Malignant Central Airway Obstruction

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Contents

Abstract

Malignant central airway obstruction (MCAO) is seen in 15–20% of lung cancer patients as well as with metastases from other cancers, like breast, kidney, etc. It is defined as 50% or greater obstruction of trachea, mainstem bronchi, bronchus intermedius, and lobar bronchi. The patients with MCAO often present with life-threatening complications and have a poor prognosis. The management of these patients varies widely between institutions and specialties involved which has a negative impact on outcomes.

Patients with MCAO should undergo detailed clinical assessment including CT scan of the chest. The main approach to management is therapeutic bronchoscopy under general anesthesia. Multimodality, therapeutic bronchoscopy provides the best chance of procedural success. In addition, these patients should be treated with definitive chemoradiation and/or surgery. A multidisciplinary, patient-centric approach is the key to optimize the outcomes.

Keywords

Central airway obstruction · Malignant central airway obstruction · Endobronchial mass · Airway tumor · Lung cancer · Therapeutic bronchoscopy · Airway stent · Airway ablation

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1 Introduction

Malignant central airway obstruction (MCAO) is defined as 50% or greater narrowing of the central airways, including trachea, mainstem bronchi, bronchus intermedius, and lobar bronchi, by a malignancy [1, 2]. It can lead to debilitating symptoms and is associated with poor patient outcomes [3, 4]. CAO is an independent risk factor for death in patients with lung cancer [5]. The management of MCAO involves multiple medical and surgical specialties, and there is a wide variation in clinical practice which leads to poor outcomes [1, 6]. With the standardization and accreditation of interventional pulmonology fellowship in the United States, competency assessment tools for rigid bronchoscopy, and societal guidelines, the management of MCAO will be streamlined and the patient outcomes are anticipated to improve [1, 7–11].

2 Etiologies

While lung cancer remains the leading cause of cancer mortality worldwide, the prevalence of MCAO remains incompletely characterized. It is estimated to vary between 13% and 17% of contemporary lung cancer cohorts, notably decreased from the older studies estimating 20–30% of patients with lung cancer [4, 5]. The shift in MCAO could be related to the lung cancer screening efforts and change in pathology from central squamous cancer to peripheral adenocarcinoma [1, 12]. As such, lung cancer is the most common cause of MCAO, but an extensive array of other thoracic and extrathoracic cancer metastases are implicated in MCAO, most commonly including breast, esophageal, thyroid, renal, and colorectal malignancies [1, 13]. Malignant central airway obstruction can also be caused by primary airway tumors, including adenoid cystic carcinomas, mucoepidermoid carcinomas, and carcinoid tumors [4]. Finally, growth of malignancies of nearby structures including the thyroid, esophagus, and mediastinum can result in extrinsic compression of the central airways as can metastatic involvement of the mediastinal and hilar nodes [4].

3 Classification

MCAO can be classified based on the anatomy of airway compromise into intrinsic or endobronchial, extrinsic, and mixed (Fig. 1) [1]. MCAO is considered “intrinsic or endobronchial” when it is generally confined to within the airway lumen, while an “extrinsic” airway obstruction is entirely extraluminal compromising the airway due to mass effect. Airway obstruction is classified as “mixed” if it has both an intrinsic and extrinsic component. The tumors causing mixed CAO are often adjacent to the airway, causing compression and erode through the airway wall into the lumen. Carefully considering this classification scheme has important implications for therapeutic management of the MCAO, as will be discussed later in this chapter [1, 14]. In addition, studies have shown that survival of patients with endobronchial CAO is better than extrinsic or mixed CAO [15, 16].

4 Presentation

MCAO has the potential to impose a profound symptom burden, most commonly manifesting as dyspnea which may have positional aggravation with lying flat [4, 5]. These patients often present with stridor or unilateral wheeze on examination [5]. Other symptoms arise directly from tissue compression or invasion by the airway tumor and may include cough, hemoptysis, chest pain, hoarseness, or dysphagia [4]. Compression of the airway can lead to persistent or recurrent postobstructive pneumonia due to impaired mucus clearance with associated symptoms of infection. Many patients develop respiratory failure requiring mechanical ventilation [17]. Compression of adjacent vascular structures may lead to pulmonary arterial thrombus or SVC syndrome, and vigilance is required to detect these complications as these merit an intensive multidisciplinary approach to treatment which must proceed concomitantly or precede the management of MCAO [18]. The interventional pulmonologist should carefully evaluate each patient prior to considering diagnostic and therapeutic approaches with consideration of the symptoms severity, respiratory compromise, patient reserve, and concurrent comorbidities.

