Peer review file
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Reviewer A
Comment 1: Thank you for this interesting report on an innovative technique. The manuscript is well written. I wonder whether a recommendation of TPC as the preferred option is justified by the data presented, since no direct comparison with other treatment options are given.
Reply 1: Thank you for pointing this out. Based on your comments, I put emphasis on the effectiveness of Total Pleural Covering itself, rather than its superiority to other treatments.
Changes in the text: We have modified out text as mentioned above (see Page 3, line57, Page14, line361 and Page15, line397).

Reviewer B
Comment 1: Many thanks for submitting your manuscript entitled "The effects of total pleural covering on pneumothorax recurrence and pulmonary function in lymphangioleiomyomatosis patients without history of pleurodesis or thoracic surgeries for pneumothorax" to the Journal of Thoracic Disease.
In this retrospective single centre study you report your experience with an innovative surgical technique called total pleural covering (TPC) in 52 female patients in whom the surgery was performed for LAM-related pneumothorax over the 16-year period on a native (pleurodesis free) lung. You evaluate the efficacy of TPC by assessing the post-operative recurrence and lung function.
Although LAM is a rare disease, with not fully known mechanism and progression pattern, its pulmonary complications can become a therapeutic challenge for the respiratory physician and thoracic surgeon. Therefore, I find the topic relevant for the professionals dealing with refractory pneumothorax. Preserving the pleural cavity from adhaesions is important as the LAM patients with impaired pulmonary function are potential lung transplantation candidates. However, pleurodesis is no longer considered as an absolute contraindication for the lung transplantation.
The manuscript is well structured, and the study objective is well defined. The patient selection criteria have been well described. The result of your well performed statistical analysis demonstrated that TPC can prevent pneumothorax recurrence in LAM patients without reducing the lung function.
However, in my opinion there is potential for improvement of the submitted manuscript.
Comment 1: In the abstract's background you did not define the purpose of the study.
Reply 1: As suggested by the reviewer, I changed words in the last sentence of the abstract's background.
Changes in the text: I added "The purpose of this study is to" in the last sentence of the abstract's background (see Page2, line31).

Comment 2: In the subsection "Study design and sample" of the Materials and methods section you duplicated the information included in the Results section. The lines 97-106 should be included in the Results.
Reply 2: Thank you for your advice. In accordance with your comments, I deleted the detailed information on exclusion (original lines 97-106) from the Materials and methods section, and added them in the Results section.
Changes in the text: I moved the original lines 97-106 to the lines 171-178 in the Results section.

3. mTOR = "mechanistic target of rapamycin" (line 45) or maybe "mammalian target of rapamycin"?
Reply 3: Thank you for pointing this out. In order to avoid causing confusion among readers, I realized that I should write both "mechanistic" and "mammalian" together.
Changes in the text: I wrote "Mechanistic/ mammalian" (see Page2, line45).

4. You compared the lung function test results between pre-TPC patients with pneumothorax vs. post-TPC patients without pneumothorax. Based on those results you concluded that TPC did not reduce the lung function. Do you think that performing the lung function test on a collapsed lung due to pneumothorax is of relevance? Secondly, after successfully managed pneumothorax I would rather expect better lung function that preoperatively.
Reply 4: We apologize for making you confused. We, of course, think that performing the lung function test on a collapsed lung due to pneumothorax is not relevant, therefore we always perform the lung function test only when pneumothorax has resolved. Thus, "pre-TPC" lung function data mean the data that was obtained at the nearest occasion before TPC when a patient had no pneumothorax.
Changes in the text: No change was made.

5. Lines 316-318 are a duplication of the lines 313-315.
Reply 5: Thank you for pointing this out. I deleted original lines 316-318.
Changes in the text: I deleted the sentence (see Page14, line358-360).

6. I understand that TPC is a surgical option for the management of the refractory pneumothorax in LAM patients, and potential alternative to pleurodesis. Why did you mention in the Discussion the general BTS recommendations for the initial management of any form of pneumothorax (lines 320-323)?
Reply 6: Thank you for your comments. I mentioned the general BTS guideline for the management of primary spontaneous pneumothorax (PSP) because simple aspiration and/or small-bore chest tube drainage recommended by the guideline, could be combined with TPC for the treatment of pneumothorax in LAM. In comparison with treatments utilized for PSP, we would like to show that treatments for PSP alone are not enough for pneumothorax in LAM, considering progressive nature and propensity of recurring pneumothorax in LAM.
Changes in the text: No change was made.

7. You conclude that TPC is a "preferable" treatment option for LAM-associated pneumothorax. I think "preferable" sounds like better than other options. Based on your analysis, where you retrospectively analysed only the efficacy of TPC, without comparing it to other treatment options, you cannot state that TPC is preferable. Maybe "effective", "good" or "safe" would better describe this technique. Summarising, I would suggest a thorough revision of the manuscript prior to its potential publication in the JTD.
Reply 7: Thank you for your suggestion. Based on your comments, I put emphasis on the effectiveness of Total Pleural Covering itself, rather than its superiority to other treatments.
Changes in the text: We have modified out text as mentioned above (see Page 3, line57, Page14, line361 and Page15, line397).

