

Peer Review File

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Reviewer A

I have read your paper and found it very well described and the content very interesting. I cannot guarantee the quality of the English editing, and I would appreciate your confirmation.

Reply: We appreciate your positive feedback on our research. We understand your concern regarding the quality of English editing, and we have taken this feedback seriously. In the revised manuscript, we have carefully reviewed and edited the English language to ensure clarity and accuracy. We kindly ask you to review the revised version to ensure it meets the English presentation standard. Once again, thank you for your time and constructive comments.

Reviewer B

Comment 1: I respect the fact that authors conducted a prospective study to demonstrate the effectiveness of suction drainage in drainage management procedure. Unfortunately, despite the prospective enrollment of patients, the allocation was left to the judgment of the surgeon. I believe that considerable selection bias occurred here. Furthermore, if the decision to allocate patients was not made preoperatively, but rather after postoperative drain placement, bias is likely to have occurred in two areas: patient background and intraoperative findings. I wonder why the allocation was left to the surgeon's discretion at the study design stage.

Reply 1: Thank you for your valuable and insightful feedback. We appreciate your concern regarding the allocation of patients, which was left to the judgment of the surgeon. However, it's important to note that this study was designed as a real-world investigation, aimed at providing insights into actual clinical practice. Prior to surgery, we carefully screened patients with similar baseline characteristics and scheduled surgical information to minimize differences between the two groups. Nevertheless, we acknowledge the inherent limitation of a non-randomized study design, which may still pose a risk of selection bias. We have duly emphasized this aspect in the limitations section of the manuscript to transparently

acknowledge and address any potential impact on the study's outcomes (Discussion part; P15; Line265-267). Thank you once again for your valuable input.

Comment 2: The purpose of this study was "This prospective observational cohort was conducted to investigate the optimal procedure of chest drainage following pulmonary resection.". The primary endpoint was chest tube duration, with several secondary endpoints. Unfortunately, the primary endpoint did not show the expected reduction in tube duration with suction drainage. In the secondary endpoints, several variables were significantly different: Suction drainage was associated with lower drainage volume and shorter hospital stay, which may be effective for drainage management. However, there was no significant difference in postoperative complications. This study was not designed to statistically validate non-inferiority with respect to postoperative complications. Therefore, "Suction drainage strategy is a safe and effective strategy for managing postoperative drainage." Is a definitive statement and should be limited to a possibility.

Reply 2: We are grateful for the reviewer's attention to the detail and their valuable feedback on our manuscript. We acknowledge the reviewer's point regarding the lack of statistically significant difference in postoperative complications. As such, we have revised our conclusion to state, "Suction drainage strategy may be an effective strategy for managing postoperative drainage.", refraining from language implying safety concerns. Thank you sincerely!

Comment 3: The authors state that "External suction was maintained until the drainage tube was removed." but also state " If the chest tube duration was less than 2 days, external suction was maintained until the chest tube was removed.". What did the authors do about continuous suctioning if the drain was left in place for more than 2 days? I think it is necessary to clearly describe how suctioning was done after the second operative day.

Reply 3: Thank you for your valuable and insightful feedback. We acknowledge that our original expression may have been confusing. In response to your comment, we have reorganized the language and created a pattern diagram for the drainage strategy (Method part; P7, Line 95-101; Following Figure 1). To clarify, our drainage procedure is as follows: External suction was initiated postoperatively and continued for 2 days. After this initial period, suctioning was discontinued, and

our manuscript. As the reviewer observed, the median drainage volume on POD1 is 100-200ml, and only according to our chest tube removal criteria of 300 ml/day, most of the drains should be extubated within 1-2 days. However, it's important to note that the decision to remove the chest tube is based on a combination of criteria, including drainage volume, absence of air leak, and complete lung expansion. Therefore, drainage tube removal is determined based on these three criteria together. Additionally, we acknowledge that factors such as air leak and the degree of lung dilation on X-ray may influence drainage duration. However, these factors are interconnected and can impact each other. For instance, air leaks may occur at various stages of drainage, influencing the overall duration. Therefore, while these factors are important, exploring their individual impact on drainage duration in this study may not be suitable. Upon reevaluation of our data, we have added an analysis regarding intralobular fissure development and the degree of adhesion. However, we found no significant differences between the suction and non-suction groups in terms of these indicators (P21, Table 1). Thank you sincerely!

