

Peer review file

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Reviewer A

Although LigaSure has been available on the medical market for many years, results of the studies regarding its usefulness in anatomical pulmonary resections are inconclusive. For this reason, it is very important to continue research in the field.

The title of the paper is very well written, it is short and but descriptive, and contains all the most important information about the study. The authors could possibly consider including the name “LigaSure” in the title, as this could help other authors searching for the literature in this area to find a paper more easily.

The abstract comprehensively describes the background, methods, results, and conclusions.

The main text is divided into appropriate sections. In the “Background” section, the authors clearly discuss the rationale for undertaking the research.

Regarding “Methods”, the part “Subjects and study design” includes all the necessary information, but the order of the text could be rearranged for its better clarity. I would suggest starting with information about the approval of the study by Institutional Review Board, followed by the dates of the study, type of study, exclusion and inclusion criteria, and type of the data included. Since Table 1 contains the results of analysis and it is referred to later in the “Results” section, I would suggest that you do not quote it in Line 68. “Operative procedure” and “Statistical analysis” are very well written.

“Results” section contains all the necessary information. However, it could be arranged in a slightly clearer and more structured way:

Comment 1: Line 114 – phrase “On the contrary” is not necessary, I suggest deleting it.

Reply 1: We would like to thank you for your valuable comment. We confirm that we have now deleted the indicated phrase from our manuscript and replaced it with “while” to increase readability.

Changes in the text: (Line 114).

Comment 2: Line 114 – I suggest adding range of volume of blood loss: “median blood loss ... was 100 mL (50-250 mL)”

Reply 2: We would like to thank you for your valuable suggestion. Following your

comment, we have now added the range of volume of blood loss to our revised manuscript.

Changes in the text: The median amount of intraoperative blood loss for all patients was 100 ml (50-250 ml) (Line 116).

Comment 3: The “Results” should contain only pure information on the results of the study. The elements of the discussion should not be included here, therefore I propose to delete all sentence beginning in the line 119 and ending in the line 122 (“Murakami...”).

Reply 3: We would like to thank you for your insightful suggestion. We completely agree with you and we would like to inform you that we have now deleted the mentioned sentence.

Changes in the text: (Line 121).

Comment 4: Line 123 – word “Further” is not necessary, I suggest deleting it.

Reply 4: We would like to thank you for your valuable comment. We have now deleted the above-mentioned word from our manuscript, as suggested.

Changes in the text: (Line 122).

Comment 5: Most of results of the comparison of VSS and CM groups reported from line 130 to line 137 are also included in Table 4. For better clarity of the text, I would suggest including information on the time of surgery and postoperative hospitalization in one shorter sentence, for example: “surgery time and hospitalization time did not differ significantly between the groups”, which could be included in the end of this part of the text. Line 123 – word “Further” is not necessary, I suggest deleting it.

Reply 5: We would like to thank you for your insightful suggestion. We have now revised our manuscript to address your comment.

Changes in the text: “Operating time and postoperative stay did not differ significantly between the two groups” (Lines: 129-130).

Comment 6: Line 138 – I suggest a change to: “Of the 11 patients with chylothorax, 10 were....”

“Conclusions” section starts with a summary of the results. The authors discuss all their findings and refer to the current literature. I have only one remark:

1. The exact figures regarding intraoperative blood loss and postoperative drainage time were already provided in the text and it is not necessary to repeat them in the conclusions (Line 152 – 153). I suggest a change to: “The intraoperative blood loss and chest tube duration was significantly lower in the VSS group”.

Reply 6: We would like to thank you for your insightful suggestion. We confirm that we have now revised the above-mentioned sentences as indicated.

Changes in the text: “Of the 11 patients with chylothorax, 10 were male” (Line 129). “Intraoperative blood loss and chest tube duration were significantly lower in the VSS group” (Line 131).

Reviewer B

I have read with great interest the manuscript titled “Vessel sealing system for video-assisted lung cancer resection reduces chylothorax and bleeding” in which the authors present their experience with the use of the LigaSure system when performing oncological lung resections, with lymph node dissection for accurate post-operative staging. This is a well written manuscript with a good number of cases included and appropriate statistical analysis of the outcomes to produce significant conclusions. I believe publication of the results will be of benefit to the community of thoracic surgeons as it addresses two important concerns with regards to potentially preventable peri- and post-operative complications.

I would propose however that the authors consider revisions as follows:

Major:

Comment 1: Line 30, Line 101. It is not very clear which values are presented as means and which are presented as medians. Furthermore, the range selected to be presented next to the median values (interquartile) is not defined early in the text and this causes some confusion to the reader until reaching line 137 of the text. Median drain duration for CM was 3 days with an interquartile range of 3-3 days while median chest drain duration for VSS was 2 days with a range of 1-3 days. Was there a thought process behind drain stay decisions which may have affected the results? Were the surgeons choosing to leave their drains stay longer affected by which sealants and ligatures were used during surgery? Or reversely, did surgeons who used sealing systems feel more confident to remove drains earlier? Were there uniform fluid criteria regarding drain removal? What were the limits? This should be noted and discussed in the text, or at least in the discussion as a potential limitation of the study.

Reply 2: We would like to thank you for your insightful comment. We would like to inform you that we have now revised the Methods section of our manuscript to address your concerns regarding our statistical analysis and to increase clarity. Furthermore, we have now added to the same section a description of the criteria used in this study to determine drain removal used in this study.

