

Peer Review File

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Reviewer A

Thank you for the opportunity to review this manuscript which assessed COPD diagnostic test rate, prevalence, and treatment rates among a population of hospitalized lung cancer patients.

Comment 1. The topic is important and management of COPD among lung cancer patients is not well-studied. However, there was a lack of clarity in the abstract and manuscript regarding 'COPD diagnosis'. It was unclear if COPD was not diagnosed based on the spirometry results during hospitalization, which were consistent with COPD (ex missed opportunity for diagnosis), or if it was simply not documented in the discharge record. It was also unclear if this was a retrospective study as the authors stated they followed 300 patients for up to 46 months. Among this subpopulation which was followed, the authors state that data on exacerbation frequency and healthcare utilization was obtained but these results are not included in the manuscript.

Reply: We thank the Peer Reviewer for this comment. We apologize for this confusion. (1) The diagnosis of COPD in the investigated LC patients was made based on spirometry results during their hospitalization. However, we found that there were cases of spirometry-diagnosed COPD that were not documented in the patients' discharge diagnosis records, thus we designed this study to assess information about whether they were aware of their underlying COPD condition (referred to as COPD awareness in this study), were on or not on COPD inhalation therapy and their adherence to the therapy. Changes in the text:

a) We have re-arranged the whole Methods section to make our intended meaning clearer and provided the specific definitions in the Method, section COPD diagnosis. Changes in the text: "In this study, the diagnostic rate of COPD was determined as the proportion of LC patients who underwent spirometry during hospitalization, were spirometry-defined COPD and had COPD mentioned in their discharge diagnosis. Treatment rate was determined as the percentage of patients with spirometry-defined COPD who received inhaled therapy starting from hospitalization following spirometry-defined COPD, such as a long-acting muscarinic antagonist (LAMA), a combined LAMA and long-acting β 2 agonist (LABA), a combination of inhaled corticosteroids (ICS) and LABA, or triple therapy (ICS/LABA/LAMA). Further, COPD awareness was defined as the proportion of LC patients with spirometry-defined COPD who were aware of their underlying COPD condition at last follow-up (September 2022), irrespective of a COPD diagnosis documented in the discharge diagnosis." (please view the Yellow highlight lines:198-208)

b) Also in the follow-up in the Method, section Follow-up.

Changes in the text: "The LC patients with COPD undergo long-term follow-up every 3 months in our hospital. In this study, we followed up all the included spirometry-

defined COPD LC patients until September 2022 to obtain information about whether they were aware of their underlying COPD condition (referred to as COPD awareness in this study) and adherence to COPD inhalation therapy after discharge. The longest follow-up time was 46 months.” (please view the Yellow highlight, lines: 211-216)

(2) This study is a retrospective study in both the Abstract and Main Text Methods. In addition, we have provided clearer details about the follow-up of the 300 patients in the:

a) Method, section Follow-up

Changes in the text: “The LC patients with COPD undergo long-term follow-up every 3 months in our hospital. In this study, we followed up all the included spirometry-defined COPD LC patients until September 2022 to obtain information about whether they were aware of their underlying COPD condition (referred to as COPD awareness in this study) and adherence to COPD inhalation therapy after discharge. The longest follow-up time was 46 months.” (please view the Yellow highlight, lines: 211-216)

b) Results, section Awareness of COPD and adherence to inhaled therapy

Changes in the text: “Follow-up was performed for all the 690 spirometry-defined COPD patients; however, only 300 were successfully contacted because 285 had died and 105 were lost to follow-up and their contacted patients' relatives could not provide accurate follow-up information.”(lines 303-306).

(3) We apologize for such issues and have now deleted contents regarding the "exacerbation frequency and healthcare utilization", mainly because acute exacerbation is related to the treatment effect and prognosis of COPD, which we will collect survival and prognosis data for further study.

Comment 2. Additionally, there was no data on whether COPD had been previously diagnosed in any of these patients. Ex. there were approximately 37% of patients in the respiratory medicine department who did not receive spirometry. It would be of interest to know how many of these patients had a prior diagnosis of COPD, or had COPD documented in their discharge record. It is also unclear whether inhaled therapies for COPD were initiated during this hospitalization upon COPD diagnosis, or whether these patients had already been prescribed these therapies prior to the hospitalization. Additionally, lung cancer outcomes are not reported which would have strengthened the manuscript, particularly if they were reported for patients who received therapy for COPD. The treatment rate should also be reported only for those who were diagnosed with COPD during the hospitalization.

