

Peer Review File

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Reviewer A:

Comment: Dear Authors,

good job, it is always pleasant to have this kind of narrative review.

few mistakes, such as syntax error, L13, EMBASE

An oversight in the precision of acronyms, L171 LMA, L259 DLT (double lumen tube mentioned in L258)

Concerning the Medications part, L109, a focus on General anesthesia with continuous, intravenous, short-acting agent is necessary. In our thoracic center, we make extensive use of this strategy, in order to reverse rapidly the general anesthesia. Patients usually leave the operating room in spontaneous ventilation, avoiding intubation.

The paragraph L269-276 can be reorganized, to have a shorter text. (degassing first and then, lavage procedure).

L341 : I think you have to underline dangers of Jet ventilation : in ex, the appropriate adjustment of the ventilator settings (pause pressure and peak inspiratory pressure) to reduce the risk of barotrauma.

L351 or elsewhere : It is important to remember to check the integrity of the teeth at the end of the procedure !

Nasopharyngeal trumpets : important to remember its importance, to ensure good ventilation, particularly when the physician is just starting out in rigid bronchoscopy.

ECMO part : please mention that ECMO is now widely insert by percutaneous ways/under ultrasonography, with limitation of morbidity. To my opinion, the text from L365 to L370 seems out of place, if they speak about trauma/surgical repair. Preferable to call back that ECMo is usually used under anticoagulation with an increased risk of fatal hemorrhage, and new circuits heparin-free limit this risk.

your bibliography looks good to me, with a wide panel of high-quality papers.

Reply:

Line 13: Will make corrections.

Line 171: Will add on laryngeal mask airway (LMA) in line 33

Line 258 and 259: Will add on double lumen tube (DLT)

Line 269 – 276: Revised as follows:

Most centers prefer to treat the more diseased lung (determined by chest imaging) first. After ensuring a sealed circuit and toleration of single lung ventilation, a degassing procedure may be performed before the initial lavage to create a more homogeneous distribution of fluid. Forced lung deflation with negative airway pressure after 100% oxygen ventilation followed by airway occlusion for ten to fifteen minutes to complete absorptive atelectasis effectively degasses the target lung. The target lung is then instilled with warmed normal saline in 0.5 to 1L aliquots. Warm saline is used to avoid inducing hypothermia.

Line 341: Revised as follows:

Some institutions use jet ventilation via the rigid bronchoscope as their preferred ventilation mode. Common complications of jet ventilation include hypercarbia, hypoxia and hypotension. Associated risk factors include baseline oxygen saturation of < 95% on room air, ASA score of IV, obesity and restrictive lung disease.⁴³ Barotrauma- associated injuries including pneumothorax, pneumomediastinum and subcutaneous emphysema may occur. Measures to ameliorate these complications include keeping the expiratory pathway of the rigid barrel unobstructed and limiting inspiratory duration to 30-40% of respiratory cycle. If jet ventilation is used, adequacy of ventilation is assessed by sufficient chest rise and continuous transcutaneous CO₂ measurement.⁴⁴

Nasopharyngeal trumpet

Although may be used in rigid bronchoscopy in ventilation, has not been widely described in our review or used in our institution thus not included.

ECMO part:

This pertains to cautious use of ECMO in patient with CAO and subsequent significant bleeding with the concern that systemic anticoagulation may worsen bleeding. The articles cited demonstrates safety of heparin-free ECMO to ameliorate complications from systemic AC.

Reviewer B:

Comment: This is a review article that introduce the anesthesia considerations for bronchoscopy. This article is interesting and well written, but I have a few questions.

Comment 1. About “Diagnostic bronchoscopy” section, it seemed that general anesthesia is assumed. It is true that if you perform TBB by robot-assisted bronchoscopy and some cases of electromagnetic navigational bronchoscopy, the patients undergo under general anesthesia so to speak deeper sedation. But you know, in global clinical setting, TBB by flexible bronchoscopy is usually performed under maintained conscious state (e.g., administering midazolam, fentanyl). I think it may seem strange to classify local anesthesia but it is disconcerting to call it general anesthesia that you mention to the complications and settings of ventilation. It would be better to describe anesthesia methods with some specificity or specify the classification.

