

## Peer Review File

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### Reviewer A

In this article, authors have analyzed the short-term outcomes of patients operated by a minimally invasive approach after the implementation of an ERAS protocol.

Concerning the introduction:

**Comment 1:** The introduction is well written, no major concerns

**Reply 1:** We thank the reviewer for this feedback.

**Changes in text:** None required.

Concerning the methodology:

**Comment 2:** Population: No major concerns

**Reply 2:** We thank the reviewer for this feedback.

**Changes in text:** None required.

ERAS protocol:

**Comment 3:** I'm a little bit astonished to read the systematic insertion of a Foley catheter.

**Reply 3:** We thank the reviewer for drawing our attention to this point. The Foley catheter is inserted because it is part of our protocol and it is removed on POD1 per our protocol. We closely track our urinary retention and UTI rates and they are low and unchanged between our pre and post-ERAS groups.

**Changes in text:** None required

**Comment 4:** Your protocol is in accordance with the ERAS society recommendations.

**Reply 4:** We thank the reviewer for this feedback.

**Changes in text:** None required

**Comment 5:** But you only have a phone call by your nurse practitioner? You don't have a day care surgery including nurse practitioner, physiotherapy and aesthetics consultation?

**Reply 5:** We do not have an evaluation by a physiotherapy team or dedicated preoperative physiotherapy program. We are in a resource limited hospital and do not reliably have access to these resources. This has now been addressed in methods under the ERAS protocol description, since if other hospitals do have access to these programs, they should undoubtedly be a part of their ERAS pathways.

Changes in text: Page 4, lines 131-136.

**Comment 6:** How is your pre operative physiotherapy program?

**Reply 6:** See comment and response number 5. We do not have these programs in place, primarily due to a lack of resources. This has been addressed in the methods section under the description of our thoracic ERAS protocol.

**Changes in text:** Page 4, lines 131-136.

**Comment 7:** Patients are admitted the day before or the day of the surgery?

**Reply 7:** We thank the reviewer for drawing our attention to this point. Patients are admitted the morning of surgery. This has been clarified in the methods under ERAS protocol description

**Changes in text:** Page 5, line 159-160

**Comment 8:** a synthetic table with all your ERAS items will be interesting and clarify the lecture.

**Reply 8:** We thank the reviewer for this suggestion. We have created a table with all of our ERAS items. These are now tables 1 (perioperative) and table 2 (postoperative).

**Changes in text:** Addition of new table 1 and table 2 with all ERAS items.

**Comment 9:** Data: No major concerns

**Reply 9:** We thank the reviewer for this feedback.

**Changes in text:** None required

Surgery:

**Comment 10:** Can you describe your surgical approach for VATS and RATS?

**Reply 10:** We thank the reviewer for this comment. We have clarified our intraoperative technique and approach in the methods section. For our lung resections, they are performed under general Anesthesia is used with a with double lumen endotracheal tube. Arterial line, large bore IV and Foley are placed prior to the operation. We do not use a central line. The VATS and RATS operations are done via 5 small incisions. A complete intercostal nerve block is performed at the beginning of the case with liposomal bupivacaine. All operations for cancer include a mediastinal and hilar lymphadenectomy. Attempts are made to minimize fissure dissection in patients with incomplete fissure. Staples are used for division of parenchyma, vessels, and airway. A Single chest tube placed after surgery. The use of pleural sealant is surgeon specific. Other than the use of pleural sealant, the operative technique is consistent between all surgeons in the division.

**Changes in text:** Page 5, lines 173-183.

**Comment 11:** Do you use sealant mesh or glue to avoid air leaks ?

**Reply 11:** The use of pleural sealant is variable and surgeon dependent. This has been addressed in our description of our operative technique.

**Changes in text:** Page 5, Lines 179-182.

**Comment 12:** Concerning the statistical analysis conducted: No major concerns about it.

**Reply 12:** We thank the reviewer for this feedback.

**Changes in text:** None required

Concerning the results

**Comment 13:** Results are well reported and clearly presented. Concerning the mortality 90-day mortality is more interesting than 30-day mortality. Can you analyze this?

