Peer Review File

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Reviewer A

Congratulations on a detailed prospective study. The only revision I see necessary is from the Result section in the first sentence. The sentence is awkward and I am not sure what "didn't meet the exclusion criteria" is referring to.

Answer: Thanks for your kind suggestion. The new sentence is changed as “A total of 504 patients went through the procedure of screening and were selected.”

Changed in the text: Page 6/Line 164.

Reviewer B

Congratulations to you on your successful new design of an instrument, speeding up the lymph nodes dissection procedure. However, there are several questions which should be addressed before the article can be considered for publication.

Comment 1: You stated that 'since 1990 VATS became the standard surgical procedure for early stage lung cancer'. Please give references.

Answer: Thanks for your kind suggestion. Indeed，the sentence is note accurate. The new sentence is “since its first report in the 1990s (3), VATS has became the standard surgical procedure for early stage lung cancer in recent years ”. The references is added.

Changed in the text: Page 3/Line 72-74.

Comment 2: What is the cost of the new aspirator ?

Answer: The engineer told me the price is about 7-8000 CNY, because there will be discount in different district. But the aspirator has not been officially on sell, as there are still some details are under improving.

Changed in the text: N/A

Comment 3: Is the new aspirator disposable ?

Answer: No, it is reusable, after cleaning and disinfection.

Changed in the text: N/A

Comment 4: Is there any difference when used for the left and the right lung ?

Answer: Our practice showed no clear difference when used for the left and the right lung.

Changed in the text: N/A

Comment 5: In line 174, prone to collision and interference.... you can write as 'sword fighting'.
Answer: Thanks for your kind suggestion. According to the comments of other reviewers, this paragraph has been deleted as it was redundant.
Changed in the text: N/A

Comment 6: From line 175 to 182, the language is lousy and difficult to understand. Please rephrase.
Answer: Thanks for your kind suggestion. According to the comments of other reviewers, this paragraph has been deleted as it was redundant.
Changed in the text: N/A

Comment 7: Please cancel the figure of traditional procedure and just show those of the new one.
Answer: Thanks for your kind suggestion. We deleted former figure 4&5.
Changed in the text: N/A

Comment 8: Please explain and describe more clearly how the new device work.
Answer: Thanks for your kind suggestion. The working process of new device is described more clearly "On the basis of a traditional surgical aspirator, the clamping function of the front plier-like structure is added. Besides, our new tool adds a ring button (with spring for returning) located on the handheld end, and a rod to conducting the force. Under normal conditions, the button is in the initial position, and the pliers remain closed. When surgeon presses the button , the force transmit to the pliers through the rod, drives the pliers open, and the aspirator is ready to clamp tissue. After the button is released, the pliers return to the closed state, and the tissue is tightly clamped. The structure (including button, spring, rod and pliers) is shown in Figure 1"
Changed in the text: Page 5/Line 124-130.

Reviewer C

The presented device seems like a very interesting innovation for the realization of VATS, congratulations for the idea. However, I think there are aspects that need to be clarified on paper:

Comment 1: P. 2 – l. 43: The 7R and 7L nodal region does not exist. Authors should correctly explain what they mean, even if it is imaginable.
Answer: Thanks for your kind suggestion. The explanation is added. "No. 7R/L (No.7 lymph nodes resected through right or left side)"

Changed in the text: Page 2/Line 44.

Comment 2: In the abstract, in the Methods section the description of the statistic should be more detailed.

Answer: Thanks for your kind suggestion. More detailed description of the statistic is provided "Mann-Whitey U test was applied to analyze sex and pathological type, an independent-samples T test was applied to analyze surgery time and age."

Changed in the text: Page 2/Line 46-47.

Comment 3: In the abstract, at the beginning of Results the number of patients should be expressed in number, not in letters.

Answer: Thanks for your kind suggestion. The number is expressed as "250" now.

Changed in the text: Page 2/Line 48.

Comment 4: P. 3 – l. 73-74: This is a biased statement, since only 20% of patients diagnosed with lung cancer are candidates for surgery at the time of diagnosis. The authors will mean that up to 85% of patients potentially candidates for surgical treatment opt for surgery. It is also striking that this statement is based on an article on small cell lung cancer.

