

Peer Review File

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Reviewer A

The need for 4L dissection for left side tumors is an interesting and controversial topic. The reviewed paper intends to give some responses to it.

The increased risk of 4L affection when hilar or station 5 lymph nodes are positive makes recommendable to perform left paratracheal dissection. However, the increase on survival and disease free survival argument might be confusing. In my opinion, the differences regarding postoperative treatment may explain differences on survival and should be reported on results if available. In addition, its impact on results should be more clearly discussed.

Minor: Line 134. The probability of positive L4 with positive L10 was..." Do the authors mind L5?

Comment 1: The increased risk of 4L affection when hilar or station 5 lymph nodes are positive makes recommendable to perform left paratracheal dissection. However, the increase on survival and disease free survival argument might be confusing. In my opinion the differences regarding postoperative treatment may explain differences on survival and should be reported on results if available. In addition, its impact on results should be more clearly discussed.

Reply 1: We are grateful for the questions raised by reviewer. Different treatment methods of postoperative patients may lead to differences in survival and disease-free survival. However, since the selected researches which patients were generally patients before 2018, the postoperative treatment of NCCN guidelines before 2018 have not been updated to bring the EGFR-TKI into first line treatment, which makes the treatment plan have a certain consistency. So we did not find these postoperative treatment were in essence different. It is not to suggest that there is no difference in treatment after surgery. This argument needs to be further confirmed by multicenter prospective studies.

Comment 2: The probability of positive L4 with positive L10 was..." Do the authors mind L5?

Reply 2: This is a clerical error and I have corrected it.

Changes in the text: (in Page 9,line 185)

Reviewer B

The authors present a systematic review and analyze the prognostic significance of L4 dissection in left lung cancer. They found a correlation between L10 metastasis and L4 metastasis and conclude that intraoperative L10 examination should guide the decision for L4 removal. The topic is of potential interest even though data of good quality is scarce.

I have several comments:

1. Abstract, results section: line 17: should be L5 instead of L10?
2. Abstract, conclusion section: the indication to radio- or chemotherapy cannot be deduced from the data.
3. Abstract, conclusion section: lines 29-31 are the only conclusions that can be drawn from the data. The recommendation to perform frozen section should be placed at the end of the conclusion section as a personal comment.
4. Introduction line 41 is lobectomy, not lobotomy and systematic not systemic
5. Introduction line 43 is guideline not guidance
6. Results section, line 107: the quality of the table 'patient characteristics' is very poor as it does not contain any relevant information about the patients, however, only the selected studies are listed
7. Results section: line 108: average age not shown in table
8. Results section, line 149: belongs to the methods section.
9. Discussion section: line 172: I do not understand the statement about thoracoscopy.
10. Table 1: wrong case number in Fang et al. 48 patients in 4LD+ group.
11. Authors should discuss the development of mediastinal nodal staging or provide information about the procedures used in the 4 papers. Did patients undergo routine EBUS, MESk, PET, CT only)
12. I cannot access reference no 24 which has been included in the final analysis, however it is not correctly stated in the reference list
13. The complete manuscript needs very intensive language editing.

Comment 1: The probability of positive L4 with positive L10 was..." Do the authors mind L5?

Reply 1: This is a clerical error and I have corrected it.

Changes in the text: (in Page 2, line 38)

Comment 2: Abstract, conclusion section: the indication to radio- or chemotherapy cannot be deduced from the data.

Reply 2: Thanks to reviewers for your questions. I quite agree with your opinion, and delete this inaccurate statement.

Comment 3: Abstract, conclusion section: lines 29-31 are the only conclusions that can be drawn from the data. The recommendation to perform frozen section should be placed at the end of the conclusion section as a personal comment.

Reply 3: Thank you for your recommendation, and I have carefully modified it.

Changes in the text: (in Page 3,line 50-51)

Comment 4: Introduction line 41 is lobectomy, not lobotomy and systematic not systemic

Reply 4: Thank you for your carefully review. I have corrected it in the new edition of manuscript.

Changes in the text: (in Page 3,line 64)

Comment 5: Introduction line 43 is guideline not guidance

Reply 5: Thank you for your carefully review. I have corrected it in the new edition of manuscript.

Changes in the text: (in Page 3,line 66)

Comment 6, 7: Results section, line 107: the quality of the table 'patient characteristics' is very poor as it does not contain any relevant information about the patients, however, only the selected studies are listed

Reply 6, 7: Thank you for your good advice. For there were not median age data in all of these researches, I attempted to calculate the median age from the data of some of these researches in different ways. I added them in Table 19 and I still can't calculate the median age of some of these researches.

Changes in the text: (in Page 19,Table 1)

Comment 8: Results section, line 149: belongs to the methods section.

Reply 8: We are so sorry for this and corrected this mistake.

Comment 9: Discussion section: line 172: I do not understand the statement about thoracoscopy.

Reply 9: We sincerely apologize for this and we changed it to "thoracoscopy technology" for more accuracy.

