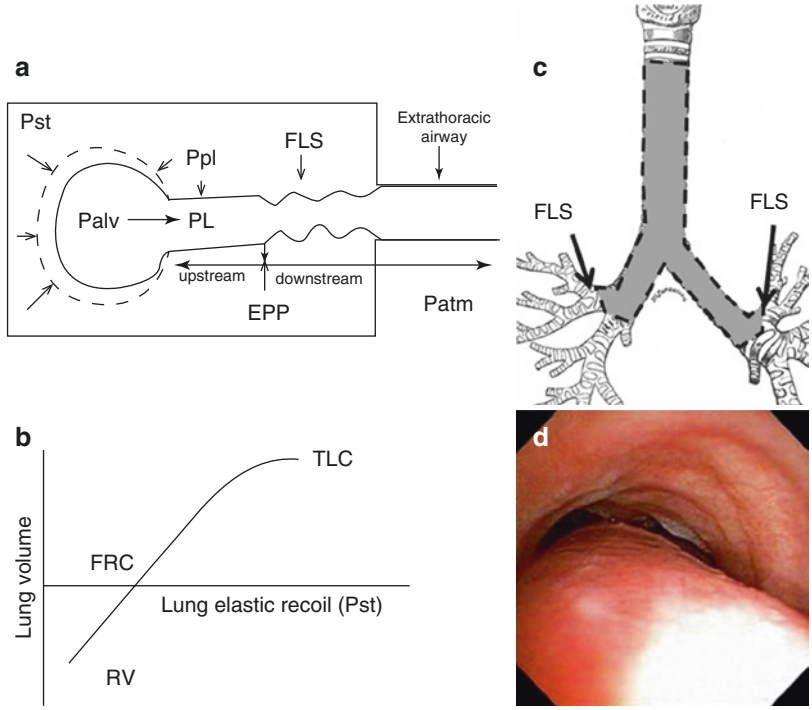

Fig. 13.5 Choke point physiology based on Starling resistor. (**a**) The alveolar pressure (Palv) is the driving pressure that causes gas to flow through airways during expiration and is approximately equal to the recoil pressure of the lungs (Pst) plus the pleural pressure (Ppl): Palv = Ppl + Pst. Normally, a pressure drop is required to accelerate a gas as it moves from an upstream (alveolarward) region of low velocity to a downstream (toward the mouth) region of high velocity. Because of this pressure drop, the intraluminal pressure (PL) eventually becomes equal to pleural pressure (Ppl). The point within the airway at which this occurs is called the equal pressure point (EPP). This equal pressure point (EPP) divides the airways into upstream segments (alveolarward from the EPP) at which transmural pressure is positive and downstream segments (mouthward from the EPP) at which the transmural pressure is positive within the extrathoracic airways and negative within the intrathoracic airways. At a given lung volume, driving pressure upstream from the EPP would be equal to lung elastic recoil, while downstream from the EPP, airways would be compressed during expiration. This region of compression of intraluminal caliber is referred to as a flow-limiting segment (FLS) or "choke point." (**b**) As lung volume decreases from TLC toward RV, the elastic recoil (Pst) decreases as well, and pleural pressure (Ppl) increases during forced expiration. (**c**) Thus, the EPP migrate upstream, resulting in a lengthening of the increasingly narrow downstream segment. This increases airway resistance and prevents further increases in expiratory airflow, causing the EPP to become fixed when airflow becomes constant. FLS has tracheal location at high lung volumes, (i.e., TLC), whereas others found FLS in lobar and segmental airways over a range in volume approximating TLC to functional residual capacity (FRC). As lung volume decreases during exhalation, the FLS move peripherally to the lobar/segmental and at most subsegmental bronchi. (**d**) Therefore, if the choke points (FLS) in humans are often located in the lobar bronchi, a mainstem bronchial or tracheal collapsibility should not result in any pressure drop between the mouth and the choke point and should not affect flow. Thus, bronchoscopic or radiologic detection of expiratory tracheal or mainstem bronchial compression (excessive dynamic airway collapse) should trigger a search for causes of airflow obstruction within the lung, not the central airways

(alveolarward) from the EPP would be equal to lung elastic recoil, because pleural pressure (Ppl) equals the intraluminal pressure (PL); downstream from the EPP (mouthward), airways would be compressed during expiration. This region of compression of intraluminal caliber is referred to as a flow-limiting segment (FLS) or "choke point." As lung volume decreases and pleural pressure (Ppl) increases during forced expiration, the EPP migrates upstream, resulting in a lengthening of the increasingly narrow downstream segment. This increases airway resistance and prevents

further increases in expiratory airflow, causing the EPP to become fixed when airflow becomes constant. EPP and therefore the FLS have tracheal location at high lung volumes (TLC), but as lung volume decreases during exhalation, the FLS moves peripherally, but they still stay in the central airways, in the lobar/segmental, the farthest in subsegmental bronchi [64]. Therefore, if the choke points in humans are often located in the lobar bronchi, a mainstem bronchial or tracheal collapsibility in the form of EDAC, often seen on CT or bronchoscopy, should not result in any pressure drop between the mouth and the choke point and should not affect flow. In fact, physiologists suggest bronchoscopic or radiologic detection of expiratory tracheal or mainstem bronchial compression (EDAC) should trigger a search for causes of airflow obstruction within the lung, not the central airways [65]. Loss of pressure in the abnormally narrowed peripheral airways in patients with asthma, COPD, or bronchiolitis will lead to decreased intraluminal pressure by the time that airflow reaches central airways, so that these airways (trachea and mainstem bronchi) will collapse at the weakest point, which is the posterior membrane. Thus, EDAC is most often a reflection of peripheral airway disease, but it can also be seen with morbid obesity due to increased pleural pressure and possible flow limitation at rest. A study of patients with obesity and COPD and normal volunteer controls found that EDAC was significantly associated with BMI (69% tracheal collapse among morbidly obese patients with BMI $\geq$ 35 compared to 57% in others, $p = 0.002$) [66]. EDAC has been documented in 22% of patients with COPD assessed by dynamic chest CT and in morbidly obese patients under general anesthesia likely due to positive pressures throughout the chest [67]. This does not mean that EDAC is responsible for flow limitation. In fact, even when defined as forced expiratory collapse of >80%, according to some reports, EDAC is not flow limiting as there is no significant correlation between end-expiratory or dynamic expiratory collapse and percent predicted FEV_1 [68].

That being said, recent epidemiologic studies show that EDAC is responsible for worse QOL in smokers [69]. A total of 8820 patients from 21 clinical centers were enrolled in the COPD gene study. On paired inspiratory-expiratory dynamic CT (measurements at aortic arch, carina, and bronchus intermedius), EDAC was found in in 443/8820 patients (5%). The primary outcome variable, quality of life (QOL) as measured by SGRQ, was worse in EDAC, which was also responsible for increased frequency and severity of exacerbations. In addition, some patients may improve their functional status after stent placement in the central airways not only for malacia but also for EDAC; one explanation is that improved central airway stability, regardless of which wall is collapsing, makes the flow less turbulent, similar to heliox, which was shown to improve exercise capacity in patients with moderate to severe COPD, even though these patients typically have choke points in the small airways (of 2 mm or less) [70]. It is possible than in the future, in addition to bronchoscopic and imaging methods, new physiologic or imaging studies may have a role in identifying the choke point physiology in CAO. For instance, using impulse oscillometry (IOS), increased resistance (i) at a low oscillation frequency (5 Hz) reflects an increase in total respiratory resistance suggestive of airway obstruction such as that found in patients with COPD, while increased R at a higher frequency (20 Hz) reflects more specifically increased central airway resistance such as that found in patients with malacia [71]. Until these methods are validated in large studies, a trial and error approach is still clinically used: temporarily place a stent and test whether the patient improves clinically; if they do, a surgeon may perform an external splinting procedure; if not, the stent is removed [72]. Another assessment method, more accurate but minimally invasive, is the intraluminal pressure monitoring using a small pressure catheter. As pointed above, dynamic airway compression causes the formation of FLS in the central airways during forced expiration. Both in animal and human studies, these FLS could be located with the use of intraluminal airway catheters by measuring lateral airway pressure (Plat) during induced flow limitation generated by either an increase in pleural pressure or a decrease in downstream pressure.