Reply:

(1) This study mainly included lung cancer patients. All lung cancer patients have not been diagnosed with COPD in the past and have not received inhalation therapy. After admission, lung function screening was conducted as we found that some proportion of the patients were not screened. The reason is that many grassroots hospitals do not pay attention to the screening of COPD in lung cancer patients but only focus on diagnosing and treating lung cancer. One of the purposes of this study is to investigate the COPD screening rate of hospitalized lung cancer patients and understand the current situation.

The research results show that the screening rate of lung cancer combined with COPD is low, which needs to be taken seriously by clinical doctors.

Thus, to avoid any confusion and to ensure an accurate COPD diagnosis, COPD diagnosis was only confirmed based on our spirometry examination.

Changes in the text: We have now clarified the following in the Method section

- Results, section Baseline data and characteristics: "Of note, all the investigated LC patients had no past COPD history and had not received related inhalation therapy." (please view the Yellow highlight, lines: 237-238)

- Method, section COPD diagnosis 1st paragraph: "To ensure an accurate COPD diagnosis, the COPD condition was determined for the investigated patients in this study only if they underwent spirometry at our hospital during this current hospitalization." (please view the Yellow highlight, lines: 185-187)

(2) Concerning the therapy initiation, we have now provided more details in the Method, section COPD diagnosis 2nd paragraph

Changes in the text: "Treatment rate was determined as the percentage of patients with spirometry-defined COPD who received inhaled therapy starting from hospitalization following spirometry-defined COPD ..." (please view the Yellow highlight, lines: 198-205); mentioning that it indeed started from hospitalization.

(3) In regard to cancer outcomes, we are thankful to the Peer Reviewer's comments. However, due to the low proportion of these patients receiving clinical outcomes during the follow-up stage and the lack of data maturity, we are currently unable to conduct in-depth analysis of survival. We will continue to follow up and conduct further in-depth analysis when the data is mature.

Comment 3. In the discussion (lines 356 to 361) the wording seems to put responsibility on the patients to request spirometry and treatment plans. Instead, shouldn't the responsibility be on the physicians to screen for COPD and to improve documentation and treatment of COPD based on the results of spirometry testing? The results suggest missed opportunities to diagnose and treat COPD and the message should be reframed around this finding. The manuscript does have some important findings however it requires substantial revision to improve the clarity of the results and clinical implications.

Reply: Indeed, we agree with the Peer Reviewer and apologize for these writing issues. We have now revised the whole text (including the Discussion) to avoid such confusing descriptions and to make our intended meaning clearer.

Changes in the text: Major English writing revision was performed in this whole text. Due to the large modification range, it is not possible to label the specific location.

Reviewer B

The Authors investigated by performing spirometry the prevalence, awareness and treatment of COPD in two series of patients with lung cancer who were hospitalized in a critical care medical division or in a thoracic surgery division of a large Hospital in China.

Despite its retrospective nature, the study is interesting and potentially contributing to the field.

However, in the present version it suffers from flaws.

Major flaws.

Comment 1. The English require an in-depth revision. Some sentences are hardly understandable.

Reply: We thank the Peer Reviewer for all these great and instructive comments. We apologize for these issues. We have had this manuscript revised by a native English speaker, and we have double-checked that all the written text is understandable and clear.

Changes in the text: Major English writing revision was performed in this whole submission. Due to the large modification range, it is not possible to label the specific location.

Comment 2. Lung cancer is now actively investigated with Low Dose CT screening. The Authors should include in their report the available information about the prevalence of COPD, defined by spirometry, in LC screening studies (see for instance Young RP et al. Airflow Limitation and Histology Shift in the National Lung Screening Trial. The NLST-ACRIN Cohort Substudy. *Am J Respir Crit Care Med* 2015;192:1060-7

Young RP et al. Lung cancer-specific mortality reduction with CT screening: outcomes according to airflow limitation in the ACRIN-NLST study (N=18,475). *Am J Respir Crit Care Med* 2016;193:A6166.

