

Peer Review File

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Reviewer A

In their study, the authors raised a very current and exciting problem of continuous intraoperative neuromonitoring of the recurrent laryngeal nerve during lung operations. It seems that neuromonitoring, for example, in thyroid operations, is currently a standard, while there is still marginal interest in thoracic surgery, and its utility has not been adequately confirmed. You can see the experience and the author's familiarity with the subject matter. The article is well written, although it is quite long and needs correction in some places. In order to help the authors in correcting their paper, I have allowed myself a few significant remarks to help improve this article.

First of all, the manuscript requires some English editing. Several mistakes to correct, for example:

Line 67 - " microaspiration" write it together, corrected in the text

Line 78- "the retrospective", corrected in the text

Line 89 - comma before "therefore", corrected in the text

Line 95 - comma after "cases", corrected in the text

Line 105 - "a left-sided" corrected in the text

Line 128 - "chloride-coated " - I suggest writing it with a dash, corrected in the text

Line 131 - comma before "there", corrected in the text

Line 139 - I suggest writing " laterally", corrected in the text

Line 144 - skip the comma after "electrode", corrected in the text

Line 147 - it should be "demonstrates", corrected see text

Line 280 - I think it should be "described", corrected see text

Line 291 - I think it should be "easily", corrected see text

Line 293 - "is" instead of "being", corrected see text

Line 298 - "the purpose of" is unnecessary; skip it. Corrected see text

Introduction - In my opinion, the Introduction is way too long - there are too many details, and the reader loses interest quickly. The introduction should briefly outline the problem and the research objectives. For example, I suggest moving the content of sentences in Lines 70- 80 to the Discussion. In the introduction, please only briefly outline the percentage range of recurrent laryngeal nerve paralysis in thoracic surgery- the reader should know what order of magnitude the problem is and why your study is so important. This thought can be developed in the discussion.

Reply: For us, it was important to point out that postoperative recurrent paresis can also occur in other surgical areas such as esophageal or cardiac surgery. Continuous neuromonitoring of the recurrent nerve could therefore also be used there.

Results- In my opinion, the description is far too long and hard to read - I suggest

shortening, simplifying, and writing it so that it is known what is the most important find in your study. The biggest problem I have with the Results is Lines 215-231. Listing patients by numbers and mentioning individual cases is uninteresting and challenging to get through. I suggest leaving this information in the Tables you did and shortening their description in the text to a minimum.

Tables should be technically corrected - they should not have vertical or transverse borders. Please see the tables in the research articles.

Conclusions I wouldn't say I like how the conclusions are described. In this section, I would like to read the essential conclusions from your study, not conclusions from the literature about things you have not researched in your paper.

Reply: In the discussion, we wanted to give an overview of the previous efforts of other authors to establish thoracic neuromonitoring of the recurrent nerve. Compared to these techniques, ours is absolutely promising, this was shown by our study.

I would like to ask if there have been cases of recurrent laryngeal nerve injury during left-sided thoracic procedures in your practice? What percentage/how many cases per year do you usually record?

Reply: In the clinic, recurrent paresis occurs again and again after left-sided thoracotomies on the left. Most often, if there are significantly enlarged lymph nodes in lymphadenectomy or tumors near the aortopulmonary window. Every year we record about 3-4 postoperative recurrent paresis.

Reviewer B

This manuscript demonstrated to assess the feasibility of continuous intraoperative neuromonitoring technique with the use of a double-lumen tube for single-lung ventilation. The main research findings of this paper will be important for the actual medical site.

This study is performed with anterolateral left-sided thoracotomy, but thoracoscopic, robot, and uniportal VATS are performed in actual surgery.

Can this technique be applied in these minimal invasive surgeries?

Discussion and validation of the applicability of this technique in these minimal invasive surgeries are needed.

Reply: Our work initially focuses on the feasibility of continuous neuromonitoring in open left-sided lung surgery. In principle, it was necessary to clarify where the electrodes were to be placed on the double lumen tube, so that a signal could be derived. In addition, a saxophone electrode was applied intrathoracically around the vagus nerve above the aortic arch. The vagus nerve was stimulated via this electrode. In our study we have shown that continuous monitoring of the function of the recurrent nerve is possible. The technique can also be used minimally - invasively. The technical feasibility would not have to be modified. We want to address the importance of

continuous neuromonitoring in the context of minimally invasive operations in further clinical studies.