The measurements of lateral pressure in malacia before and after stent insertion show that before stenting, a large pressure difference is seen between the upper trachea and right lower bronchus and carina. After stenting, the pressure difference could vanish for both inspiration and expiration, and a regular respiratory cycle is seen [73]. By measuring lateral airway pressure on each aspect of the airway narrowing (proximal and distal) and plotting the two pressures against each other (pressure-pressure curves) during quiet breathing intraoperatively, the site of maximum obstruction and the degree of airway narrowing can be determined quantitatively [74]. Analysis of the pressure difference and the angle of pressure-pressure curve allow intraoperative estimation of the outcomes of a particular interventional bronchoscopic procedure. However, stents may improve flow but the choke points migrate distally. This process can be addressed either by additional stent insertion or by the use of noninvasive positive-pressure ventilation. Detection of choke point migration can be demonstrated bronchoscopically or by dynamic computed tomography (CT) in the form of airway wall collapse distal to the stent.

Stent Selection Criteria

Stent retrievability is an important criterion in patients with benign disease and with malignancy for which a temporary stent placement is expected. For example, for patients with malignant CAO who will undergo further systemic chemotherapy and/or radiation therapy and respond to treatment, the stent may become loose, migrate, and require removal [75]. Inserting a stent into the patient is not always the biggest challenge encountered in caring for these patients. It is advisable to select a stent that can be removed if necessary without causing further tissue damage. Another selection criterion is based on the stent's *morphology and positioning*: for instance, T-tubes require a tracheostomy, straight indwelling stents splint open the trachea and the mainstem bronchi, while bifurcated stents are placed at the main carina and sometimes at secondary carinas. One criterion to consider prior to insertion is the *stent material*. In fact, the traditional way to classify stents was based on material type: metal, polymers, and hybrid stents partially covered or fully covered.

The type of stent, however, should also be decided based on the *biomechanical characteristics* (dependent on the material but also on design and thickness) because stents differ greatly in their elasticity and resistance to angulation [76, 77]. The expansile force (strength) and ability to withhold angulation (buckling) varies among different types of stents. In this regard, the studded-silicone type stent and Polyflex stents have a high expansile force [60] and may be preferred in obstruction due to severe and extensive airway compression. However, for a distorted, curved airway, angulation properties become important because they determine whether the stent can conform to an acutely angulated airway and still remain patent, such as is often the case in patients with left main bronchial obstruction due to extrinsic compression (Fig. 13.6). In these cases, the Ultraflex stent may be a better choice than a straight silicone stent because of the Ultraflex stent's known resistance to angulation. A study evaluating the role of interventional bronchoscopy for malignant CAO showed that the most common stent used in the trachea and right mainstem bronchi (relatively straight airways) was the Dumon stent, while the most common one for the left mainstem bronchus (curved, tapered airway, often distorted in the setting of malignancy) was the Ultraflex stent, likely because of its better ability to withhold angulation[5] [78]. Therefore, stent biomechanics bench testing data such as the crush (expansile) force, infolding (angulation) properties, and fatigue life, which are for the most part considered confidential and proprietary information, may be very useful to the interventional bronchoscopist. For instance, fatigue life may become important in patients with benign etiology of CAO, especially

[5] In this study, patients with esophageal carcinoma involving the airway mostly required only stent placement without laser-assisted debulking, probably because the main problem was extrinsic compression.

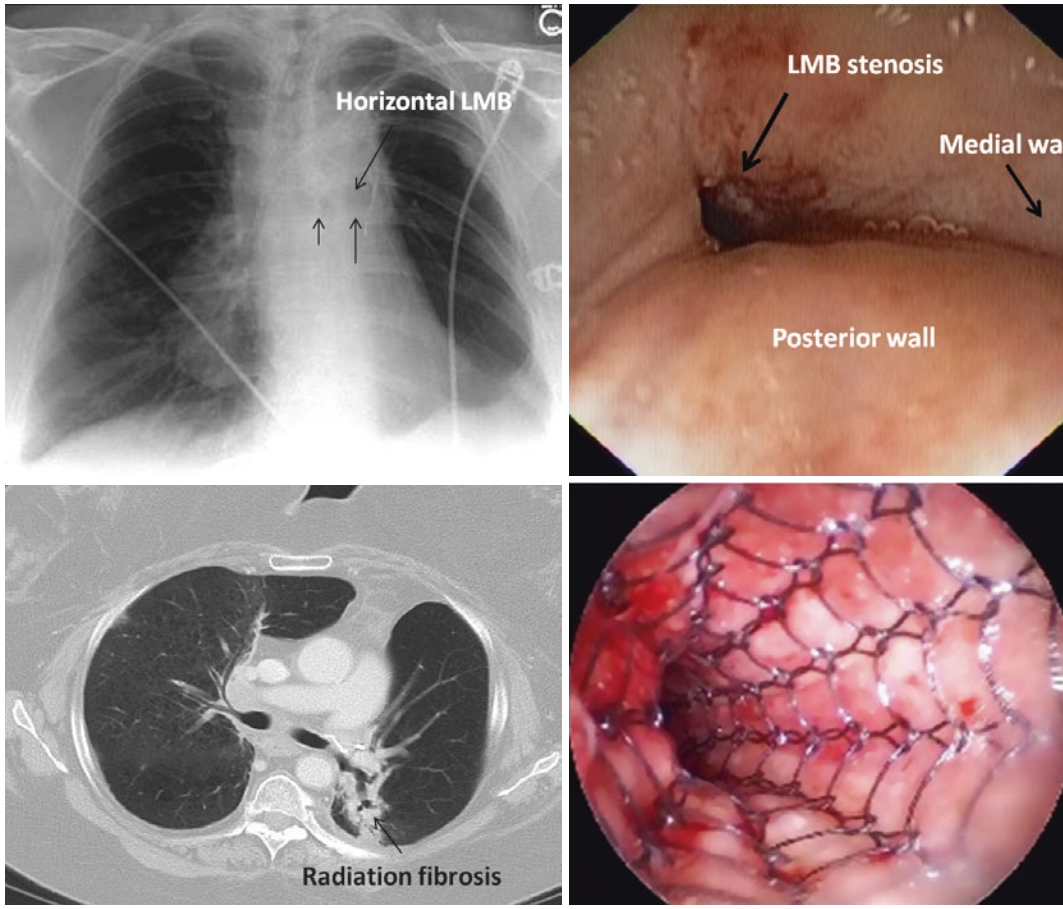

Fig. 13.6 Example of how airway anatomy impacts stent selection. Chest radiograph reveals nearly horizontal left main bronchus (*upper left*). Chest computed tomography shows that this was in part caused by volume loss from radiation fibrosis (*lower left*). Bronchoscopy revealed significant torsion of the left main bronchus and mid-distal left main bronchial stenosis (*upper right*). Due to its resistance to angulation, a partially covered self-expandable metallic stent was inserted to restore airway patency

malacia, in which cycled compression of the stent with each exhalation may lead to stent fracture and its associated complications.

In regards to *size*, following dilation, usually a stent with a diameter that is bigger than the remaining stenosis should be inserted. The actual size of the stent could be objectively determined by carefully evaluating the airway diameter using CT, measuring devices or even radial probe EBUS, or long range, anatomical optical coherence tomography. Many experienced rigid bronchoscopists, however, do not need or use these technologies and often choose the size of the stent based on the "tactile feedback" resulting from the viscoelasticity property of the airway; in general, the stent is slightly larger (1–2 mm) than the size of the dilating bronchoscope. However, if CT scanning is used to determine the stent size, one should remember that for mainstem bronchi, contrary to trachea, the diameter of the airway on the CT is different than the actual airway diameter, and corrections are necessary (Fig. 13.7) [79].