5 Diagnostic Evaluation

The diagnosis of MCAO is established on the history, physical examination, and imaging [1, 4]. A comprehensive clinical history and physical exam can provide important details regarding the severity of symptoms and patient’s trajectory which can direct the team about the urgency of therapeutic management. It has been well established that there are greater odds of successfully relieving MCAO when the lesion is promptly acted upon [16, 19].

While chest X-rays may be readily available, the findings may be nonspecific as the airway anatomy is poorly defined [20]. The computerized tomography (CT) of the chest remains the most reliable means of diagnosing and characterizing MCAO [4]. However, radiographic detection of MCAO is highly variable in the “real-world” with evidence of underdiagnosis of central airway compromise [21]. CT imaging of the chest for MCAO has also been shown to underestimate the extent of airway obstruction as compared

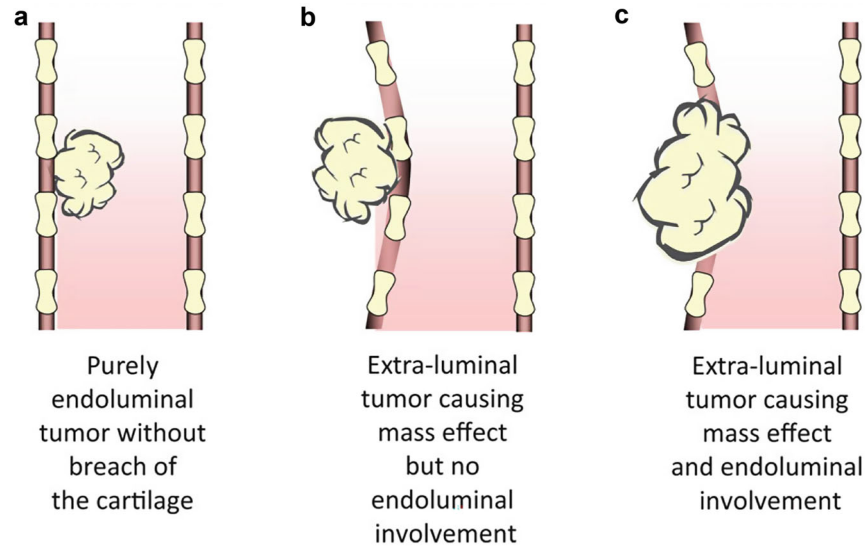

Fig. 1 Classification of central airway obstruction. (**a**) Intrinsic or endobronchial, (**b**) extrinsic or extraluminal, and (**c**) mixed. (Adapted from Fig. 25.2 from previous chapter by Michaud)

to contemporaneous bronchoscopy but may overestimate the degree of obstruction in cases where mucus or blood masquerade as tissue obstruction [20].

Visualization of a patent distal airway either radiographically or bronchoscopically has been shown to be an indicator of successful relief of MCAO and may portend more favorable bronchoscopic outcome [19]. Duration of lobar atelectasis of greater than four weeks may suggest the atelectatic lung is irredeemable [20].

Functional testing including spirometry in the setting of MCAO may not be feasible, particularly when the patient is presenting with profound symptoms or acute respiratory failure. That noted, spirometry may show patterns of expiratory, inspiratory, or combined flow-volume loop flattening which have been associated with variable intrathoracic, variable extrathoracic, or fixed obstruction, respectively [4].

6 Therapeutic Approach and Treatment

Therapeutic management of MCAO is multidisciplinary and multimodal; therapeutic bronchoscopy is the backbone of this approach [1, 2, 4]. Multiple studies have shown that therapeutic bronchoscopy palliates symptoms like dyspnea and improves the quality of life (QOL) and survival [16, 22–30]. Not only does it palliates symptoms, therapeutic bronchoscopy serves as a bridge to definitive treatment like chemotherapy, radiation, and even surgery [1, 31, 32]. Evidence suggests that patients who underwent successful therapeutic bronchoscopy for CAO had a prognosis similar to patients who did not have CAO [3].

