

## Peer Review File

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### Reviewer A Comments:

Comment 1: When referring to clinical outcomes, I would also consider whether a patient subsequently goes on to receive further anti-cancer treatment as an endpoint of value. Frequently, patients with MCAO are too breathless and frail for further treatments. However, airway intervention can improve their exercise tolerance and frailty status to a level that permits further anti-cancer treatment. I would suggest that this metric is another clinically relevant measure of the value of bronchoscopic intervention.

Reply 1: Thank you for the comments. A sentence in the Survival section highlighting the potential explanation for improved survival in patients who received therapeutic bronchoscopy.

Changes in text: The last section of the first paragraph in “Survival” has been changed to:

When compared with patients with MCAO who refused TB, patients who underwent TB had a longer survival after matching for age, comorbidities, type of malignancy and type of obstruction (4 $\pm$ 3 months and 10 $\pm$ 9 months respectively).<sup>23</sup> This may be due to the potential improvement in their functional status which would allow patients to receive further anti-cancer therapy.

Comment 2: In line 71 you refer to “left mainstem disease”. In the context of airway obstruction, it is not clear whether this refers to disease of the left main bronchus, or concomitant coronary artery disease with left mainstem involvement. This should be clarified.

Reply 2: Thank you for your comments. That was changed to “Left mainstem involvement” to allow further clarification.

Changes in text. The sentence has been changed to:

On the other hand, American Society of Anesthesiology (ASA) score 3, renal failure, primary lung cancer and left mainstem involvement were associated with failure.

Comment 3: One area of practice that you haven’t mentioned is the need for concomitant intervention. The two scenarios I can think of here are airway intervention (usually stenting) with concomitant SVC stenting for SVCO and airway intervention (usually stenting) with concomitant oesophageal stenting for oesophageal malignancy. Perhaps the management of these specific scenarios could be briefly discussed.

Reply 3: We would like to thank the reviewer for their comments. The objectives of the manuscript were to describe specifically the clinical outcomes of therapeutic bronchoscopy for malignant central airway obstruction that are based on some clinical evidence from prior studies. We tried to focus specifically on therapeutic bronchoscopy. Unfortunately, there isn’t enough data to suggest how much improvement in outcomes does concomitant management of SVC obstruction would provide to patients. A sentence was added to the Dyspnea section addressing the potential value of double stenting.

Changes in text: A sentence was added to the dyspnea section as follows:

Stenting the esophagus as well as the airway in cases of esophageal malignancy have also led to improvement in both dysphagia and respiratory symptoms. The lack of comparator limits the ability to clearly measure the value of double stenting.<sup>22</sup>

Comment 4: When discussing complications you mention a mortality rate of between 0.5% and 1.3%. Whilst I do not disagree, it is perhaps worth mentioning that for patients who undergo anaesthesia for potential bronchoscopic intervention and are found to have pathology which is not amenable to treatment, the rate of morbidity and mortality is much higher and that inability to treat the problem is frequently associated with a rapid decline thereafter.

Reply 4: We would like to thank the reviewer for the comments. That section is addressing mortality from the procedure itself (e.g. as a result of bleeding, hypoxia, etc.). Therefore, the pathology of the disease itself may not necessarily have an impact on the rate of complications. The impact of pathology on survival was mentioned in the survival section.

Changes in text: No changes were performed.

#### **Reviewer B Comments:**

Comment 1: Lines 22 and 43: “The clinical impact therapeutic bronchoscopy (TB)” . I believe the word “of” is missing.

Reply 1: We would like to thank the reviewer for their comment. Changes were made to the sentence accordingly

Changes in text: The sentence was changed to:

The clinical impact of therapeutic bronchoscopy (TB) may have must then be weighed against the potential complications to justify its value. Early studies of TB for CAO included patients with both malignant and benign etiologies.

Comment 2: The authors should provide a more informative abstract. Currently it looks more like an introduction, rather than an abstract. The authors may add some key results and findings from this review, as well as an outlook for future research.

Reply 2: We would like to thank the reviewer for their comments. A paragraph was added to the abstract.

Changes in text: A paragraph was added to the abstract as follows:

Therapeutic bronchoscopy has been shown to have a clear impact on weaning from mechanical ventilation, dyspnea, health-related quality of life, survival and quality adjusted survival. The potential impact of therapeutic bronchoscopy on these outcomes should be weighed against the potential risk of complications. Understanding the factors associated with improved clinical outcomes will help physicians decide when and if TB is helpful. Future studies should focus on creating a decision analysis tool to further define decision thresholds.

Comment 3: I would suggest the authors add the background information about the definition of CAO and the percentage of MCAO cases in the Introduction.

Reply 3: The text was modified to address the reviewer's comments.

Changes in text:

Central airway obstruction (CAO), defined as obstruction of the trachea and/or mainstem bronchi, is a debilitating condition with a significant impact on patient's quality of life and risk of hospitalization from respiratory failure.

Another sentence added to the introduction as follows:

In a cohort review, MCAO was found in up to 13% of patients with newly diagnosed lung cancer.

Comment 4: I would also suggest the authors consider adding the information about the types of MCAO before the sentence "For endoluminal disease, hot and cold ablative..." . Just like the statement "There are three main types of malignant airway obstruction: endobronchial obstruction, extrinsic compression, and mixed pattern" .

Reply 4: We would like to thank the reviewer for their input. The types of MCAO are mentioned prior to the ablative statement. The sentences in the introduction are as follows:

The obstruction may occur either due to endoluminal disease, extrinsic compression, or a combination of both. Several bronchoscopic tools are available to manage such obstruction. For endoluminal disease, hot and cold ablative therapies as well as mechanical debulking may help reestablish patency of the airway.<sup>4</sup> Airway stenting may be beneficial in cases of extrinsic compression. In cases of MCAO due to a combination of extrinsic and endoluminal disease, a combination of the aforementioned modalities may be used.

Changes in text: No changes were made to the text.

Comment 5: Lines 179-180: "Although TB may prolong life, most patients benefit from the improvement in quality of life during that time" . The use of "Although" is not appropriate.

Reply 5: We thank the reviewer for their input. "Although" was changed to "While".

Changes in text: Sentence changed to:

While TB may prolong life, most patients benefit from the improvement in quality of life during that time.