Answer: Thanks for your kind suggestion. It is indeed a misrepresentation. NSCLC takes up to 85% of all lung cancer patients.

Changed in the text: Page 3/Line 72.

Comment 5: P. 4 – l. 89: The authors possibly mean that the aspirator may be useful for VATS in many patients, not just some patients.

Answer: Thanks for your kind suggestion. We replaced "some" with "most".

Changed in the text: Page 4/Line 90.

Comment 6: P. 4 – l. 97-99: I don't quite understand what the authors mean, it should be better explained.

Answer: Thanks for your kind suggestion. Every patient has a hospital number. If the number is odd (with last digit 1, 3, 5, 7, 9), the patient will be allocated into traditional aspirator group (control). If the number is even (with last digit 0, 2, 4, 6, 8), the patient will be allocated into new aspirator group (intervention).

Changed in the text: Page 4/Line 98-101.

Comment 7: P. 4 – l. 105: The use of anticoagulants does not contraindicate surgery, it only requires an adequate preoperative and perioperative adjustment.

Answer: Thanks for your kind suggestion. Our previous description was not accurate. The redescription is "use of anticoagulant drugs in one week".

Changed in the text: Page 4/Line 107-108.

Comment 8: P. 4 – l. 109: The sixth exclusion criterion may imply a selection bias; it is too imprecise.

Answer: Thanks for your kind suggestion. We use "other situations VATS mediastinal lymph node dissection could not proceed, such as has converted to open surgery" To replace our previous sentence.

Changed in the text: Page 4/Line 111-112.

Comment 9: P. 4 – l. 111-113: The authors do not explain whether the new instruments were tested under experimental surgery conditions on non-human models; this aspect may present ethical controversies.

Answer: Thanks for your kind suggestion. The new aspirator passed experimental surgery on pig before clinical trial.

Changed in the text: Page 5/Line 134-135.

Comment 10: P. 4 – l.115-117: Were adverse effects such as lacerations of the esophagus or of the tracheobronchial membrane, recurrent nerve injuries, etc. not taken into account?. In short, they are tissue damage that could occur, and that should be considered during data collection. If they were considered but did not occur, the authors should specify that tissue damage did not occur; some aspect related to this appears in Discussion and Table 3, and yet it should already be clear in this part of the text.

Answer: Thanks for your kind suggestion. In the revised manuscript, we stated "there were no other accidental tissue injury or postoperative adverse events related to mediastinal lymph node dissection."

Changed in the text: Page 6/Line 187-189.

Comment 11: The Methods section does not clearly define the variables studied; consequently, the statistical analysis subsection is confusing.

Answer: Thanks for your kind suggestion. In the revised manuscript, we defined the variables and redescribed the statistical analysis.

Changed in the text: Page 5/Line 138-155.

Comment 12: P. 9 – Fig. 1: I think the drawing corresponding to the closed position of the pliers presents the explanatory arrow of the operating mechanism inverted.

Answer: Thanks for your kind suggestion. The button is annular. Press any part of the button can achieve same effect. The structure is redescribed in detail.

Changed in the text: Page 4/Line 124-131.

Reviewer D

In this prospective non-randomized single-institutional study, the authors investigated the efficacy of a novel aspirator in mediastinal lymph node dissection by uniportal VATS. I have some comments.

Comment 1: Before the mediastinal dissection, lobectomy is performed by uniportal VATS. Was a traditional aspirator used for lobectomy both in traditional aspirator groups and new aspirator groups? If a new aspirator was used for lobectomy in new aspirator groups, were there any differences in total operation time or the amount of bleeding?

Answer: Thanks for your kind suggestion. The new aspirator has been used in the lobectomy, but the difference in total operation time and the amount of bleeding is not compared. In our preliminary study, we found the efficacy of new aspirator in lobectomy is less than that in lymph node dissection, as lymph node resection demands more grasping; Meanwhile, there are several factors that influent lobectomy, such as interleaf fissure development, degree of lymph node calcification, degree of connective tissue porosity and anatomic variation. Both these two factors may cover the difference in total operation time and the amount of bleeding. Therefore, we decided not to compare the efficacy of new aspirator in lobectomy.