Contrary to size, the *length* of the stent does not have an important impact on flow dynamics [62]. That is simply because the resistance to flow is linearly and directly proportional to the length of stenosis and inversely proportional to the radius of the airway narrowing at

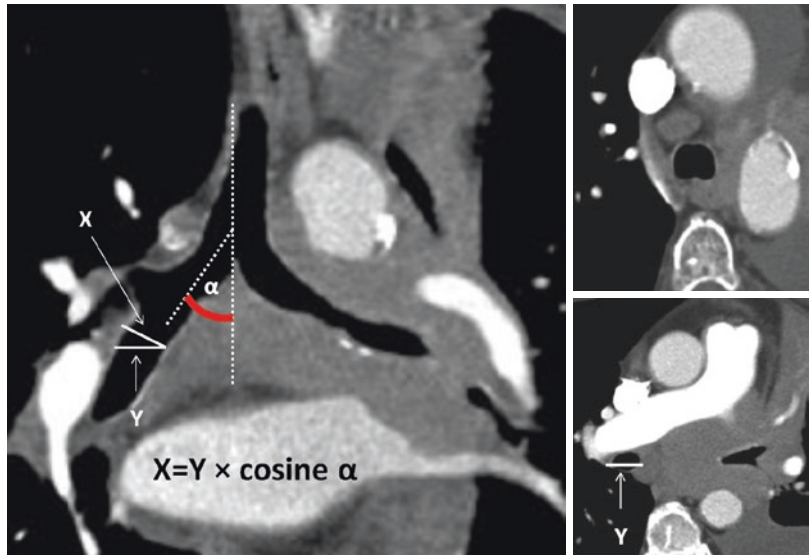

Fig. 13.7 Chest computed tomography use for stent size selection. Contrary to trachea (*upper right*), for mainstem bronchi and bronchus intermedius (*lower right*), the diameter of the airway on the CT (*Y*) is different than the actual airway diameter, and corrections are necessary (*right panel*). *Y* represents the measured transverse diameter of the bronchus on chest tomography, and *X* represents the corrected transverse bronchial diameter. *α* denotes the angle between the central axis of the trachea and bronchus, which equals the angle between *Y* and *X*

the power of 4 (for laminar flow). In simulation studies, for instance, long stenoses show a modest difference in pressure profile with a slightly bigger magnitude of total pressure drop than the web-like stenosis of comparable airway narrowing (90%) [62]. The extent of the narrowing is important, however, for surgical decisions and for stent's length selection. In general, the length of the stent should be longer than the actual stenosis, to avoid migration and obviously to properly palliate the airway narrowing. In general the stent should exceed the stenosis by 0.5–1 cm on both sides. This principle may be difficult to apply in short airway such as the right main bronchus, when the stent may need to be customized on-site in order to provide ventilation to the right upper lobe. The exact length can be measured based on previously performed chest CT scanning for a different indication. Given the risk of radiation and alternative methods, ordering a CT scan for the sole purpose to determine stent size or length may not be warranted or cost-effective. The operator can use the scope itself, the telescope or accessory instruments (available sizing devices) to measure the extent of stenosis during bronchoscopy.

All these stent factors (size, length, morphology, material, and biomechanics) become important in selecting a particular stent for a specific type of obstruction. For instance, the dynamic features of TBM can make the selection of the type and size of the stent being inserted problematic. Sometimes very large stents (20–22 mm diameter) are required for those patients with tracheobronchomegaly. In addition, the expansile force has to be high enough to prevent significant collapse during expiration. Even though they rarely migrate, we use Y-shaped stents infrequently because we try to preserve as much normal mucosa as possible and thus decrease the likelihood of stent obstruction by tenacious mucous secretions, a common complication, especially in patients with chronically inflamed airways. In addition, Y-stent insertion in a patient with complete airway collapse and inflamed and friable airway mucosa is not always straightforward and could be complicated by lack of unfolding, airway perforation and subsequent ventilation, oxygenation, and hemodynamic disturbances.

Technique and Equipment

Airway stents can be placed via flexible (for SEMS) or rigid bronchoscopy (SEMS or silicone). The principles are the same: first, the operator will dilate the lesion (extrinsic compression, stricture, or significant residual obstruction after other endobronchial therapies); second, a stent large enough is deployed inside the airway to prevent migration and properly restore airway patency.

In case of *rigid bronchoscopy*, the scope is introduced through the mouth and then between the vocal cords under direct visualization to assure a secure airway at all times. We usually choose large rigid bronchoscopes (12–13 mm diameter) to allow deployment of a large tracheal/bronchial stents and facilitate easy passage of accessory instruments (large grasping forceps or large suction tubing that may become necessary in severe airway bleeding). The beveled tip of the scope facilitates lifting of the epiglottis and atraumatic passage of the scope through the vocal cords, but also assists for dilation and removal of exophytic endoluminal lesions (i.e., rigid bronchoscopic debulking). Operators should be familiar with the length of their scope and be able to decide how much the stent introducer should be inserted inside the scope in order to avoid deployment of the stent too distally (beyond the stenosis) or too proximally (inside the rigid bronchoscope). There are two techniques of straight silicone stent insertion, as one can expulse the stent either beyond the stricture and then pull it back or to directly deploy it within the stricture itself. There are also two techniques to deploy a Y-stent, and the operator can choose the one he or she is most familiar with: the "push" technique, in which the stent is ejected from the bronchoscope above the carina and then is pushed down with an open rigid grasping forceps placed at stent bifurcation, and the "pullback" technique, in which both bronchial limbs are placed within one bronchus (usually the one involved with most disease) and then the stent is pulled back slowly until the shorter limb pops out. While this has not been studied, the "pullback" technique may be safer in patients with abnormal airway wall (friable, infiltrated mucosa, preexistent fistula) because of potential reduced risk of pushing the stent into the mediastinum. Accessory instruments such as grasping forceps may be needed post deployment to assist with stent unfolding and positioning in the desired location. If the operator works through an open system, he or she may occasionally need to use Vaseline petroleum gauze packing strip or Kerlex gauze roll to pack the nose and the mouth, respectively, in case of significant air leak and subsequent impaired ventilation and oxygenation.

Flexible bronchoscopy is used by many operators to insert SEMS. This procedure can even be performed while the patient is on the ventilator in the intensive care unit. The technique of placing these stents under fluoroscopic guidance is well described [80], but fluoroscopy in the intensive care unit is cumbersome and often unavailable. There are techniques for placing these stents without fluoroscopy, one of which will be described here. First, the bronchoscope is inserted in the mouth through a bite block alongside the endotracheal tube (ETT), after deflating the ETT cuff, and advanced into the space between the tracheal wall and the ETT. The scope is then positioned proximal to the stenosis. A guide wire is inserted through the bronchoscope and passed alongside the lesion, after which the bronchoscope is withdrawn, leaving the guide wire in place. The scope is reinserted into the ETT to confirm guide wire location. A stent delivery catheter is advanced over the guide wire, and the stent is deployed under bronchoscopic visualization. The delivery catheter and guide wire are withdrawn together, leaving the stent in position. If necessary, the stent can be repositioned by grasping its proximal loop with a flexible alligator forceps.

Stent-Related Complications

Complications following stent placement can be divided into procedure-related complication and long-term sequelae of the physical presence of an airway stent. While rarely reported, procedure-related complications can occur during stent

insertion and as a result of their deployment and include perforation of the airway wall resulting in broncho-mediastinal fistula, massive hemorrhage (from large vessel laceration) and potentially mediastinal misplacement of the stent, and hypoventilation and hypoxemic respiratory failure caused by the large stent not unfolding satisfactorily or by occlusion of the stent with mucus or blood immediately following deployment.

A study of the aforementioned AQuIRE registry found that in patients undergoing any type of bronchoscopic intervention (including stenting) for malignant CAO, the overall severe 30-day complication rate was 4%. Overall complication risk was increased by moderate sedation (as opposed to general anesthesia), urgent or emergent procedures, American Society of Anesthesiologists (ASA) score > 3, and redo therapeutic bronchoscopy. The rate of significant bleeding necessitating intervention was 0.5%. The risk for significant bleeding was increased in patients undergoing urgent and emergent procedures, APC use, redo therapeutic bronchoscopy, and patients who were never smokers. The rate of procedurally related death was 0.5%. Risk of death as a result of procedural complication was increased in urgent or emergent procedure and in never-smoking patients. In these patients with malignant CAO, the post-procedure 30-day overall mortality was 15%. Risk of death within 30 days increased with the use of stents, and Y-stents in particular had a significantly higher risk of 30-day mortality compared to straight "tube" stents: it is unclear if this is a result of the stent itself or, more likely, the increased severity and extent of disease which necessitates a stent and more-so a Y-stent. In addition, the risk of 30-day mortality was increased in patients with a Zubrod performance status score > 1, ASA score > 3 or any intrinsic or mixed obstructive disease. Overall the rate of immediate procedurally related complications is rare. Of the modifiable risk factors, the two most pertinent are utilizing general anesthesia instead of moderate sedation, a judicious decision for the use of stenting, and the type of stent employed [81].

