Management of Central Airway Obstruction

An American College of Chest Physicians Clinical Practice Guideline

Kamran Mahmood, MD, MPH; Lindsy Frazer-Green, PhD; Anne V. Gonzalez, MD, MSc; Scott L. Shofer, MD, PhD; Angela Christine Argento, MD; Ian Welsby, MD; Russell Hales, MD; Samira Shojaee, MD, MPH; Donna D. Gardner, DrPH; Joe Y. Chang, MD, PhD; Felix J. F. Herth, MD, PhD; and Lonny Yarmus, DO, MBA

BACKGROUND: Central airway obstruction (CAO), seen in a variety of malignant and nonmalignant airway disorders, is associated with a poor prognosis. The management of CAO is dependent on provider training and local resources, which may make the clinical approach and outcomes highly variable. We reviewed the current literature and provided evidence-based recommendations for the management of CAO.

METHODS: A multidisciplinary expert panel developed key questions using the Patient, Intervention, Comparator, and Outcomes (PICO) format and conducted a systematic literature search using MEDLINE (PubMed) and the Cochrane Library. The panel screened references for inclusion and used vetted evaluation tools to assess the quality of included studies and extract data, and graded the level of evidence supporting each recommendation. A modified Delphi technique was used to reach consensus on recommendations.

RESULTS: A total of 9,688 abstracts were reviewed, 150 full-text articles were assessed, and 31 studies were included in the analysis. One good practice statement and 10 graded recommendations were developed. The overall certainty of evidence was very low.

CONCLUSIONS: Therapeutic bronchoscopy can improve the symptoms, quality of life, and survival of patients with malignant and nonmalignant CAO. Multi-modality therapeutic options, including rigid bronchoscopy with general anesthesia, tumor/tissue debridement, ablation, dilation, and stent placement, should be utilized when appropriate. Therapeutic options and outcomes are dependent on the underlying etiology of CAO. A multidisciplinary approach and shared decision-making with the patient are strongly encouraged.

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KEY WORDS: airway stenosis; airway stent; carcinoid; central airway obstruction; clinical practice guidelines; jet ventilation; lung cancer; rigid bronchoscopy; therapeutic bronchoscopy; tracheal stenosis

ABBREVIATIONS: AQuIRE = American College of Chest Physicians Quality Improvement Registry Evaluation and Education; CAO = central airway obstruction; CHEST = American College of Chest Physicians; ERMT = endoscopic carbon dioxide laser resection with adjuvant medical therapy; HR = hazard ratio; PDT = photodynamic therapy; QoL = quality of life; RCT = randomized controlled trial

AFFILIATIONS: From the Division of Pulmonary, Allergy and Critical Care (K. H. and S. L. S.), Department of Medicine, Duke University, Durham, NC; Allergy & Asthma Network (L. F.-G. and D. D. G.), Fairfax, VA; Respiratory Division (A. V. G.), McGill University Health Centre, Montréal, QC, Canada; Johns Hopkins University (A. C. A. and L. Y.), Baltimore, MD; Department of Anesthesiology (I. W.), Duke University, Durham, NC; Department of Radiation Oncology (R. H.), Johns Hopkins University, Baltimore, MD; Vanderbilt University (S. S.), Nashville, TN; Department of Radiation Oncology (J. Y. C.), MD Anderson Cancer Center, Houston, TX; and Department of Pneumology and Critical Care

Summary of Recommendations

1. **For patients with suspected central airway obstruction, we recommend a comprehensive history and physical examination with a focus on the respiratory system, a CT scan of the chest, and appropriate laboratory investigations pertinent to nonmalignant central airway obstruction and preoperative assessment** (Good Practice Statement).

2. **For patients with symptomatic *malignant or nonmalignant* central airway obstruction, we suggest therapeutic bronchoscopy as an adjunct to systemic medical therapy and/or local radiation** (Conditional Recommendation, Very Low Certainty of Evidence).

3. **For patients with symptomatic *malignant or nonmalignant* central airway obstruction, we suggest the use of rigid bronchoscopy over flexible bronchoscopy for therapeutic interventions** (Conditional Recommendation, Very Low Certainty of Evidence).

4. **For patients with symptomatic *malignant or nonmalignant* central airway obstruction, we suggest the use of general anesthesia/deep sedation over moderate sedation for therapeutic bronchoscopy** (Conditional Recommendation, Very Low Certainty of Evidence).

5. **For patients with symptomatic *malignant or nonmalignant* central airway obstruction undergoing rigid therapeutic bronchoscopy with general anesthesia, we suggest the use of either jet ventilation or controlled/spontaneous assisted ventilation** (Conditional Recommendation, Very Low Certainty of Evidence).

6. **For patients with symptomatic *malignant or nonmalignant* central airway obstruction with endobronchial disease, we suggest the use of tumor or tissue excision and/or ablation to help achieve airway patency** (Conditional Recommendation, Very Low Certainty of Evidence).

7. **For patients with *nonmalignant central airway obstruction with stenosis* undergoing therapeutic bronchoscopy, we suggest airway dilation be performed either alone or in combination with other therapeutic modalities** (Conditional Recommendation, Very Low Certainty of Evidence).

8. **For patients with symptomatic *malignant or nonmalignant* central airway obstruction, we suggest stent placement if other therapeutic bronchoscopic and systemic treatments have failed and when feasible for the underlying disorder** (Conditional Recommendation, Very Low Certainty of Evidence).

9. **For patients with *malignant or nonmalignant* central airway obstruction with stent placement, we suggest either routine surveillance bronchoscopy or bronchoscopy when patients are symptomatic** (Conditional Recommendation, Very Low Certainty of Evidence).