**Reply 13:** We do not collect 90 day mortality, as it is not reported in the institutional STS database.

**Changes in text:** Unable to provide this variable, therefore no changes in the text were made.

**Comment 14:** In the ERAS group, according to your protocol it's impossible to check 100% of the ERAS items for each patient, so what is the percentage of deviations from the ERAS protocol?

**Reply 14:** We thank the reviewer for drawing our attention to this point. Unfortunately, we did not analyze. There was 100% surgeon agreement and adoption and all residents and nursing staff were required to follow the protocol beginning on 3/1/2019. It would be a worthwhile future area of study to look into compliance with the protocol.

**Changes in text:** Page 4, Lines 125-127.

**Comment 15:** Did implementing the ERAS protocol require recruiting staff?

**Reply 15:** The implementation of the protocol did not require recruiting staff. Residents and nursing staff were informed of the protocol and began implementing it at our start date of 3/1/2019. There was 100% surgeon agreement and adoption. This has been clarified in our methods section.

**Changes in text:** Page 4, Lines 125-127.

Concerning the discussion:

**Comment 16:** It's a well written discussion well documented with good references. Nice paragraph and interesting about the "decision fatigue manifests".

**Reply 16:** We thank the reviewer for this kind feedback.

**Changes in text:** None required.

**Comment 17:** Limitations are well described.

**Reply 17:** We thank the reviewer for the feedback.

**Changes in text:** None required.

Concerning the conclusion:

**Comment 18:** It's a well written, easy reading and interesting article, that need some little precisions. Congratulations to authors for this work.

**Reply 18:** We thank the reviewer for the kind feedback.

**Changes in text:** None required.

## **Reviewer B**

**Comment 1:** This is an ERAS report on minimally invasive surgery, but it lacks novelty. Furthermore, considering the stated objectives of the report, there is limited information on the surgical approach. VATS and RATS procedures are different. And surgical skills might be simply improved. There is a significant bias in the background, and there is a possibility that the results have not been properly assessed.

**Response 1:** We thank the reviewer for his thoughts and for reviewing the manuscript. It is valid that skills have improved over time. However, there was no significant change in surgical approach or technique over the course of our study. We have analyzed the outcomes for our VATS and RATS lung resections and found that there was no significant difference between the two approaches for length of stay or postoperative outcomes. We acknowledge that the retrospective study design presents potential inherent biases, particularly with operative variables and this has been addressed in the limitations section of our manuscript.

**Changes in text:** No changes that we are able to directly address.

## **Reviewer C**

This paper focuses on ERAS, a popular topic and serves as a possible "how-to" paper on implementing ERAS into a thoracic surgery program.

**Comment 1:** There is no hypothesis or aim stated in the introduction.

**Response 1:** We thank the reviewer for drawing our attention to this point. Our initial hypothesis was that implementation of this protocol would streamline patient care and reduce our hospital length of stay. This has been addressed in the introduction section.

**Changes in text:** Page 4, lines 118-120.

**Comment 2:** Much of my feedback is based on the lack of details on your ERAS program. What is the goal of your ERAS protocol - discharge by a certain day? "Some patients are discharged on POD 1" - doesn't really explain who/why/what. Later you write "when ready, patients are discharged."

**Response 2:** We thank the reviewer for this comment. Our standard discharge criteria is chest tube out, on room air, voiding independently, and on PO pain medication. Depending on patient preference and clinical status, sometimes we send people out with chest tubes, with oxygen, and with foleys. However, by and large, there was no systematic change in our discharge criteria. This has been addressed in our methods section.

**Changes in text:** Page 6, lines 228-235.

**Comment 3:** You state your protocol involves 4 weeks of counseling on smoking and alcohol cessation for 4 weeks. Does this delay surgery by at least 4 weeks on these patients? Do they have to successfully stop or what is the endpoint?