A study from multicenter, prospective registry American College of Chest Physicians Quality Improvement Registry, Evaluation, and Education (AQuIRE) included 1115 therapeutic bronchoscopies on 947 patients with MCAO [33]. Clinically significant improvement in dyspnea occurred in 90 of 187 (48%) patients measured and improvement in health-related QOL was seen in 76 out of 183 (42%) patients measured. In another prospective study of 53 patients with CAO, including 24 with MCAO, there was a significant improvement of about 500 ml in FVC and FEV1 [22]. Dyspnea as measured by San Diego Shortness of Breath Questionnaire (SOBQ) decreased significantly by about 15 points, and there was an improvement in almost all domains of QOL measured by 36-Item Short Form Survey (SF-36). The median survival of MCAO patients who had a successful therapeutic bronchoscopy compared to patients with unsuccessful procedure was 229 vs 115 days [22]. A study has shown that this improved survival and palliation is maintained long term [16]. There is evidence to support that in patients with MCAO and respiratory failure, therapeutic bronchoscopy can lead to weaning from mechanical ventilation [17, 34]. In a retrospective study, 30 patients with acute respiratory failure secondary to MCAO underwent therapeutic bronchoscopy [17]. Twenty-eight (93%) patients were successfully extubated within 48 hours. In addition, there is evidence to suggest that early therapeutic bronchoscopy can improve survival [16, 19]. The complications reported with therapeutic bronchoscopy in the AQuIRE registry included procedure-related deaths (0.5%), escalation in level of care (4.4%), bleeding requiring intervention (0.5%), and refractory hypoxemia (2.2%) [35]. These complications should be carefully discussed with the patients and referring providers to decide the management options. Examples of cases with intrinsic, extrinsic, and mixed central airway obstruction are shown in Figs. 2, 3 and 4. A management algorithm is proposed in Fig. 5.

