

## Peer Review File

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### Reviewer A

This study is a very interesting and important study.  
I have some comments.

Comment 1. Just reading this title, I could not understand it as a study of pleurodesis for pneumothorax.

**Reply:** We agree this is unclear. We adjusted the title, making it easier to interpret. (See title. Page 1, line 6-7)

Comment 2. Abbreviations are used frequently in the abstract, making it difficult to read.

**Reply:** After consideration of this remark, we think omitting the abbreviations until the main body of text would provide better readability. We hope this in line with your expectations. (See page 2, line 5-30)

Comment 3. It would be easier to understand the grading system summarized in Table 1 if it was explained not only in text but also with images and videos. I also think it will improve universality with respect to results.

**Reply:** Thank you for this outstanding idea. We have edited a compilation of ultrasound clips and added this to the supplement for online viewing. (see video: 'Grading System')

Comment 4. Who performed the ultrasound evaluation of the degree of adhesion? Was it the surgeon? Was it a diagnostic imaging physician? One person? More than one?

**Reply:** We agree that sonographic assessments are operator dependent, and experience is key. Ultrasound of the pleura was performed during this study by two clinicians with extensive experience in thoracic ultrasound, and who received formal training in evaluation of the pleura. Added to manuscript: page 03, line 34-40.

Comment 5. Page 5, line 11: "Generally, treatment options for pneumothorax attempt to create pleurodesis." I do not agree with this statement.

**Reply:** Thank you for notifying us regarding this erroneous statement, since this did not reflect our thoughts. We adjusted the sentence, adding context en nuance. page 05, line 11-12.

### Reviewer B

Comment. I appreciate to the authors for presenting this meaningful study which showed the

progression of pleurodesis after surgical pleurectomy can be evaluated by bedside sonography. As the authors stated, this study can serve as a foundation for studies identifying patients at risk for ineffective pleurodesis and evaluating the effectiveness of pleurodesis agents. What I want to point out with this study is that it was a single-arm study in which the subject consisted only of patients who underwent surgical pleurectomy, which makes it to be inconclusive that the sonographic findings over time after surgery in this experimental group were entirely due to surgical pleurectomy, because it is not unknown to what extent lung sliding and pleural thickening occur in patients who underwent VATS bullectomy alone. In addition, it would be more helpful if it was clarified whether there was a correlation between the location of pleurectomy and the site of pleurodesis found in sonography.

**Reply:** Thank you for critically reviewing our manuscript. We agree that this is a single-arm study in which both pleurectomy and bullectomy was performed. Since the population received 'complete' pleurectomy (added to manuscript: page 3, line 19), and bullectomy was 'apical' in general (added supplemental table S1), we believe any sonographically observed pleural changes have to be attributed to the pleurectomy. The upper most part of the lung, where the bullectomy took place, is not readily accessible due to overlying ossal structures.

#### **Reviewer C**

Manuscript summary:

In this study the authors assessed the feasibility of monitoring the process of pleurodesis after surgical pleurectomy with thoracic ultrasound. The authors found progressive increase in US grades for lung sliding and pleural thickening during the first postoperative days after pleurectomy that is probably attributable to progressing pleurodesis.

General comments:

The manuscript reviews an important topic in chest imaging and the manuscript methodology is adequate. The main limitation of the study is the small number of patients and lack of clarity with regards to the effect of the results seen on clinical outcomes.

Specific comments:

Title:

None.

Abstract:

Comment 1. Page 2 line 6: "information on the extent and duration of pleurodesis", not sure what the word duration refers to.

**Reply:** This word is indeed confusing and is the result of a bad translation. We have changes the word to development (speed). See page 2, line 7, and page 3, line 14

Comment 2. Page 2 line 26: "complete pleurodesis in this series was only incidentally reached before discharge", I would rephrase that to say that only a minority of patients reached complete pleurodesis.

**Reply:** We have corrected this sentence. See page 2, line 29-30

Comment 3. Page 2 line 16-17: Please add “±” to the numbers noted in the results.

**Reply:** Thank you for noting this error. We have added the sign. See page 2, line 18-19 and page 4, line 16-18.

Introduction:

Comment 4. No comments.

Materials and Methods:

Comment 5. What is the US experience/training of the US operator and the second observer?

**Reply:** (See also reviewer A, comment 4.) We agree that sonographic assessments are operator dependent, and experience is key. Ultrasound of the pleura was performed during this study by two clinicians with extensive experience in thoracic ultrasound, and who received formal training in evaluation of the pleura. Added to manuscript: page 03, line 34-40.

Results:

Comment 6. Given that the majority of patients achieved peak mean values close to 1 (1=questionable) for the presence of lung sliding a good definition of what constitutes a questionable result of is needed to try and decrease uncertainty.

