

Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-23-651>

Reviewer A

1. **Comment:** Title: appropriate

Response: Thank you. We are very pleased to receive the reviewer's comments.

2. **Comment:** Abstract: appropriate

Response: Thank you. We are very pleased to receive the reviewer's comments.

3. **Comment:** Introduction: The authors should not use LC for lung cancer. Otherwise, some readers may get confused with laparoscopic cholecystectomy.

- Line 58: The authors should describe full name for US before.

Response: Thank you very much for the reviewer's suggestion, we have modified it.

Changes in the text : line 64

4. **Comment:** Method:

- The authors should describe that this study was conducted based on the criteria of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).

- According to the PRISMA, the authors should present the full search for all database and include the register code of the trial for example PROSPERO number.

- The authors should completely describe the details of inclusion and exclusion criteria. Not just describe only age > 18 .

- The authors should mention whether non-English studies were included.

Response: Thank you very much for the reviewer's comments. We have modified them.

Changes in the text: line101-103, line 112, line 115

5. **Comment:** Results

- Figure 4, 6, 8, 10, 11 and 13, the authors should label which sides were Favor DEx or Favor control.

- Figure S2 should be mentioned before Figure S1 because these inflammatory markers were primary end points.

- Table 1. Outcome should describe as the real outcomes instead of using F1-F10.

Response: Thank you very much for the reviewer. We have modified it.

Changes in the text: table 1 and Figure 4, 6, 8, 10, 11 and 13,

6. **Comment:** Discussion and conclusion: appropriate

This is an interesting study in order to describe the effect of DEx on inflammatory and pulmonary function in VATS by performing the systematic review for RCTS. The statistical analysis was performed appropriately. However, I found that the authors should describe more information according to the queries and recommendation in order to improve their manuscript.

I also have some queries about the registration code in the website for example PROSPERO this is recommended by the criteria of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). I think this study should be considered for publication if the authors can answer the queries appropriately.

Response: Thank you very much for the reviewer's comments, which have been added.

Reviewer B

I would like to share my comments as the followings:

1.Comment: For abstract on page 2 line 53-54, I suggest the authors to add a word which is represented PICO including the primary outcome in Keywords for example “serum inflammatory factors”, “inflammatory reaction” or “postoperative inflammation”.

Response: Many thanks to the reviewers, we have already added.

Changes in the text: line 58

2.Comment: Following the template for original article of Journal of Thoracic Disease, Highlight Box is placed after abstract and no more than 150 words. The manuscript has 160 words in Highlight Box.

Response: Many thanks to the reviewers, we have already added.

Changes in the text: line 60-78

3.Comment: From the PRISMA 2020 Checklist, most of checklist items and line numbers are not correlated and need to be corrected carefully.

Response: Thank you for your comments. We have modified it and Uploaded the updated PRISMA 2020 Checklist.

4.Comment: About methods, have the study been registered on PROSPERO? If so, I suggest the authors to add the detail including the number in manuscript.

Response: I agree with the reviewer's opinion very much. We have added.

Changes in the text: line 121-123

5.Comment:For literature retrieval on page 3 line 96-98, are there any other terms (keywords) that also impact the data selection? I suggest the authors to insert the table of search terms and search strategies? Did the authors retrieve only English & Chinese publications or any languages? Please identify the language of publications instead of the region.

Response: I agree with the reviewer's opinion very much. We have added.

Changes in the text: line 131-132

6.Comment: For exclusion criteria on page 3 line 107-108, please clarify the terms “experimental designs that are unreasonable” and “unusable data”. Did you contact the authors before exclusion unobtainable full-text?

Response: I agree with the reviewer's opinion very much.

Changes in the text: line 142-144

7.Comment: The extracted data on page 4 line 118-120, I suggest the authors to collect the data about underlying disease especially cardiovascular and pulmonary disease (except lung cancer). According to these are confounding factors. Some medical conditions may affect to inflammatory response. Previous pulmonary disease may affect to postoperative pulmonary function. Previous cardiovascular disease may affect to cardiovascular event. Adverse reactions also should be described more in details.

Response: We very much agree with the reviewer's opinion, but this information is very little mentioned in the paper, we will pay attention to in the future research.

8.Comment: The result on page 5 line 154 “11 (14, 17-26) RCTs were finally included.....”, however the reference number 14 is a retrospective observational study not RCT. This study should be excluded for analysis as it does not meet eligibility criteria. Reference number 17; intervention group received dexmedetomidine and dezocine which may affect to primary outcome. I suggest the authors to reanalysis and reconsideration of outcome and conclusion.