The remainder of this section will address long-term adverse events related to the presence of indwelling airway stent. In this regard, stents are indeed foreign objects inside the airway, and adverse events are therefore expected. Several complications have been identified and reported as incidence proportion[6] [9] in case series, but only recently this issue has been systematically approached using clear definitions and statistics using incidence rate[7] rather than proportions to report these adverse events [9]. Because of different biomechanics, significant differences exist between airway stent types in terms of long-term complications related to stent infection, granulation tissue, mucus plugging, stent migration, and stent fracture which could injure the airway wall or the adjacent mediastinal vessels [82]. While perioperative complications are rare and the immediate effects of stent insertion could be gratifying, both bronchoscopists and patients should be aware that long-term complications are common and potentially life threatening [83].

Granulation Tissue

This complication may also promote the development of secondary stenoses [84]. The exact prevalence of stent obstruction by granulation tissue versus tumor overgrowth or ingrowth in patients with malignant obstruction is somewhat confounded by the fact that studies tend to report them together rather than separately but when it occurs may be clinically significant in approximately 25% of patients [85]. The estimated incidence proportion of recurrent obstruction from either granulation tissue or tumor is 9–67% in patients with metal stents and 6–15% in patients with silicone stents [86]. The likely mechanism for granulation tissue formation consists of excessive pressure on the airway wall, which may lead to ischemic necrosis due to capillary closure. From physics standpoint, if the expansion force of a stent would be distributed equally over its com-

[6] An incidence proportion is defined as the number of cases with complications divided by the number of cases overall and is an appropriate measure for analyzing immediate perioperative complications [6].

[7] It measures events per person-time at risk [6].

plete outer surface, this would result in a relatively small contact pressure on the airway wall. However, if the stent wall touches a small portion of the inner tracheal wall (as may be the case with cylindrical stents for stomal, triangular stenoses), then the local pressure at that contact zone would be much higher and would result in considerable impairment of mucosal blood flow promoting further tissue ischemia and damage. This process could be worse if a SEMS is used. Though such a stent may have the same overall expansion force as a silicone stent, it can shut down the mucosal blood flow at spots where the thin wires come in contact with the tissue (Fig. 13.8). Thus the ciliated epithelium is replaced by fibroblasts and granulation tissue. Oversizing the stent has been suspected as a risk factor especially when stents are placed in the upper trachea or subglottis. In one study, Dumon stent insertion for benign tracheobronchial stenoses showed an incidence proportion of 28% for granulation tissue after a mean period of follow-up of 303 days. The stent-to-airway diameter ratio of 90% was found to be the critical cutoff point for predicting granulation tissue formation (OR, 47.5285) [79]. The optimal ratio between the stent and the airway diameter that could reduce granulation tissue formation has yet to be determined. Friction between the sharp edges of the stent and airway mucosa and the formation of galvanic currents may cause granulation tissue formation; this is especially true if electrocautery is used, and these currents are generated[8] around the metal wires [85]. This granulation tissue ingrowth can make removal difficult and result in substantial airway wall trauma [87]. It is likely that factors such as stent kinking or fracture also contribute to granulation tissue formation. Overall, however, granulation tissue formation is not easily predictable but seems to be more common in patients with keloids and in those with chronic airway infection [88]. Management of this problem is complicated by the difficulty of removing metal stents [88, 89]. Interestingly, one study addressing malignant CAO, compared with Ultraflex stents, both silicone stents and Aero stents seem to be more likely to lead to granulation tissue formation [9]. In the multivariate model, however, only silicone stents (HR = 3.32) and lower respiratory tract infection (HR = 5.69) were associated with increased risk for granulation. It is likely that the observed differences in granulation tissue may be related to repetitive motion trauma and infection. Coated stent models such as polyurethane-coated metallic stent may reduce the histobiological reaction to foreign bodies in animal experiments (i.e., granulation tissue formation) and still maintain sufficient expansion force [90]. In vivo human studies are warranted.

[8] An electrical current in which the electron flow is in only one direction; galvanic currents cause fibroblasts proliferation resultant increase in collagen synthesis, property used for wound healing and also implicated in keloid formation.

Stent Fracture

This is a rare complication seen with metal stent insertion, but it may result in airway wall perforation and hemoptysis, potentially fatal events [9, 29, 91]. United States Food and Drug Administration warned that metallic tracheal stents in patients with benign airway disorders should be used only after thoroughly exploring all other treatment options (such as surgical procedures or placement of silicone stents) [29]. The use of these stents as a bridging therapy to surgery is also not recommended, because the removal of these stents is associated with significant complications.

Stent-Associated Lower Respiratory Infection and Mucus Obstruction

When a definition of respiratory infection is based on the presence of clinical findings (fever, increased volume and purulence of sputum, and worsening cough), with or without radiographic evidence of pneumonia but requiring the managing physician to prescribe antibiotics, the incidence proportion of lower respiratory tract infections was 36–39% in patients suffering from cancer [9]. The authors of this study found that

respiratory infections led to significant morbidity and mortality: over half the patients were hospitalized, and 23% of patients with respiratory infections died within 14 days of their infection. Respiratory infections were more frequent in patients with Aero stents compared with silicone or Ultraflex. Various degrees of obstruction by mucus are not uncommon. This tends to be more common in patients with ineffective cough and in smokers. In patients with malignant CAO, having a left-sided stent (HR = 3.07), age (HR = 0.97), having a silicone stent (HR = 2.72) versus Ultraflex stents, and having chemotherapy post-stent placement (HR = 0.32) had significant impact on time to mucus impaction. The higher risk with left-sided stents makes sense; because of the sharper angle[9] between the left main bronchus and trachea, the patient may have difficulty in raising secretions. In addition to obstructing the airway, in time this could also lead to halitosis because the stent becomes covered chronically with a biofilm (Fig. 13.8). Recent in vitro studies evaluated a new methodology to create highly hydrophobic micro-/nanostructured silver antibacterial surfaces against Gram-positive and Gram-negative bacteria, using low-pressure plasma. This micro-/nanostructured silver coating demonstrated antibacterial properties causing a reduction of Gram-positive and Gram-negative bacteria viability on airway stents [92].

Migration

While an oversized stent could cause granulation tissue formation, an undersized stent would likely migrate. In one study, stent migration was 5.26%, 6.06%, and 15.38% in patients in whom the stent-to airway diameter was between 90% and 100%, 80% and 90%, and <80%, respectively [79]. The migrated stent, in addition to not palliating the airway narrowing for which was initially placed, could result in inability to clear secretions, in continuous friction between the wall of the stent and the airway mucosa, and cause granulation as well. Ideally a stent is well compressed once is deployed, but even if it is sized appropriately and placed properly and sitting tightly at the end of the procedure, it can still migrate later because of the visco-elastic properties of the tracheal tissues (Fig. 13.8). This complication is seen more commonly in benign disease or in patients with cancer undergoing therapy, likely because patients with benign disease survive longer and because of the changes in airway viscoelastic properties (in time the airway stenosis progressively dilates). This probably explains why about 20% of patients with strictures may have their stent removed after ~18 months. For patients with ECAC, silicone stent insertion improves functional status immediately post-intervention, but is associated with a high rate of adverse effects with quite frequent stent migration. In fact, in one study of malignant CAO, among various stents (Ultraflex, Aero, and silicone), only silicone tube stents had a significant effect on migration risk with an HR of 3.52 [9]. Stent migration requires a revision procedure to maintain satisfactory airway patency and prevent further complications.