Changed in the text: N/A

Comment 2: The authors only compared the outcomes in mediastinal lymph node dissection. Total operation time, the amount of bleeding, the duration of chest drainage and the duration of hospital stay should be also investigated.

Answer: Thanks for your kind suggestion. As we explained above, the efficacy of new aspirator in lobectomy is not statistically significant, according to our preliminary study, so we just compare the factors related to lymph node dissection.

Changed in the text: N/A

Comment 3: Although there are statistically significant differences in the procedure time of mediastinal lymph node dissection between the traditional aspirator group and the new aspirator group, those differences have little influence in clinical practice, for the procedure time in the traditional aspirator group is short enough.

Answer: Thanks for your kind suggestion. In Nowadays, the VATS has been a mature technology. On the other hand, the room for its improvement is limited, and it's difficult to achieve even a little progress. Though the improvement for VATS brought by the new aspirator

is not so much, it still has clinical significance. We hope more achievements can be made to make the procedure time of VATS shorter and shorter.
Changed in the text: N/A

Comment 4: The authors did not compare the procedure time of left upper mediastinal lymph node dissection (#4L, #5, #6). Are there any data on that?
Answer: Thanks for your kind suggestion. In our preliminary study, the procedure time of #5/#6 didn't show significant difference, as the time of dissection #5 and #6 is short (much easier than #2/4R and #7), the new aspirator is not able to show its advantage. Meanwhile, we found the variance of time spent in dissection of #4L is large in our preliminary study, which may because the actual size, number and location (near arterial ligament or closer to the bulge) of #4L differs, and the three factors have great influence for the procedure time of #4L. By contrast, the size and location of #2/4R and #7 are relatively fixed, and the procedure time for their dissection has enough space for descend. That's why we set #2/4R, 7R and 7L as our target lymph nodes.
Changed in the text: Page 8/Line 228-242.

Comment 5: The orientations of figures and videos should be added in the revised manuscript (for instance, caudal/cranial; ventral/dorsal).
Answer: Thanks for your kind suggestion. The orientations of figures and videos are added in the manuscript. All the operation are single-portal VATS, and the incision locates between posterior axillary line and midaxillary line, fourth intercostal.
Changed in the text: Page 4/Line 117-118, Page 11/Line 330-331, Page 12/Line 335-336, Page 12/Line 347-348, Page 12/Line 352-353.

Comment 6: About the p value of No.7 lymph node in Table 2: it should be replaced to <0.001.
Answer: Thanks for your kind suggestion. The number "0.000" has been replaced to <0.001.
Changed in the text: Page 13/Line 360.

Comment 7: Since much of the discussion section was the duplication of the introduction section, the discussion is redundant. The authors should make discussions based on the results of this study.
Answer: Thanks for your kind suggestion. We deleted paragraphs in the discussion section that similar to introduction section, and extra discussions based on the results are made.
Changed in the text: Page 7/Line 205-255.

Comment 8: The number of references are little. Some manuscripts should be cited in the revised manuscript.

Answer: Thanks for your kind suggestion. Several citations have been added in the revised manuscript. As there are little literatures on similar topic, the number of added citations is not so much.

Changed in the text: Page 10/Line 309-318.

Reviewer E

Review of the paper entitled: "Enhanced efficacy of a novel aspirator in uniportal video-assisted thoracoscopic mediastinal lymph node dissection: a nonrandomized prospective clinical trial" by Luo1 et al, Department of Thoracic Surgery, Zhejiang Cancer Hospital, Hangzhou, China. The authors reported the clinical application of a new device, an aspirator which opens the distal tip ensuring a better traction and tissue dissection in term of reduced operative time and complication similar to the traditional curve device. I think the new device could have some application and it is a very interesting device. The paper needs some modifications almost regarding the paragraph methods and results:

Comment 1: I suggest inserting the approval code and date from ethics committee.