10. **For patients with *malignant or nonmalignant* central airway obstruction undergoing therapeutic bronchoscopy, we suggest either using or holding local bronchoscopic therapy** (Conditional Recommendation, Very Low Certainty of Evidence).

Remark: Local bronchoscopic treatment is defined as a non-ablative bronchoscopic therapy that may reduce the recurrence or progression of an endobronchial disorder.

11. **For patients with *nonmalignant* central airway obstruction, we suggest either open surgical resection or therapeutic bronchoscopy** (Conditional Recommendation, Very Low Certainty of Evidence).

12. **For patients with *malignant* central airway obstruction with endobronchial tumor, we suggest either surgical resection or therapeutic bronchoscopy for relief of initial obstruction** (Conditional Recommendation, Very Low Certainty of Evidence).

Remarks: There is limited evidence to suggest surgical benefit for non-carcinoid malignant central airway obstruction because of advanced locoregional or metastatic disease. Surgery with curative intent might be considered in patients with central airway obstruction related to a localized primary lung and airway cancer, including carcinoid.

Background

Central airway obstruction (CAO) is a life-threatening disorder that leads to debilitating dyspnea and is associated with a poor prognosis, especially for proximal obstruction.[1,2] It is defined as a 50% or greater occlusion of the trachea, mainstem bronchi, bronchus intermedius, or lobar bronchi.[3,4] Lung cancer, the leading cause of oncologic mortality, is the most common etiology of malignant CAO,[2] but primary

Medicine (F. J. F. H.), Thoraxklinik, and Translational Lung Research Center (TLRCH), University of Heidelberg, Heidelberg, Germany.

CORRESPONDENCE TO: Kamran Mahmood, MD, MPH; email: k.mahmood@duke.edu

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airway malignancy or any cancer that metastasizes to the airway or surrounding mediastinum can cause CAO.[1] Nonmalignant disorders affecting the respiratory tract can also lead to CAO (Table 1). Anatomically, CAO can be classified into three distinct categories: intrinsic, extrinsic, or mixed (Fig 1).

The management of CAO is supported by limited high-quality evidence amidst significant heterogeneity of patients and disorders, compounded by wide variability in training and practice patterns.[4-6] Although with novel targeted systemic therapies, lung cancer screening efforts, and a shift in lung cancer epidemiology from central squamous cell to peripheral adenocarcinoma, the overall incidence of CAO is decreasing, the life-threatening presentation and complexity of management necessitate a systematic approach.[7] Fortunately, there is an increased awareness along with rapid growth in interventional pulmonary training and clinical programs specializing in CAO management.[6] Therefore, we evaluated the current evidence systematically and utilized expert consensus to provide clinical guidance as well as highlighted gaps for meaningful research with patient-centric outcomes.

TABLE 1] Etiologies of Nonmalignant Central Airway Obstruction

1. Postintubation/tracheostomy-related tracheal stenosis
2. Idiopathic tracheal or bronchial stenosis
3. Inflammatory a. Granulomatosis with polyangiitis b. Relapsing polychondritis c. Radiation d. Other inflammatory, like sarcoidosis, inflammatory bowel disease, etc.
4. Infections, like TB, fungal, recurrent respiratory papillomatosis, rhinoscleroma
5. Lung transplantation-related stenosis and bronchomalacia
6. Expiratory airway collapse: a. Tracheobronchomalacia and excessive dynamic airway collapse b. Mounier Kuhn Syndrome
7. Nonmalignant airway tumors/lesions a. Benign growths like hamartoma, lipoma, etc. b. Amyloidosis c. Tracheobronchopathia osteochondroplastica
8. Mechanical compression by surrounding structures, like goiter, aortic aneurysm

Methods

A multidisciplinary expert panel conducted a systematic review addressing 11 questions developed using the PICO (Patient, Intervention, Comparator, and Outcomes) format (Table 2). The population of interest is patients with symptomatic CAO, including inpatients and outpatients. The panel employed the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach for assessing the certainty of evidence and formulating and grading clinical recommendations. The strength of recommendation and supporting evidence is expressed as shown in Table 3.[8]

For detailed methodology, see e-Appendix 1.

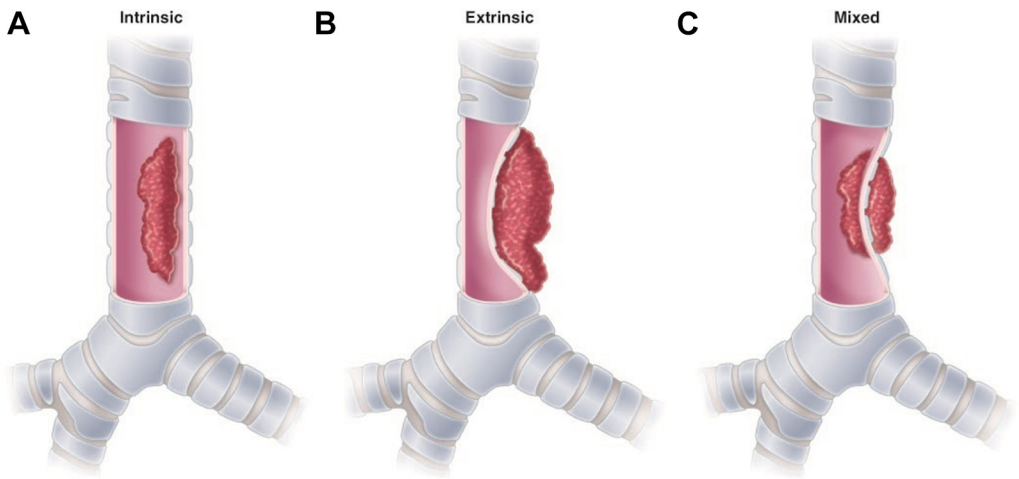

Figure 1 – *A-C, Classification of central airway obstruction. A, Intrinsic or endoluminal. B, Extrinsic or extraluminal. C, Mixed. Reproduced with permission from Loscalzo et al. Harrison's Principles of Internal Medicine Vol 2, 21st Edition, ISBN: 9781264268481.*