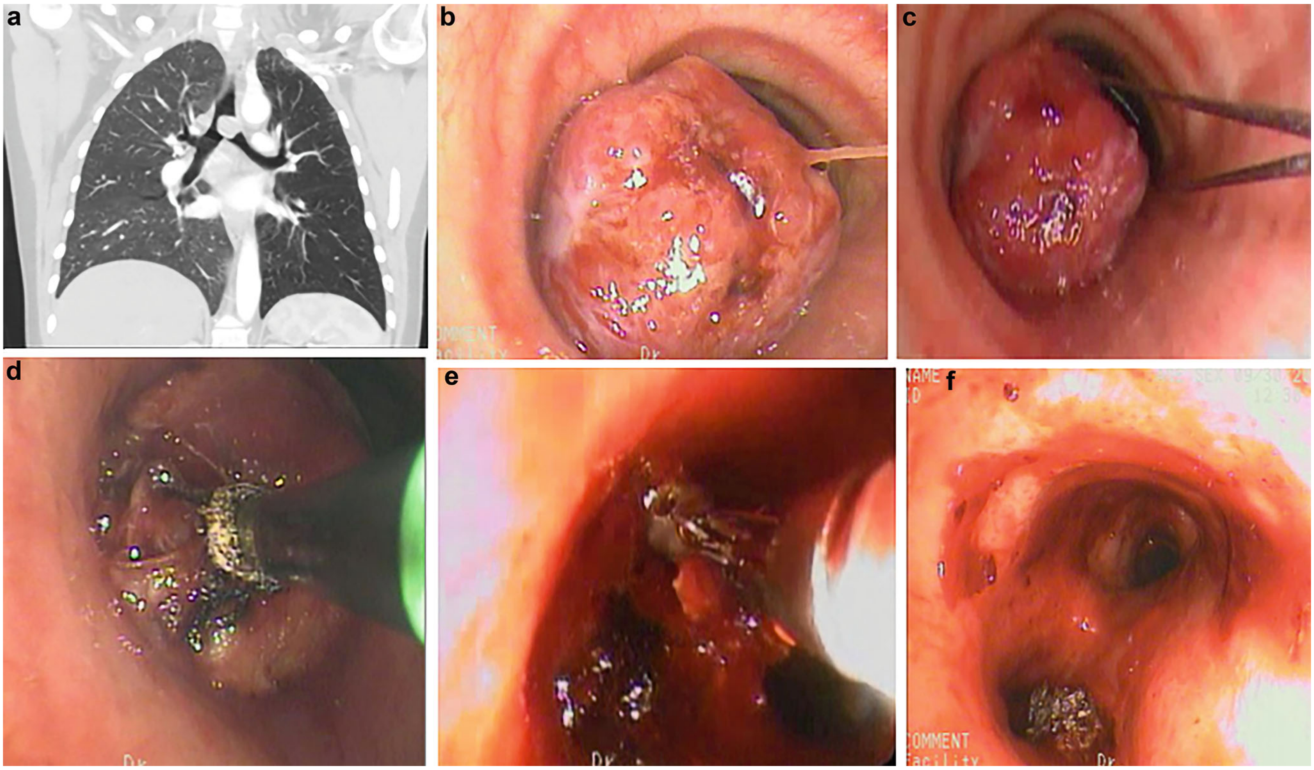

Fig. 2 Intrinsic or endobronchial central airway obstruction. (**a**) CT chest showing endobronchial mass with significant tracheal obstruction, (**b**) bronchoscopic view, (**c**) insertion of electrocautery snare around the mass, (**d**) flexible electrocautery probe ablation, (**e**) flexible forceps debridement, and (**f**) carina after debridement of the tracheal mass. The mass was carcinoid tumor, and patient underwent subsequent surgical sleeve resection of the trachea and carinal reconstruction

6.1 Patient Assessment

A careful assessment of the patient is essential for planning therapeutic bronchoscopy, including the anesthesia approach, intubation preparation, and ECMO back-up [1]. Besides the detailed history and clinical examination, especially evaluating the airway and respiratory system, following components of examination can inform the difficulty of endotracheal tube placement or rigid bronchoscopy:

1. Mouth opening (normal >3 finger breadths) [36]
2. Teeth, like loose, missing or prominent [36]
3. Modified Mallampati score [37, 38]
4. Neck mobility (Normal >90°) [36]
5. Thyromental distance (normal >3 finger breadths) [36]

6.2 Rigid Versus Flexible Bronchoscopy

For therapeutic approach to MCAO, rigid bronchoscope has several technical advantages over flexible bronchoscope. These include establishment of secure airway for mechanical ventilation, ability to use the beveled end of rigid bronchoscope to core an obstructing tumor, and provision of a conduit through which flexible bronchoscope, rigid forceps, large suction catheters, and stents can be deployed [1]. The silicone stents can only be deployed through the rigid bronchoscopes [39]. These advantages are particularly important for large and proximal central airway tumors. The flexible bronchoscopes might be adequate for distal and smaller airway lesions and is used as an adjunct with almost all rigid bronchoscopy cases. Therefore, the American College of Chest Physicians (ACCP) guidelines for management of central airway obstruction suggested rigid over flexible bronchoscopy for therapeutic interventions [1].

In the AQuIRE registry, out of 1115 therapeutic bronchoscopies, flexible bronchoscope was used in 382 (34.3%) and rigid bronchoscope in 733 (65.7%) procedures. Success rate, defined as reopening the airway lumen to >50% of the normal diameter, was 92.7% vs. 93.5% ($P = 0.62$) for flexible and rigid bronchoscopy, respectively [33]. The complications were similar with both modalities [35]. Similar outcomes have been reported by other studies as well [40, 41]. However, rigid bronchoscope has been used more often for proximal and bulkier disease [40]. A study has shown that less procedures were needed with rigid vs. flexible bronchoscopic approach [42].