Answer: Thanks for your kind suggestion. The approval code and date from ethics committee has been inserted.

Changed in the text: Page 5/Line 120-121.

Comment 2: I suggest a whole statistical review and in particular: how were categorical data resumed? what was the statistical test used to calculate differences between sex and complications for example? Fisher's test? chi-square?

Answer: Thanks for your kind suggestion. The “Statistical analysis” part was rewritten, the categorical data was deemed. Independent-samples T-test was applied to analyze the differences in sex and complications.

Changed in the text: Page 5/Line 138-155.

Comment 3: what was the distribution of the data? normal or not?

Answer: Thanks for your kind suggestion. We’ve tested the data with SPSS, and it fit normal distribution.

Changed in the text: N/A

Comment 4: what was the selection criteria between the new device and the traditional one? I did not find this crucial information into the paper;

Answer: Thanks for your kind suggestion. Enrolled patients were allocated according to the parity of the hospital number: odd hospital number (with last digit 1, 3, 5, 7, 9) to the traditional

aspirator group (control) and even hospital number (with last digit 0, 2, 4, 6, 8) to the new aspirator group (intervention).
Changed in the text: Page 4/Line 98-101.

Comment 5: I suggest including in the paragraph methods what dissection device was used by the two surgeons (hook? ultrasound dissector? bipolar?). did the authors analyze the impact of the different energy devices? This is a crucial information because different devices have different operation time and electrocautery and dissection characteristics.
Answer: Thanks for your kind suggestion. Every thoracic surgeon has his own pathway and method in mediastinal lymph node dissection. In this study, we didn't determine the device used by two surgeons, give them the space to produce a full effect of the aspirator, no matter traditional or new aspirator. In the actual process, both of them use ultrasound dissector in most part of dissection, and hook also plays a role in the process. Neither of them uses bipolar. In the revised manuscript, we added the discussion about the effect of different devices.
Changed in the text: Page 8/Line 250-255.

Comment 6: L140 this sentence contains redundant information, please correct it.
Answer: Thanks for your kind suggestion. This redundant has been corrected.
Changed in the text: Page 6/Line 164.

Comment 7: I suggest including the conversion rate is available.
Answer: Thanks for your kind suggestion. In our study, all of the enrolled patients receiver mediastinal lymph node dissection in VATS. If one patient was converted to open surgery before mediastinal lymph node dissection, he/she would be excluded. There were 21 patients were excluded because of this reason.
Changed in the text: N/A

Comment 8: I think references should be implemented.
Answer: Thanks for your kind suggestion. Several citations have been added in the revised manuscript. As there are little literatures on similar topic, the number of added citations is not so much.
Changed in the text: Page 10/Line 309-318.

Reviewer F

The authors propose a new instrument that unites two surgeon functions, suction and grasping, in one device during uniportal thoracoscopic lung resection. They report an open-label comparison trial of roughly 250 patients each undergoing lung resection for presumed or

confirmed lung cancer with either a conventional or the new instrument. They find differences in length of lymph node dissection and operative events between the two methods. They conclude that the new instrument is superior to conventional suction aspiration.

Comment 1: Since an unknown numbers of study subjects enter the operating room without a histological diagnosis of lung cancer (inclusion criterium II of IV), it follows that some study participants never underwent lymph node dissection because they were not found to have lung cancer. These participants are not mentioned but should be accounted.

Answer: Thanks for your kind suggestion. 77 patients failed the procedure of screening. The reason including the result of cryopathology didn't suggest mediastinal lymph node dissection (such as benign or carcinoma in situ), conversion to open surgery before mediastinal lymph node dissection, patient's condition fluctuates during surgery and a compromise resection is performed, et al.

Changed in the text: Page 6/Line 158-163.

Comment 2: Differences of mean dissection time between two methods were 37 seconds for station 2/4 R lymph nodes and 42 seconds for station "7R" lymph nodes (given that station 7 nodes are midline, this reviewer assumes that "7R" refers to dissecting 7 nodes from the right side). The difference for "7L" nodes was 59 seconds. Thus, while a total difference of 1 minute 36 seconds in right sided lymph node dissection may be statistically different, it is clinically irrelevant. Or at least the authors have not demonstrated clinical relevance. A time advantage that is clinically irrelevant does not mean the surgeon should not use the instrument, it only means the reason for switching to the instrument occurs for subjective, and not objective, differences.