TABLE 2] PICO Questions

Question No.	Question
1	Should patients with symptoms of suspected CAO undergo a complete clinical evaluation?
2	Should therapeutic bronchoscopy along with systemic medical therapy and/or local radiation be performed for symptomatic malignant or nonmalignant CAO compared to systemic medical therapy and/or local radiation only?
3	Should therapeutic bronchoscopy for symptomatic malignant or nonmalignant CAO be performed using rigid bronchoscopy compared to flexible bronchoscopy?
4	Should therapeutic bronchoscopy for symptomatic malignant or nonmalignant CAO be performed with general anesthesia/deep sedation compared to moderate sedation?
5	Should therapeutic rigid bronchoscopy with general anesthesia for malignant or nonmalignant CAO be performed with jet ventilation compared to controlled ventilation or spontaneous assisted ventilation?
6	Should patients with symptomatic malignant or nonmalignant CAO who have endobronchial disease undergo therapeutic bronchoscopy with tumor or tissue excision/ablation compared to therapeutic bronchoscopy without excision/ablation?
7	Should patients with symptomatic nonmalignant CAO with stenosis undergo therapeutic bronchoscopy with airway dilation compared to therapeutic bronchoscopy without dilation?
8	Should patients with symptomatic malignant or nonmalignant CAO treated with therapeutic bronchoscopy undergo stent placement compared to no stent placement?
9	Should patients with malignant or nonmalignant CAO who have undergone stent placement receive routine bronchoscopy surveillance compared to no surveillance or symptom-driven bronchoscopy?
10	Should patients with malignant or nonmalignant CAO undergo therapeutic bronchoscopy with local bronchoscopic therapy compared to no local bronchoscopic therapy?
11	Should patients with symptomatic malignant or nonmalignant CAO undergo surgical resection compared to therapeutic bronchoscopy?

CAO = central airway obstruction; PICO = Patient, Intervention, Comparator, and Outcomes.

Results

A total of 9,688 unique citations were screened (e-Fig 1), and 31 relevant studies were identified (e-Table 1) and the following recommendations were proposed (Fig 2).

Question 1: Should patients with symptoms of suspected CAO undergo a complete clinical evaluation?

American College of Chest Physicians (CHEST) Recommendation 1: For patients with suspected central airway obstruction, we recommend a comprehensive history and physical examination with a focus on the respiratory system, a CT scan of the chest, and appropriate laboratory investigations pertinent to nonmalignant central airway obstruction and preoperative assessment (Good Practice Statement).

Justification. In patients with suspected CAO, including outpatients and inpatients, detailed history taking should encompass symptoms, comorbid conditions, including cervical spine disorders, medications (eg, antiplatelets or anticoagulants), and previous therapies (eg, thoracic surgery, chemoradiation).[1] The physical examination should include a comprehensive evaluation of the upper and lower airways.[1] The following parameters, that may impact the approach to rigid bronchoscopy or endotracheal tube intubation, should be assessed:

TABLE 3] Certainty of Evidence

Certainty of the Evidence	Level of Confidence in the Estimate of the Effect[8]
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