**Response 3:** We thank the reviewer for drawing our attention to this point. In short,

patients do not absolutely have to stop and we do not want this to be a reason to delay their surgery. In patients who do stop, it is very rare that we do surgery within 4 weeks of booking due to limited OR access and so the 4 week timeline will not delay their operation. In summary, we operate even if they are currently smoking, but smoking cessation is provided to all smokers.

**Changes in text:** Page 4, lines 137-140

**Comment 4:** The protocol does not seem strict - the descriptions can be quite nebulous or imprecise: "patients are allowed clear liquids" or "use of opiates is minimized" or "euvoemia is maintained" or "chest tube is put to suction" or "acetaminophen and gabapentin are given to all patients". It would be useful to summarize exactly what your protocol is/isn't with dosages etc. in a table.

**Response 4:** We thank the reviewer for this comment. We have added tables 1 and 2 to help elucidate the specifics of our ERAS program. This also has been addressed in more detail in our methods section.

**Changes in text:** Pages 4-6, lines 131-235

**Comment 5:** What is the type of MIS technique that is used, VATS and/or robotics? Was there a temporal trend using one over the other and did this impact the clinical outcomes? Do they have the same number of incisions, do you do it port-based, with an access incision, etc?

**Response 5:** The MIS technique used was a combination of robotic and VATS lung resections. Due to increased availability of console time, there was an increase in the proportion of robotic lung resections. This has been added to Table 3 with the preoperative demographics. We subsequently performed an analysis of all of our robotic vs VATS lung resections performed over this time and there was no significant difference in overall median or mean LOS. We have provided this in supplementary table 4. Clarifications to these points have been added in the results section.

**Changes in text:** Pages 7-8, Lines 274-277

**Comment 6:** How many surgeons and anesthesiologists are utilized in this protocol, do they all follow the same rules?

**Response 6:** We thank the reviewer for drawing our attention to this point. There were 3 surgeons and 10 anesthesiologists/CRNAs, all of whom followed the protocol. This has been clarified in the methods.

**Changes in text:** Page 5, lines 157-159

**Comment 7:** What determines going to the ICU vs. ward from the OR?

**Response 7:** This has been addressed in our discussion section. It is based on clinical decision making of anesthesia and surgery.

**Changes in text:** Page 9, lines 328-330.

**Comment 8:** What is the percent of prolonged admission between groups? This is different than the mean or median LOS.

**Response 8:** We thank the reviewer for this comment. However, we do not have a dedicated “prolonged admission” data point in our database. We have looked into incorporating this, but it seems that the definition of “prolonged admission” varies widely by study and institution. Therefore, we have not included a new “prolonged admission” variable, but we can look into including this if the reviewer had a specific definition of prolonged admission that he would like used.

**Changes in text:** No changes that we were able to address based off the initial comment

**Comment 9:** You report "postoperative pneumothorax" on line 209 - what is this defined as, a space on a postop CXR? Collapse requiring intervention after chest tube removal?

**Response 9:** We thank the reviewer for this comment. We have added a specification that this was requiring chest tube reinsertion.

**Changes in text:** Page 9, line 315.

**Comment 10:** You seem to be conflating better outcomes with better patient workflow. For example, LOS is better and there are less ICU admissions, yet the overall complication rate is the same. The only clinical outcome that was better was a decrease in postop pneumothorax with ERAS; however, the trend was to discharge more patients with chest tubes in the ERAS group. Can you comment in the discussion about this distinction - is it truly better patient outcomes?

**Response 10:** We thank the reviewer for drawing our attention to this. We agree that part of the benefits of these protocols is derived from improved patient workflow. However, lower length of stay is frequently used as a surrogate for clinical outcomes and we believe appropriate endpoint. Similar findings have been reported in the ERAS literature, and we have added a more in-depth discussion of this point to our discussion section. It is likely an amalgamation of small improvements in patient care/outcomes, along with improved workflow that make these pathways so effective.