Reviewer C

The reviewer is honored to review an article about the continuous intraoperative neuromonitoring of the recurrent laryngeal nerve during lung operations. The paper is interesting in terms of the reproducibility of this cIONM technique. There are several points to be revised, as follows:

Regarding a title, if the authors want to include lung resections, they should write the introduction more specifically on lung resections. In lung resections, issues of recurrent laryngeal nerve palsy would be more limited in left upper lobectomy and lymph node dissection of upper mediastinal nodes. They cited many papers such as aortic surgery and esophageal surgery.

Reply: For our feasibility study to establish continuous neuromonitoring of the recurrent laryngeal nerve, we used left-sided lung surgery. In the context of lung interventions, especially with lymphadenectomy in the aorto-pulmonary window, the recurrent nerve may be at risk. Nevertheless, we have also cited papers from other areas such as esophageal or aortic surgery, because we believe that continuous neuromonitoring can also be used advantageously to prevent nerve lesions in such procedures.

This paper focused on the newly developed device and its preliminary usage. Therefore, the authors should describe this device with more detailed explanation using some schemas. They used only 2 figures (Figure 1 and 4). More about its mechanism should be explained with several schemas.

Reply: We have not included any further schemes to explain the technical structure, as it corresponds to the structure used in thyroid surgery. In our figures 1 and 4 we want to focus on special aspects. Figure 1 shows the positions of the tube electrodes and how the colored cables are connected to the multichannel connector. Figure 4 is intended to show the conduction signals of the proximal and distal electrodes seen on the monitor. We would like to demonstrate how such a derivative signal looks at all.

- 1) In discussion, the authors should add more descriptions about the future clinical usages in lung resections more specifically.

Reply: At the end of the discussion, we refer to further prospective clinical studies that are intended to demonstrate the importance of the use of continuous neuromonitoring of the recurrent nerve in the context of lung operations, with a focus on tumor surgery. In particular, we plan to establish neuromonitoring for minimally invasive procedures. In principle, we consider this technically feasible.

- 2) Regarding Figure 3, the discrepancies between the figure and the figure legend should be corrected. For example, “NV” and “VN”. “NLR” and “RLN”. “AB” and “AA”.

Thank you for your comment, we have corrected our figure legend (please see in the manuscript).

Reviewer D

I find it a very interesting topic because research concerning patient's safety and "non-nocere" techniques should be garranted.

Although I find it a very complete work, I think you should revise it again and clarify some points.

- Regarding the abstract. I find a little bit confusing de M&M paragraph.

Following thoracotomy, the vagus nerve alongside the aortic arch was exposed. A continuous stimulation probe (Saxophone® electrode, Dr. Langer Medical, Waldkirch, Germany) was placed around the nerve.....As it is written it sounds that you are neuromonitoring the vagus and not de RLN?¿

Reply: The saxophone electrode is applied to the vagus nerve, since the recurrent nerve is part of the vagus nerve, it is stimulated. Through the adhesive electrodes on the tube, however, only the function of the recurrent nerve is detected.

- Introduction. Line 86. You have also monitored the cricoarytenoid muscle...but I do not see anything related to it in the results...just the clinical phoniatic evaluations.

Reply: On the monitor, the muscle potential of the cricoarytenoid muscle is indicated by the electrodes placed at the level of the vocal cords. If such a potential is proven, the functionality of the muscle can be assumed. The results were confirmed by a phoniatic examination.

- M&M. Evaluation.

You have talked about height and DLT sizes...but no differences between sex? Have you selected the tube size according just to the height? Explain please.

Reply: The size of the double lumen tube is selected according to the size of the patient (see Table 1). The gender of the patient does not matter. This procedure corresponds to the usual anesthesiological practice.

I find a lack of information regarding the statistical analysis. Also, range must be expressed between [] and no with ().

Reply: Thank you for your comment we correct this point in the manuscript.

Moreover, range only must be used if the variable does not reach normality...something I do not know if it has been tested because you have not talked about variables, analysis and their expression.

Remember otherwise using SD if necessary.

- Discussion. Correct.

- Conclusion. Correct.

- References: must be review. In some of them the title is between [] but not in others;?

Reply: We have correct this point in the references

- Tables.

Error in table 2. I guess that you want to say N=18 and not n=17?

Reply: we have correct this point in the table

Table 3 must be re-written. I find a lack of information regarding the variables and how to express them properly (numeric ones must be express as mean and SD or range when appropriate; categoric ones as number and percentage). As a suggestion, you should erase the variable "number" and include the n in the main ones:

Signal (n=18) Group OD = E1+ and E2- Group B = E1+ and E2+ -->

Signal (n=18) Group OD = E1+ and E2- (N=14) Group B = E1+ and E2+ (N=4)

Reply: Thank you for your comment, we have revised the whole table, please check.