Kaaks R, et al. Lung function impairment in the German Lung Cancer Screening Intervention Study (LUSI): prevalence, symptoms, and associations with lung cancer risk, tumor histology and all-cause mortality. *Transl Lung Cancer Res.* 2022 Sep;11(9):1896-1911. doi: 10.21037/tlcr-22-63. PMID: 36248328; PMCID: PMC9554689.

Reply: Thank you very much for this comment. We have added the suggested descriptions in the Introduction section's first paragraph.

Changes in the text: Introduction section 1st paragraph: " In addition, COPD has been shown to be an important factor that may significantly increase the risk and severity of LC, especially in those with other accompanying factors such as smoking, airflow limitation, and others, but it could be significantly reduced if these high-risk patients undergo adequate and timely screening." (please view the Yellow highlight, lines: 98-102)

Comment 3. The rationale and expected (measured in other contexts) benefit of inhalation therapy for COPD should be indicated in the introduction or discussion.

Reply: We are grateful to the Peer Reviewer for this very good suggestion. We have added corresponding descriptions in the Discussion section.

Changes in the text: Discussion: "Inhalation therapy is a common treatment option for

LC patients with coexisting COPD. The rationale behind this therapy is to deliver medication directly to the lungs, allowing for maximum therapeutic benefit while minimizing potential systemic side effects and increasing treatment adherence, as well as being more practical and easier to use." (please view the Yellow highlight, lines: 411-414)

Comment 4. They skipped testing the diffusing capacity of lung for carbon monoxide (DLCO) that complements spirometry for assessment of COPD, with particular relevance for emphysematous changes. This should be recognized as an additional limit of the study.

Reply: We thank the Peer Reviewer for this insight. DLCO testing can provide the following benefits: (1) Early detection of emphysematous changes: DLCO testing can detect early changes in lung function that may not be picked up by spirometry, which may help identify emphysematous changes before significant lung damage occurs, allowing for earlier interventions and treatment, as well as (2) better differentiation of COPD subtypes: DLCO testing can help differentiate between different subtypes of COPD, such as emphysema and chronic bronchitis, which can have different treatment approaches.

Further, as shown by our study results, due to the low awareness and focus on COPD in lung cancer patients, the utility of DLCO in this present setting is not very the most important aspect of this study, as we have to first sensitize more oncologists and physicians on the importance of adequately assessing and managing COPD in lung cancer patients. As a next step, we will aim to delve into this topic more. Also, due to cost and availability, DLCO testing is not widely performed in lung cancer patients.

However, based on the Peer Reviewer comments, we acknowledge that this might be a limitation of this study, thus, we have now clarified this in the Limitation section.

Changes in the text: Discussion, "Limitation": "Fourth, since the patients did not undergo diffusing capacity of lung for carbon monoxide (DLCO) testing, this might have affected the evaluation of lung cancer combined with emphysema." (please view the Yellow highlight, lines: 454-457)

Minor flaws

Comment 1. The insisted difference between reference to chinese studies and "foreign" (.....) studies is untenable. The Authors should make a more equilibrated mention of prior studies, maybe indicating the other countries in which the study was performed, or, better, avoiding to outline the geographical location of the studies.

Reply: We agree with the Peer Reviewer. We have now revised the whole text for such issues and abstained from using terms such as "domestic, abroad, foreign".

Changes in the text: We have deleted such terms from the Introduction and Discussion.

Comment 2. The graphic representation in Fig. 2 of the relationship between awareness of COPD and inhalation therapy is a bit strange and not essential.

Reply: We have cross-checked with the other authors of this study, and after discussion, we still believe that this is quite an innovative approach of showing these data in a more

appealing way to the readers compared to conventionally used bar charts or histograms. However, if the Peer Reviewer insists and the Editors believe that this figure is not suitable for publication, we could consider revising it. Hope the Peer Reviewer can understand. Thank you very much in advance.

Reviewer C

The authors reported a retrospective study of 3,578 lung cancer patients hospitalized at a single center's department of Respiratory and Critical Care Medicine and Thoracic Surgery from January 2019 to December 2020. The main finding of the study is that COPD is remarkably underdiagnosed and undertreated among lung cancer patients. The rate of COPD diagnosis and treatment for lung cancer patients is higher in the department of Respiratory and Critical Care Medicine than the Thoracic Surgery department. Furthermore, a discharge diagnosis of COPD can increase the rate of inhalation treatment and awareness of COPD condition in lung cancer patients.