Bronchoscopy is currently the standard for the detection and treatment of stent-related complications and, in nonurgent situations, usually involves a two-step procedure. Initially, diagnostic flexible bronchoscopy is performed to detect and characterize a stent complication; if a treatable complication is detected, rigid bronchoscopy may be required for therapeutic intervention. In this regard, from regulatory perspective, the stent insertion package should probably contain information about stent's biomechanics, sterilization (although this may not affect the infection rate) [9] in addition to reporting indications, expected results, incidence rates of long-term complications, as well as potential contraindications to stent insertion.

Contraindications

There are certain circumstances when stent insertion should not be offered. For instance, in idiopathic or secondary benign subglottic stenosis

[9]Especially in patients with tumors who might have a nearly horizontal left main bronchus due to large subcarinal adenopathy.

(within 2 cm from the vocal cords), stents may extend the length of the stenotic segment [93]. This is particularly true for metallic stents. In one study, all patients with laryngotracheal stenosis who had undergone covered or uncovered metallic stent placement developed new strictures or granulation tissue that precluded definitive surgical treatment or required more extensive resections [93]. In fact, some tracheal surgeons believe that SEMS should never be used in patients who are potential candidates for resection because these are likely to cause additional airway injury

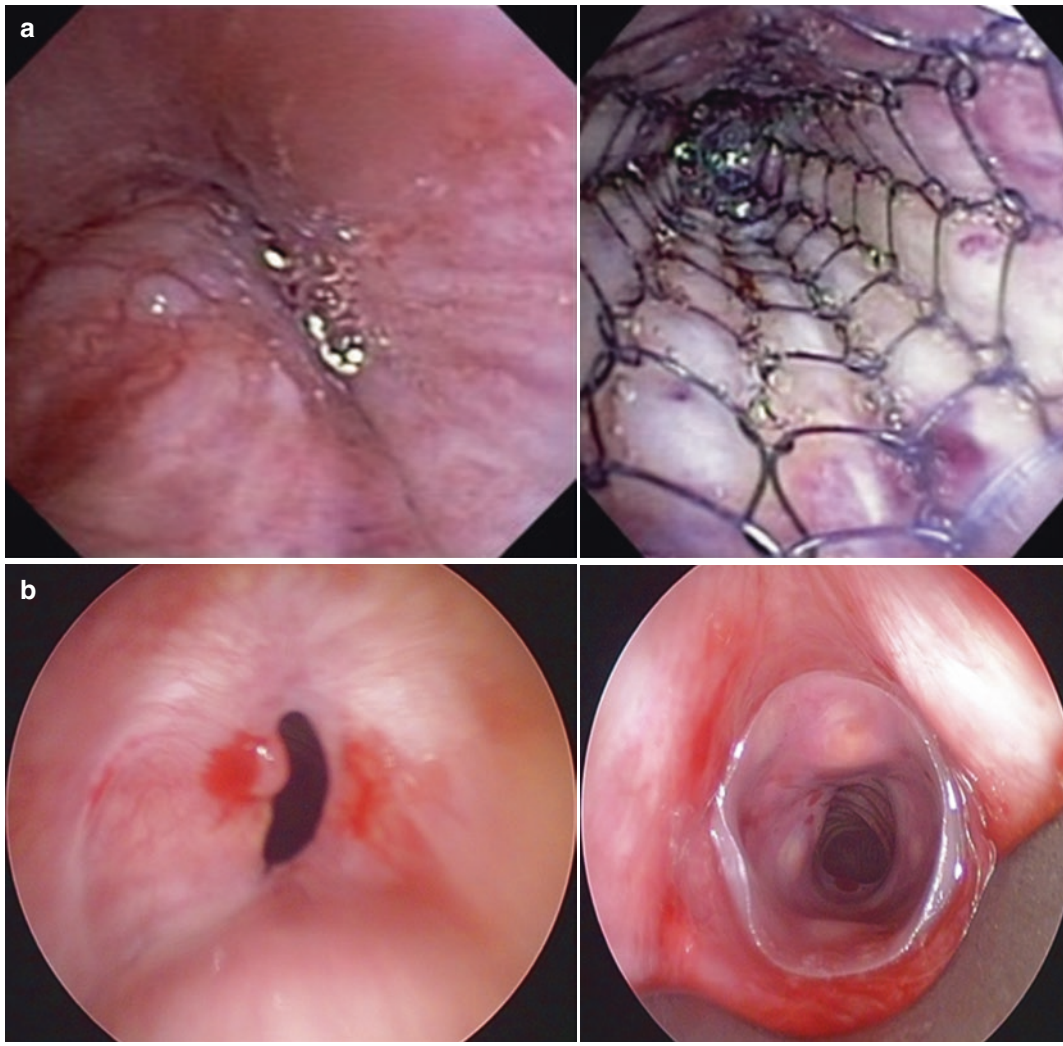

Fig. 13.8 (**a**) Severe, complete left main bronchial obstruction due to extrinsic compression and mucosal infiltration (*left panel*); a partially covered self-expandable metallic stent was inserted which caused at blanching spots where the thin wires come in contact with the tissue, suggesting mucosal ischemia from mucosal blood flow compromise (*right panel*). (**b**) Post-tracheostomy-related tracheal stenosis with chondritis and hypertrophic tissues (*left panel*). Post-dilation; a straight silicone stent was placed which was well compressed after deployment (*right panel*). (**c**) In the same patient, several months later, bronchoscopy showed that the stent migrated downward to the main carina (*left panel*); this resulted in significant obstruction of the left main bronchus and inability to clear secretions (*right panel*). (**d**) Computed tomography performed 3 months prior to bronchoscopy showed complete absence of aeration in the right lower lobe, thus precluding bronchoscopic intervention to restore airway patency (*left panel*); bronchoscopy in this case showed mucosal infiltration and friability and no evidence of airway patency distal to the obstruction (*right panel*)

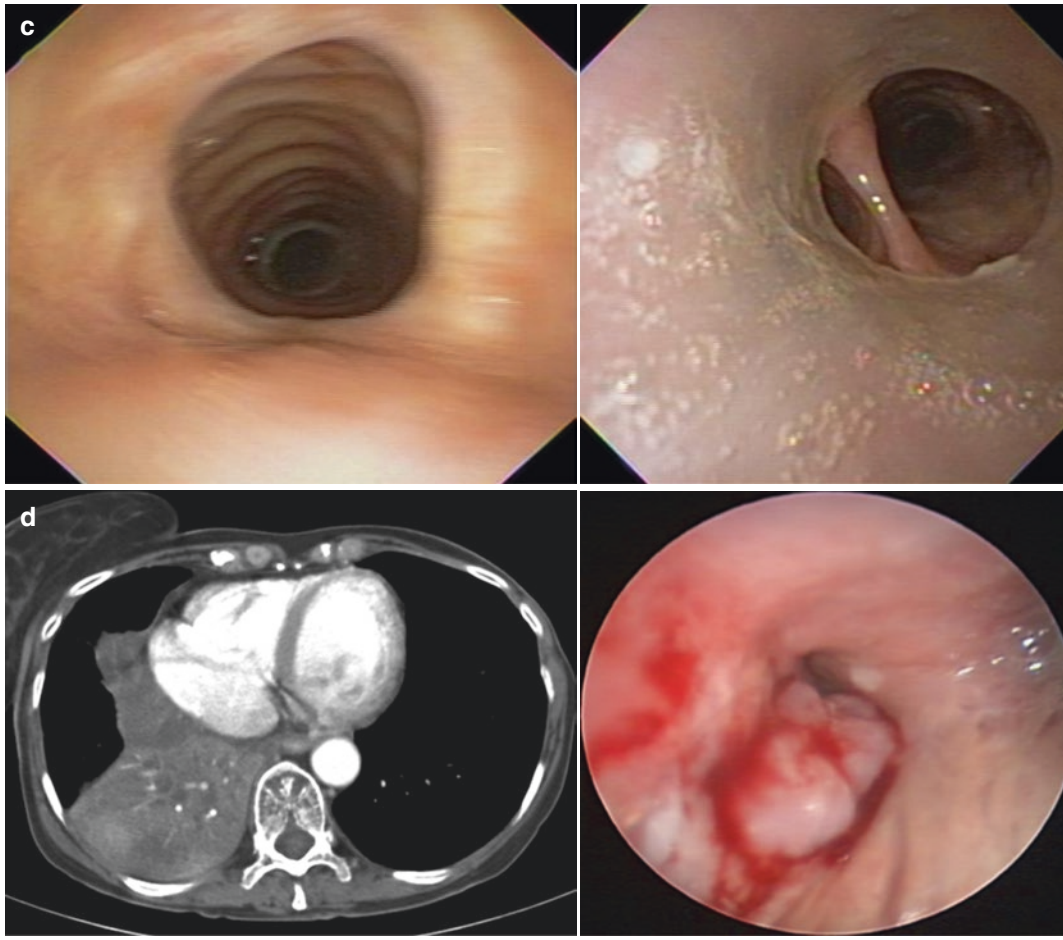

Fig. 13.8 (continued)

and possibly make a potentially resectable patient unresectable[10] [93].