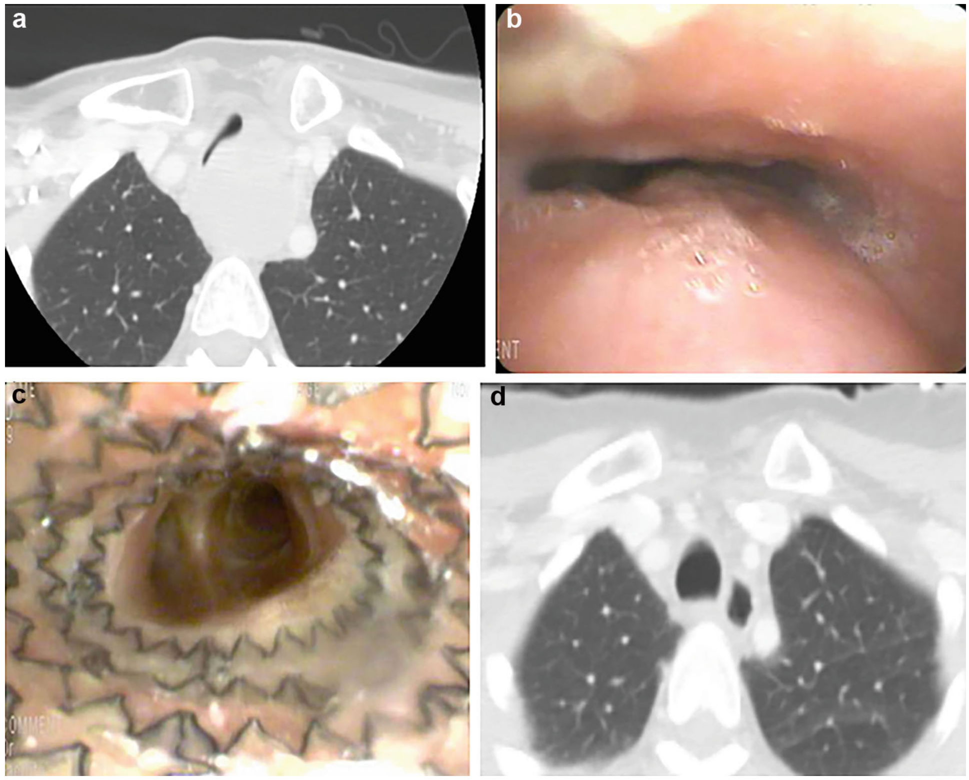

Fig. 3 Extrinsic central airway obstruction. (**a**) CT chest showing mediastinal mass with significant tracheal extrinsic compression, (**b**) bronchoscopic view, (**c**) hybrid stent placed in trachea, and (**d**) CT chest showing resolution of tracheal obstruction after radiation and chemotherapy for lymphoma and stent removal

6.3 Anesthetic Approach for Therapeutic Bronchoscopy

General anesthesia with paralytics is associated with less complications and is more effective for therapeutic bronchoscopy. In the AQuIRE registry, 961 therapeutic bronchoscopies were done with general anesthesia/deep sedation and 154 with moderate sedation [33, 35]. The technical success was similar, but less complications were observed with general anesthesia/deep sedation vs. moderate sedation (OR = 0.42; 95% CI, 0.21–0.83; P = 0.013). Also, the use of paralytics was associated with less complications (3% vs. 6.7%, P = 0.006). A randomized controlled trial (RCT) also reported lower complications with paralytics vs. without paralytics for therapeutic bronchoscopy [43]. Evidence suggests that more procedure sessions are required for therapeutic bronchoscopy with moderate sedation compared to general anesthesia [42]. The ACCP guidelines suggest the use of general anesthesia/deep sedation with paralytics for therapeutic bronchoscopy [1]. Multidisciplinary collaboration with anesthesiology team is essential to plan the optimal anesthesia approach for these patients.

6.4 Ventilator Support for Therapeutic Bronchoscopy

For patients undergoing general anesthesia for therapeutic bronchoscopy, different modes of ventilation including jet ventilation and controlled or spontaneous assisted ventilation can be used [44]. In the AQuIRE registry, controlled or spontaneous assisted, volume cycled ventilation was used in 714 (64%) and jet ventilation in 230 (20.6%) patients with MCAO [33, 35]. The technical success rate and complications were similar with both approaches. A study has reported more hypercapnia with controlled vs. jet ventilation [45]. The ACCP guidelines suggest the use of either jet or controlled/spontaneous assisted ventilation for therapeutic bronchoscopy under general anesthesia [1].

In patients with severe tracheal or bilateral mainstem bronchial obstruction with concern for respiratory arrest or complete collapse of airway lumen on anesthesia induction, extracorporeal membrane oxygenation (ECMO) can offer a safe bridge for anesthesia [46].

6.5 Tumor Debridement

Tumor debridement is generally the first step to recanalize airway with endobronchial or mixed obstruction. It is generally performed with flexible or rigid forceps and tumor is