**Changes in text:** Page 12, lines 438-448

## **Reviewer D**

Structure:

**Comment 1:** the article reflects the standard layout of a scientific article.

**Response 1:** We thank the reviewer for this feedback.

**Changes in text:** None required

Materials and methods:

**Comment 2:** patient selection is on point, and groups are built to highlight supposed differences between the same type of lung resection (anatomic and non anatomic, lobectomy and wedge) in pre-ERAS and ERAS pathways,

**Response 2:** We thank the reviewer for this feedback.

**Changes in text:** None required

**Comment 3:** ERAS society recommends opiates avoidance in favor of NSAIDS in the guidelines, but, since no strict consensus is present, every center decides which pain-killing protocols to adopt.

**Response 3:** We thank the reviewer for this comment and agree that this is variable between centers. We have included dosing and medications in table 1 and 2, to help share our own practices. Our group has published on pain after thoracic surgery, and we try to limit narcotics as much as possible. However, we have been unable to replicate what other centers do with opioid free pain control.

**Changes in text:** Incorporation of table 1 and table 2 with medication dosing

**Comment 4:** In the post-ERAS group I did not find a precise definition of aerostatic techniques, and the author keeps it vague. Recent studies show that the use of aerostatic material and reinforced staplers during surgery, for example, is linked to a lower occurrence of prolonged air leaks. This is usually defined as the main culprit of prolonged hospital stay, therefore an ERAS protocol lacking clear standardized intra-operative practices to avoid air leaks, or failure to collect data on the matter, is an incomplete one, and the data following it could have a surgical bias that is hard to determine.

**Response 4:** We thank the reviewer for drawing our attention to this point. We have added clarification to our methods section regarding our operative technique and practices to avoid air leaks. Other than variable use of pleural sealant between surgeons, operative technique is consistent throughout the division.

**Changes in text:** Page 5, lines 173-183

**Comment 5:** Apart from post-op day zero and post op day one, concurrent days are not well defined in the handling of the chest tube, is it not standardized? (duration of air leaks? Quantity of pleural effusion?).

**Response 5:** We thank the reviewer for this comment. We have included the chest tube fluid outputs in the methods section. Regarding air leaks, the chest tubes can be removed once air leaks cease. This is consistent between surgeons. Clarifications to these points have been incorporated in the methods section.

**Changes in text:** Page 6, line 216

**Comment 6:** The rest of the protocol respects ERAS guidelines.

**Response 6:** We thank the reviewer for this feedback.

**Changes in text:** None required

Results:

**Comment 7:** Post-ERAS and pre-ERAS groups are similar in terms of population, comorbidity and post-operative complications.

**Response 7:** We thank the reviewer for this feedback.

**Changes in text:** None required.

**Comment 8:** Procedure type is not comparable between the two groups ( $p=0,014$ )

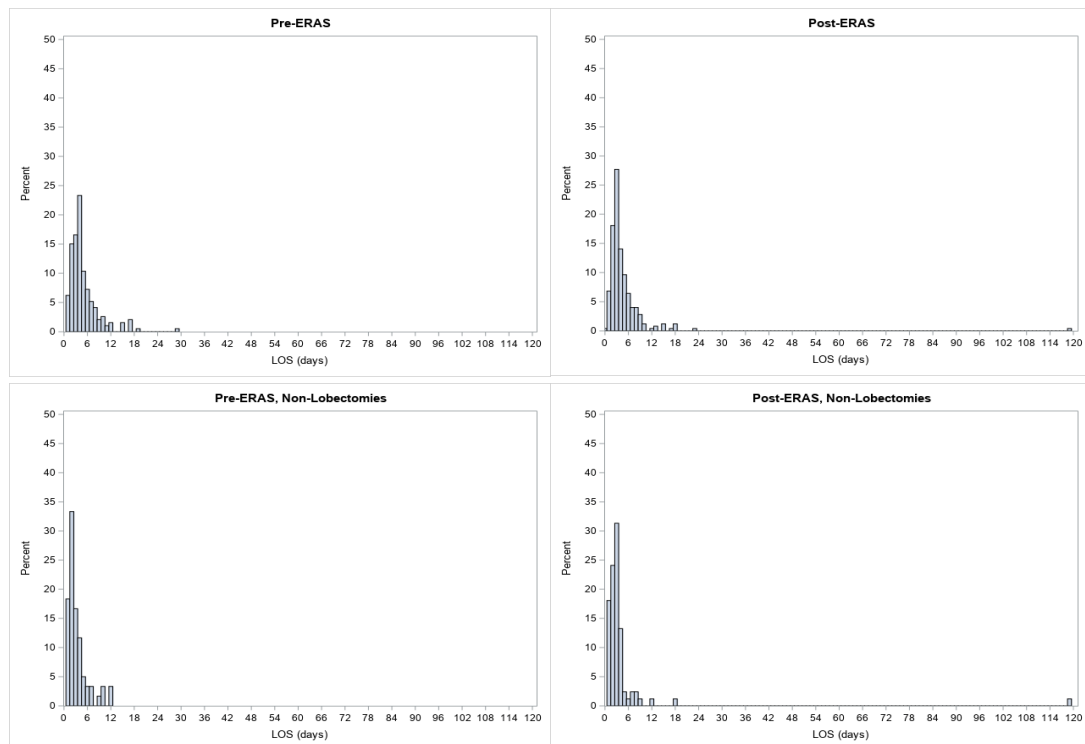
therefore it could have been a confounding factor.