Reviewer C

I would like to thank the authors for their work regarding suction drainage after Uni-VATS. It is indeed a controversially discussed issue if suction is needed when using chest drains after thoracic surgery, or whether atmospheric pressure is enough to prevent a postoperative lung collapse. This is in fact important regardless of the operative technique, whether open or thoracoscopic. The manuscript in my opinion is lacking novelty and it needs significant language and methodological improvements. I have added some comments as suggestions on how to improve the manuscript.

Comment 1: Line 9-10: this is the first sentence of the paper and it does not make sense. "Remain little consensus" is not correct English. Please correct by a native speaker.

Reply 1: We appreciate the feedback on the clarity of our opening sentence. In the revised manuscript, we have carefully rephrased the sentence to ensure it accurately conveys our intended meaning. We hope this improvement enhances the overall readability of the paper. We thank you for your constructive input!

Comment 2: Line 12: “scheduled for UniVATS” implies that the operation was planned but not necessarily carried out. This needs to be more concise. The word scheduled is used throughout the publication and should be replaced by a more concise word which reflects that the surgery was not only planned (scheduled) but was also carried out. For example, “all patients which were treated/operated/resected using UniVATS technique” would be much better.

Reply 2: Thank you for your suggestions in helping us improve the quality of the article. We have taken your feedback into consideration and replaced the word "scheduled" with "patients who underwent/received UniVATS" throughout the manuscript. We believe this modification will improve the accuracy and conciseness of our descriptions. Thank you sincerely!

Comment 3: Line 16: which pain score?

Reply 3: Thank you for your valuable comments. We have taken your suggestion into account and further clarified in the methodology section that postoperative pain scores were assessed using the visual analog scale (VAS). (Method part; P8; Line 112-113). Thank you sincerely!

Comment 4: Line 20: remove the word finally at the beginning of the sentence.

Reply 4: Thank you for your helpful suggestion. We have revised the sentence by removing the word "finally" and replacing it with "A total of" (Abstract; P2; Line35). Thank you sincerely!

Comment 5: Line 43-46: you state that you have performed a meta-analysis which shows that sunction drainage is superior, but then say that it still warrants further investigation. You will need to elaborate on why this is the case, otherwise your sentence effectively contradicts the need for your study.

Reply 5: Thank you for your valuable comments. We understand the potential confusion caused by the statement in our manuscript. Our intention was to highlight the existing heterogeneities in the previous meta-analysis, which included variations in participants, study protocols, and surgical techniques such as thoracotomy and multi-port VATS. We acknowledge the need for further exploration to address these heterogeneities and provide more conclusive evidence. In response to your comment, we have reorganized the language in the background section (Page 5; P5; Line 57-61) to clarify this point. We hope this revision addresses your concerns and improves the coherence

of our manuscript.

Comment 6: Why would the drainage of UniVATS patients be any different from the drainage in normal VATS patients? Can you explain the need to differentiate between these groups?

Reply 6: Thank you for your valuable comments. We appreciate the opportunity to clarify the rationale for differentiating between UniVATS and normal VATS patients in our study. UniVATS has emerged as a rapidly growing less invasive approach compared to multi-portal VATS, constituting over 90% of all VATS procedures in our center. Previous studies have suggested that UniVATS may offer advantages such as shorter chest tube duration and fewer postoperative complications^{1,2}. However, despite these promising outcomes, there is still a need for further investigation into this relatively new approach. By focusing specifically on UniVATS patients, we aimed to provide valuable insights into the effectiveness of external suction on chest tube drainage in this particular surgical population. Given the lack of evidence regarding the impact of external suction on postoperative outcomes after UniVATS, our study sought to fill this gap in the literature and contribute to a better understanding of optimal perioperative management strategies for UniVATS patients. We hope this explanation clarifies the rationale for our study design and the importance of differentiating between UniVATS and normal VATS patients. Thank you for your valuable feedback.

