Peer Review File

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Review comments

Reviewer A

The authors described the technqie of Videomediastinoscopic lymphadenectomy (VAMLA).
The view, that such technique may be useful in the middle income and low income countries is correct, in my opinion and I am convinced that VAMLA should be promoted in such countries.

Comment 1: The disadvantages of the manuscript include lack of any results of the author's institution. Only the results from the other centers are reported.
It is necessary to know the author's own results, even if they are the initial ones.

Reply 1: We work in three different institutions in Bogotá, Colombia, in a very heterogeneous condition as is usual in our country even when we work in the country's capital. One of them is a public institution. This is our initial experience with different resources and we have not registered our results. One of the disadvantages of our practice is that we work in more than one institution and in these places we don't have proper record keeping systems or people to help us keep good records. Only one of these institutions has a Linder Dahan video mediastinoscope; the other two institutions does not have this device.

Comment 2: The other shortcomings of the study regard the attached videos illustrating the technique of VAMLA, which is imperfect and can hardly be called lymphadenectomy.
Lymphadenectomy of the mediastinum should not be performed with the technique based on traction ond removal of the pieces of individual nodes.
The proper technique means dissection of the nodes and the surrounding fatty tissue as a whole. Therefore, dissection should be performed along the major structures as a trachea or the azygos vein to mobilize a packages of the nodes plus mediastinal fat and remove them in one piece. This applies to removal of the stations 7, 4R and 10R but station 4L and 2 L nodes should be removed individually
On the attached videos, dissection of station 7 nodes was relatively the best, the dissection of the other stations was unacceptable.

Reply 2: We are showing our evolution from the traditional mediastinoscopy to VAMLA, and as Reviewer 6 proposes, we decide to change the name of the article:

“From Video-Assisted Mediastinoscopy (VAM) to Video-Assisted Mediastinal Lymphadenectomy (VAMLA) surgical technique in a low-to-middle income country”

However, even with the traditional Carlens mediastinoscope, we are resecting complete nodes, although on the right we are not resecting all the fatty tissue. According to your recommendation, we changed the video that shows 4R dissection.

Comment 3: It is incomprehensible for me, why the author did not used the Linder Dahan mediastinoscope to dissect all nodal stations.
What was done with the use of the Linder Dahan mediastinoscope was relatively the most similar to lymphadenectomy. Everythink done with the tube-like mediastinoscopy at the utmost, this technique is something like mediastinoscopy, maybe a little more but not a lymphadenectomy.

Reply 3: It is because a Linder Dahan video-mediastinoscope is not available in two of the three institutions where the authors work, it is also not available in most places in our country as we mentioned in the article.

The authors want to thank the reviewer A for the comments.

Reviewer B

This is a surgical technique report about the usefulness of VAMLA in low- and middle-income countries.
Although the authors confidently report the VAMLA procedure on video, there are some major problems.

Comment (1) First, there is a major problem with terminology of using “lymphadenectomy”. There are various types of lymph node dissection for lung cancer: systematic nodal dissection (complete lymphadenectomy), selected lymph node biopsy, sampling, systematic sampling, lobe-specific systematic node dissection, and extended lymph node dissection.

I’m afraid that your videos are not called as “lymphadenectomy” but biopsy. Lymphadenectomy means performing by excising all tissues in the compartment surrounded by anatomical tissue, with en bloc and without destroying the capsule. In the video, the lymph nodes are separated and the surrounding tissue is not sufficiently removed. So it's hard for us to call them a “lymphadenectomy”. I can agree with as a biopsy. Therefore, do not emphasize “systemic lymphadenectomy”.

Reply 1: The authors changed the title of the article as proposed by reviewer 6 and also uploaded a new video (4R dissection). The authors are aware that some videos show biopsies but the resections performed usually are more than just biopsies.

