

## Peer review file

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### Reviewer A

**Comment:** The authors suggest that some of the cases may have had ‘emphysema pneumothorax’ (an expression I had not previously heard and which I take to mean secondary pneumothorax). As both patient groups had very low tobacco exposure this seems unlikely and I would not favor using CT in this way because of the radiation exposure. The small difference in smoking history (only 3.3 pack years) seems unlikely to have had such an impact on recurrence rates. The letter rather concentrates on the recurrence rate issue rather than emphasising the main findings of as rapid symptom relief, shorter hospital stay etc, and particularly the huge difference in adverse events and serious adverse events.

As surgeons the authors suggest surgery as an option. I would suggest that operating on patients with a first spontaneous primary pneumothorax is inappropriate given that the condition is a nuisance rather than being dangerous and that in 70% or more it will not recur. Interestingly the recurrence rate in the surgically managed group in the Olesen paper they quote was 13%. In the conservatively managed group in our study it was 8.8% in the first year when most recurrences occur. Olesen et al were performing pleural abrasion to effect pleurodesis. Much lower recurrence rates have been reported with talc poudrage alone (Cardillo et al. Thorax 2016;71:847-53). The number needed to treat by VATS to prevent one recurrence is 4.8. My own approach has been to explain the risks of recurrence to the patient and if they wish offer pleurodesis by talc poudrage using local anaesthetic medical thoracoscopy. What may well affect that decision will be the recurrence rate in those conservatively managed given a longer follow up period. If this remains low then the NNT for surgery is likely to become even more unacceptably high.

**Reply:** Firstly, thanks for your comments! Meaning of emphysema pneumothorax is that pneumothorax is associated with pulmonary emphysema and emphysematous lesions .I fully agree with you that it belongs to secondary pneumothorax. Chest X-ray

is a routine examination for outpatient diagnosis and evaluation of primary spontaneous pneumothorax, however, it's not always easy to identify emphysematous lesions. Computed tomography (CT) is more sensitive to the diagnosis of pulmonary emphysema and emphysematous lesions than chest radiographs. Meanwhile, low-dose CT could reduce radiation dose and it doesn't make much impact on health.

The difference of mean pack-yr of smoking (about 3.3 pack years) seems small between two groups in Brown's study, but standard deviation is big difference (23.3 pack years vs 7.8 pack years) and it means data dispersion of interventional group is significant difference from conservative group. SD should be controlled.

In our opinion, recurrence rate is an important index to evaluate treatment effect and meanwhile other index (like hospital stay, adverse events etc) can not be ignored.

According to current research, maybe it's controversial to perform operation for first primary spontaneous pneumothorax. However, we should recognize the good outcome of surgery for primary spontaneous pneumothorax. In a 10-year experience, Herrmann et al demonstrated treatment of first episode of PSP by VATS is a safe procedure, with a very low rate of recurrence and a high patient satisfaction (recurrence occurred in 4 patients (2.2%); ten-year freedom from recurrence was 96.2%; procedure-related morbidity rate was 7.6%). [Herrmann et al, Eur J Cardiothorac Surg 2016; 49:854-859] So surgery is still an effective option for primary spontaneous pneumothorax.

#### **Reviewer B**

**Comment:** In the first paragraph, however, "a diameter of 2 cm or more" and "less than 2 cm in diameter" seem to be inappropriate. The term "diameter" may be replaced with "depth", referring to the guidelines.

**Reply:** Firstly, thanks for your comments! We have modified our text as advised (see Page 2, line 23, 28)

Changes in the text: Page 2, line 23, 28

#### **Reviewer C**

## Comments

### Major comments

1. Although this article was titled “Comments on Therapy Option for Primary Spontaneous Pneumothorax”, you mainly described the conservative and interventional therapies and the relationship with smoking habit for PSP. The options of surgical procedure are various and controversial. As you know, in European countries, intraoperative pleurodesis is often used. Meanwhile, in Asian countries, absorbable sheets are used for reinforcement around the staple line to prevent postoperative recurrence. You may describe it in detail, too.

2. You showed that smoking habit is risk factor of PSP according to relatively old report in 1987. It may be acceptable comment generally. However, there were some reports which described that smoking habit prevented postoperative recurrence, recently. Anyway, you may not argue the relationship between smoking habit and PSP for your theme.

### Minor comments

You often used the term as “primary pneumothorax”. I recommend to use “primary spontaneous pneumothorax” or “PSP”.

**Reply:** Thanks for suggestions about difference of operative choice between the European and the Asian, and relationship between smoking habit and PSP. Those two topics actually could arouse reader's interest, but they are not main topics of this letter. So, apologize, we'll not add those topics in our letter.

We have modified our text according to Minor comments (see Page2, line19,37; Page 3, line41,42,46; Page 4, line71,72,74,79; Page 5, line82-84,92-93; Page6 , line104,116,119)

Changes in the text: Page2, line19,37; Page 3, line41,42,46; Page 4, line71,72,74,79; Page 5, line82-84,92-93; Page6 , line104,116,119

## **Reviewer D**

### **Comments**

(1) The Authors state that “Conservative treatment mainly relies on the reabsorption of gas by pulmonary capillaries to eliminate pneumothorax” [Northfield T C. Oxygen therapy for spontaneous pneumothorax. *BMJ* 1971;4(5779):86-88].

However, some Authors have demonstrated that this process of “air removal from the pleural space rests only on the resorption capabilities of the visceral pleura” and that “air resorption from the pleural cavity is accomplished by the process of simple diffusion of gases through the semipermeable pleura to the subpleural venous system.” So maybe this last detail should be specified and highlighted, instead of generally speaking of a process of reabsorption “by pulmonary capillaries”. I have attached this article for you. [Ivan P. Novakov IP, Hadzhigeorgiev GN, Safev GP. Resolution of experimental pneumothorax by room air. *Folia Medica* 2011; 53(1): 60-64].

(2) Moreover the Authors state that “In a 10-year retrospective study, Bense et al. found that 88% of patients with primary pneumothorax had a history of smoking. Compared with non-smokers, the risk of pneumothorax increased 9 times in 83 female smokers and 22 times in male smokers. In Brown et al.’s study, smoking was not matched between the two groups,...”. In fact, the Authors confirm that “Thus it could be speculated that different smoking conditions may affect the healing and recurrence of primary pneumothorax patients, resulting in data deviation and affecting the accuracy of the results.”

Recently, some Authors have demonstrated the presence of cannabinoids and particular pathologic alterations in lung tissues of young cannabis smokers operated for PSP, supporting the correlation between this disease and cannabis abuse and suggesting spontaneous pneumothorax "secondary to cannabis" as a new nosological entity. So, together with tobacco smoke, the Authors should mention cannabis smoking too, citing this research, as even cannabis smoking can be a contributing factor “resulting in data deviation and affecting the accuracy of the results”. I have attached this article for you. [Bisconti M et al. Cannabinoids Identification in Lung Tissues of Young Cannabis

Smokers Operated for Primary Spontaneous Pneumothorax and Correlation With Pathologic Findings. *Respiration*. 2019;98(6):503-511].

**Reply:** Thank you very much for providing us with the latest mechanism of air resorption of spontaneous pneumothorax. It is helpful for readers to state detail of air resorption, but due to the word limit, generally speaking of a process of reabsorption is sufficient.

As you stated, cannabis smoking is another important risk factor for primary spontaneous pneumothorax. So we have modified our text as advised( see Page 5-6, line96-104)

Changes in the text: Page 5-6, line96-104