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Peer Review File

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Reviewer A

Pneumothorax after CTNAB is one of the annoying complications. This report presents an interesting method of CTNAB to prevent pneumothorax.
Although this retrospective study is very suggestive and interesting, it has some problems that need more information and discussions.

My comments
1.What is the mechanism of blood patching to prevent pneumothorax? Did injected blood spread through the pleural space? If so, how did the authors know the injected blood into the pleural space? Did they use real-time CT monitoring?

Reply 1: Mechanism of blood patching: blood/ clot plugging the tact created by the needle. After the biopsy specimens are obtained and immediately before the coaxial introducer needle is removed, plasma is slowly separated from the blood/clots in the syringe and the remaining blood/clots are injected into the tract as the guiding needle is slowly removed. The injection is continued up to and just past the pleura. Typically, 4-6 ml is injected, depending on the tract length. SO, to answer the question: the blood was injected in the biopsy tract (lung paranchyma) and not specifically in the pleural space.

Changes in the text: None. Answer can be seen: page 8, line 20 – 22 and page 9, lines 1 – 2

2.I could not follow the patient selection method. Did authors perform blood patching at CTNAB in all patients after 2016? Or did author select the patients for blood patching after 2016? In the latter case, how did author select patients.?

Reply 2: Blood patching was performed in all patients between 2016 and 2019.

Changes in the text: Blood patching was not performed in patients from 2013-2015, however, all patients who underwent CT-guided lung biopsy from 2016 to 2019 received blood patching.

3.Authors analyzed the impact of COPD to develop pneumothorax. However, subpleural emphysema or honeycomb formation may also influence the likelihood of developing pneumothorax after CTNB. Please add information about emphysema or bullae formation in studies patients.

Reply 3: As documented on page 11, lines 13 to 15, COPD history was obtained from patient chart review and not by radiological evidence of emphysema. Information about radiological evidence of emphysema and bullae formation was outside the scope of this study and we have added it as one of the limitations. We can review the correlation between CT features of emphysema and pneumothorax and effect of blood patching of the tract as a separate study.

Changes in the text: Thirdly, evaluation of subpleural emphysema or honeycomb formation in patients without COPD was beyond the scope of this study and may influence the likelihood of developing pneumothorax after CTNB.

4.Authors mentioned multivariable analyses had been performed in this study. However, I could not find the result of multivariable analyses. As this is a retrospective study, many confounding factors should be carefully evaluated including, for example, using propensity score method.

Reply 4: The reviewer made an excellent point. We wanted to suggest that multivariate analysis may be needed to adjust for possible and potential imbalances and mistakenly mentioned that it was performed. We have made edits to the text and have added it as one of the limitations.

Changes in text: Lastly, additional multivariate analyses maybe needed to perform to adjust for any potential imbalances which was beyond the scope of this study.

Reviewer B

The authors performed a retrospective chart review from two institutions comparing patients who did and did not receive an intraparenchymal blood patch following percutaneous CT-guided biopsy.

Intro

1. Did the metanalysis include studies that used IBP? Please include information on the rate of chest tube placement and hospitalization from this study and other studies, since those are also outcomes you examined in your study.

Reply: The metaanalysis does not mention about the use of sealing technique but is a good study to get incidence rates of complications. We have added the results of the remaining studies as suggested.

Changes in text: Changes in text: A meta-analysis of 32 studies investigating complications of lung biopsy reported pneumothorax incidence rates between 22.2% to 28.6% in patients undergoing core lung biopsy, with 4.3% to 7.3% of the patients requiring either manual aspiration or chest tube placement and/or hospitalization(1).

There have been mixed results in the literature from studies investigating the efficacy of blood patching. Bourgouin et al. (2) , did find a decrease in the incidence of pneumothorax with blood patching from 34.1% to 28.8%, along with a decrease in the incidence of pneumothorax requiring chest tube placements from 9.1% to 7.7%. Similar results were demonstrated by Herman and Weisbrod (3), with a decrease in incidence of pneumothorax with blood patching from 30% to 24%, however an insignificant increase was noted in patients needing chest tube placement in the blood patching group (2.2%, 1/46 vs 2.1%, 1/47), but the findings were not statistically significant in both studies (2, 3).