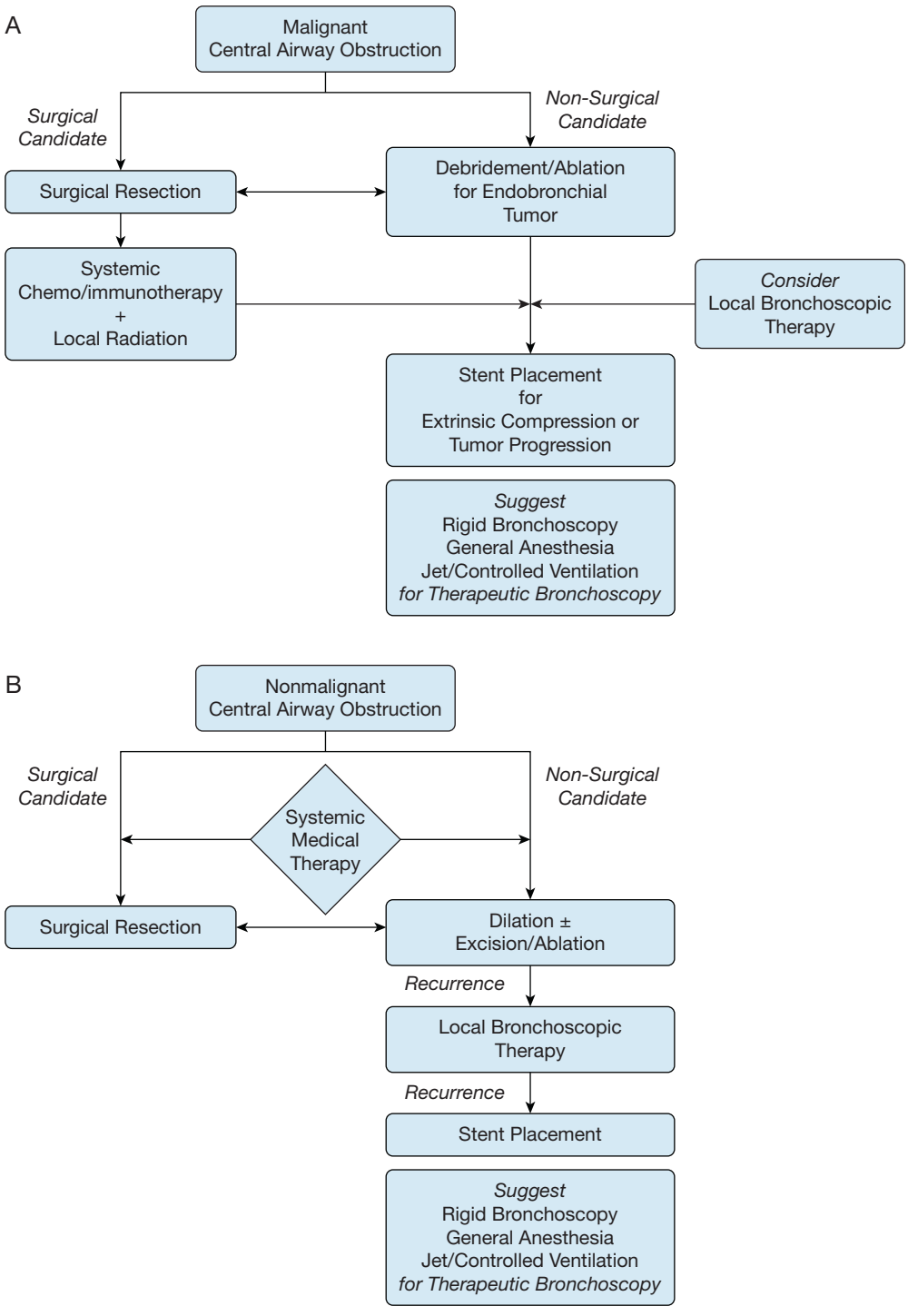

Figure 2 – *A, Suggested approach for the management of malignant central airway obstruction. B, Suggested approach for the management of nonmalignant central airway obstruction.*

1. Mouth opening (Normal > three patient-finger breadths).[9]
2. Teeth, especially prominent, missing, or loose teeth.[9]
3. Modified Mallampati score.[10,11]
4. Neck mobility (Normal > 90°).[9]
5. Thyromental distance (Normal > three finger breadths).[9]

Laboratory investigations for pre-operative assessment and serological studies to determine the etiology of nonmalignant CAO, especially when there is concern for vasculitis or connective tissue disorders, can assist with primary diagnosis and monitoring of therapeutic response. Spirometry and flow-volume loops can help

assess the functional limitation of airway obstruction, response to intervention, and long-term monitoring.[1,12] The imaging of choice for CAO is CT scan of the chest and neck to establish the diagnosis and severity of obstruction and plan therapeutic approaches and follow-up.[1,13] Special attention should be paid to central airways as radiographic diagnosis of CAO is often missed or delayed.[14]

Question 2: Should therapeutic bronchoscopy along with systemic medical therapy and/or local radiation be performed in symptomatic patients with malignant or nonmalignant central airway obstruction compared to systemic medical therapy and/or local radiation only?

CHEST Recommendation 2: For patients with symptomatic ***malignant or nonmalignant*** central airway obstruction, we suggest therapeutic bronchoscopy as an adjunct to systemic medical therapy and/or local radiation (Conditional Recommendation, Very Low Certainty of Evidence).

Justification. Therapeutic bronchoscopy can be leveraged as a bridge and adjunct to definitive treatment of the underlying disorder. In malignant CAO, therapeutic bronchoscopy can be used to relieve the airway obstruction, allowing patients to receive local radiation, chemo-immunotherapy, and targeted therapies as indicated. In certain cases of nonmalignant CAO, such as vasculitis or airway infections like endobronchial TB or fungal infections, appropriate systemic medical treatments should be pursued concurrently.

One prospective and two retrospective studies, and one randomized trial, comparing therapeutic bronchoscopy and systemic medical therapy, including local radiation, to systemic medical therapy alone were identified.[15-18] Although of very low quality due to small and heterogeneous patient cohorts, the evidence suggests that addition of therapeutic bronchoscopy results in a statistically significant improvement in symptom control, quality of life (QoL), spirometry, and survival (e-Table 2).

A prospective study compared 34 patients with non-small cell lung cancer who underwent therapeutic bronchoscopy to 12 patients who declined therapeutic bronchoscopy.[16] Patients in both groups received chemo-radiation. Mean survival time was 10 $\pm$ 9 and 4 $\pm$ 3 months with therapeutic bronchoscopy and control, respectively (log rank $P = .005$). Dyspnea decreased and global health and physical function improved with therapeutic bronchoscopy for up to 6 months of follow-up. A retrospective study compared patients with lung cancer-associated CAO undergoing therapeutic bronchoscopy *with* chemo-radiation (n = 60) and patients (n = 40) receiving chemo-radiation only.[15] With therapeutic bronchoscopy, survival was better (hazards ratio [HR], 2.1; 95% CI, 1.1-4.8; $P = 0.003$), symptom-free interval prolonged, and atelectasis and rehospitalizations decreased. Radiation therapy should be carefully planned in patients with malignant CAO with airway stenting, as anatomic distortion and scattered radiation dose to the airway from the metal stent can lead to higher complications.[19]

Research priorities. The existing but limited comparative effectiveness evidence, favorable safety profile, and clinical experience supporting bronchoscopic intervention pose ethical challenges for designing a randomized controlled trial (RCT) withholding therapeutic bronchoscopy from symptomatic patients.[1] However, prospective clinical trials comparing therapeutic bronchoscopy to radiation and combination modalities, especially in patients with advanced malignant CAO, are needed.