Response: We very much agree with the reviewer's opinion. We have carefully read the following, which is indeed not a randomized trial, so we change the randomized controlled study in this paper to a controlled study, so the conclusion we get based on this study also has its limitations! Thank you very much for your suggestions. However, the outcome of the study involving 14 was only fev1 and adverse events, which had little impact on the main conclusion of the paper.

9.Comment: This study included 11 RCTs (reference14, 17-26) as mentioned on page 5 line 154-155. However, reference number 14 is a retrospective observational study which does not meet the eligibility criteria. Reference number 17; intervention group received dexmedetomidine and dezocine which may affect to primary outcome. Most of the data is needed to be re-analyzed. In my opinion reanalysis and reconsideration of outcome and conclusion is very necessary.

Response: We very much agree with the reviewer's opinion. We have carefully read the following, which is indeed not a randomized trial, so we change the randomized controlled study in this paper to a controlled study, so the conclusion we get based on this study also has its limitations! Thank you very much for your suggestions. However, the outcome of the study involving 14 was only fev1 and adverse events, which had little impact on the main conclusion of the paper.

Reviewer C

1. Figure 1

a) In figure 1, there's no “others”, please check.

Responds: Thanks very much to the editor, we have changed it.

162 **##Literature retrieval**

163 We performed a computer search of the databases of PubMed, Embase, Cochrane
164 Library, Web of Science, and **others** for controlled trials (CTs) about the effect of Dex
165 on inflammation and lung function after thoracoscopic surgery for [lung cancer](#). The

- Records identified through
- Database searching (n=268)
 - PubMed (n=57)
 - Embase (n=84)
 - Cochrane (n=63)
 - Web of science (n=64)

b) Please remove the symbols in red box.

Responds: Thanks very much to the editor, we have removed it.

- Records identified through
- Database searching (n=268)
 - PubMed (n=57)
 - Embase (n=84)
 - Cochrane (n=63)
 - Web of science (n=64)

2. Figure 10

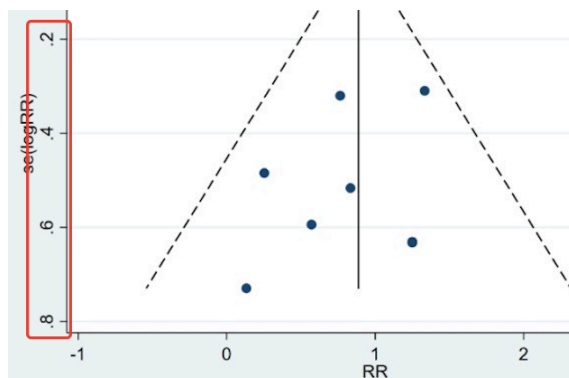
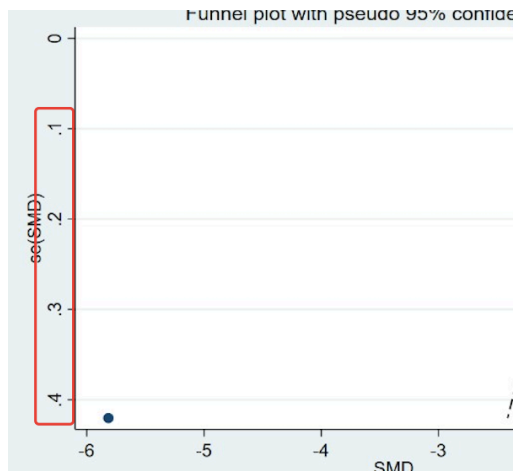
Please check the author's name.

Lco SH 2016

Responds: Thanks very much to the editor, it was Lee SH 2016.

3. Figure S1 and S2

Please revise the Y-axis. “.1, .2, .3, .4” should be “0.1, 0.2, 0.3, 0.4”; “.2, .4, .6, .8” should be “0.2, 0.4, 0.6, 0.8”.



Response: Thanks very much to the editor, we have modified it.

4. References/Citations

Please double-check if more studies should be cited as you mentioned “studies”.

149 lungs, and other important organs, improving perioperative pulmonary function. Other
 150 studies have also reported that Dex can diminish the production of reactive oxygen
 151 species (ROS) and the release of cytochrome C in lung tissues, therefore it can reduce
 152 the apoptosis of alveolar epithelial cells (16). The influence of Dex on lung injury and

Responds: Thanks very much to the editor, we have changed it.