2. Please discuss the current standard of care

Reply: Added to introduction.

Changes in text: Current standard of care guidelines and recommendations do not warrant the instillation of autologous blood routinely, likely due to lack of enough evidence, but does mention the benefit noted in the literature (6).

Methods:

1. Please include the IRB approval number.

   Reply: IRB number has been added to the methods section.

   Changes in text: This retrospective study is compliant with the Health Insurance Portability and Accountability Act and approved by the Institutional Review Board (IRB number: 1589530-1).

2. Please define “large” pneumothorax.

Reply: Pneumothorax size was calculated using the equation $Y = 4.2 + [4.7 \times (A + B + C)]$, $r = .98$, $p < .0001$, developed by Collins et al. (1995). It mentions enlarging pneumothorax (not large pneumothorax) on page 9, line 20

Changes in text: Patients with a large pneumothorax found immediately after biopsy on CT-imaging, even before removal of the biopsy needle, were excluded from the study. Pneumothorax size was calculated using the equation $Y = 4.2 + [4.7 \times (A + B + C)]$, $r = .98$, ($p < .0001$), developed by Collins et al (6).

3. What size chest tubes were used?

   Reply: 8.5 Fr Cook multipurpose d

Changes in text: Patients with a symptomatic pneumothorax, enlarging pneumothorax, or pneumothorax >25% volume were treated with 8.5 Fr Cook multipurpose-d chest tubes that were placed under CT guidance

Discussion:

1. You refer to “documented alternatives” to blood patching but never discussed these in the intro section. Please include this content in the introduction.Please check the attached original manuscript.

   Reply: Alternatives to IBP are added.

   Changes in text: There are several documented alternatives to blood patching that are utilized in effort to avoid pneumothorax complications including hydrogel plugs, fibrin glue, collagen foam plugs, absorbable haemostat gelatin powder, injection of normal saline tract sealant and even techniques like patient breath-hold after deep exhalation before needle extraction., however widespread use of a particular method has not yet been adopted.

2. Consider summarizing your key findings again.

Reply: key findings summarized just before limitations.

Changes in text: Moreover, our study shows a derease in not only the incidence (37% to 14.6%) of pneumothorax, but also in the severity 16% to 9%), need for chest tube placement (17.2% to 3.9%), and the hospitalizations rate (16.4% to 2.9%) suggesting that blood patching is a safe and effective technique that can be considered when performing percutaneous CT-guided lung biopsies.

3.Please acknowledge the limitations associated with a retrospective study like this.

Reply: Done as suggested.

Changes in text: Lastly, this is a retrospective study and any differences found could be due to the reason the patient received the blood patch and not necessarily to the blood patch itself.

4. How did the providers decide who received IBP? Did this introduce selection bias?

Reply: IBP became the standard of care at the given institutions in 2016 due to clinical consensus and limited, but useful literature evidence. This has been described in the methods section. This did not introduce selection bias as the basic demographic characteristics between the 2 groups were not significantly different.

Changes in text: Blood patching was not performed in patients from 2013-2015, however, all patients who underwent CT-guided lung biopsy from 2016 to 2019 received blood patching.

5. Add content on how this manuscript adds to the current body of literature.

Reply: Done as suggested.

Changes in text: Previously, very few studies have been performed to compare the incidence rates of complications in patients undergoing CT-guided lung biopsy. Moreover, mixed results were found in previous studies, which underscores the importance of the current study.

Conclusion

5. Caution should be exercised when drawing conclusions from retrospective, observation, non-controlled studies.

Reply: Added in the limitations.

Changes in text: Caution should be exercised when drawing conclusions from retrospective, observational, and non-controlled studies.