Reviewer C
Comment 1: You spend much effort to give a good overview of the management of patients with recurrence of pneumothorax as a complication of lymphangioleiomyomatosis.
Due to the fact, that lymphangioleiomyomatosis is a rare disease the cohort is small. Nevertheless the results of recurrence and impairment of lung function are very good.
The discussion is well structured and the manuscript corresponds to the STROBE criteria. The grammar and syntax are fine.

The authors calculated many variables, like the relation between pulmonary function and mTORI initiation. Probably it might have been more expressive, if the authors would have focused on rate of recurrence and postoperative pulmonary function.
In conclusion: You cover an interesting topic with good results and your discussion is well thought out.
Reply 1: While we appreciate the reviewer's feedback, we still think the analysis of pulmonary function and postoperative pneumothorax recurrence in relation to mTORI initiation is essential because mTORI initiation serves as an indicator of the disease severity and/or activity of LAM. Additionally, we believe the rate of patients who required mTORI initiation after TPC is worth reporting because there is no report on post-TPC treatment options.
Changes in the text: We made no change.

Reviewer D
Comment 1: The article regarding the assessments of effects of total pleural covering in patients with LAM and pneumothorax presents a 16- years' experience of the leading Japanese center.
The article is interesting and suitable for publication, but only after introducing improvements.
1. How many patients suffered from: chylothorax, chyloperitoneum, lymphangioma?
Reply 1: Among 52 patients, chylothorax was found in 4 patients, chyloperitoneum in 2 patients, and lymphangioleiomyomas in 4 patients. Actually, pleural effusion was observed in 5 patients, but its property wasn't examined in one patient. Similarly, 8 patients had ascites, but only 2 were examined to be chyle.
Changes in the text: We have added information of comorbidities on Table1.

Comment 2: How many patients received sirolimus before the pneumothorax?
Reply 2: There is a patient who had received sirolimus as of her first pneumothorax on the operative side. Since the patient's pulmonary function data was not available, all the cases included in the analysis of pulmonary function are free from the influence of sirolimus.
Changes in the text: We have annotated on Table 1.

Comment 3: It was shown that patients with LAM, who smoked cigarettes, had a higher risk of pneumothorax. Please present the smoking history of your patients.
Reply 3: Among 52 patients, 7 had a history of smoking.
Changes in the text: We have added smoking history on Table1.

Comment 4: What was the mean number of sheets used in the group below 10 and over then 10 sheets? Was any statistical difference observed? Previously, it was presented by your group, that for the left lung pneumothorax there were less sheets used. Was this observed in this study?
Reply 4: The mean number of sheets used in the group below 10 was 6.9, while that of the group over than 10 sheets was 11.9. Unlike the result of our previous study, no statistically significant difference in the probability of recurrence-free hemithorax post TPC was found between two groups categorized by the number of ORC sheets. The mean number of sheets used for the right lung was 11.5, while that for the left lung was 11.0 with no statistical significance ($p=0.436$). The median number of sheets used for the right lung was 12, while the left lung was 11 ($p=0.467$).
Changes in the text: Please see Page 8, line 195-196.

Comment 5: There was no statistical difference in pneumothorax recurrence between the groups in which <10, and over than 10 sheets of ORC were used.
The hypothesis that the lower recurrence of free survival was caused by different experience of surgeons or by the comorbidities should be supported by evidence and adequate analysis.

Reply 5: Thank you for your comments. According to your advice, we analyzed our inference process.
Changes in the text: Please see Page 11, line 280-290.

Comment 6: It was suggested that recurrent pneumothorax might be connected to higher activity of the disease - similarly to the serum concentration of VEGF-D. Did you perform an assessment of VEGF-D?
Reply 6: Thank you for raising this important point. However, pneumothorax or its recurrence doesn't always relate to disease severity when the impaired degree of lung function or cystic destruction is defined as the measure of disease severity from Japanese epidemiological study (Hayashi M et al. Respirology 2007;12: 523–530). Therefore, we don't measure serum VEGF-D level routinely.
Changes in the text: No change was made.

Comment 7: An analysis of postoperative complications should be presented.
Reply 7: We have added the suggested content to the manuscript. We graded the postoperative complications according to the Clavien-Dindo classification of surgical complications.
Changes in the text: We added a new paragraph for postoperative complications in the Results section (see page3, line53-54, page5, line113, page10, line262-268).

Comment 8: Conclusions: The study presents results of only one type of treatment, without comparison to other treatment options. As a consequence, it is impossible to assess, that, the total pleural covering is a preferable type of treatment.
Reply 8: Thank you for pointing this out. Based on your comments, I put emphasis on the effectiveness of Total Pleural Covering itself, rather than its superiority to other treatments.
Changes in the text: We have modified out text as mentioned above (see Page 3, line57, Page14, line361 and Page15, line397).