Reference:

1. Bertolaccini L, Batirel H, Brunelli A, et al. Uniportal video-assisted thoracic surgery lobectomy: a consensus report from the Uniportal VATS Interest Group (UVIG) of the European Society of Thoracic Surgeons (ESTS). *Eur J Cardiothorac Surg.* 2019;56(2):224-229.
2. Hirai K, Usuda J. Partial lung resection by uniportal video-assisted thoracoscopic surgery: technique and pitfalls. *Eur J Cardiothorac Surg.* 2020;58(Suppl_1):i106-i107.

Comment 7: Weakness: -10 to -15 cmH₂O suction: why did you not standardize this if you were able to prospectively enroll patients in a study? It would be different if it were a retrospective study, but you had the chance to standardize before you started. This does not appear like a sound scientific approach.

Reply 7: Thank you for your valuable comments. As mentioned in our method part, this study is a prospective observational study, where we did not intervene in the postoperative drainage strategy

for patients. Furthermore, the negative pressure suction range of -10 to -15 cmH₂O is in alignment with the varying pleural cavity pressure, and based on our clinical experience, does not have a significant impact on postoperative drainage. This range was chosen to reflect routine clinical practice and to provide data that is applicable to real-world clinical decision-making. Our study design aims to minimize potential bias by enrolling patients with matched baseline and surgical information, thus ensuring the reliability of our findings. Thank you very much!

Comment 8: Line 131: 88% never smokers in a study which looks at lung cancer appears extremely unlikely. How do you explain this extraordinary percentage of never smokers with lung cancer?

Reply 8: Thank you for your valuable review comments. We appreciate the opportunity to address your concerns regarding the high percentage of never smokers in our study population. The observed predominance of never smokers in our study may indeed reflect the demographic composition of our sample. Specifically, our study included a higher proportion of female participants (72%), among whom never-smokers constituted a significant portion (80%). This demographic distribution may contribute to the seemingly extraordinary percentage of never smokers with lung cancer in our study. Furthermore, we have carefully reviewed our data to ensure its accuracy. However, we acknowledge that our study sample size is limited and may not fully represent the true epidemiological characteristics of lung cancer. Despite these considerations, it's important to note that the differences in smoking status between the two groups were balanced, which should not significantly impact the validity of our study results. Thank you sincerely!

Comment 9: 198-204: I do not believe there is any scientific evidence to support these hypotheses. It does indeed appear unlikely that suction drainage led to less fluid extraction, as stated by the authors. This has been shown in previous studies.

Reply 9: Thank you for your valuable review comments. While some studies have reported higher drainage volume with suction drainage, our results suggest a different trend, favoring lower drainage volume with external suction in UniVATS patients. Firstly, our findings also aligned with some previous studies that have similarly suggested a trend of decrease in postoperative drainage volume with external suction^{1,2}. However, the observed discrepancy in drainage volume between our study

and some previous research may be influenced by various factors, including differences in surgical techniques, patient populations, and drainage protocols. We acknowledge the possibility of contradictory effects of suction drainage, as discussed in the manuscript (Discussion part; P12-13; Line209-223). Further investigation is warranted to elucidate the underlying mechanisms driving these divergent outcomes and to validate our findings in larger, multi-center studies. Thank you for bringing up this important point for discussion.

Reference:

1. Brunelli A, Salati M, Pompili C, Refai M, Sabbatini A. Regulated tailored suction vs regulated seal: a prospective randomized trial on air leak duration. *Eur J Cardiothorac Surg.* 2013;43(5):899-904.
2. Brunelli A, Monteverde M, Borri A, et al. Comparison of water seal and suction after pulmonary lobectomy: a prospective, randomized trial. *Ann Thorac Surg.* 2004;77(6):1932-7; discussion 1937.

