Peer Review File

Article information: https://dx.doi.org/10.21037/tlcr-24-484

Reviewer #A

Major comments

Comment 1 (C1): The authors have cited intraoperative R-EBUS images as a predictive factor for successful bronchoscopy in diagnosing PPLs. However, R-EBUS imaging is influenced by the presence or absence of a bronchus sign on CT, as the R-EBUS image results from whether the devices can reach the target lesion during procedures. Therefore, it seems inappropriate to consider R-EBUS imaging as a preoperative predictor of diagnostic success.

Response 1 (R1): Thank you for your insightful comments. We agree with the reviewer that R-EBUS image was not used as a preoperative predictor of diagnostic success. However, we did not analyze the clinical factors associated diagnostic success according to before or during procedure. It is consistent with previous studies that included RP-EBUS image as clinical factors associated with diagnostic yield[1]. However, review`s comment is reasonable. Thus, we added this point as the limitation.

Page 14, lines 304-308

"Finally, within the lesion on the EUBS image was the strongest factor associated with diagnostic yield in this study. However, this factor is not available before EBUS is performed. Although bronchus sign on CT no longer has a significant association with diagnostic yield after adjusting for EBUS image, physicians may consider the bronchus sign on CT as a clinical factor before performing EBUS in patients with COPD."

Reference

1. Kim SH, Chung HS, Kim J, et al. Development of the Korean Association for Lung Cancer Clinical Practice Guidelines: Recommendations on Radial Probe Endobronchial Ultrasound for Diagnosing Lung Cancer - An Updated Meta-Analysis. *Cancer Res Treat*. 2024;56(2):464-483.

C2: Why was bronchoscopy performed on patients with COPD without fluoroscopy guidance, knowing they were at risk of pneumothorax associated with TBB?

R2: Our hospital does not have access to fluoroscopy, which may have played a role in the development of the pneumothorax. However, our results may suggest that RP-EBUS-TBLB can be performed with relatively low risk of pneumothorax in centers without access to fluoroscopy. We have included this points as a limitation of our study.

Page14, lines 300-305

"Third, the diagnostic yield and complications of RP-EBUS-TBLB may be affected by the use of additional modalities, such as GS, fluoroscopic guidance, virtual bronchoscopic navigation, and transbronchial needle aspiration. At our center, we only used the GS to perform RP-EBUS-TBLB. Combining different modalities may improve diagnostic yield and reduce complications. Further studies are needed to clarify the benefits of these modalities in RP-EBUS-TBLB in patients with COPD."

C3. The new findings in this study are unclear. If the only difference is the number of patients being higher than in previous studies, it is not novel.

R3: *Thank you for your comments. A previous study reported safety and diagnostic accuracy in a relatively small number of patients with COPD, but our study analyzed safety and diagnostic accuracy in a relatively large number of patients with COPD, as well as factors associated with diagnostic success in patients with COPD. To our best knowledge, there were no data on this topic.*

Minor comment

C1. There is a typographical error (EUBS) on page 3, line 110.

R1. We apologize for the inaccuracy. We revised it.

Reviewer #B

C1: There was a correlation between CT-scan findings, airflow limitation and location of lesions? Emphysema could play a role in lower diagnostic yield for lesions in upper lobes?

R1: Thank you for your insightful comments. We have performed additional analysis to assess the association between emphysema and diagnostic yield, and the results showed that there was no significant association. We have added this point to Table 4 and Methods section.

Page 8, line 146-153

"*Emphysema was assessed visually and was defined as a low-attenuation lung area without a clear wall. The degree of emphysema was categorized into three groups: mild, moderate and severe. Mild emphysema included mild centrilobular emphysema (scattered lucencies affecting an estimated 0.5-5% of a lung zone) and mild paraseptal emphysema (less than 1 cm, well-demarcated rounded juxtapleural lucencies). Moderate emphysema was defined as many centrilobular emphysema occupying more than 5% of any lung zone. Severe emphysema included confluent emphysema, advanced destructive emphysema, panlobular emphysema, and substantial paraseptal emphysema (12).*"

C2: Rate of complications: please, add more details: there were complications other than pneumothorax? infections? hemoptysis? early? late? How they were identified?

R2: Thank you for your valuable comments. The complication rate was reported in Table 2. We have added this points to the Methods and Results sections.

Page 8, lines 164-172

"All bronchoscopy procedures were performed on an inpatient basis to monitor for procedure-related complications. Vital signs and the development of any complications were monitored for at least 24 hours after the procedure. Chest radiographs were obtained immediately after the bronchoscopy procedure and on the next day to investigate the development of pneumothorax. Physicians closely monitored patients for signs of hemoptysis immediately after the bronchoscopy procedure and during the 24-hour observation period. Infectious complications were defined as new respiratory symptoms (fever>37.8℃ body temperature, cough, sputum, or chest pain) or new lung infiltrates on chest radiograph after bronchoscopy."

Page 10, lines 208-215

"Regarding complication rate, there were no early terminations of the procedure, deaths or life-threatening complications during or after bronchoscopy. The incidence of pneumothorax was higher in patients with COPD compared to those without COPD (4.6% vs. 1.1%, respectively, P = 0.008). The complication rate did not differ according to the severity of airflow limitation in patients with COPD (mild, 3.1%; moderate = 10.5%; severe to very severe, 8.3; P = 0.266) (Figure 2). Hemoptysis occurred after RP-EBUS in five patients (2.9%) with COPD and 11 patients (2.5%) without COPD (P = 0.498). None of the patients with COPD and 6 (1.4%) of the patients without COPD developed infectious complications (P = 0.132)."

C3: The only sampling instrument used was the forceps: the use of needle in case of eccentric lesions could have improved the diagnostic yield?

R3: Thank you for your insightful comments. We agree with the reviewer that transbronchial needle aspiration may improve diagnostic accuracy, especially for eccentric lesion on EBUS image. Unfortunately, we were not able to perform transbronchial needle aspiration during the study period. We added this point as the limitation of our study.

Page14, lines 300-305

"Third, the diagnostic yield and complications of RP-EBUS-TBLB can be affected by the use of additional modalities, such as GS, fluoroscopic guidance, virtual bronchoscopic navigation, and transbronchial needle aspiration. At our center, we used only the GS to perform RP-EBUS-TBLB. The diagnostic yield can be improved and complications can be lowered by combining various modalities. Further studies are needed to clarify the benefits of these modalities in RP-EBUS-TBLB in patients with COPD."

C4: please add more details regarding the safety of procedure: airflow limitation can be related to complications rather than diagnostic accuracy

R4: Thank you for your insightful comments. We added this point to the Result section.

Page 10, lines 208-214

"Regarding complication rate, there were no early termination, deaths or life-threatening complications during or after bronchoscopy. The incidence of pneumothorax was higher in patients with COPD compared to those without COPD (4.6% vs. 1.1%, respectively, P = 0.008). The complication rate did not differ according to the severity of airflow limitation in patients with COPD (mild, 3.1%; moderate = 10.5%; severe to very severe, 8.3; P = 0.266) (Figure 2). Hemoptysis occurred after RP-EBUS in five patients (2.9%) with COPD and 11 patients (2.5%) without COPD (P=0.498). None of the patients with COPD developed infectious complications (P=0.132)."