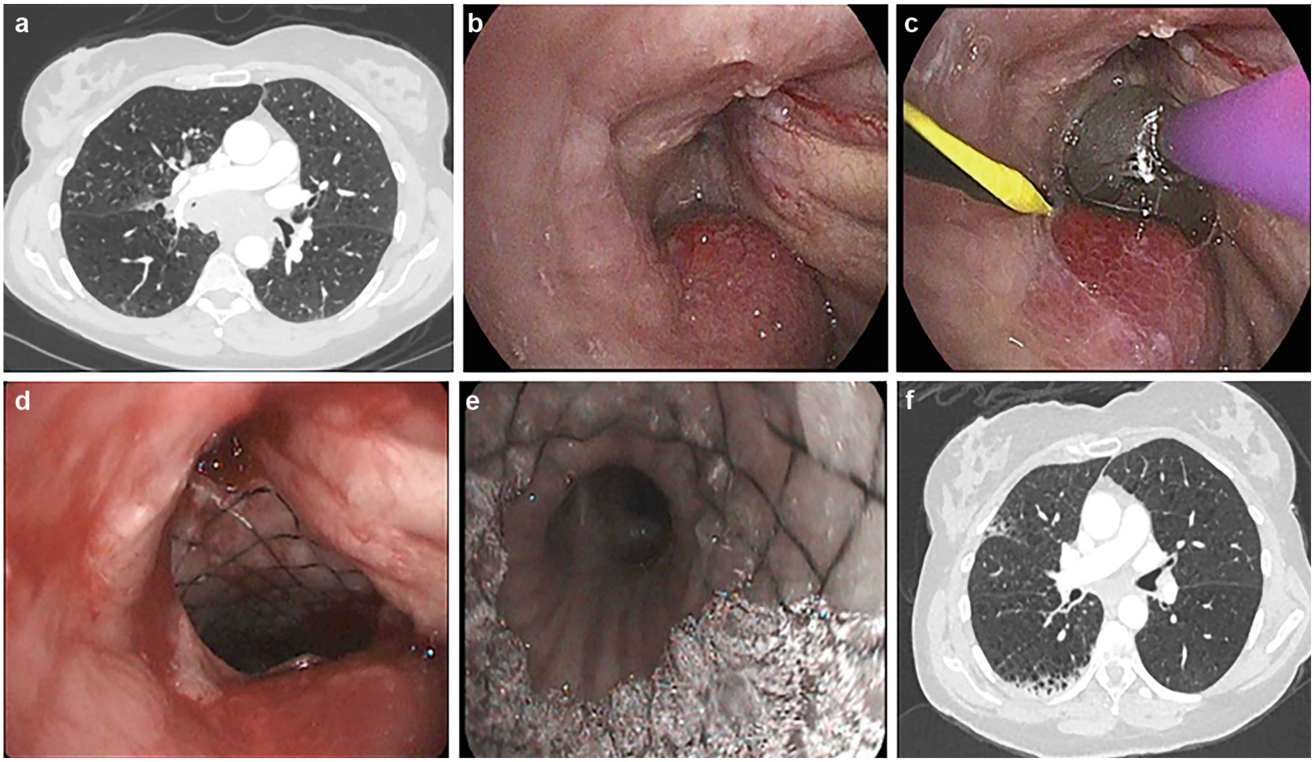

Fig. 4 Mixed central airway obstruction. (**a**) CT chest showing mixed extrinsic and intrinsic obstruction of right mainstem bronchus and bronchus intermedius, (**b**) bronchoscopic view showing endobronchial disease as well as extrinsic compression of right mainstem bronchus and bronchus intermedius, and (**c**) balloon dilation of bronchus intermedius. Guidewire has been inserted into distal airways. (**d**) Hybrid stent placed in bronchus intermedius, (**e**) distal view of the stent, and (**f**) CT chest showed resolution of bronchus intermedius obstruction after radiation and chemotherapy for nonsmall cell lung cancer and subsequent stent removal

excised from the airway [1]. The beveled end of rigid bronchoscope can be used for coring through the proximal