Comment 1. Firstly, the introduction requires more background information and context regarding the research question. The novelty of the article may be limited, as previous studies have also reported the underdiagnosis and undertreatment of COPD in lung cancer patients. For example, a study published in *Respirology* in 2013 (doi: 10.1111/j.1440-1843.2012.02282.x) that is cited by the authors reached similar conclusions.

Reply: We thank the Peer Reviewer for this comment, which has made us reassess this whole study.

(1) We have almost entirely revised the Introduction section and, specifically, added more context regarding the research question.

(2) In regard to the novelty of this study, we have now more clearly described the limitations in existing literature in the Introduction section (Changes in the text: please view the Yellow highlight "However, current data on the status of COPD management in LC patients are limited, as previous studies primarily focused on LC patients undergoing thoracic surgery or those with early-stage non-small cell LC (17,19), thus paid less attention to the coexisting COPD condition. In addition, most of the existing literature did not elaborately assess and compare the screening, management and follow-up of COPD in LC patients treated in surgical and non-surgical wards.", lines: 127-133)

(3) Our present study is quite different from existing literature, and specifically, compared to the mentioned study (doi: 10.1111/j.1440-1843.2012.02282.x): (i) the authors themselves mentioned in their published work that "Data on the current status of COPD management in patients with lung cancer remains limited", and despite that their study was performed in 2013, till present there is not enough data and awareness on this topic is still highly needed; (ii) our study assessed the rate of screening of COPD among all LC cases treated at our hospital during this period of time; (iii) we assessed the drugs and regimen used in these COPD LC patients; and (iv) most importantly, we compared the screening, management and follow-up of COPD in LC patients treated in

the Department of Respiratory and Critical Care Medicine (non-surgical ward) versus the Department of Thoracic Surgery (surgical ward), as well as assessing the screening and prevalence of COPD.

Changes in the text: As described above in (2), thank you.

The authors need to explain the novelty of the study, which is the fundamental problem of the study

Reply: Indeed, thank you again for this comment. We have addressed the issue in the just-above responses (2) and (3)

Changes in the text: As described above in (2) and (3), thank you.

Comment 2. In the methods section, the authors should provide more detailed information on the inclusion and exclusion criteria. Particularly, for the 300 patients that were followed up, there is no information about them.

Reply: Thank you very much for these comments.

(1) We have now clarified the inclusion and exclusion criteria of this study. Methods, section Patient selection: “The study inclusion criteria were: (1) patients with primary bronchopulmonary carcinoma confirmed by histopathology or cytopathology;(4) primary diagnosis of other diseases, such as the heart (i.e., congestive heart failure), lungs (i.e., active pulmonary tuberculosis), and others that may affect patients' lung function (i.e., abnormalities in large airways).”(lines: 150-161).

(2) In addition, we did not specifically select 300 patients from the 690 assessed spirometry-diagnosed COPD; in fact, the study authors tried individually to follow up all the 690 patients but 285 of them had died and 105 could not be contacted. We have now clarified these in the Results as well.

a) Method, section Follow-up.

Changes in the text: “The LC patients with COPD undergo long-term follow-up every 3 months in our hospital. In this study, we followed up all the included spirometry-defined COPD LC patients until September 2022 to obtain information about whether they were aware of their underlying COPD condition (referred to as COPD awareness in this study) and adherence to COPD inhalation therapy after discharge. The longest follow-up time was 46 months.” (please view the Yellow highlight, lines: 211-216)

b) Results, section Awareness of COPD and adherence to inhaled therapy

Changes in the text: “Follow-up was performed for all the 690 spirometry-defined COPD patients; however, only 300 were successfully contacted because 285 had died and 105 were lost to follow-up and their contacted patients' relatives could not provide accurate follow-up information.”(lines 303-306).

Comment 3. Line 157: Could you please clarify whether the data collected in this study includes information on COPD treatment?

Reply: We thank the Peer Reviewer for this comment. We have now added that we also retrieved data about COPD treatment in Methods, section Data collection,

Changes in the text: “COPD-related treatment” (please view the Yellow highlight, lines:

175-176)

Comment 4. Line 174: Since the longest follow-up is 46 months, it may be worthwhile to conduct an analysis of the survival rates of the patients and to perform a Kaplan-Meier analysis of the influencing factors.