About the systematic lymphadenectomy, we included in introduction:
"The International Association for the Study of Lung Cancer (IASLC) includes systematic lymphadenectomy within its definition of complete resection, but it can be either complete systematic lymphadenectomy or selective systematic lymphadenectomy that includes lobe-specific systematic nodal dissection (in addition to achievement of tumor-free margins in lung resection) (7)."

Comment (2) While highlighting its benefits in low- and middle-income countries, you use Harmonic and LigaSure. These advanced energy devices are costly single-use devices. I think it would be cheaper to use an monopolar devices. What do you think?

Reply 2:
We included in surgical technique:
"Advanced energy devices are more expensive than monopolar devices, but they are safer during dissection within the mediastinum. Special care must be taken with the active blade of ultrasonic devices, because it can cause severe burns. These devices are always available at our institutions but have restrictive reuse policies."

Comment (3) EBUS-TBNA and EUS are effective and minimally invasive for diagnosis. There is little description of this point, and please describe how to use it properly with VAMLA. VAMLA requires general anesthesia, but EBUS-TBNA and EUS can be performed with local anesthesia. For staging purposes, EBUS-TBNA and EUS are more safer and cheaper.

Reply 3: We included in comments:
"If videomediastinoscopes are scarce in Colombia, EBUS is even scarcer. Furthermore, pulmonologists and thoracic surgeons are just beginning on the learning curve. The costs of the two procedures in our country are probably similar because endobronchial ultrasound-guided transbronchial fine needle aspiration (EBUS-TBNA) is always performed under general anesthesia. Even so, EBUS is safer than VAM or VAMLA."

Comment (4) When Harmonic active blade contacts the surrounding mediastinal organs, there is a risk of serious complications due to the drilling effect. Please describe this point.

Reply 4: We included in technique:
"Special care must be taken with the active blade of ultrasonic devices, because it can cause severe burns."

Comment (5) Video 1 and Video 5 are unnecessary. Video 5 showed only touching the lymph nodes and did not dissect them.

Reply 5: the authors are completely agreed and removed Video 1 and 5.

The authors want to thank the reviewer B for the comments.

Reviewer C

It is an interesting review about VAMLA based mainly on techincal aspects. I find it useful in order to learn the technique to perform VAMLA. The videos presented explain correctly the different steps of this technique with a nice view and understandable explanations. Furthermore, this article is also useful for low and middle-income countries to know the way of performing VAMLA in the cases that a videomediastinoscope is not available.

I would like to add some comments in order of appearance in the manuscript:

Comment 1-Introduction section, line 75: the systematic lymphadenectomy is not always "essential" in the treatment of lung cancer. That sentence sounds strange.

Reply 1: we changed “essential” for “useful”.

Comment 2- Comments section, line 160: It would be interesting to show here the variation of the % of complications after the learning curve.

Reply 2: In Comments we included:
“Complication rates of these surgeons decreased from 18-19% to 3-5%.”

Comment 3- Comments section, line 176: after explaining the technical advantages of VAMLA I am not sure the last sentence is appropriate. Furthermore, with the present accuracy of CT and PET in mediastinal staging there is no robust evidence for the requirement of doing a lymphadenectomy prior to surgery.

Reply 3:
We included:
“Assessment of the lymph nodes prior to resection is clearly indicated for central tumors, tumors larger than 3cms, and when N1 is suspected because of PET-CT or CT. In these cases, VAMLA offers more precise staging and favors administration of more appropriate treatment.”

Comment 4- Comments section, line 204: the authors comment that perhaps VAMLA without a videomediastinoscope does not offer the same safety and in the opinion of some authors is mandatory to have a videomediastinoscope to perform it. Along the manuscript the authors explain that it is possible to perform VAMLA

without it but perharps is necessary to make clear if the authors recommend doing it without a videomediastinoscope.