Question 3: Should therapeutic bronchoscopy for symptomatic malignant or nonmalignant CAO be performed using rigid bronchoscopy compared to the flexible bronchoscopy?

CHEST Recommendation 3: For patients with symptomatic ***malignant or nonmalignant*** central airway obstruction, we suggest the use of rigid bronchoscopy over flexible bronchoscopy for therapeutic interventions (Conditional Recommendation, Very Low Certainty of Evidence).

Justification. A prospective registry and four retrospective studies comparing the outcomes of flexible and rigid bronchoscopy were identified.[3,20-24] Rigid bronchoscope serves as a conduit for ventilation, can be used to "core through" large tumors, allows excellent suction and ability to tamponade during airway bleeding, and facilitates insertion of instruments like flexible bronchoscopes, rigid forceps, and silicone stents.[21,25] In most cases of rigid bronchoscopy, flexible bronchoscope is used as an adjunct tool, especially for distal airway interventions. Comparative studies showed similar success rates with flexible and rigid bronchoscopy, but fewer procedure sessions were required to achieve airway patency with rigid bronchoscopy. There were no significant differences in complications, but data suggest more bleeding-related

deaths with flexible bronchoscopy (e-Table 3). Although evidence is of very low certainty, the expert panel favors rigid bronchoscopy for therapeutic interventions in symptomatic CAO, especially for proximal and critical obstruction, because of the distinct multimodality procedural advantages.

The prospective multicenter American College of Chest Physicians Quality Improvement Registry, Evaluation and Education (AQuIRE) registry assessed the effectiveness and complications of therapeutic bronchoscopy for malignant CAO.[3,20] The registry included 947 patients who underwent 382 flexible and 733 rigid therapeutic bronchoscopies. Success rate, defined as reopening the airway lumen to > 50% of the normal diameter, with flexible vs rigid bronchoscopies was 92.7% vs 93.5% ($P = .62$). Complication rates and complication-related mortality were similar across modalities. Several other studies reported similar outcomes, but rigid bronchoscopy was more commonly used for proximal and bulkier disease.[21-23] A study demonstrated that fewer treatment sessions were required with rigid vs flexible bronchoscopy (1 vs 2 sessions, $P < 0.001$).[24]

Research priorities. Further research is needed to compare success, safety, and patient-centered outcomes between flexible and rigid bronchoscopy for management of CAO, with specific focus on the utility in proximal vs distal airway locations.

Question 4: Should therapeutic bronchoscopy for symptomatic malignant or nonmalignant CAO be performed with general anesthesia/deep sedation compared to moderate sedation?

CHEST Recommendation 4: For symptomatic patients with ***malignant or nonmalignant*** central airway obstruction, we suggest the use of general anesthesia/deep sedation over moderate sedation for therapeutic bronchoscopy (Conditional Recommendation, Very Low Certainty of Evidence).

Justification. Two prospective registry studies and a retrospective study were identified.[3,20,24] The available very low certainty evidence suggests general anesthesia/deep sedation is safer compared to moderate sedation for therapeutic bronchoscopy and associated with fewer complications and lower mortality (e-Table 4). Although no significant difference was found in the rate of technical success between the use of general anesthesia/deep sedation and moderate sedation during CAO procedures, more treatment sessions were required under moderate sedation, presumably due to the inability of the patient to tolerate long procedures. The use of general anesthesia with paralytics compared to spontaneous ventilation was associated with a significant reduction in intraoperative respiratory complications. The panel suggests a multidisciplinary approach involving the proceduralist and anesthesiologist for optimal anesthesia planning to minimize complications.

In the AQuIRE registry, 961 therapeutic bronchoscopies were performed with general anesthesia/deep sedation and 154 with moderate sedation.[3,20] There was no difference in the technical success rate, but general anesthesia/deep sedation was associated with a significant decrease in the risk of complications compared to moderate sedation (multivariate OR, 0.42; 95% CI, 0.21-0.83; $P = .013$). In addition, the use of paralytics with anesthesia was associated with a further significant reduction in complications (3% vs 6.7%; $P = .006$). Another study reported a similar success rate but more procedure sessions were required and more fatal bleeding complications observed with moderate sedation vs general anesthesia.[24] An RCT showed that rigid bronchoscopy under general anesthesia with paralytics vs without paralytics was associated with fewer desaturation events and hypercapnia.[26]

Research priorities. Studies should be performed to assess the outcomes of therapeutic bronchoscopy with general anesthesia/deep sedation vs moderate sedation.

Question 5: For patients with symptomatic CAO undergoing rigid therapeutic bronchoscopy with general anesthesia, should jet ventilation be used compared to controlled ventilation or spontaneous assisted ventilation?

CHEST Recommendation 5: For patients with symptomatic ***malignant or nonmalignant*** central airway obstruction undergoing rigid therapeutic bronchoscopy with general anesthesia, we suggest the use of either jet ventilation or controlled/spontaneous assisted ventilation (Conditional Recommendation, Very Low Certainty of Evidence).

Justification. In jet ventilation, high-pressure oxygen is delivered through the open rigid bronchoscope in short bursts either manually at a rate of 10-14 breaths per minute (Sander's technique) or using a high frequency, automated machine at 60-300 breaths per minute.[27] In controlled ventilation, the anesthesia circuit is attached to a sealed rigid bronchoscope, and minute ventilation is maintained by positive pressure with a mechanical ventilator or bag ventilation. For spontaneous assisted

ventilation, oxygen is delivered through the rigid bronchoscope, and sedation is titrated to allow spontaneous ventilation by the patient with assisted ventilation if prolonged desaturation.