Reply 1. Moderate sedation is mentioned as one of the strategies used in flexible bronchoscopy

under the medications section. Guided bronchoscopy is specifically pertaining to strategies in robotic or navigational bronchoscopy given special considerations in considering anesthesia strategies.

Comment 2. In L323, you write “The procedure is performed with general anesthesia with or without neuromuscular blockage”. It is true, but I think it should be administered if possible (Okamoto S, et al. *Anesth Analg* 2020; 131: 893-900.).

Reply 2. Revised as follows:

The procedure is performed with general anesthesia with or without neuromuscular blockade. Although a balanced anesthetic technique with short-acting neuromuscular blocking agents may be more desirable to decrease anesthetic dose, minimize airway injury, reduce cardiovascular side effects.

Reviewer C:

Thank you for your invitation to review this manuscript. Although I have found the title of the manuscript, I’m disappointed with the text content. It is hard to guess based on its content what is the overall aim of the authors to write about procedures, anesthesia, or ventilation. Based on this the text I chaotic although divided into paragraphs. Manuscript selection for the revision is methodologically poor. The title does not reveal the text content.

Comments to the authors:

Major points:

The authors write in the methods: “The search strategy employed a combination of keywords, subject headings, and author, with recognized experts in the field to ensure a comprehensive and focused retrieval of literature”- if so a definition of recognized expert should be defined to avoid colleague citations. On top of this the search criteria seems to be strangely chosen why Atelectasis AND navigational bronchoscopy was chosen as a search criteria when terms which are much more related to the topic of the paper such as: respiratory failure and bronchoscopy, dyspnea and bronchoscopy or NIV and bronchoscopy where not chosen. Or Abdelmalak AND whole lung lavage, especially that pulmonary alveolar proteins may be treated with other bronchoscopy methods than whole lung lavage. But most importantly bronchoscopy is being broadly, most frequently performed in sedation not anesthesia that is why this term should have been used. Moreover the non anesthesiological anesthesia is being widened with new approaches such as Propofol delivered by non-anesthesiologists. Which shows that the key words have been chosen in a narrowed way.

The authors write “Two independent reviewers screened the articles and abstracts of ...: it should be written whether there have been differences between those reviewers in the article selection. This would be better presented with a use of flow chart.

The authors write in line 97: “The total lidocaine dose must be tracked to avoid toxicity”, however the dose of lignocaine in clinical practice is rather not measured therefore such strong statement may be misleading for less experienced readers.

In the whole text term bronchoscopy is being used. Unfortunately this may be misleading because most readers may interpret it as rigid bronchofiberoecopy, therefore this should be changed into bronchofiberoecopy in cases where bronchofiberoecopy is being explained.

Line 111 when “guidelines from the American Society of Anesthesiologists” is being discussed this should be compared with other guidelines. For example with exception for whole lung lavage I have never used a temperature monitor which is not indicated for most procedures which last typically several minutes.

In lines 115-116 the authors write that “The most common combination is Propofol and fentanyl.” Unfortunately this is not true for most bronchofiberoecopies which are performed in an intravenous shallow sedation delivered by pulmonologist who use Propofol rarely. However in case the authors intention was to write only about procedures performed with the assistance of an anesthesiologist the title of the manuscript should have been changed into another which would clearly indicate this.

In lines 116-118 the author write about paralysis indicated for longer procedures – this should be more precisely described, because in real life in procedures performed not by anesthesiologist neuromuscular blockade is being rarely used, whereas it is much more performed by anesthesiologist which frequently are much more ready to intubate the patient than to use NIV to facilitate bronchofiberoecopy performance.

Based on the title of the manuscript :Lines 126-147 seems to be outside of the scope of the manuscript. Moreover chapter named Diagnostic Bronchoscopy: should explain first standard diagnostic bronchoscopy purposes not navigational-bronchoscopy which is used in narrowed indications.

In lines 166-172 the authors write about the narrowed tracheal lumen in case when the procedure is being performed in a intubated patient, whereas it has been described that bronchofiberoecopy may be also performed in procedures lasting several hours In an non-intubated patient. This was described for example for the use of Lung lavage facilitated with NIV for the pulmonary alveolar proteinosis treatment.

178-186 In the authors explain preoxygenation, - in the text the disadvantages are being explained however nothing is being written about HFNC-FOB which may addressed some problems which are being observed in patients

Line 208 Therapeutic Bronchoscopy: starts with therapeutic lung volume reduction whereas the most common indication for therapeutic bronchoscopy is airway clearance in patients with severe pneumonia.