Reply: Indeed, we agree with the Peer Reviewer that survival rate analysis would be useful, however, since there are already literature on this topic, adding such would not improve the novelty of this study. Although the longest follow-up was 46 months, most patients have much shorter follow-up, we are waiting for data maturity for survival analysis as we want to conduct a 5-year survival assessment for these patients in our future studies.

Thus, due to the low proportion of these patients receiving clinical outcomes during the follow-up stage and the lack of data maturity, we are currently unable to conduct in-depth analysis of survival. We will continue to follow up and conduct further in-depth analysis when the data is mature.

Comment 5. In the results section, the descriptions should be clearer, and the subtitles should be accurate to avoid any possible misunderstandings. Additionally, there are too many tables, and some of them can be presented as graphics to give a better impression and make the results easier to understand. To improve the novelty of the study, I suggest adding survival analysis to provide new information.

Reply: We thank the Peer Reviewer for this comment. In regard to cancer outcomes, we are thankful to the Peer Reviewer's comments. However, due to the low proportion of these patients receiving clinical outcomes during the follow-up stage and the lack of data maturity, we are currently unable to conduct in-depth analysis of survival. We will continue to follow up and conduct further in-depth analysis when the data is mature.

In regard to the tables, we have deleted tables 3 and 7 and directly mentioned their corresponding data in the text. Changes in the text:

a) Results, section COPD inhalation treatment [lines: 290-300]: "As shown in Table 5, ... dual bronchodilator therapy (LAMA/LABA) was the least commonly used (37/312, 11.9%)."

b) Results, section Documentation of COPD diagnosis in LC patients at discharge [lines: 267-275]: "Of the 2,762 LC patients who underwent spirometry....suggesting that doctors in the non-surgical ward paid significantly more attention to the underlying COPD condition than those in the surgical ward.").

However, since Tables 5 and 6 contain important statistical data that cannot be converted into figures, we still suggest keeping these tables as their presented data are quite relevant to the study findings and conclusions. We thank the Peer Reviewer in advance for understanding.

Comment 6. Line 206: The title "Patient characteristics in the LC+COPD group" may not be appropriate, as it also mentions the lung cancer group. If your aim is to highlight the paper on COPD, please rewrite it.

Reply: We thank the Peer Reviewer for this important suggestion. We have double-

checked and revised all the subtitles of the Results section, restructured the whole Results section and made sure that the current subtitles are specific and more appropriate.

Changes in the text: All subtitles in the Results section (please view the Yellow highlighted subtitles).

Comment 7. Line 249: Could you please clarify the difference in missed diagnosis of COPD between the Department of Respiratory and Critical Care Medicine and the Thoracic Surgery department? Please ensure that Respiratory Medicine refers to Respiratory and Critical Care Medicine to avoid any misunderstandings.

Reply: We thank the Peer Reviewer for this comment.

First, we have provided a definition of "missed diagnosis" in the text (Changes in the text: Results, section Missed COPD diagnosis in LC patients at discharge, lines: 278-281): "Although COPD was confirmed in 690 patients by spirometry, patients who did not have COPD recorded in their hospital discharge diagnosis (i.e., LC only as discharge diagnosis rather than LC and COPD) were considered as missed COPD diagnosis in this study."

Second, we have clarified the rates in subsequent sentences as " Further, the missed COPD diagnosis rate in the Department of Respiratory and Critical Care Medicine was significantly lower than that in the Department of Thoracic Surgery (30.9% vs. 92.5%, χ^2 , 244.370, $P < 0.001$). [Changes in the text: please view the Yellow highlight, lines: 282-284]".

Third, we have revised Figure 1 and clarified all important rates differences between the two departments. Lastly, we have made sure to only use "Department of Respiratory and Critical Care Medicine" in the whole text to avoid any misunderstandings.

Comment 8. Line 269: What's the selection criteria used for the 300 patients to be followed up?

Reply: Thank you very much for these comments.

(1) We have now clarified the inclusion and exclusion criteria of this study. Methods, section Patient selection: "The study inclusion criteria were: (1) patients with primary bronchopulmonary carcinoma confirmed by histopathology or cytopathology; ... (4) primary diagnosis of other diseases, such as the heart (i.e., congestive heart failure), lungs (i.e., active pulmonary tuberculosis), and others that may affect patients' lung function (i.e., abnormalities in large airways)." (lines: 150-161).

