Peer Review File

Article information: https://dx.doi.org/10.21037/med-22-44

Reviewer A Comments:

Comment 1: Thank you for allowing me to review the article titled "Overview of Malignant Central Airway Obstruction". The manuscript reads very well and contains most of the published data in regard to MCAO. There are areas that are more pertinent to benign CAO (detailed stenosis classification, description of radial cuts prior to balloon tracheoplasty etc) and I would recommend keeping the manuscript focused on MCAO as much as possible.

Reply 1: Thank you for your thoughtful review and the detailed comments for edits.
We agree that the detailed stenosis classification systems are more pertinent to non-malignant CAO, but they are still applicable to MCAO (i.e. Freitag classification system includes structural abnormalities such as endobronchial tumors) and therefore we would like to include this in the discussion to provide a more general foundational understanding of CAO prior to discussing the more technical aspects of MCAO management.
Changes in the text: none

Other minor points:

Comment 2. Consider discussing the risk of increasing dead space with airway recanalization if an area with no or low blood perfusion gets recanalized.

Reply 2: Agree with this suggestion and added two sentences in the text after line 557 with two new references.
Changes in the text: "One potential exception to the benefits described here is in patients with significant concomitant pulmonary artery occlusion. Airway debulking procedures may be associated with worsened gas exchange in this population because of increased dead space ventilation and worsened ventilation/perfusion mismatch (79,80)."

Comment 3. Consider discussing a balloon (Fogarty, CRE) utilization to visualize a distal airway past the obstructing lesion.

Reply 3: Thank you for this suggestion. A sentence has been added on line 346.
Changes in the text: "In addition to therapeutic dilation, various balloons (controlled radial expansion, Fogarty, etc.) may be useful for procedure planning purposes by providing at least transient visualization of airways distal to endobronchial tumor."

Comment 4. Line 211 - remove the word 'often'.

Reply 4: We agree with this correction and edits have been made.
Changes in the text: "often" was removed from the text on line 211.

Comment 5. Line 243 add the word 'Malignant' at the beginning of the sentence.

Reply 5: We agree with this revision suggestion and edits have been made.
Changes in the text: "Malignant" was added at the beginning of the sentence in line 243.

Comment 6. Lines 254/255: Consider changing the sentence as it currently reads as only IP can manage malignant CAO. Suggested option: Hospitals without the ability and expertise to perform therapeutic bronchoscopy should proceed with an urgent transfer to a tertiary care facility. Airway stabilization with an ET tube and bronchoscopy to suction excessive secretions may be needed

prior to the transfer.

Reply 6: Thank you for this suggestion and agree with this change. Changes have been made to the text on lines 254-258.

Changes in the text: "Hospitals without the ability and expertise to perform advanced therapeutic bronchoscopy should proceed with urgent transfer to a tertiary care facility. Airway stabilization with intubation and clearance of mucus in the distal airways with a fiberoptic bronchoscope may be necessary prior to transfer to stabilize the patient, keeping in mind the potential risks associated with tumor manipulation in a critical airway (32)."

Comment 7. Lines 360: Consider changing the sentence regarding SEM stents as they are being able to be placed via flexible bronchoscopy only in small sizes. Consider also mentioning the use of fluoroscopy when SEM is not deployed under direct visualization with FOB.

Reply 7: Agree with this clarification. Text updated and sentences added beginning on line 360.

Changes in the text: "Silicone stents typically require the use of rigid bronchoscopy whereas self-expandable metallic stents (SEMS) may be placed via flexible bronchoscopy in some instances. SEMS are available for placement via direct vision through the working channel of a flexible bronchoscope at small diameters, but larger diameter SEMS are typically placed under direct visualization during rigid bronchoscopy or via fluoroscopic guidance, often over a guidewire."

Comment 8. Discuss the benefit of therapeutic bronchoscopy prior to surgical resection as described in the paper by Prashant Chhajed et al. Therapeutic bronchoscopy interventions before surgical resection of lung cancer (PMID: 16631682).

Reply 8: Thank you for suggesting this article. This adds to the perspective of the interaction between therapeutic bronchoscopy and surgical management of MCAO which we did not otherwise include. Text and reference added to the document beginning on line 561.

Changes in the text: The following text has been added with a reference to the paper by Prashant Chhajed et al.: "The utility of therapeutic bronchoscopy in the management of patients with MCAO considered for curative resection has also been established. Pre-surgical therapeutic bronchoscopy using single or multiple interventional therapies often provides more detailed endobronchial staging compared to conventional bronchoscopy which may allow for increased utilization of parenchymal sparing surgeries. Therapeutic bronchoscopy is also beneficial in the treatment of post-obstructive pneumonia and for optimization of patient functional status prior to definitive resection (82)."

Reviewer B Comments:

Comment: The authors have submitted an excellent review of malignant central airway obstruction with an emphasis on the bronchoscopic diagnosis and management of malignant CAO. The article is well-organized, very clearly written, and addresses the subject in a comprehensive manner. The figures chosen also add significantly to the information conveyed, and Figure 1 in particular did a nice job of demonstrating clearly the various types of CAO relative to the airway lumen.

Reply: Thank you.

Reviewer C Comments:

Comment: After review the article, it's important to add more contents in this paper to review the most recent researches in the field, which will be the main advantage of this article. It's not enough to mention the progress in just one section. Moreover, the references should be updated as

well. Only 10 articles cited in this paper were published in 2021 and 2022.

Reply 1: Thank you for your comments and recommendations. This was an invited review article as part of a series with the request to provide a general overview of malignant central airway obstruction. We did clarify the expected contents and were asked to just briefly cover each treatment modality, general therapeutic outcomes, etc. as each of these things will be covered in detail in other invited articles for this series. Given the scope of our article and word limitations, we did not include all available descriptions and data for these topics, however, we have updated some of the text and reference list to include more recent publications per your recommendation. Much of the data for the therapeutic modalities has not substantially changed throughout the years (APC, cryo, basic electrocautery) except for the newer modalities of radiofrequency and microwave ablation (also some PDT), but we acknowledge it is important to provide up to date data when available.

Changes in the text: Added text and reference on line 479: "Endobronchial ultrasound transbronchial needle-guided placement of laser catheters in extrabronchial tumors causing MCAO has also recently been reported (65)."

Added text and reference starting on line 294: "Overall, technical success after therapeutic bronchoscopy is usually reported to be over 90% and a recent prospective, single-center study of 100 patients with newly diagnosed MCAO determined distal airway patency on thoracic CT predicts technical success of therapeutic bronchoscopy (38). Conversely,"

Added text and reference starting on line 488: "An exploratory study using Surveillance, Epidemiology, and End Results Medicare linked data evaluated all-cause and cause-specific mortality in patients with stage III and IV non-small cell lung cancer receiving various treatment modalities. Despite some limitations, this large study demonstrated that PDT use as part of a multimodal treatment approach may add value to the management of MCAO with improved outcomes compared to non-PDT ablation techniques (67)."

Added other more recent references (plus others specifically in response to comments from other reviewers): (80) Dutau 2022 line 557, (72) Jantz 2021 line 509.