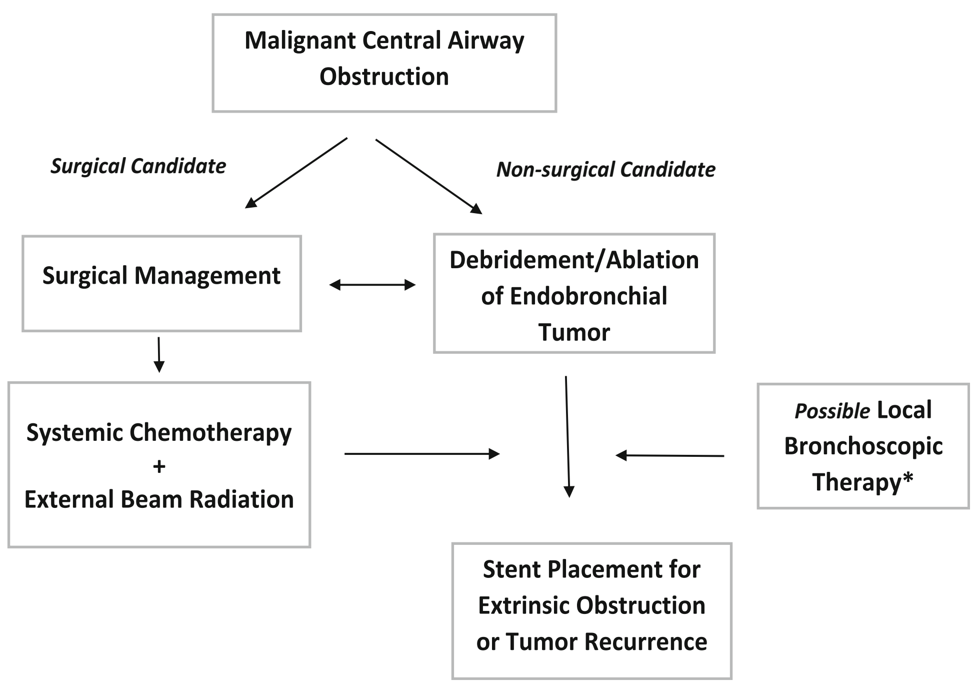

Fig. 5 Suggested algorithm for the management of malignant central airway obstruction. *Local bronchoscopic therapy may include photodynamic therapy, brachytherapy, cryotherapy, or intratumoral chemotherapy injection.

tumors. Cryoprobe can be used for debridement, has been shown to be effective in several case series, and makes the debridement process more efficient compared to forceps [47, 48].

6.6 Ablative Therapies with Immediate Effect

Multiple ablative therapies are available and can help with tumor debridement and recanalizing the airways [48]. The details of these ablative therapies are addressed in another chapter. These modalities include contact electrocautery devices like flexible and rigid probes, electrocautery snare, and knife [49]. The noncontact ablative therapies include argon plasma coagulation (APC) and laser [50, 51]. The role of ablative therapies is to achieve hemostasis with tumor debridement and tumor destruction or vaporization. It is important to know the variable depth of tissue destruction with different devices and settings, as the heat effect goes deeper than the surface ablation. In addition, it is critical to decrease the fraction of inhaled oxygen (FiO_2) to ≤ 0.4 and keep the active tip of the ablative probes away from flammable devices like flexible bronchoscope or endotracheal tube to decrease the risk of airway fire [1]. The ACCP guidelines suggest tumor excision with ablative therapies to achieve airway patency [1].

6.7 Ablative Therapies with Delayed Effect

Ablative therapies with delayed effect include photodynamic therapy (PDT), brachytherapy, and cryotherapy [48]. The details of these therapies are addressed in other chapters. While brachytherapy and cryotherapy have fallen out of practice because of limited data around their efficacy, PDT is still utilized to recanalize the airways and decrease the tumor regrowth. There is also some emerging data around injection of chemotherapy into the endobronchial lesions [52]. Multiple, small studies have explored the efficacy of PDT [53, 54]. In a retrospective study of NSCLC patients with CAO, PDT with chemoradiation ($n = 39$) was compared to non-PDT ablation and chemoradiation ($n = 558$) [53]. Mean time for repeat intervention in PDT vs. non-PDT groups was 147 vs. 98 days ($P = 0.20$). All-cause mortality was lower in the PDT group. PDT treatment is associated with photosensitivity and patients need to avoid sunlight for up to eight weeks after the treatment. In addition, airway stenosis can be seen as a complication of PDT. ACCP guidelines suggests to consider these “local therapies” that prevent tumor regrowth for MCAO management in select patients [1].

6.8 Airway Stents

The airway stents are important adjuncts in maintaining the patency of airways in MCAO by relieving extrinsic compression or prevent tumor regrowth. The stents provide more durable control of dyspnea and decrease the need for repeated therapeutic bronchoscopies [1, 11]. Silicone or fully covered hybrid metal stents are used in MCAO, and there is no difference in the efficacy of either stent type [55]. Details of the airway stents are discussed in other chapters. The airway stents should be considered in patients with extrinsic compression for palliation or while adjunct chemoradiation needs time to shrink the tumor [1]. In endobronchial CAO, the stents have a role after tumor debridement in patients who have failed the initial chemoradiation or previous therapeutic bronchoscopies [1].