Answer: Thanks for your kind suggestion. As a prospective controlled study, the only variable between the two groups is the aspirator, or the grasping ability of the new aspirator, to be specific. According to our experience, the time advantage is from the better exposure induced by pulling the lymph nodes. The new aspirator can move the lymph nodes to almost every direction and expose its every side to dissociate, when it is relatively difficult for traditional aspirator to expose the bottom and dorsal side (relative to camera perspective) of lymph nodes. The advantage in exposure brings the difference of time. We added the clinical relevance in the discussion part of revised manuscript.

Changed in the text: Page 7/Line 208-214.

Comment 3: Nowhere does this study measure a usual outcome variable of the quality of lymph node dissection, the number of dissected lymph nodes. One may infer from the chylothorax rate that dissection must have been thorough, but nodal count by the surgeon or the pathologist would have been helpful. Yes, lymph nodes do fracture and multiply during dissection, but the surgeon could have accounted for that difference.

Answer: Thanks for your kind suggestion. We collected the number of harvested lymph nodes. The number was added in Table 1.
Changed in the text: Page 5/Line 141, Page 13/Line 357.

Comment 4: The third inclusion/exclusion criterium relates to the indication for mediastinal lymph node dissection. This indication should be explained in the Methods section: all lung cancers, selected lung cancers?
Answer: Thanks for your kind suggestion. The third inclusion criteria in the revised manuscript is "diagnosed as invasive lung cancer and has the surgical indication of systematic mediastinal lymph node dissection;"
Changed in the text: Page 4/Line 104.

Comment 5: The three injuries occurring with the "traditional" suction device are indeed concerning. Each is unusual, particularly for the experienced surgeons selected here to perform these operations. One possible explanation is that surgeons were rushed by operating against a clock and another that rapid instrument changes may be occurring in uniportal approaches that then cause unique injuries. These injuries should receive a separate comment in the Discussion.
Answer: Thanks for your kind suggestion. The first case happened in the process of dissecting No.7L, as bleeding of lymph nodes obstructed the exposure of contralateral bronchial, which was injured by ultrasound dissector. In the second case, the 4R lymph node is calcifying, and showed tight adhesion with the wall of the superior vena cava; the bleeding happened when the surgeon trying to dissociate with hook. The third case is similar, the 4R lymph node adhered tight with the wall of azygos vein arch, which is injured when the surgeon trying blunt dissection. This part was added in the revised manuscript.
Changed in the text: Page 8/Line 220 - 227.

Comment 6: Related to comment 5, the "crucial" role of aspirators as described by the authors results from a self-imposed limitation in uniportal access to resection, the condition in which each hand of the surgeon must provide more than one instrument function. This imposition is perhaps regarded by surgeons like the authors as entirely acceptable, indeed favorable. Yet in its ultimate consequence, where even the length of the single incision is progressively shortened, resecting a lung cancer becomes a "devil's work ball" (鬼工球) where artistry is an end to itself. Yet only the imperfect ivory ball may be discarded. No study has ever demonstrated a clinically relevant advantage of uniportal thoracoscopy over multiple incisions.
Answer: Thanks for your kind suggestion. Indeed, we agree with your opinion, that uniportal thoracoscopy showed clinical advantage over multiple incisions. Instrument interference is an important shortcoming of uniportal thoracoscopy, when in VATS with multiple incisions, this problem is almost non-existent. However, in actual clinical work, a considerable number of

thoracic surgeons are accustomed to uniportal thoracoscopy. This new aspirator was invented for them, trying to reduce the interference of instruments and facilitate the operation procedure.
Changed in the text: N/A

Comment 7: Almost half of all lung resections were left sided. Dissection of aorto-pulmonary station 5 lymph nodes is routine at least in upper lobe cancers, yet not a word is lost on station 5. A left sided mediastinal lump node dissection of only station 7 would generally be regarded as insufficient. The omission is peculiar and must be explained.