Two prospective registry studies and one prospective cohort study comparing jet and controlled/spontaneous assisted ventilation were identified.[3,20,28] Technical success rates were similar, but complication rates were lower with jet ventilation (e-Table 5). Controlled ventilation is preferred over spontaneous assisted ventilation as the former is associated with decreased intraprocedural respiratory complications.[26] Extracorporeal membrane oxygenation may be considered for therapeutic bronchoscopy in patients with critical tracheal or bilateral mainstem bronchial obstruction, but ideal patient selection and complication profiles are poorly understood.[29]

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 malignant CAO.[3,20] There was no significant difference between the controlled/spontaneous assisted ventilation and jet ventilation in therapeutic success rates (92.9% vs 96.1%, respectively), improvement of dyspnea or QoL, complications, or complications-related mortality. In one study, rigid bronchoscopy with controlled ventilation was associated with more significant hypercapnia compared to jet ventilation.[28]

The panel suggests a multidisciplinary partnership with the anesthesiology team and the best use of available equipment to optimize patient outcomes.

Research priorities. Comparative studies are needed to establish the safety and efficacy of controlled/spontaneous assisted ventilation, jet ventilation, and extracorporeal membrane oxygenation with a focus on investigating specific indications for these modalities.

Question 6: Should patients with symptomatic malignant or nonmalignant CAO who have endobronchial disease undergo therapeutic bronchoscopy with tumor or tissue excision/ablation compared to therapeutic bronchoscopy without excision/ablation?

CHEST Recommendation 6: For patients with symptomatic ***malignant or nonmalignant*** central airway obstruction with endobronchial disease, we suggest the use of tumor or tissue excision and/or ablation to help achieve airway patency (Conditional Recommendation, Very Low Certainty of Evidence).

Justification. Two comparative retrospective studies and one prospective study assessing tissue excision/ablation in nonmalignant CAO were identified, but the quality of evidence was very low (e-Table 6).[30-32] No studies comparing malignant tumor excision and/or ablation with other bronchoscopic therapeutic modalities were identified. Tumor excision is an essential procedure that can be performed with multiple techniques, including manual debridement with flexible or rigid forceps, rigid bronchoscope coring, microdebridement, or cryodebridement.[33] These techniques are often performed in conjunction with heat ablative modalities to control bleeding.[34] Several non-comparative case series demonstrate the effectiveness and safety of commonly used modalities, including laser, electrocautery, and argon plasma coagulation.[25,33,35-37]

Laser or electrocautery resection can be used to excise scar tissue in *nonmalignant* CAO, mostly in tracheal stenosis. A prospective multicenter study of 810 patients with idiopathic subglottic stenosis compared dilation, endoscopic carbon dioxide laser resection with adjuvant medical therapy (ERMT), and cricotracheal resection.[32] At 3 years, the recurrence rate of stenosis was 28% with dilation and 12.4% with ERMT (adjusted propensity-matched HR, 3.16; 95% CI, 1.82-5.51). Compared to dilation, ERMT showed better breathing score, voice score, and global physical health score at one year. At 5 years (n = 487), dilation and ERMT were associated with recurrence rates of 50% and 30%, respectively.[38] Some subgroups of patients with nonmalignant CAO, like lung transplant-related airway stenosis, may not need tissue excision or ablation.

The panel suggests excision of endobronchial tumor/tissue in conjunction with ablative therapies. When using heat ablative therapies, appropriate safety precautions should be followed, including reducing the F_{IO_2} to ≤ 0.4 and keeping the ablation catheters away from flammable devices to decrease the risk of airway fire.[34]

Research priorities. The comparative effectiveness of different ablative therapies should be assessed.

Question 7: Should patients with symptomatic nonmalignant CAO with stenosis undergo therapeutic bronchoscopy with airway dilation compared to therapeutic bronchoscopy without dilation?

CHEST Recommendation 7: For patients with ***nonmalignant*** central airway obstruction ***with stenosis*** undergoing therapeutic bronchoscopy, we suggest

airway dilation be performed either alone or in combination with other therapeutic modalities (Conditional Recommendation, Very Low Certainty of Evidence).

Justification. One prospective and two retrospective studies were identifed.[30-32] The strength of evidence comparing dilation to nondilation approaches for nonmalignant CAO with stenosis is very low. Dilation is considered first-line therapy and can be performed alone or in combination with laser or electrocautery incisions and local bronchoscopic injection therapies. Evidence suggests dilation compared to laser resection or steroid injection is associated with increased time to reintervention (e-Table 7). But, when dilation is compared to laser resection with adjuvant medical therapy, the recurrence rate is higher.

A retrospective cohort study of 101 patients with subglottic stenosis secondary to idiopathic, post-intubation, granulomatosis with polyangiitis, and other autoimmune etiologies reported a statistically nonsignificant difference in mean time to reintervention with dilation (96 procedures; 463 ± 530 days) vs laser incisions (6 procedures; 179 ± 193 days).[30]

In a prospective, multicenter study of 810 patients with idiopathic subglottic stenosis, the recurrence rate of stenosis was 28% with dilation and 12.4% with ERMT at 3 years.[32] At 5 years (n = 487), dilation and ERMT were associated with a recurrence rate of 50% and 30%, respectively.[38] A multimodality approach utilizing dilation, ablative resection, and medical treatment is more likely to achieve optimal outcomes.

Research priorities. Robust evidence is needed to understand the role of dilation, either alone or as an adjunct, to other bronchoscopic therapies.