**Response 8:** We thank the reviewer for drawing our attention to this. This trend is indicative of the current changes in practice surrounding sublobar resection and it certainly could have introduced bias into our study. We have added a discussion to this point in the limitations section.

**Changes in text:** Page 12, lines 455-458

**Comment 9:** Median length of stay of pre-ERAS in table 2 is 4.0 (IQR 3.0-6.0) while ERAS is 3.0 (IQR 2.0-5.0) ( $p=0.03$ ), however in table 3 I found that median length of stay for sub groups is at a glance incompatible with that result. The median stay for anatomic lung resection is the same (4.0,  $p=0.018$ ) between pre- and post-ERAS, while non anatomic resection in the post-ERAS groups is higher, or at least equal due to not being statistically significant (3.0 vs 2.0,  $p=0.86$ ). How is it that the overall median length is lower in the post-ERAS group while subgroups are both equal or higher than the pre-ERAS group? Is it a miscalculation or an oversight?

**Response 9:** The distributions of LOS by ERAS and type of resection are shown below. There is one patient in the post-ERAS non-lobectomy group whose extreme value pulls the median value for that subset higher than the median for the pre-ERAS non-lobectomy subset. In the larger overarching groups of pre/post ERAS that extreme value has less influence on the median, hence the seemingly contradictory Mann-Whitney U test results. We hope that this helps to clarify the reviewer's concerns regarding inconsistency in the median length of stay data.



**Changes in text:** None required

**Comment 10:** A higher proportion of patients were discharged with a chest tube in the



post-ERAS group, perhaps due to hospital policy of COVID related issued (as stated by the author), but I could not find the table with the “adjusted” results of LOS stated in row 205-206, which is stated as significant ( $p=0,008$ ) and the main point of which the study revolves around.

**Response 10:** We thank the reviewer for this comment. As this was just one variable that we examined, we opted to not include it in the LOS table, so as not to confuse readers. The data is presented below in table form, and all components of the table are provided in the results section. If the reviewer would prefer, we can upload this table below with our supplementary file, but we did not feel that inclusion of a standalone table with the “adjusted” LOS results was needed.

Variable	Pre-ERAS (n=191)	Post-ERAS (n=239)	p-value
Hospital Length of Stay, median (IQR)*	4 (3, 6)	3 (2,5)	0.008

*\*Patients who were discharged home with a chest tube were excluded from this analysis. There were 2 patients in the Pre-ERAS group and 10 patients in the ERAS group who were excluded.*

**Changes in text:** None required

**Comment 11:** ICU stay is significantly lower in the post-ERAS group ( $p=0,02$ ) but the author herself states that it was a consequence of a policy rather than an intrinsic benefit to the application of an ERAS method. It could have been an interesting point of discussion if the author collected data on unnecessary ICU admissions to support the discrepancy. Therefore, this data should not be presented as a highlight of the study.