**Reply:** We agree with your remark. Personally, I believe there is a need for development in quantitative (lung) ultrasound. In this study, the assessment is in part qualitative and the ‘grade 1’ is negatively defined, as in: nor 0, nor 2. To give more context regarding the grading system, we have edited a compilation of ultrasound clips and added this to the supplement for online viewing. (see video: ‘Grading System’).

Comment 7. Did the results of US evaluation affect in any way the duration of tube drainage or discharge? If not, what parameters were used to decide remove the tube drainage and was there a correlation between these parameters and US results?

**Reply:** Our local hospital protocol uses a chest tube drainage duration of at least 72 hours, theoretically allowing pleural adhesions to develop and reducing the recurrence of pneumothorax (page 3, line 4-6), resulting in 3 and sometimes 4 days to chest tube removal (see supplement). Longer times before chest tube removal were due to persistent airleak (>10ml/min airflow). In this study there were only three patients with a (clinically significant) longer chest tube drainage time, and since a chest tube duration for 72h was ‘mandatory’ causing confounding, a correlation was/could not calculated.

US was not used in any way to influence chest tube drainage or discharge. However, this is a very interesting and important topic, for which this pilot may break ground for a more patient-tailored approach. See also the discussion on page 5, line 14-23.

Discussion:

Comment 8. Page 5, line 10: “and broad accessible diagnostic mode”, needs to be revised to “and broadly accessible diagnostic modality”.

**Reply:** Thank you for marking this error, we have revised the sentence. Page 5, line 10.

References:

No specific comments.

Tables:

No specific comments.

Figures:

No specific comments.

#### **Reviewer D**

Comment. <https://pubmed.ncbi.nlm.nih.gov/34634246/>

I think this is worth publishing. But I am afraid that the future work they have suggested has already been done: Please have a look at the paper suggested above, as it shows how TUS by physicians can reduce length of stay post pleurodesis. How did the authors choose their 6 points? Can they comment on how this differs from the above paper? And why theirs might be better?

I would expand the discussion section and reference above.

**Reply:** Thank you for reviewing our manuscript and your constructive remarks. We are aware of this interesting and recent publication, which we listed in our references (see reference 9). It was shortly discussed on page 5, line 2-4. The main, and important, difference with this study is de patient population. Our study consisted of patients with a pneumothorax (with therefore relatively healthy pleura) and had a surgical treatment to reach pleurodesis; pleurectomy. The study by Psallidas et al., consisted of a group of patients with malignant pleural effusion and used talc for pleurodesis. The study by Psallidas et al., is promising to say the least. In conjunction with our study, which confirms TUS might also be useful after treatment for pneumothorax, this might be a starting point for further research on the clinical implementation of TUS in the treatment of pneumothorax. Of course future research has to focus on hospital length of stay, or more importantly, long term outcome such as recurrent pneumothorax.

With regard to the 6 point (this study) versus 9 point system (Psallidas et al.), there remains a large variation in practice regarding ultrasound protocols and the number of locations assessed. The 6 point system might be quicker, however if that comes at the cost of accuracy is yet to be determined.

We elaborated on the above on page 5, line 4-7, and further.

## Reviewer E

The idea of your case review is very interesting because it could have potentially a big impact on LOS and chest tube removal after surgery in patients who undergo surgery due to pneumothorax.

I have some comments:

Comment 1. In your supplemental table 1 you classified only 1 patient as SSP but in table 2, 3 patients have Asthma/COPD, please explain

**Reply:** Thank you for your meticulous review. We used the diagnosis of the treating physician for classification in supplemental table S1. The three patients with asthma/copd were patient #4, #5, and #9. Patient #4 has asthma (diagnosed in primary care) and did not seem to relate to de pneumothorax, patient #5 had the buffalo chest syndrome as main diagnosis (but also COPD), and patient #9 has COPD with emphysema, classified as SSP.

Comment 2. In supplemental table 1 how you define days in the last column? after discharge? or after surgery?

**Reply:** After surgery (added to table S1). The recurrent pneumothorax of patient #6 was found during ultrasound examination, after chest tube removal (wrong number of days till pneumothorax due to automated calculation in the previous version).

Comment 3. Which chest tube drainage System do you use in your hospital? It could be helpful to know it because a digital system could give more information about air leak for example

**Reply:** We use the digital drainage system (Thopaz Chest Drain System, Medela, Switzerland). Added to manuscript: page 3, line 24-25.

Comment 4. Was the Chest tube under suction post-operatively?

**Reply:** Yes, a standard drainage pressure of -8 cm H<sub>2</sub>O is used. Added to manuscript: page 3, line 24-25.