Question 8: Should patients with malignant or nonmalignant CAO treated with therapeutic bronchoscopy undergo stent placement compared to no stent placement?

CHEST Recommendation 8: For patients with symptomatic ***malignant or nonmalignant*** central airway obstruction, we suggest stent placement if other therapeutic bronchoscopic and systemic treatments have failed and when feasible for the underlying disorder (Conditional Recommendation, Very Low Certainty of Evidence).

Justification. One RCT, three prospective studies, and seven retrospective studies comparing stent placement to other bronchoscopic therapies were identified.[3,20,39-45] The very low certainty evidence suggests stent placement is associated with technical success, more durable improvement in dyspnea, and decreased need for repeat therapeutic bronchoscopies, especially in patients with malignant CAO (e-Table 8). The benefits of stent placement are more evident in malignant CAO with extrinsic compression where oncologic therapy will require time for response, or in patients with endobronchial disease who have failed first-line chemotherapy and receiving radiation or palliative care compared to chemotherapy-naive patients.[39] Evidence about the stent complications should be considered in decision-making.[4,46] Because of stent complications like mucus plugging, granulation tissue formation, migration, fracture, and infections, stent use should be carefully contemplated, avoided if airway debridement can achieve airway patency, and reserved for indications when airway patency cannot be maintained without the stent or prior treatment has failed.[4]

An underpowered RCT randomized 78 patients with *malignant*, endobronchial CAO due to non-small cell lung cancer to silicone stent or no stent after tumor debridement.[39] There was no difference in recurrence-free or overall survival, but stent placement led to longer improvement in dyspnea and decreased need for repeat therapeutic bronchoscopies. The beneficial effect of the stent on local recurrence was significant in the subset of patients for whom first-line chemotherapy failed or who received radiation or palliation only as compared to the treatment-naive group (HR, 0.21; 95% CI, 0.06-0.74; $P = .007$). In the AQuIRE registry, 406 stents were placed during 1,115 therapeutic bronchoscopies.[3,19] Stent placement was associated with technical success (multivariate OR, 11.9; 95% CI, 5.1-27.8; $P < .0001$) but was not associated with improvement in dyspnea, QoL, or complications.

Although the evidence for stent placement is more limited in *nonmalignant* CAO, the panel suggests a stent trial for patients requiring repeated dilations who have failed local bronchoscopic therapy. Alternative options for stent placement should be considered in patients with subglottic tracheal stenosis due to anatomical constraints and stent migration. In a retrospective study of central airway stenosis in lung transplant recipients, stenting compared to dilation was associated with a greater improvement in FEV_1.[47] The US Food and Drug Administration issued a public health notification in 2005 about the complications of metallic stents in benign tracheal disorders,[48] although the new-generation, fully covered metal stents may be safer.[4,49]

Research priorities. Clinical trials are needed to assess optimal use of airway stents, management of airway secretions and granulation tissue, and the impact of chemotherapy and radiation around stent insertion. In view of the US Food and Drug Administration warning, the safety of the new-generation, fully covered metal stents in nonmalignant CAO, especially in the trachea, and the use of local therapies to avoid or delay stent insertion warrant well-designed trials. Drug-coated and 3D-printed stents should also be further evaluated.

Question 9: Should patients with malignant or nonmalignant CAO who have undergone stent placement receive routine bronchoscopy surveillance compared to no surveillance or symptom-driven bronchoscopy?

CHEST Recommendation 9: For patients with ***malignant or nonmalignant*** central airway obstruction with stent placement, we suggest either routine surveillance bronchoscopy or bronchoscopy when patients are symptomatic (Conditional Recommendation, Very Low Certainty of Evidence).

Justification. One retrospective study assessing surveillance bronchoscopy was identified.[50] The certainty of evidence is very low (e-Table 9). Patients with CAO who undergo stent placement should be clinically followed, as they can develop stent-related complications or stents may need to be removed after treatment of the underlying disorder. In addition, we suggest the use of mucociliary clearance interventions (eg, hypertonic saline nebulization) and the use of chest CT scans for assessment of stent or airway patency to potentially limit the need for additional invasive procedures.

A retrospective study of patients with malignant and nonmalignant CAO who underwent silicone stent placement and were available for follow-up compared routine surveillance bronchoscopy (n = 39) within 3 months of stent insertion to bronchoscopy only when the patients were symptomatic (n = 31).[50] Stent-related complications were detected in 16 of 39 patients (41%) in the surveillance group, most of whom were symptomatic as well, and 26 of 31 (84%) symptomatic patients in the control group. The authors concluded that routine surveillance bronchoscopy did not detect stent complications unless patients were symptomatic.

Research priorities. Comparative studies are needed to investigate the utility of surveillance by routine or symptom-driven bronchoscopy and CT scans.

Question 10: Should patients with malignant or nonmalignant CAO undergo therapeutic bronchoscopy with local bronchoscopic therapy compared to no local bronchoscopic therapy?

CHEST Recommendation 10: For patients with ***malignant or nonmalignant*** central airway obstruction undergoing therapeutic bronchoscopy, we suggest either using or holding local bronchoscopic therapy (Conditional Recommendation, Very Low Certainty of Evidence).

Remark: Local bronchoscopic treatment is defined as a non-ablative bronchoscopic therapy that may reduce the recurrence or progression of an endobronchial disorder.

Justification. Several local bronchoscopic therapies including photodynamic therapy (PDT), brachytherapy, cryotherapy, and intralesional injection/application of medications (eg, intratumoral chemotherapies for malignant CAO and steroid or mitomycin C injection/application for nonmalignant CAO) have been utilized. Two retrospective studies assessing the effectiveness of local therapy were identified.[31,51] Overall, the certainty of evidence is very low and comes with a significant bias, but favors the use of local therapy for increased success and prolonged time to reintervention with no significant complications (e-Table 10). The panel recommends a personalized approach to assess risks and benefits of each intervention (eg, post-PDT airway stenosis and photosensitivity).