Comment 10: 10. 225: I think you need to mention your ERAS standards in postoperative care and how you achieved these low pain scores. Earlier chest drain removal could facilitate better physical activity postoperatively, but it does appear likely that the shorter LOS is down to less fluid extraction.

Reply 10: Thank you for your insightful comment. We appreciate the opportunity to provide further clarification on our postoperative care standards and pain management approach. In our study, we implemented Enhanced Recovery After Surgery (ERAS) standards in postoperative care, which included a comprehensive multimodal analgesia approach. This approach involved preoperative education, a systematic pain assessment system, multimodal analgesic protocols, and rehabilitation training (Discussion part; P14; Line246-248). These concerted efforts likely contributed to the achievement of low pain scores observed in our study. Regarding the potential impact of earlier chest drain removal on postoperative physical activity, we agree that it could facilitate better patient mobilization. However, we attribute the shorter length of hospital stay (LOS) primarily to the observed differences in fluid extraction between the suction and non-suction drainage groups. The lower drainage volume and shorter drainage duration associated with suction drainage likely facilitated the early initiation of patient rehabilitation training, ultimately contributing to the reduction in LOS. Thank you sincerely!

Reviewer D

Thank you for submitting your manuscript. I have reviewed the article titled "Suction versus non-suction drainage strategy after uniportal thoracoscopic lung surgery: a prospective cohort study". This article suggest interesting and good topics. I believe that your paper caries important lessons and messages for thoracic surgeons. However, your paper needs minor revision in order to improve these messages. I have three questions.

Comment 1: Referring to the baseline characteristics of the non-suction and suction groups, there are differences in areas related to lymph nodes. I think that these differences can affect the results. Additionally, the drainage strategy was determined by the surgeon's decision. I think a randomized design study would have been sufficiently possible, but what do you think about the possibility of selection bias due to the surgeon's discretion?

Reply 1: Thank you for providing us with your review comments. Before surgery, we screened patients with similar baseline and scheduled surgical information to minimize differences between the two groups. Most variables that could potentially affect postoperative drainage were already balanced between the two groups (except for lymph nodes dissection). Therefore, considering the potential impact of lymph nodes dissection on postoperative outcomes, in addition to directly comparing the effects of the two drainage methods on outcomes, we conducted a sensitivity analysis (regression analysis) to analyze outcomes that differed between the two groups. The results indicated that lymph nodes dissection had no impact on postoperative outcomes. Furthermore, as the reviewer mentioned, non-randomized study designs may not account for potential confounding factors, and we have emphasized this limitation in the discussion section. Thank you sincerely!

Comment 2: There are many researches on the benefits of physical activity as early ambulation. Are all patients transferred to a general ward rather than ICU after surgery? How many hours after surgery is it usually recommended to patients to start walking? I also wonder if there was any difference between the two groups.

Reply 2: Thank you for your valuable review comments. Almost all patients are initially transferred to the anesthesia recovery room postoperatively, and after successful recovery, they are then

transferred to the general ward. In our center, patients are typically encouraged to mobilize the first day after the surgery. All difference between the two groups have been presented in the manuscript. Thank you sincerely!

Comment 3: Postoperative drainage volume may be related to inflammatory changes after surgery. Regarding postoperative drainage volume, I suggest a mention of estimated blood loss and adhesion presence. Were there any complications such as pneumonia? It would be also good to mention laboratory findings such as CRP.

Reply 3: Thank you for your valuable comment. As requested by the reviewer, we have included information on estimated blood loss and pleural adhesions in the manuscript (P21; Table1). We found no significant differences in intraoperative blood loss and the presence of pleural adhesions between the two groups. Regarding postoperative complications such as pneumonia, upon careful review of the data, we did not observe postoperative pneumonia in our study cohort. This could be attributed to the various measures we implemented to reduce postoperative complications, including the ERAS protocol and prophylactic antibiotic use. Regarding inflammatory markers, specifically CRP, we did not collect data on CRP levels postoperatively as routine practice unless there were specific indications such as suspected infection. Therefore, we were unable to include CRP findings in our analysis. Thank you sincerely!