The absence of a functional "distal airway" such is the case with significant and chronic (usually >1 month) distal parenchymal tumor infiltration or confirmed lack of perfusion of underlying lung are also contraindications to stent insertion and, for the same reasons, for any endoluminal therapy aimed at restoring airway patency. In patients with CAO (lobar or mainstem bronchi), assessing the functionality of the lung parenchyma distal to the obstruction is useful when considering interventions meant to establish airway patency. Functionality of the lung distal to the obstruction may not be restored in patients who have had chronic complete obstruction and lack of ventilation (Fig. 13.8). Determining whether there is functional airway and lung beyond an obstruction is essential to any successful bronchoscopic intervention,[11] in part because significant friability of bleeding from thin infiltrated bronchial mucosa, or lack of lung perfusion[12] despite restored

[10] In this regard, histologically benign CAO should be treated surgically or for nonsurgical candidates, with silicone stents whenever possible.

[11] Other conditions include experienced bronchoscopist and team, experienced anesthesiologist, control of patient's overall performance status, additional systemic or local therapy still possible, and control of comorbidities.

[12] One way to assess the perfusion status of lung parenchyma distal to an airway obstruction is to attempt bypassing the stenosis using a high-resolution EBUS radial probe.

airway patency might preclude intervention. In one study, 71% of patients who initiated radiation therapy within 2 weeks after radiological evidence of atelectasis had complete re-expansion of their lungs, compared with only 23% of those irradiated after 2 weeks [94]. Studies pertaining to successful bronchoscopic treatment and time to treatment are lacking. In addition, significant mucosal friability and bleeding of bronchial mucosa might also preclude interventions because stent insertion may result in broncho-mediastinal fistula, loss of the stent within the mediastinum, or hemorrhage (Fig. 13.8).

Follow-Up and Patient Education

Immediately after stent insertion, a chest radiograph is performed to confirm its location. Because stents are associated with significant adverse events, a stent alert card should be given to the patient upon discharge from the hospital; this provides information both for patients and for the doctors that may encounter patients with airway stents. They are informed that even though some stents (i.e., silicone) are not radiopaque, one can still identify them on the chest radiographs as straight lines. In addition, the card includes the patient's name, indication for stent insertion, type, location and size of stent inserted, contact information, and instructions for both patients and physicians in case of stent-related complications. Also, if intubation is necessary for whatever reason, bronchoscopic intubation using a cuffless # 6 ETT to avoid stent dislodgement or mucosal trauma is advisable.

Granulation tissue, secretions, migration, tumor progression, and fistula formation are usually detected during follow-up bronchoscopy or on chest CT. Studies show that the extent of air pockets around the stent on follow-up chest CT correlates with the success of stent removal, indicates regression of stenosis, and may help guide the optimal time for stent removal [95]. Stent-related complications, however, are usually detected by the onset of new respiratory symptoms and do not necessitate systematic (scheduled) routine flexible bronchoscopy. In those patients suspected of having stent-related adverse effects, however, bronchoscopy should be performed for diagnosis and potentially for therapy. While routine follow-up bronchoscopy in the lack of symptoms may not be warranted in all patients after stent insertion, given that most complications occur within 6 weeks post-stent insertion [9, 11, 12], one could choose to perform surveillance bronchoscopy in patients at high risk for complications after stent insertion. There are reports, however, suggesting that time to granulation tissue detection after SEMS insertion is longer in patients with dynamic airway obstruction than in those with structural airway obstruction (396 vs. 95 days $p = 0.02$) [84], so a need for prolonged follow-up in these patients may be warranted. Some physicians perform routine bronchoscopy every couple of months, while others only do it when patients complain of new symptoms [96]. Preventive measures for obstruction by mucus such as aerosol therapy, respiratory physiotherapy, and clinical visits are advocated. Also, while not a universal practice, saline nebulization is offered by many bronchoscopists to keep the stent humidified in order to avoid excessive mucus plugging. In fact, severely disabled patients such as those who are bedridden and with poor cough or impaired metal status are unlikely to benefit from indwelling airway stents since the risk of obstruction by mucus may outweigh the benefit gained by placing the stent and only temporarily restore airway patency.

Summary and Recommendations

Airway stents improve symptoms of selected patients with malignant and benign central airway obstruction, esophagorespiratory, and bronchial stump fistulas, but in general, their insertion should be reserved to patients for whom curative open surgical interventions are not feasible or contraindicated. Metallic stents should be avoided in benign disease unless surgery or silicone stent placement is not possible or feasible. For malignant disease, stents are placed with a palliative intent. They should therefore be placed by operators able to handle intraoperative, short-term, and long-term complications. Long-term

complications after placing such prostheses are not uncommon and can occasionally be fatal. Not all stents are equivalent in terms of biomechanics and stent-tissue interactions. Currently, this information may be considered confidential; proprietary and regulatory bodies do not mandate its reporting. However, manufacturers should probably describe some key biomechanical properties including the resistance to angulation, expansile force, and mechanical failure to help physicians predict successful airway patency restoration and immediate and long-term stent-related complications.