Answer: Thanks for your kind suggestion. In this study, the operation time of left upper mediastinal lymph node dissection, such as No.4L, No.5 and No.6, were not compared between the two groups. In our preliminary study, we found the variance of time spent in dissection of No.4L is large, which may because the actual size, number (some patients have only one or even no No.4L lymph nodes, when others may have three or more) and location (near arterial ligament is difficult to expose, when closer to the bulge is easy for exposure) of No.4L differs, and these factors have great influence for its procedure time. Meanwhile, we found the new aspirator can show some advantage in the operation time of No.5 and No.6, but not significant. We regarded the result as the exposure of No.5 and No.6 is relatively easy, and the time of dissection is short (compared to that of No. 2/4R, No. 7R and No. 7L), and the convenience of new aspirator can not fully play its role. By contrast, the size and location of No. 2/4R, No. 7R and No. 7L are relatively fixed, and the operation time for their dissection has enough space for descend. In the formal phase of study, the results meet our expectations.
Changed in the text: Page 8/Line 228-242.

Comment 8: The authors state that their current version of suction grasper has “defects”. This is entirely understandable, and further versions may show improved function. This reviewer has noted the sharp tip of the current version and suggests to blunt the tip in order to reduce the risk of injury.

Answer: Thanks for your kind suggestion. The degree of sharpness of the tip is an important point in the process of invention. Figure 1 showed our design, and we’ve found the tip was too sharp, and then improved the design. In figure 2&3, the tip was equal thick as traditional aspirator.
Changed in the text: N/A

Comment 9: Beginning a manuscript with a sentence describing lung cancer as a leading cause of mortality is like stating that the earth is round. Both statements are correct but irrelevant. The need for a new instrument and combining instrument functions arises from the limitations of uniportal thoracoscopy - that is the introduction.

Answer: Thanks for your kind suggestion. The sentence describing lung cancer as a leading cause of mortality has been deleted.

Changed in the text: Page 3/Line 70 (deleted).

Reviewer G

The suction with the function of grasping tissue is very unique, and seems useful to perform appropriate lymphadenectomy.
As the author said, appropriate lymphadenectomy is crucial in surgical treatment for patients with non-small cell lung cancer in oncological perspective. Although uVATS is being expanded worldwide, surgeons occasionally struggle to perform appropriate lymphadenectomy via this single small sized incision. This suction device might be useful to defeat the technical difficulty in performing lymphadenectomy via uVATS.
However, the author evaluated only the duration of the lymphadenectomy the surgeons spent, which is major problem in this study.
Although the operating time is one of the important things, other oncological factors should be evaluated such as N-upstage or the number of harvested lymph nodes.

Additionally, there were some minor problems as below:
Comment 1: The author defined the duration of lymphadenectomy as "The time spent for lymph node dissection was defined as the time taken from incision of mediastinal pleura to lymph node clearance and cessation of bleeding.". I think it might be difficult to calculate the real time only for lymph node dissection because other procedure such as exposure of pulmonary vessels are related with lymph node dissection. For example, when we expose inferior pulmonary vein, we incised parietal pleura. This was the prospective study. If the author prohibited performing lymphadenectomy in the middle way to some degree, it should be mentioned.
Answer: Thanks for your kind suggestion. For other mediastinal lymph nodes, such as No.5, the real time for lymph node dissection is difficult to distinguish with other procedure. However, lymph nodes in No.2/4R and No.7 are relatively independent, and the procedure to dissect them can be separate with procedure to deal with pulmonary lobes. Besides, when the pathological result is confirmed, we perform mediastinal lymph nodes dissection first, then to perform lobectomy. Therefore, the time of dissecting No.2/4R, No.7R and No.7L can be accurate.
Changed in the text: N/A

Comment 2: Figure 1-3 should be revised to make them easy to understand for readers.
Answer: Thanks for your kind suggestion. The Figures and their legends are revised with more detailed information.
Changed in the text: Page 11/Line 323 - Page 12/Line 336.