**Response 11:** We thank the reviewer for this comment. We have added to the commentary of our ICU admissions in the discussion section. Unfortunately, we do not have data on unnecessary ICU admissions. However, we believe that our findings may still be of interest to other institutions considering adopting a thoracic ERAS protocol.

**Changes in text:** Page 9, lines 338-349

Conclusions:

**Comment 12:** Doubts persists in the consistency of the data used to state a benefit of the applied protocol.

**Response 12:** We thank the reviewer for this feedback.

**Changes in text:** None required

**Comment 13:** ICU admission rate was lower due to an implementation of a policy rather than an improved patient condition, and therefore scientifically inconsistent without proper analysis (ICU admissions not really needed to begin with? It’s a whole point altogether).

**Response 13:** We thank the reviewer for this comment. We have added a more extensive discussion on ICU admission practices in the discussion section, as we still

believe that this finding may be of benefit to other institutions.

**Changes in text:** Page 9, lines 338-349

**Comment 14:** In regards to decision fatigue, the author states that chest tube management is one of the main culprits, and that the process of standardization could help. However the author doesn't give a standard for chest tube management, which is the main point of disagreement among specialist in a non-complicated post-op patient.

**Response 14:** We thank the reviewer for this comment. The chest tube is placed to waterseal in PACU. It is removed when air leak ceases and when output is less than 300, 400, or 500cc/24hr (surgeon specific). These requirements have been added to the methods section, as well as are incorporated in table 1 and table 2.

**Changes in text:** Table 1 and Table 2. Page 6, line 216

References:

**Comment 15:** References are on point.

**Response 15:** We thank the reviewer for this feedback.

**Changes in text:** None required

Language clarity:

**Comment 16:** Language is clear and understandable.

**Response 16:** We thank the reviewer for this feedback.

**Changes in text:** None required.

Recommendation of acceptance:

**Comment 17:** This article needs to address the points given above to be considered for acceptance, and as such I do not recommend acceptance as of this version.

**Response 17:** We thank the reviewer for this feedback. We have worked whenever possible to address all of the reviewer's comments and hope that our revised version is suitable for publication.

**Changes in text:** None required

Constructive Feedback:

**Comment 18:** Review the tables and present data stated in the discussion. Integrate if necessary.

**Response 18:** We thank the reviewer for the constructive feedback. We have reviewed the tables and data stated in the discussion and have addressed all points raised by the reviewer whenever possible.

**Changes in text:** None required.

**Comment 19:** Focus on results due to the best clinical practice rather than hospital policy. ICU is always a point of discussion between anesthesiologists and surgeons, perhaps a rate of admission to ICU despite first indication of ward monitoring could be useful to support the decision?

**Response 19:** We agree with the reviewer that this is always a point of discussion

between anesthesiologists and surgeons. Unfortunately, rate of ICU admission despite first indication of ward monitoring is not a data variable that is collected in our institutional STS database. Regardless, we believe that the finding that patients were sent to the floor without an ICU level care in the PACU, and still had comparable complications and reduced length of stay is worthwhile for other institutions to learn of who are considering adopting a thoracic ERAS protocol. Commentary to this point has been added to the discussion section.

**Changes in text:** Page 9, lines 338-349

**Comment 20:** Try to focus on confounding factors and ways to exclude them. Match pre-ERAS with post-ERAS with a stronger statistical analysis (propensity score matching?).

**Response 20:** We thank the reviewer for this suggestion. We looked into matching based off cancer/non-cancer, ASA score, and operative approach, but this resulted in an approximately 30% reduction in our study population for both pre and post-ERAS groups, potentially reducing generalizability of this study and significantly lowering our sample size. Therefore, matching the groups is not possible with our current data set.

**Changes in text:** None required

#### **Reviewer E**

**Comment 1:** I read your manuscript and found many interesting data and results. My compliments. However, I would encourage you to ameliorate this manuscript with revision.