Changes in the text: (in Page 11,line231)

Comment 10: Table 1: wrong case number in Fang et al. 48 patients in 4LD+ group.

Reply 10: Thanks to the reviewer for carefully finding the clerical error here, I have revised it.

Changes in the text: (in Page 19, see Table 1)

Comment 11: Authors should discuss the development of mediastinal nodal staging or provide information about the procedures used in the 4 papers. Did patients undergo routine EBUS, MESk, PET, CT only).

Reply 11: Preoperative clinical staging has been shown in Table 1. Postoperative routine examinations, such as a plain chest x-ray; computed tomography scan of the thorax, head, and abdomen; and ultrasound of neck and abdomen, were generally performed every 3 months for the first 2 years after surgery and every 6 months after that for 5 years.

Comment 12: I cannot access reference no 24 which has been included in the final analysis, however it is not correctly stated in the reference list.

Reply 12: We are so sorry for the difficulty of reading this article. It was a research which was published in one of Chinese top medical journals, and it was written by Chinese. I have corrected the reference list.

Comment 13: The complete manuscript needs very intensive language editing.

Reply 13: Thanks for the reviewers' valuable suggestions. We have polished the language of manuscript by the help of some company.

Reviewer C

The authors conducted a meta-analysis on the importance of 4L lymph node dissection and the risk factors for its metastasis, which included 4 retrospective articles and a total 2635 patients were analyzed. The study demonstrated that the probability of positive L4 with positive L10 was 5.11 times and with positive L5 was 3.92 times of that with negative L10. L7 was not an independent risk factor for positive L4. According to the authors' statement, 4L lymph node dissection was an independent risk factor influencing the prognosis of patients.

I have the following comments/suggestions:

Please explain what kind of situation is not favorable for 4L dissection

Please explain local radiotherapy should be performed when Station 10L (+), did the authors study in this issue? Your study did not reveal the radiotherapy effect.

Line 107: the staging of patients was based on a postoperative pathological diagnosis. The significance of this issue should be focused on clinical stages instead of pathologic stages.

Line 184: the anatomical limitations make 4L dissection more difficult and increase the surgical risk...could the authors summarized what kind of risks were recorded in this meta-analysis.

Minor:

1. Line 59: mistyping of extra brackets, please delete them.0
2. Line 172: the sentence is hard to follow, who wants to reduce lymph nodes for dissection?
3. Line 201: the conclusion was drawn from your study findings from a meta-analysis, and was not consistent with yours.
4. The discussion could be shortened.

Comment 1: Please explain what kind of situation is not favorable for 4L dissection

Reply 1: When 4L appears obvious calcification or adheres closely to adjacent structures, we believe that anatomy may cause damage to adjacent structures at this time, such as: the aortic arch, left recurrent laryngeal nerve, and thoracic duct.

Comment 2: Please explain local radiotherapy should be performed when Station 10L (+), did the authors study in this issue? Your study did not reveal the radiotherapy effect.

Reply 2: Thank you for your carefully review. We haven't done this kind of study, so this is a misstatement. I have corrected it in the new edition of manuscript.

Comment 3: Line 107: the staging of patients was based on a postoperative pathological diagnosis. The significance of this issue should be focused on clinical stages instead of pathologic stages.

Reply 3: Thanks for the reviewers' valuable suggestions. Since the literature cited is pathological staging, the results of our study are intended to guide surgery.

Comment 4: Line 184: the anatomical limitations make 4L dissection more difficult and increase the surgical risk...could the authors summarized what kind of risks were recorded in this meta-analysis.

Reply 4: 4L nodes played an important lymphatic pathway of the left lung (bounded by the aortic arch superiorly, the trachea and esophagus medially, the superior border of the main left bronchus inferiorly, and the pulmonary artery and arterial ligament anteriorly and laterally).In addition, 4L nodes are close to the left recurrent laryngeal nerve, increasing the possibility of nerve damage during dissection. Dissection of the lymph nodes here may result in damage to the aortic arch, recurrent laryngeal nerve, or even the thoracic duct.

Changes in the text: (in Page13 ,line266)

Minor:

Comment 1: 1. Line 59: mistyping of extra brackets, please delete them.

Reply 1: Thanks to reviewers for your questions. I quite agree with your opinion, therefore, delete it.

Changes in the text: (in Page4 ,line87)

Comment 2: Line 172: the sentence is hard to follow, who wants to reduce lymph nodes for dissection?

Reply 2: Thank you for your comments. We have polished our languages and made more accurate words in the new edition of manuscript.

Changes in the text: (in Page9 ,line195)

Comment 3: the conclusion was drawn from your study findings from a meta-analysis, and was not consistent with yours.

Reply 3: We apologized for the inaccurate statement and corrected in new edition of manuscript.

Changes in the text: (in Page11 ,line231)

Comment 4.: The discussion could be shortened.

Reply 4 : Thanks for the reviewers' valuable suggestions. We have deleted the duplicate content.

Changes in the text: (in Page12 ,line256)