References

1. Zhu GH, Ng AH, Venkatraman SS, et al. A novel bioabsorbable drug-eluting tracheal stent. Laryngoscope. 2011;121:2234–9.
2. Korpela A, Aarnio P, Sariola H, et al. Comparison of tissue reactions in the tracheal mucosa surrounding a bioabsorbable and silicone airway stents. Ann Thorac Surg. 1998;66:1772–6.
3. Saito Y, Minami K, Kobayashi M, et al. New tubular bioabsorbable knitted airway stent: biocompatibility and mechanical strength. J Thorac Cardiovasc Surg. 2002;123:161–7.
4. Robey TC, Valimaa T, Murphy HS, et al. Use of internal bioabsorbable PLGA "finger-type" stents in a rabbit tracheal reconstruction model. Arch Otolaryngol Head Neck Surg. 2000;125:985–91.
5. Vondrys D, Elliott MJ, McLaren CA, Noctor C, Roebuck DJ. First experience with biodegradable airway stents in children. Ann Thorac Surg. 2011;92:1870–4.
6. Antón-Pacheco JL, Luna C, García E, López M, Morante R, Tordable C, Palacios A, de Miguel M, Benavent I, Gómez A. Initial experience with a new biodegradable airway stent in children: is this the stent we were waiting for? Pediatr Pulmonol. 2016;51(6):607–12.
7. Chao YK, Liu KS, Wang YC, Huang YL, Liu SJ. Biodegradable cisplatin-eluting tracheal stent for malignant airway obstruction: in vivo and in vitro studies. Chest. 2013;144(1):193–9.
8. Stehlik L, Hytych V, Letackova J, Kubena P, Vasakova M. Biodegradable polydioxanone stents in the treatment of adult patients with tracheal narrowing. BMC Pulm Med. 2015;15:164.
9. Ost DE, Shah AM, Lei X, et al. Respiratory infections increase the risk of granulation tissue formation following airway stenting in patients with malignant airway obstruction. Chest. 2012;141:1473–81.
10. Bolliger CT. Multimodalities treatment of advanced pulmonary malignancies in "interventional bronchoscopy". Prog Respir Res. 2000;30:187–96.
11. Murgu SD, Colt HG. Complications of silicone stent insertion in patients with expiratory central airway collapse. Ann Thorac Surg. 2007;84:1870–7.
12. Ernst A, Majid A, Feller-Kopman D, et al. Airway stabilization with silicone stents for treating adult tracheobronchomalacia: a prospective observational study. Chest. 2007;132:609–16.
13. Bondaryev A, Makris D, Breen DP, et al. Airway stenting for severe endobronchial papillomatosis. Respiration. 2009;77:455–8.
14. Terrier B, Dechartres A, et al. Granulomatosis with polyangiitis: endoscopic management of tracheobronchial stenosis: results from a multicentre experience. Rheumatology. 2015;54:1852–7.
15. Plojoux J, Laroumagne S, Vandemoortele T, Astoul PJ, Thomas PA, Dutau H. Management of benign dynamic "a-shape" tracheal stenosis: a retrospective study of 60 patients. Ann Thorac Surg. 2015;99:447–54.
16. Mehta AC, Lee FY, Cordasco EM, et al. Concentric tracheal and subglottic stenosis. Management using the Nd-YAG laser for mucosal sparing followed by gentle dilatation. Chest. 1993;104:673–7.
17. Dalar L, Karasulu L, Abul Y, et al. Bronchoscopic treatment in the management of benign tracheal stenosis: choices for simple and complex tracheal stenosis. Ann Thorac Surg. 2016;101:1310–7.
18. Brichet A, Verkindre C, Dupont J, et al. Multidisciplinary approach to management of postintubation tracheal stenoses. Eur Respir J. 1999;13:888–93.
19. Galluccio G, Lucantoni G, Battistoni P, et al. Interventional endoscopy in the management of benign tracheal stenoses: definitive treatment at long-term follow-up. Eur J Cardiothorac Surg. 2009;35:429–33; discussion 933–4.
20. Cavaliere S, Bezzi M, Toninelli C, et al. Management of post-intubation tracheal stenoses using the endoscopic approach. Monaldi Arch Chest Dis. 2007;67(2):73–80.
21. Nouraei SA, Ghufoor K, Patel A, et al. Outcome of endoscopic treatment of adult postintubation tracheal stenosis. Laryngoscope. 2007;117:1073–9.
22. Cooper JD, Grillo HC. The evolution of tracheal injury due to ventilatory assistance through cuffed tubes: a pathologic study. Ann Surg. 1969;169:334–48.
23. Murgu SD, Colt HG, Mukai D, et al. Multimodal imaging guidance for laser ablation in tracheal stenosis. Laryngoscope. 2010;120:1840–6.
24. Patelli M, Gasparini S. Post-intubation tracheal stenoses: what is the curative yield of the interventional pulmonology procedures? Monaldi Arch Chest Dis. 2007;67:71–2.
25. Zias N, Chroneou A, Tabba MK, et al. Post tracheostomy and post intubation tracheal stenosis: report of 31 cases and review of the literature. BMC Pulm Med. 2008;8:18.
26. Martinez-Ballarin JI, Diaz-Jimenez JP, Castro MJ, et al. Silicone stents in the management of benign tracheobronchial stenoses. tolerance and early results in 63 patients. Chest. 1996;109:626–9.

27. Wain JC Jr. Postintubation tracheal stenosis. Semin Thorac Cardiovasc Surg. 2009;21:284–9.
28. Liu HC, Lee KS, Huang CJ, et al. Silicone T-tube for complex laryngotracheal problems. Eur J Cardiothorac Surg. 2002;21:326–30.
29. U.S. Food and Drug Administration. Metallic tracheal stents in patients with benign airway disorders. 2005. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm153009.htm; Accessed 7 Aug 2016.
30. Gildea TR, Murthy SC, Sahoo D, et al. Performance of a self-expanding silicone stent in palliation of benign airway conditions. Chest. 2006;130:1419–23.
31. Jog M, Anderson DE, McGarry GW. Polyflex stent: is it radiopaque enough? J Laryngol Otol. 2003;117:83–4.
32. Jeong BH, Um SW, Suh GY, et al. Results of interventional bronchoscopy in the management of postoperative tracheobronchial stenosis. J Thorac Cardiovasc Surg. 2012;144:217–22.
33. Ost DE, Ernst A, Grosu HB, et al. Therapeutic bronchoscopy for malignant central airway obstruction: success rates and impact on dyspnea and quality of life. Chest. 2015;147(5):1282–98.
34. Stanopoulos IT, Beamis JF Jr, Martinez FJ, et al. Laser bronchoscopy in respiratory failure from malignant airway obstruction. Crit Care Med. 1993;21:386–91.
35. Lo CP, Hsu AA, Eng P. Endobronchial stenting in patients requiring mechanical ventilation for major airway obstruction. Ann Acad Med Singap. 2000;29:66–70.
36. Jeon K, Kim H, Yu CM, et al. Rigid bronchoscopic intervention in patients with respiratory failure caused by malignant central airway obstruction. J Thorac Oncol. 2006;1:319–23.
37. Oviatt PL, Stather DR, Michaud G, Maceachern P, Tremblay A. Exercise capacity, lung function, and quality of life after interventional bronchoscopy. J Thorac Oncol. 2011;6:38–42.
38. Razi SS, Lebovics RS, Schwartz G, et al. Timely airway stenting improves survival in patients with malignant central airway obstruction. Ann Thorac Surg. 2010;90:1088–93.
39. Okiror L, Jiang L, Oswald N, et al. Bronchoscopic management of patients with symptomatic airway stenosis and prognostic factors for survival. Ann Thorac Surg. 2015;99:1725–30.
40. Lemaire A, Burfeind WR, Toloza E, et al. Outcomes of tracheobronchial stents in patients with malignant airway disease. Ann Thorac Surg. 2005;80:434–8.
41. Furukawa K, Ishida J, Yamaguchi G, et al. The role of airway stent placement in the management of tracheobronchial stenosis caused by inoperable advanced lung cancer. Surg Today. 2010;40:315–20.
42. Guidelines for intensive care unit admission, discharge, and triage. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine. Crit Care Med. 1999;27:633–8.
43. Murgu S, Langer S, Colt H. Bronchoscopic intervention obviates the need for continued mechanical ventilation in patients with airway obstruction and respiratory failure from inoperable non-small-cell lung cancer. Respiration. 2012;84:55–61.
44. Deschamps C, Bernard A, Nichols FC 3rd, et al. Empyema and bronchopleural fistula after pneumonectomy: factors affecting incidence. Ann Thorac Surg. 2001;72:243–7.
45. Lois M, Noppen M. Bronchopleural fistulas. An overview of the problem with a special focus on endoscopic management. Chest. 2005;128:3955–65.
46. Han X, Wu G, Li Y, et al. A novel approach: treatment of bronchial stump fistula with a plugged, bullet-shaped, angled stent. Ann Thorac Surg. 2006;81:1867–71.
47. Shen KR, Allen MS, Cassivi SD, et al. Surgical management of acquired nonmalignant tracheoesophageal and bronchoesophageal fistulae. Ann Thorac Surg. 2010;90:914–9.
48. Wang H, Tao M, Zhang N, et al. Airway covered metallic stent based on different fistula location and size in malignant tracheoesophageal fistula. Am J Med Sci. 2015;5:364–8.
49. Freitag L, Ernst A, Unger M, Kovitz K, Marquette CH. A proposed classification system of central airway stenosis. Eur Respir J. 2007;30:7–12.
50. Rodriguez AN, Diaz-Jimenez JP. Malignant respiratory-digestive fistulas. Curr Opin Pulm Med. 2010;16:329–33.
51. Diaz-Jimenez P. New cufflink-shaped silicone prosthesis for the palliation of malignant tracheobronchial-esophageal fistula. J Bronchol. 2005;12:207–9.
52. Dumon JF, Dumon MC. Dumon-Novatech Y8-stents: a four-year experience with 50 tracheobronchial tumors involving the carina. J Bronchol. 2000;7:26–32.
53. Burt M, Diehl W, Martini N, et al. Malignant esophagorespiratory fistula: management options and survival. Ann Thorac Surg. 1991;52:1222–9.
54. Herth FJ, Peter S, Baty F, Eberhardt R, Leuppi JD, Chhajed PN. Combined airway and oesophageal stenting in malignant airway-oesophageal fistulas: a prospective study. Eur Respir J. 2010;36:1370–4.
55. Murgu SD, Colt HG. Description of a multidimensional classification system for patients with expiratory central airway collapse. Respirology. 2007;12:543–50.
56. Boiselle PM, O'Donnell CR, Bankier AA, et al. Tracheal collapsibility in healthy volunteers during forced expiration: assessment with multidetector CT. Radiology. 2009;252:255–62.
57. Sarodia BD, Dasgupta A, Mehta AC. Management of airway manifestations of relapsing polychondritis: case reports and review of literature. Chest. 1999;116:1669–75.
58. Miyazawa T, Nishine H, Handa H, et al. Migration of the choke point in relapsing polychondritis after stenting. Chest. 2009;136:81S.
59. Adliff M, Ngato D, Keshavjee S, et al. Treatment of diffuse tracheomalacia secondary to relapsing polychondritis with continuous positive airway pressure. Chest. 1997;112:1701–4.
60. Nouraei SA, Nouraei SM, Randhawa PS, et al. Sensitivity and responsiveness of the Medical