Reply 4: We included in comments:
"We believe that this procedure is safer and more comfortable to perform with a videomediastinoscope, but we also believe that, when this device is not available, surgeons can use a traditional mediastinoscope to perform more extensive resections like the ones we have presented."
And in last part of comments:
"The authors are also convinced of the benefits of this procedure in terms of time, staging and surgical results, so we strongly recommend it, even when a videomediastinoscope is not available."

The authors want to thank the reviewer C for the comments.

Reviewer D

Comment 1: Although the concept to present this technique is interesting, the manuscript lacks coherence.

- It would be interesting to know in which patients this technique is used, which place has chemotherapy, radiotherapy, immunotherapy etc.

Reply:

This is an article about surgical technique, and our objective was to show the technique, but we agree that it is important to mention indications and contraindications, so we included in introduction:

"Evaluation of mediastinal lymph nodes in non-small cell lung cancer (NSCLC) is important because N has prognostic and therapeutic implications. This evaluation begins with CT and PET-CT scans, but they are not always enough. Histological assessment of the mediastinum is indicated when the probability of N2 is greater than 10%. This occurs when adenopathies are present in images, when the tumor is central, and/ or when it measures more 3 cm or more. This evaluation can be done by VAM, VAMLA, or endobronchial ultrasound (EBUS),
When EBUS is available, it is used after CT and PET-CT in the preoperative assessment of mediastinal lymph nodes with indications for histological assessment of the mediastinum. Thus, if the patient undergoes neoadjuvant therapy, restaging is performed with VAMLA. When EBUS is not available or negative, we confirm the absence of N2 with VAM or VAMLA. However, we prefer to do VAMLA to avoid repeated mediastinoscopy especially in patients who are candidates for neoadjuvant therapy. These are the main indications for VAMLA in our practice. Relative contraindications are patients with limited neck extension, previous mediastinoscopy or irradiated mediastinum."

- Is there experience with a conventional mediastinoscopy?

Reply:

In general, in our country there are experiences with conventional mediastinoscopy among thoracic surgeons and we routinely evaluate our patients with CT and although we only have PET-CT in one of the institutions, in the other two it can be requested outside the institution, so we usually have it available in the preoperative evaluation.

- How many patients with NSCLC are operated on/what volume does this facility have? What kind of preoperative imaging is being used?

Reply:

We work in three different institutions in Bogotá, Colombia, in a very heterogeneous condition as is usual in our country even when we work in the country's capital. One of them is a public institution. This is our initial experience with different resources and we have not registered our results. One of the disadvantages of our practice is that we work in more than one institution and in these places we don't have proper record keeping systems or people to help us keep good records. Only one of these institutions has a Linder Dahan video mediastinoscope; the other two institutions does not have this device.

Comment 2: There are many typo's and the English language should be corrected. In line 179 there seems to be something lacking.

Reply 2: We agree; we've had the manuscript reviewed by a native English speaker. All the changes were highlighted.
We rephrased the paragraph that includes line 179:

"VAMLA's morbidity rate of about 4.6% (2.6% to 5.3%) is similar to that of mediastinoscopy. It has better sensitivity (93.8%) and specificity (100%), and its false negative rate is low (0.9%) (4, 12). Sensitivity, as in all the invasive mediastinal staging procedures, depends on the number of lymph nodes and stations evaluated. With VAMLA's better vision and ease of use by the surgeon, a sufficient number of nodes and stations can be evaluated more frequently than with other methods."

Comment 3:

- What is the authors idea on using high cost energy device s such as the Harmonic scalpel and the Ligasure in a low income country?

Reply:

In comments we included:

"Advanced energy devices are more expensive than monopolar devices, but they are safer during dissection within the mediastinum. Special care must be taken with the active blade of ultrasonic devices, because it can cause severe burns. These devices are always available at our institutions but have restrictive reuse policies."

- Furthermore, in Low income countries quite often a regular mediastinoscope is not available all together....