**Response 1:** We thank the reviewer for the kind feedback. We have worked whenever possible to incorporate all suggested changes and address the concerns of the reviewer. We hope that our revised manuscript is suitable for publication.

**Changes in text:** Changes detailed below

**Comment 2:** Key findings: specify that you refer to a median difference in LOS. As you discussed in the main text, anatomical resections mainly towed the difference.

**Response 2:** We thank the reviewer for this feedback

**Changes in text:** None required

**Comment 3:** Revision of the text for typos

**Response 3:** We thank the reviewer for drawing our attention to this point. We have gone back and revised the text for typos. Several were corrected throughout the manuscript.

**Changes in text:** Several small typos edited throughout manuscript.

**Comment 4:** build up a table for your Institutional ERAS protocol (at least the first three PODs).

**Response 4:** We thank the reviewer for this suggestion. We have created table 1 and

table 2, which summarize our perioperative care of patients, as well as the first 3 PODs (POD0, POD1, POD2) of our ERAS protocol. After POD2, all postoperative days are essentially treated equivalently, so we only have included up to POD2.

**Changes in text:** Incorporation of table 1 and table 2

**Comment 5:** it should be helpful to understand if there are critical differences with your pre-ERAS protocol for the same set of patients. Please add information and build up a table similar to the one suggested for the ERAS protocol.

**Response 5:** We thank the reviewer for this comment. Unfortunately, there was no clear pattern prior to our ERAS protocols and different components of the care differed for each surgeon. This is why we developed our ERAS protocol. Therefore, we do not believe there is a clear and concise way to summarize key differences since it was entirely surgeon and patient dependent prior to implementation of our protocol.

**Changes in text:** None addressed

**Comment 6:** It should be interesting to explain what kind of physiotherapy protocol you applied before and after surgery. This publication should help you "Bertani A, Ferrari P, Terzo D, Russo E, Burgio G, De Monte L, Raffaele

**Response 6:** We thank the reviewer for this comment. As we have mentioned in the earlier comments, we do not have a dedicated physiotherapy program, as we practice in a resource limited hospital and community. However, we have incorporated the reference into the manuscript, as other institutions may benefit from learning more about these protocols and incorporating them into their own ERAS protocols.

**Changes in text:** Page 4, line 133-135

## **Reviewer F**

**Comment 1:** This is a well written manuscript on the application of ERAS to minimally invasive thoracic surgery, which is undoubtedly a hot topic. It reports the experience of adopting an ERAS protocol for perioperative management of minimally-invasive treated thoracic patients in a single Institution. The English language is good and only few typos should be amended.

Nevertheless, I think some key points should be addressed before considering the manuscript suitable for publication.

**Response 1:** We thank the reviewer for his kind feedback. We have worked whenever possible to address all the concerns raised and hope that the revised version is suitable for publication in Journal of Thoracic Disease.

**Changes in text:** Changes detailed below and incorporated throughout the text.

Major concerns

**Comment 2:** Several studies have examined the impact of ERAS on VATS lung resections, much more than those cited by the Authors:

*D'Andrilli A, Rendina EA. Enhanced recovery after surgery (ERAS) and fast-track in video-assisted thoracic surgery (VATS) lobectomy: preoperative optimisation and care-plans. J Vis Surg. 2018 Jan 5;4:4. doi: 10.21037/jovs.2017.12.17.*

*Gonfiotti A, Viggiano D, Voltolini L, Bertani A, Bertolaccini L, Crisci R, Droghetti A. Enhanced recovery after surgery and video-assisted thoracic surgery lobectomy: the Italian VATS Group surgical protocol. J Thorac Dis. 2018 Mar;10(Suppl 4):S564-S570. doi: 10.21037/jtd.2018.01.157.*

*Bertolaccini L, Brunelli A. Devising the guidelines: the techniques of uniportal video-assisted thoracic surgery-postoperative management and enhanced recovery after surgery. J Thorac Dis. 2019 Sep;11(Suppl 16):S2069-S2072. doi: 10.21037/jtd.2019.01.62.*