Reviewer E

This is a prospective cohort study in which the choice of suction or non suction drainage is a surgeon choice. I would suggest, if possible to explain which are the criteria they adopted to choose between the 2 different drainage. Minor language revision.

Reply: Thank you for providing us with your review comments. We appreciate your suggestion to provide insight into the criteria used by surgeons to choose between suction and non-suction drainage. While the choice of drainage strategy was largely left to the discretion of the surgeons, it's important to note that this decision was influenced by various factors including the surgeon's preference, institutional protocols, and patient-specific factors such as intraoperative findings and anticipated postoperative course. However, due to the nature of our study design, we were unable

to provide specific criteria for the selection of drainage strategy. We have emphasized in the methods section that the drainage strategy was largely determined by the surgeons, and their habits regarding external suction were relatively fixed. Moreover, we have meticulously reviewed and modified the English language in the revised manuscript. Please see if the revised version met the English presentation standard. Thank you sincerely!

Reviewer F

Thank you for giving me opportunity to review the original article entitled ‘Suction versus non-suction drainage strategy after uniportal thoracoscopic lung surgery: a prospective cohort study’. While excellent postoperative results after uniportal anatomical resection, this study raised some flaws regarding study design and interpretation of the results as below.

Comment 1: Due to its non-randomized study, how did the authors allocate the patients to suction and non-suction groups prospectively?

Reply 1: Thank you for your valuable and insightful feedback. As a prospective observational study, this study did not intervene in the choice of drainage strategy for patients. We mainly focused on the preoperative assessment and recruitment of patients with matched baseline and scheduled surgical information to minimize inter-group differences. However, due to the non-randomized design, there may indeed be potential unbalanced factors. Thus, we have emphasized this in the limitation section (Discussion part; P15; Line265-267), acknowledging the need for further validation through additional research. Thank you sincerely!

Comment 2: Although sample size was determined based on the hypothesis where suction drainage extended period of the chest tube drainage, the chest tube duration was comparable between suction and non-suction group. Authors should put more emphasis on this result in the conclusion, since the chest tube duration would be the primary outcome in the current study.

Reply 2: Thank you for your valuable comment. Firstly, we note that while there is no significant difference in chest tube duration, the suction drainage group exhibits a numerically lower drainage duration, approximately by 1 day, which holds clinical significance. We have compared our findings with previous research and further delved into the reasons behind the shorter drainage duration in

the suction drainage group (Discussion part; P12; Line198-208). Additionally, we have explored the potential correlation between the numerically shorter suction duration and the shorter hospital stay observed in the suction drainage group (Discussion part; P13; Line228-230). Thank you sincerely!

Comment 3: Did the authors use traditional or digital drainage system?

Reply 3: Thank you for your valuable feedback. In this study, patients included in this study use traditional drainage system. Thank you sincerely!

Comment 4: Authors should discuss that suction drainage would influence the incident of persistent air leak.

Reply 4: Thank you for your valuable and insightful feedback. We have included a discussion about PAL in the manuscript's discussion section, addressing the potential influence of suction drainage on PAL. We have acknowledged the controversy surrounding the association between external suction and PAL, attributing it to varying surgical types and definitions of PAL. Additionally, we have highlighted the clinical interventions available to reduce the incidence of PAL (Discussion part; P14-15; Line250-259). Thank you sincerely!

Comment 5: While the duration of chest tube was comparable between suction and non-suction groups, suction drainage exhibited significantly decreased postoperative length of hospital stay. I wondered these conflicting results because the chest tube duration would influence on the length of hospital stay.

Reply 5: Thank you for your valuable comment. As observed by the reviewer, there is no statistical difference in drainage time between the two groups, but the median drainage time in the external suction group (1.96 vs. 2.58, $P = 0.08$) is numerically one day less than the non-suction group. This corresponds to the one-day shorter hospital stay in the external suction group compared to the non-suction suction group. Furthermore, we have discussed this issue in the discussion part (P13; Line228-230). Thank you sincerely!