WLL explained in line 260 may as the use of 10-15 liters of saline according to the literature is frequently extended to 40 liters, whereas >10 liters may be used in not intubated patient supported by NIV.

ECMO- reading the paragraph a reader has an impression that the reason for ECMO implantation may be bronchoscopic procedure such as hemoptysis- this is not true as ECMO requires time and anticoagulation which both are not assessable in a patient with massive hemophthysis. I would rather emphasize that patient on ECMO may undergo any kind of bronchofiberoecopy assessment because when ECMO is applied pulmonary ventilation is not required, however in general the anticoagulation is a problem moreover in ECMO patients most common indication for bronchoscopy performance is airway clearance and culture collection.

The overall perspective is that it is difficult to reveal whether the authors want to concentrate on

an anesthesia indicated by the title or on the bronchoscopy procedures. The authors concentrate in a large extent on ventilation however the text does not mention other options than invasive mechanical ventilation or ECMO, whereas there is no data on NIV or HFNC and bronchoscopy. Numerous sophisticated procedures are explained but there is not data about most common indications which in general are lung cancer diagnosis for diagnostic procedures and cultures with airway management in case of therapeutic bronchoscopies. In this perspective there is no data about the shallow sedation performed without the involvement of anesthesiologist. This makes the revision not coherent with current practice. The title does not reveal the text content.

Minor points:

- 1)The text should be assessed to get rid of double spacing
 - 2)The authors in lines 34-38 write in a future tense however this should be written in past tense.
- The manuscript is difficult to read, I would suggest to include some diagrams.

Comments to reviewer C:

The search terms were selected as the purpose of this article is to discuss advanced diagnostic and therapeutic bronchoscopy. The intent of this paper was not to discuss flexible bronchoscopy for BAL, aspiration of secretions, etc. For similar reasons, the focus was on deep sedation and general anesthesia as the literature supports that even based advanced diagnostics are better tolerated and have more thorough staging when performed in a non-moderate sedation approach (though a diagnostic EBUS could be done through this approach)

Line 97: Again as this is discussing approaches to cases performed with the use of general anesthesia, lidocaine doses should be tracked. Our anesthesia colleagues often use 4% lidocaine which increases the risk of toxicity.

National Institutes of Health workshop summary. Summary and recommendations of a workshop on the investigative use of fiberoptic bronchoscopy and bronchoalveolar lavage in individuals with asthma. *J Allergy Clin Immunol.* 1985;76:145–147.

Day RO, Chalmers DR, Williams KM, Campbell TJ. The death of a healthy volunteer in a human research project: Implications for Australian clinical research *Med J Aust.* 1998;168:449–51

Jöhr M Local anesthetics – wonderful drug or dangerous toxins. 2008 Cape Town The 14th World Congress of Anaesthesiologists.

Line 111: Again, this manuscript focuses on lengthier procedures which often exceed an hour in length. The ASA guidelines are referenced as a result

Line 115-116: Again, this manuscript is focusing on a different procedure type, and deep/general sedation. These procedures are not routinely performed with shallow sedation

Lines 116-118: Again, this manuscript is focused on procedure types where paralysis is recommended. This increases the ease of insertion of rigid bronchoscopy and allows for longer breath holds to be performed in robotic bronchoscopy cases where small nodules are sampled.

Lines 126-147: This chapter is intended to focus on advanced bronchoscopy procedures which is

why this is included.

Line 166-172: Standard of care is emphasized in this manuscript not rare approaches to cases

Lines 178-186: Again, preoxygenation is described given the anesthetic approach (general) which is the focus of the manuscript

Line 208: This paper focuses on airway based therapeutics as defined by the AABIP (which includes BLVR). Aspiration of secretions is not considered an airway based therapeutic and would not be an acceptable cases for procedure logs, nor would cryoextraction cases

Line 260: WLL volumes are average volumes as there may be extremes in certain cases

ECMO: Several cases are reported of heparin free ecmo runs and this can be achieved from cannulation and throughout the run with appropriate set up and circuit flows

Reviewer D:

Comment: It is well written manuscript of comprehensive narrative review on the anesthetic considerations for flexible and rigid bronchoscopy.