Peer review file

Article information: http://dx.doi.org/10.21037/jtd-20-1557B

Reviewer A

Comment 1: The authors report a series of emphysema patients with pneumothorax evaluating the possible risk factors for recurrence. The way the first pax episode was treated is extremely heterogeneous (tube, tube plus talc, thoracoscopy with talc). This significantly reduces the power of the study making the conclusions weak.

Reply 1: We also understand your concern. However, in the clinical practice, various treatment methods are selected depending on the patient's general condition and the degree of lung function deterioration. This study has reflected these situations. In addition, we have identified the recurrence rate for each treatment method in patients with PE and pneumothorax.

Reviewer B

Comment 1: Information is lacking on details of inclusion criteria for multivariable analysis. Usually, an upper threshold *P*-value using univariable analysis must be defined for inclusion into multivariable analysis (e.g. *P*-value < 0.1).

Reply 1: Thank you for your thoughtful comment. We have described the ‘details of inclusion criteria for multivariable analysis’ at Statistical analysis section. "A multivariable Cox proportional hazard regression analysis with backward stepwise selection, with $P < 0.05$ for the entry of variables and $P > 0.10$ for the removal of variables, was used to identify

prognostic factors associated with recurrence." See page9, line 96.

Comment 2: Why did the authors have chosen a Cox regression model, which is used for survival analyses? I think, this is wrong. Please, use logistic regression analysis. Similarly, the authors should use Odd's ratio rather than Hazard ratio.

Reply 2: Time interval between the completion of treatment and recurrence of pneumothorax was different for each patient. In this study, the median time interval between the completion of treatment and recurrence of pneumothorax was 12.4 months (interquartile range, 2.4 – 38.4 months). Considering these results, the difference in the time interval was considered as important factor in the analysis. However, in the logistic regression analysis, it did not reflect the time to recurrence of pneumothorax. Therefore, we performed a Cox proportional hazard regression analysis.

Comment 3: Why was the reason, CO_2 was not entered into multivariable analysis, although it was significant in the unilateral analysis?

Reply 3: CO_2 was excluded through backward stepwise selection method mentioned above.

Comment 4: Height is an established and important risk factor of pneumothorax. However, the authors only use BMI. I recommend to include height into statistical analysis. Either BMI or height should perhaps be entered into multivariable analysis.

Reply 4: Thank you for your suggestion. We did further analysis on the height you mentioned. We added to the results in page 9, line 108; and at the Table 4.

Comment 5: What is the meaning of presented Hazard ratio (better would be Odd's ratio), for example for FEV_1. There was a multivariable HR 0.423. But, what does this mean for FEV_1? The authors have to define this for continuous (metrical) variable.

Reply 5 It meant that Hazard ratio decreased as FEV_1 increased. In conclusion, this study confirmed that the lower the FEV_1, the higher the recurrence rate.

Comment 6: On the other hand, HR of current smoking is 0.895. This would mean, that smokers have a lower risk of recurrence. This makes no sense. I would expect HR > 1.0.

Reply 6: All the patients in this study were former or current smokers. Also, it was not statistically significant that current smokers had a higher risk of recurrent pneumothorax than former smokers. If you see a table 4, *P*-value was 0.866, which had no statistical significance, and the confidential interval was 0.246 – 3.250.

Comment 7: What means "Reference" within Table 4?

Reply 7: When the hazard ratio was calculated, the reference value of each variable was described as 'Reference'.

Reviewer C

Comment 1: The definition of prolonged air leak is unclear, is it 2 or 5 days?

Reply 1: We appreciate your helpful comment. Pneumothorax guidelines have been published by the British Thoracic Society (BTS) and American College of Chest Physicians (ACCP). The definition of prolonged air leak was not uniform for each guideline. Therefore, in this study, the pneumothorax after 5 days was defined as prolonged air leak.

Comment 2: What operation was performed by VATS? It is unclear.

Reply 2: Thank you for your thoughtful comment. VATS does not mean certain lung surgeries, but only chemical pleurodesis under VATS. We have modified our manuscript as advised (see page 10, line 123; page 11, line 144; page 12, line 178~184; and at the Table 2 and 4.

Comment 3: Some analysis looking at the impact of the treatment strategy on the post pneumothorax PFT's should be done. We would expect a decline in PFT's after VATS for example.

Reply 3: We agreed with your comment. This study conducted on the patients who developed first secondary spontaneous pneumothorax. So, there was no PFT's results before pneumothorax. Therefore, the results of PFT before and after VATS could not be compared.

Comment 4: Did Some statistics should be done to compare the PFT's between the recurrence and no recurrence groups.

Reply 4: Thank you for your thoughtful comment. The comparison of PFT according to the

recurrence of pneumothorax was added to the Table 3. There were no statistical differences between the two groups.

Comment 5: Was DL_{CO} available?

Reply 5: Because this study was conducted retrospectively, DL_{CO} was not performed in all patients.

Comment 6: It seems like we are missing other potential factors for recurrence here: steroid use inhaled vs oral, O2 use, functional class, pack years, etc.

Reply 6: Considering the criteria for accreditation of South Korea insurance, bronchodilators can be used from moderate COPD ($FEV_1/FVC < 0.7$ and $FEV_1 < 80\%$ predicted) patients. However, only 26 patients in this study met the criteria. Finally, bronchodilators were used in 21 of 26 patients; 14 patients with long-acting muscarinic antagonist (LAMA) + long-acting $beta_2$-agonist (LABA) + inhaled corticosteroid (ICS), 6 with LAMA + LABA, and 1 with LABA + ICS. We did not include the usage of bronchodilators as a variable for analysis. Because, only 43% of the study population used various types of bronchodilators. Additionally, this study was conducted with a retrospective design, some potential factors could not be identified.

Comment 7: The main message here is that people with severe COPD who only get a chest tube are higher risk for recurrence. I'm not sure that is a completely novel insight.

Reply 7: The inclusion criteria of this study were secondary spontaneous pneumothorax

patients with emphysema observed in computed tomography, not COPD. This is the difference from other past studies. Twelve patients in this study were not matched the COPD definition with a ratio of FEV_1 to FVC < 0.7. In addition, previous studies used the data obtained from PFT performed before the occurrence of pneumothorax. However, there is no mention of the time interval between the assessment of PFT and development of pneumothorax. Therefore, it is not clear whether the PFT results reflect the lung function at the time of the event. In contrast, the present study performed PFT after the resolution of pneumothorax. We have described above the contents at Discussion section, page 13.