In a retrospective study of patients with non-small cell lung cancer, for a subset with *malignant* CAO, bronchoscopic PDT in combination with chemoradiation (n = 39) was compared to non-PDT ablation with chemoradiation (n = 558). Mean time to reintervention in the PDT vs non-PDT groups was 147 vs 98 days ($P = 0.20$). All-cause mortality was lower in the PDT group.[52] For *nonmalignant* CAO, a retrospective study of 20 patients with idiopathic and post-intubation/tracheostomy tracheal stenosis, reported 4-month success rates of 15%, 18.2%, and 75% for airway dilation, steroid injection, and mitomycin C application, respectively ($P < .05$).[51]

Research priorities. Well-designed studies are needed to assess the effectiveness of different current or novel local bronchoscopic therapies for CAO management.

Question 11: Should patients with symptomatic malignant or nonmalignant CAO undergo surgical resection compared to therapeutic bronchoscopy?

CHEST Recommendation 11: For patients with ***nonmalignant*** central airway obstruction, we suggest either open surgical resection or therapeutic bronchoscopy (Conditional Recommendation, Very Low Certainty of Evidence).

CHEST Recommendation 12: For patients with ***malignant*** central airway obstruction with endobronchial tumor, we suggest either surgical resection or therapeutic bronchoscopy for relief of initial obstruction (Conditional Recommendation, Very Low Certainty of Evidence).

Remarks: There is limited evidence to suggest surgical benefit for non-carcinoid malignant CAO because of advanced locoregional or metastatic disease. Surgery with curative intent might be considered in patients with CAO related to a localized primary lung and airway cancer, including carcinoid.

Justification. Two prospective and six retrospective studies comparing surgery to therapeutic bronchoscopy were identified.[32,53-59] The certainty of evidence is very low, and most of the evidence in nonmalignant CAO is related to tracheal stenosis. We suggest dilation as a primary intervention for benign, simple and subglottic tracheal stenosis with consideration of local therapy like mitomycin C on recurrence and close collaboration with thoracic surgery or otolaryngology. For repeat recurrence, especially in patients with complex tracheal stenosis, a surgical approach is suggested. Tracheostomy or rarely stent placement may be considered in some select patients who are not surgical candidates. For patients with malignant CAO secondary to typical and atypical endobronchial carcinoid tumors, surgical resection is the treatment of choice for curative intent. Therapeutic bronchoscopy may be a bridge to surgery or primary treatment if patients with typical carcinoid tumors are not surgical candidates. Surgery may be a definitive treatment option in suitable candidates with localized primary lung and airway cancer-related CAO.

Evidence suggests that the recurrence of tracheal stenosis is lower with surgical resection compared to therapeutic bronchoscopy (e-Table 11). In a prospective, multicenter study including 810 patients with idiopathic subglottic stenosis, the recurrence rates at 3 years with dilation, ERMT, and surgical resection were 28%, 12.4%, and 1.2%, respectively.[32] Breathing score and QoL were better following surgical resection, but voice scores were worse compared to other therapies. The recurrence rates at 5 years (n = 487) were 50%, 30% and 5%, for dilation, ERMT, and surgery, respectively.[38] Multiple studies in patients with tracheal stenosis comparing surgical resection to multimodality therapeutic bronchoscopy, including stent placement, found similar outcomes.[53-58]

Nonmalignant CAO can be seen with tracheobronchomalacia and excessive dynamic airway collapse.[4] Evidence suggests the utility of noninvasive ventilation as a primary intervention.[60] For patients with severe tracheobronchomalacia refractory to noninvasive ventilation, a stent trial followed by tracheobronchoplasty may be considered, but further studies are needed.[61]

For malignant CAO, the role of surgery is generally limited to carcinoid tumors based on available evidence and professional society guidelines.[62,63] In a retrospective study of patients with bronchial carcinoid, 25 patients with typical carcinoid were treated bronchoscopically with laser resection, and 48 patients with typical or atypical carcinoid underwent surgical resection.[59] Nine patients in the bronchoscopic group subsequently underwent surgical resection. At 5 years, the survival in the bronchoscopic and surgical groups was 94.4% and 94.5% ($P = .9$). For malignant CAO related to primary lung and airway cancer, surgical resection may be considered if it is curative in surgical candidates.[64,65] Therapeutic bronchoscopy can serve as a bridge to definitive surgical resection in lung and airway cancer-related CAO with localized disease.[64,65]

Research priorities. Studies focused on patient-centric outcomes are required to evaluate the role of surgery in CAO and optimal therapeutic bronchoscopic strategies in patients who are not surgical candidates.

Discussion and Summary

CAO is a syndrome that includes heterogeneous disorders, and the *specific* treatment of malignant and nonmalignant CAO should be dictated by the underlying etiology. One limitation of this guideline is that the recommendations provide an overarching approach within a hierarchical framework that may not apply to all patients with CAO. Another limitation is that most of the comparative evidence is of very low certainty, with little confidence in the estimates of benefits, harms, and burdens. Therefore, the strength of recommendations is conditional, but we believe that the desirable benefits of the recommendations likely outweigh the risks. The panel recommends shared decision-making with patients and caregivers, considering their goals and QoL. A multidisciplinary approach is suggested, and health care access and

inequities should be addressed. We call for well-designed studies to address the gaps and this guideline should be revised once the evidence is upgraded.

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