There are multiple case series documenting the safety and efficacy of different types of airway stents in MCAO [16, 17, 22, 24, 27, 28, 33, 34, 39]. An underpowered trial randomized 78 patients with NSCLC related endobronchial CAO to silicone stent placement vs. no stent after tumor debridement [14]. Although there was no difference in the local recurrence-free survival, the patients who underwent stent placement had more durable relief of dyspnea beyond three months and decreased need for repeat therapeutic bronchoscopies. In addition, local recurrence of tumor was decreased in the subset of patients who failed first-line chemotherapy or received palliation or radiation only, compared to treatment-naïve patients (Hazards ratio, 0.21; 95% CI, 0.06–0.74; $P = 0.007$).

The stents are associated with complications like growth of granulation tissue or tumor at the proximal or distal ends, mucus plugging, migration, and even erosion into surrounding mediastinal structures like esophagus and blood vessels [55]. The erosion is rare with modern stents but can be encountered in the setting of periprocedural radiation [56, 57]. Therefore, the patients with airway stents should be carefully followed and the stents should be removed as soon as there is evidence of significant tumor regression [1]. The patients should be prescribed mucociliary clearance therapies like nebulized hypertonic saline or acetylcysteine to prevent mucus plugging of the stents [11, 58]. The evidence is unclear about the role of surveillance bronchoscopies after airway stent placement [1, 11]. A retrospective study of patients with stent placement who were available for follow-up compared routine surveillance bronchoscopy within three months of stent insertion to bronchoscopy when patients were symptomatic. The patients in either group were symptomatic when stent-related complications were detected on bronchoscopy [59]. ACCP guidelines recommend either routine surveillance or symptom-driven bronchoscopy [1]. CT chest can be utilized for surveillance and assess stent patency [1, 60].

6.9 Role of Chemotherapy and Radiation

Therapeutic bronchoscopy can provide a bridge to definitive chemoradiotherapy for underlying malignancy [1]. In case of external beam radiation therapy (EBRT), treatment of central lesions is associated with an increased risk of complications, like airway and vascular fistulae, airway necrosis, and stenosis [61]. These risks may be compounded by airway stents, which may cause local airway ischemia because of the radial pressure of the stent [61], increased mucosal toxicity by the radiation due to the radiation scatter by the metal stent [56], or rapid regression of the tumor invading the airway or surrounding structures creating fistulae. In a series of 43 patients with MCAO who underwent airway stent placement and EBRT, the EBRT was stopped prematurely due to complications in 37% patients [61]. The adverse events included malignant restenosis of the stent ($n = 7$), fistula ($n = 4$), airway necrosis ($n = 3$), mediastinitis with abscess ($n = 1$), nonmalignant airway stenosis ($n = 1$), and hemoptysis ($n = 1$). The radiation for central airway tumors should be carefully planned [56, 61], and dose adjusted to minimize the toxicity [61]. For high-risk patients, concurrent chemotherapy and EBRT should be avoided, and stents should be removed as soon as feasible [61]. These risks should be addressed in a multidisciplinary fashion and discussed with the patients.

6.10 Role of Surgery

Therapeutic bronchoscopy can also facilitate surgical resection for airway or lung malignancy [1, 31]. Surgery should be considered as a definitive management in all patients who are surgical candidates [1]. Carcinoid tumors often present as airway tumors, and therapeutic bronchoscopy is performed for the relief of airway obstruction. Surgical resection should follow if the patient is a suitable candidate, as suggested by different societal guidelines including ACCP [1, 62, 63]. However, in patients who are not fit for surgery, therapeutic bronchoscopy can be considered as the primary management option [1]. In a retrospective study of patients with endobronchial carcinoid tumors, 25 patients with typical carcinoid were treated with therapeutic bronchoscopy with laser resection, and 48 patients with typical or atypical carcinoid underwent surgical resection [64]. Nine patients in the bronchoscopic group underwent surgical resection afterward. The 5-year survival was about 94% in both groups. Studies have also shown that patients with NSCLC and other airway malignancies could undergo surgical resection after therapeutic bronchoscopy [31, 65]. In a case series, 74 patients with NSCLC were able to undergo surgical resection, with parenchyma-sparing surgery (lobectomy or bilobectomy) after therapeutic bronchoscopy [31]. Multidisciplinary approach including thoracic surgery is essential for select MCAO patients.

7 Conclusion

In conclusion, patients with MCAO have a poor prognosis and present with acute symptoms and respiratory compromise. Multimodality, therapeutic bronchoscopy is essential to manage these patients. Multidisciplinary approach with different relevant specialties and patient participation can relieve symptoms, improve quality of life and survival, and minimize complications.

Competing Interest Declaration The author(s) has no competing interests to declare that are relevant to the content of this manuscript.

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