Reply

In Colombia (similar in Latin America), the availability of medical devices is heterogeneous, but institutions where there are thoracic surgery services, usually have a conventional mediastinoscope and also small lenses (5 mm). The problem is the non-availability of a videomediastinoscope.

- What is the authors idea on complete lymph node dissection and re-staging techniques?

Reply:

In comments, we included:

“and when a complete lymphadenectomy has been performed, it may avoid repeated mediastinoscopy after neoadjuvant treatment or avoid futile surgery in high risk patients (8).”

Comment 4: The manuscript lacks a discussion. It has merely a "Comments" section. Please provide a discussion incorporating the comments, strengths and limitations and a better analysis and evaluation of the literature.

Reply 4: According to the author's guidelines, this is an article on surgical technique and there is no discussion section, only comments. However, we have improved the comments section.

The authors want to thank the reviewer D for the comments.

Reviewer E

We would like to congratulate the authors on their manuscript entitled: “video-assisted mediastinal lymphadenectomy (VAMLA) in a low- and middle-income country”. Please find our comments below.

Comment 1: General notes:

• please consult a native English speaker for grammar and spelling check.

Reply:

We agree, we've had the manuscript reviewed by a native English speaker. All the changes were highlighted.

• it is not common to place a “history” paragraph before the introduction section.

Reply:

We agree; we removed the history section and we included this information in introduction.

• since the red line is missing in this study, it is hard to review, as is the readability for readers. There is no well-defined research question, method and conclusion.

Reply:
There is no well-defined research question, method and conclusion because, according to the author´s guidelines, it is a Surgical Technique paper. We described the technique and followed the steps of this type of article.

Comment 2: Introduction
- It does not become entirely clear to me what the added value is to again describe the technique of VAMLA, regardless of whether this is performed in a low- or high-income country. Moreover, what is the difference between VAMLA in a low- versus high-income country?
- The study is designed as a review. However, this is not substantiated by the manuscript.

Reply 2:
- We believe that the VAMLA is a tool that in any setting adds value in the study and treatment of selective cases of lung cancer; the point is that we do not always have a videomediastinoscope in low- or middle-income countries, for this reason we try to show how, despite not always having a videomediastinoscope, we can improve the mediastinoscopy technique to perform a systematic dissection of the mediastinal and hilar nodes.
In comments, we included:
"VAMLA's morbidity rate of about 4.6% (2.6% to 5.3%) is similar to that of mediastinoscopy. It has better sensitivity (93.8%) and specificity (100%), and its false negative rate is low (0.9%) (4, 12). Sensitivity, as in all the invasive mediastinal staging procedures, depends on the number of lymph nodes and stations evaluated. With VAMLA's better vision and ease of use by the surgeon, a sufficient number of nodes and stations can be evaluated more frequently than with other methods."

- This is not a review, is a Surgical Technique article.

Comment 3: Surgical technique
- Different surgical techniques are described, such as VAMLA, conventional mediastinoscopy, etc. This came as a surprise for me due to a non well-defined research question.

Reply 3: We are describing the VAMLA technique with and without a videomediastinoscope. We are trying to show how with a tubular mediastinoscope with a 30-degree 5 mm lens connected to a video camera, a trained thoracic surgeon could perform VAMLA. We are not answering a research question; it is an article that describes a surgical technique.

The authors want to thank the reviewer E for the comments.

Reviewer F

Comment 1: My comments and suggestions were already addressed by the most reviewers. I agree the videos do not show a VAMLA, this is a video mediastinoscopy paper. We can maybe ask the authors to change the title?
I didn't see the videos, but apparently the lymph nodes are not fully removed, but biopsied.
Otherwise, this is a well written paper.

Reply 1: We accepted your suggestion to change the title:

"From Video-Assisted Mediastinoscopy (VAM) to Video-Assisted Mediastinal Lymphadenectomy (VAMLA) surgical technique in a low-to-middle income country"

The authors want to thank the reviewer F for the comments.