Changes in the text: “With regards to descriptive statistics, continuous variables were described using means or medians (interquartile ranges), while categorical variables were described using frequencies or percentages” (Lines: 101-103).

“Chest tube was removed when the total discharge volume was lower than 5mg/kg/day and apparent air leakage and chylothorax were not detected” (Line 87).

Comment 2: Line 63. It is interesting that the authors selected to not include patients who had previously underwent chemotherapy and radiotherapy, as these are the patients who exhibit the highest risk of peri-operative bleeding and have difficult to dissect lymph nodes, thus possibly generating a strong case for the use of a sophisticated technologically advanced sealing system over conventional methods. Can the authors explain why they selected to exclude these patients from their analysis?

Reply 2: We would like to thank you for your valuable comment and apologize for not including this information in our original manuscript. We have now revised our manuscript to add this information.

Changes in the text: “Patients that required conversion to open thoracotomy or that had undergone either preoperative chemotherapy or radiotherapy were excluded from this study to simplify the investigation of VSS effectiveness in general cases” (Lines: 62-64).

Comment 3: Line 112. A significant number of patients was found to be in stage III and IV following resection, more than those in stage II. This is outside the scope of this paper however interesting as an outcome and could be useful to comment on in the discussion, especially since patients who previously received neo-adjuvant treatment were not included. Which staging systems were used? On a similar note, was there a difference in the number or stations of lymph nodes dissected between the two groups discussed in the paper? Were nodes completely removed or sampled during lung resections?

Reply 3: We would like to thank you for your insightful comment. We have now revised our manuscript to address your comment.

Changes in the text: “After anatomic pulmonary resection, mediastinal lymph node dissection (MLND) is routinely performed. While mediastinal lymph node stations #2R,

#4R, #7, #8 and #9 were dissected from the right lobes, mediastinal lymph node stations #4L, #5, #6, #7, #8 and #9 were dissected from the left lobes, according to the guidelines provided by the International Association for the Study of Lung Cancer (IASLC) []. In contrast, selective MLND was performed in patients who underwent segmentectomy. Staging was performed according to the Lung Cancer Staging Manual (7th edition) by the American Joint Committee on Cancer” (Line 78).

Comment 4: Line 121. Post-operative air leak is an important and frequently experienced complication in thoracic surgery, one which possibly contributes the most to prolonged stay and further morbidity. It is interesting that the authors have not included post-operative air leaks at all in their study because, given the limited availability of staplers in the department, one may argue that the use of LigaSure to dissect vessels and develop fissures could have been another important factor to consider when comparing methods. In this series of 948 patients only 11 developed a chylothorax and peri-operative bleeding amounted to relatively small volumes overall, probably more patients exhibited complications and prolonged stay related to incomplete aerostasis rather than haemostasis?

Reply 4: We would like to thank you for your valuable comment. We have now revised our manuscript to address your comment. we have also added the information about incidence of persistent air leaks between two groups in table4 and modified the result part accordingly.

Changes in the text: “Surgerytime, hospitalization and incidence of persistent air leaks (air leak lasts >7days) did not differ significantly between two groups”. (line134)

Comment 5: Line 134. Patients in the VSS group spent one additional day in hospital compared to patients in the CM group, even though their drains had mostly been removed one day earlier. Even though not statistically significant, arguably this is an important finding as the cumulative costs of one extra day of hospital stay for a number of patients probably outweighs gains made by thorough haemostasis peri-operatively. Can the authors explain in discussion why patients with a median drain duration of 2 days were required to remain in hospital for 9-10 days?

Reply 5: We would like to thank you for your valuable comment. We have revised our manuscript to address your comment and have now explained that the incentive to shorten post-operative stay had been quite weak in Japan.

Changes in the text: “In Japan, the National Health Insurance covers around 90% of the cost associated with patient hospitalization following lung cancer resection. The

hospitalization duration is gradually shortening according to the national medical cost reduction policy” (Line 223).

Comment 6: Lines 146-147. “Chest tube was removed at a median of 5.4 days after lung cancer surgery”. Which group of patients is this number referring to, is it for all 11 patients who developed a chylothorax or just the 8 who were treated conservatively? The authors explain that intervention for chylothorax was mostly considered for patients after 7 days following lung resection.

Reply 6: We would like to thank you for your valuable comment. We have now revised our manuscript to increase understanding.

Changes in the text: “In these 11 patients, the chest tube was removed at a median of 6 days (4-7 days) after lung cancer surgery” (Lines: 138-139).

Comment 7: Line 226. Patients in the VSS group are reported to have a shorter hospital stay but in Table 4 and Line 134 it appears they actually have had a longer hospital stay. Which one is correct?

Reply 7: We would like to thank you for your valuable comment and apologize for the lack of clarity. We have now revised our manuscript to increase understanding.

Changes in the text: “There was no post-operative hospital stay advantage in the VSS group but rather increase by one day (9 vs 10 days, $p=0.757$). It would be resulted from the situation that clear criteria for hospital discharge after surgery have not been set in this study.” (Line 237).

Minor:

Comment 1: Line 86: Comma not needed after phrase “In case”

Reply 1: We would like to thank you for your comment. We have now deleted the comma as suggested.

Changes in the text: (Line 87).

Comment 2: Line 114: replace “of all patients” with “for all patients”. Replace “on the contrary” with “furthermore”.

Reply 2: We would like to thank you for your comment. We confirm that we have now replaced “of all patients” with “for all patients” and replaced “on the contrary” with “while” to increase readability.

Changes in the text: (Line 116).