Research Council dyspnoea scale to the presence and treatment of adult laryngotracheal stenosis. Clin Otolaryngol. 2008;33:575–80.
61. Myer CM, O'Connor DM, Cotton RT. Proposed grading system for subglottic stenosis based on endotracheal tube sizes. Ann Otol Rhinol Laryngol. 1994;103:319–23.
62. Brouns M, Jayaraju ST, Lacor C, et al. Tracheal stenosis: a flow dynamics study. J Appl Physiol. 2007;102:1178–84.
63. Mead J, Turner JM, Macklem PT, Little JB. Significance of the relationship between lung recoil and maximum expiratory flow. J Appl Physiol. 1967;22:95–108.
64. Smaldone GC, Smith PL. Location of flow-limiting segments via airway catheters near residual volume in humans. J Appl Physiol. 1985;59:502–8.
65. Baram D, Smaldone G. Tracheal collapse versus tracheobronchomalacia: normal function versus disease. Am J Respir Crit Care Med. 2006;174:724.
66. Boiselle PM, Litmanovich DE, Michaud G, et al. Dynamic expiratory tracheal collapse in morbidly obese COPD patients. COPD. 2013;10(5):604–10.
67. Behazin N, Jones SB, Cohen RI, Loring SH. Respiratory restriction and elevated pleural and esophageal pressures in morbid obesity. J Appl Physiol (1985). 2010;108(1):212–8.
68. O'Donnell CR, Bankier AA, O'Donnell DH, Loring SH, Boiselle PM. Static end-expiratory and dynamic forced expiratory tracheal collapse in COPD. Clin Radiol. 2014;69(4):357–62.
69. Bhatt SP, Terry NL, Nath H, et al. Association between expiratory central airway collapse and respiratory outcomes among smokers. JAMA. 2016;315(5):498–505.
70. Hogg JC, Macklem PT, Thurlbeck WM. Site and nature of airway obstruction in chronic obstructive lung disease. N Engl J Med. 1968;278:1355–60.
71. Pornsuriyasak P, Ploysongsang Y. Impulse oscillometry system in diagnosis of central airway obstruction in adults: comparison with spirometry and body plethysmography. Chest. 2009;136:123S.
72. Murgu SD, Colt HG. Tracheobronchomalacia and excessive dynamic airway collapse. Respirology. 2006;11:388–406.
73. Handa H, Miyazawa T, Murgu SD, et al. Novel multimodality imaging and physiologic assessments clarify choke-point physiology and airway wall structure in expiratory central airway collapse. Respir Care. 2012;57(4):634–41.
74. Nishine H, Hiramoto T, Kida H, et al. Assessing the site of maximum obstruction in the trachea using lateral pressure measurement during bronchoscopy. Am J Respir Crit Care Med. 2012;185(1):24–33.
75. Witt C, Dinges S, Schmidt B, Ewert R, Budach V, Baumann G. Temporary tracheobronchial stenting in malignant stenoses. Eur J Cancer. 1997;33:204–8.
76. Chan AC, Shin FG, Lam YH, et al. A comparison study on physical properties of self-expandable esophageal metal stents. Gastrointest Endosc. 1999;49(4 Pt 1):462–5.
77. Freitag L, et al. Mechanical properties of airway stents. J Bronchol. 1995;2:270–8.
78. Chhajed PN, Somandin S, Baty F, et al. Therapeutic bronchoscopy for malignant airway stenoses: choice of modality and survival. J Cancer Res Ther. 2010;6:204–9.
79. Hu HC, Liu YH, Wu YC, et al. Granulation tissue formation following Dumon airway stenting: the influence of stent diameter. Thorac Cardiovasc Surg. 2011;59:163–8.
80. Saad CP, Murthy S, Krizmanich G, Mehta AC. Self expandable metallic airway stents and flexible bronchoscopy: long-term outcomes analysis. Chest. 2003;124:1993–9.
81. Ost DE, Ernst A, Grosu HB, et al. Complications following therapeutic bronchoscopy for malignant central airway obstruction: results of the AQuIRE Registry. Chest. 2015;148(2):450–71.
82. Agrafiotis M, Siempos II, Falagas ME. Infections related to airway stenting: a systematic review. Respiration. 2009;78:69–74.
83. Ernst A, Feller-Kopman D, Becker HD, et al. Central airway obstruction. Am J Respir Crit Care Med. 2004;169:1278–97.
84. Chung FT, Lin SM, Chou CL, et al. Factors leading to obstructive granulation tissue formation after ultraflex stenting in benign tracheal narrowing. Thorac Cardiovasc Surg. 2010;58:102–7.
85. Freitag L. Airway stents. In: Strausz J, Bolliger CT, editors. Interventional pulmonology. Sheffield: European Respiratory Society; 2010. p. 190–217.
86. Dalupang JJ, Shanks TG, Colt HG. Nd-YAG laser damage to metal and silicone endobronchial stents: delineation of margins of safety using an in vitro experimental model. Chest. 2001;120:934–40.
87. Alazemi S, Lunn W, Majid A, et al. Outcomes, healthcare resources use, and costs of endoscopic removal of metallic airway stents. Chest. 2010;138(2):350–6.
88. Matt BH, Myer CM 3rd, Harrison CJ, et al. Tracheal granulation tissue. A study of bacteriology. Arch Otolaryngol Head Neck Surg. 1991;117:538–41.
89. Lunn W, Feller-Kopman D, Wahidi M, et al. Endoscopic removal of metallic airway stents. Chest. 2005;127:2106–12.
90. Matsui H, Hiroma T, Hasegawa H, Ogiso Y. Decreased granulomatous reaction by polyurethane-coated stent in the trachea. Pediatr Int. 2014;56(6):817–21.
91. Bolot G, Poupart M, Pignat JC, et al. Self-expanding metal stents for the management of bronchial stenosis and bronchomalacia after lung transplantation. Laryngoscope. 1998;108:1230–3.
92. Gilabert-Porres J, Martí S, Calatayud L, et al. Design of a nanostructured active surface against gram-positive and gram-negative bacteria through plasma activation and in situ silver reduction. ACS Appl Mater Interfaces. 2016;8(1):64–73.
93. Gaissert HA, Grillo HC, Wright CD, et al. Complication of benign tracheobronchial strictures

by self-expanding metal stents. J Thorac Cardiovasc Surg. 2003;126:744–7.
94. Reddy SP, Marks JE. Total atelectasis of the lung secondary to malignant airway obstruction. Response to radiation therapy. Am J Clin Oncol. 1990;13:394–400.
95. Verma A, Park HY, Lim SY, et al. Posttuberculosis tracheobronchial stenosis: use of CT to optimize the time of silicone stent removal. Radiology. 2012;263(2):562–8.
96. Matsuo T, Colt HG. Evidence against routine scheduling of surveillance bronchoscopy after stent insertion. Chest. 2000;118:1455–9.