*Huang L, Frandsen MN, Kehlet H, Petersen RH. Days alive and out of hospital after enhanced recovery video-assisted thoracoscopic surgery lobectomy. Eur J Cardiothorac Surg. 2022 Aug 3;62(3):ezac148. doi: 10.1093/ejcts/ezac148.;*

These are only examples of the rich literature on this topic, and I think that some of those papers should be discussed by the Authors;

**Response 2:** We thank the reviewer for drawing our attention to these interesting studies. References to these have been incorporated into the revised manuscript.

**Changes in text:** Page 4, lines 131-132. Page 5, lines 177-181. Page 12, lines 443-446. Page 12, lines 443-446.

**Comment 3:** There is a statistically significant difference between pre- and post-ERAS groups concerning cancer vs non-cancer (more non-cancer diagnosis in the post-ERAS), I think this aspect should be explored and discussed, since cancer patients are more fragile patients than non-cancer counterparts.

**Response 3:** We thank the reviewer for this point. Regarding cancer/non-cancer and ASA, these are certainly factors that can contribute to confounding. Interestingly, though there was a lower percentage of cancer patients in the ERAS group, there was a higher proportion of patients with an ASA score of II. We have added a discussion of these points to our limitation section.

**Changes in text:** Page 12, lines 459-462

**Comment 4:** There is a statistically significant difference between pre- and post-ERAS groups concerning the surgical procedure, in particular more sublobar resection have been performed in the post-ERAS group; don't you think this could have biased the results? This aspect should be discussed;

**Response 4:** We thank the reviewer for drawing our attention to this. This trend is indicative of the current changes in practice surrounding sublobar resection and it certainly could have introduced bias into our study. We have added a discussion to this point in the limitations section.

**Changes in text:** Page 12, lines 455-457

**Comment 5:** Globally, although without statistically significance, more patients were discharged with chest tube or home O2: considering that the main favorable outcome was the reduced median LOS, the feeling is that this outcome was influenced by the choice of early discharge with chest tube (without air leak, as you have underlined) or home O2;

**Response 5:** We thank the reviewer for this feedback. We have addressed in previous comments that there was no practice change with respect to patient discharge with chest tube or home O2, though there was a significant difference observed. We do not have a single, clear explanation for this, and it was absolutely not our intention to discharge patients home with chest tubes simply to lower our hospital length of stay. Additionally, a significant difference in LOS still exists even when the patients who were discharged home with a chest tube were excluded, as we previously included in the results section.

**Changes in text:** Page 9, lines 314-318

**Comment 6:** Pneumothorax requiring chest tube reinsertion was more frequent in pre-ERAS group, why and how's it possible? ERAS encourages an early chest tube removal; if you to discuss about this aspect, you should at least report POD chest tube removal before and after ERAS.

**Response 6:** It is possible that though ERAS encourages an early chest tube removal, there are standardized criteria for removal with regard to air leak that must be met, and therefore the management may have been more conservative in the post-ERAS group. Unfortunately, we can not compare chest tube data because of change in medical record systems from prior to 2017. Therefore, the daily data from hospitalizations where we would have to manually retrieve chest tube duration from is not accessible and chest tube duration is not collected in the institutional STS database.

**Changes in text:** We are unable to collect the requested data, and therefore unable to address this comment directly in the text.

Minor

**Comment 7:** Number of VATS vs RATS should be reported

**Response 7:** We thank the reviewer for this comment. This has been incorporated in the preoperative characteristics table 3, and a comparison of LOS for VATS and RATS incorporated as a supplementary file.

**Changes in text:** Page 8, lines 274-277

**Comment 8:** number of primary lung neoplasms vs secondary neoplasms should be reported.

**Response 8:** We thank the reviewer for this comment and certainly think that this would be an interesting point of discussion. However, this variable is not collected in our institutional STS database.

**Changes in text:** No changes that we are able to implement since the requested data is unavailable to us.