(2) In addition, we did not specifically select 300 patients from the 690 assessed spirometry-diagnosed COPD; in fact, the study authors tried individually to follow up all the 690 patients but found that 285 of them had died and 105 could not be contacted. We have now clarified these in the Results as well.

c) Method, section Follow-up.

Changes in the text: "The LC patients with COPD undergo long-term follow-up every 3 months in our hospital. In this study, we followed up all the included spirometry-defined COPD LC patients until September 2022 to obtain information about whether they were aware of their underlying COPD condition (referred to as COPD awareness

in this study) and adherence to COPD inhalation therapy after discharge. The longest follow-up time was 46 months.” (please view the Yellow highlight, lines: 211-216)

d) Results, section Awareness of COPD and adherence to inhaled therapy

Changes in the text: “Follow-up was performed for all the 690 spirometry-defined COPD patients; however, only 300 were successfully contacted because 285 had died and 105 were lost to follow-up and their contacted patients' relatives could not provide accurate follow-up information.”(lines 303-306).

Comment 9. Tables 3, 5, 6, and 7 could be presented as graphics.

Reply: We thank the Peer Reviewer for this comment. We believe the Peer Reviewer intended meaning is that the no. of tables in this work seems too much. In this regard, we have deleted tables 3 and 7 and directly mentioned their corresponding data in the text. Changes in the text:

a) Results, section COPD inhalation treatment [lines: 290-300]: “As shown in Table 5, ... dual bronchodilator therapy (LAMA/LABA) was the least commonly used (37/312, 11.9%).”

b) Results, section Documentation of COPD diagnosis in LC patients at discharge [lines: 267-275]: “Of the 2,762 LC patients who underwent spirometry....suggesting that doctors in the non-surgical ward paid significantly more attention to the underlying COPD condition than those in the surgical ward.”).

However, since Tables 5 and 6 contain important statistical data that cannot be converted into figures, we still suggest keeping these tables as their presented data are quite relevant to the study findings and conclusions. We thank the Peer Reviewer in advance for understanding.

Comment 10. The tables should be presented in 3-line tables, as per the examples in the Author Instruction of the journal.

Reply: We are grateful to the Peer Reviewer for this comment. However, in the PDF that the Peer Reviewer obtain, the tables do not contain 3 line spacing, however, in the Word version of the manuscript, all tables are in the 3 line spacing format.

Comment 11. In the discussion section, the authors should provide a more in-depth interpretation of their results in the context of the current state of research. Specifically, the authors should explain how their findings contribute to our understanding of the topic and identify any areas for future research.

Reply: We thank the Peer Reviewer for this comment. We have revised the whole Discussion and provided more important context. Also, we clarified how these findings could contribute to our understanding and impact clinical practice in the future.

Changes in the text: Major revision was performed in this whole text. Due to the large modification range, it is not possible to label the specific location.

Minor points:

1. Line 70: "call for" instead of "Call for."

Reply: We thank the Peer Reviewer for this comment. We have now deleted this word

from the text.

2. Lines 84-87: The idea is repeated here. Consider revising to avoid redundancy.

Reply: We have revised the whole text and avoided repeated descriptions to avoid redundancy, where applicable.

Changes in the text: Whole manuscript.

3. Line 99: Delete the space after "alveoli."

Reply: We thank the Peer Reviewer for this comment. We have now deleted this space from the text.

Changes in the text: Introduction, line 105: "chronic inflammation of the alveoli, caused by..."

4. In some parts, "FEV1" is written as "FEV1," and in other parts as "FEV1." Be consistent throughout the manuscript.

Reply: We apologize for this issue. We have now revised all to "FEV1" to maintain consistency throughout the whole text.

Changes in the text: Whole manuscript.

5. Line 238: Delete the period.

Reply: We thank the Peer Reviewer for this comment. We have now deleted the period throughout the whole text where not needed.

6. Line 405: Delete the word "due."

Reply: We have rewritten the whole Conclusion section and omitted this word.

Changes in the text: Conclusion: "Our study highlights the feasibility of screening for and treating COPD in LC patients ...to improve their treatment outcomes, quality of life and prognosis by more accurate and timely diagnosing COPD in LC patients and implementing appropriate treatment." (please view the Yellow highlight, lines: 460-466).

7. Line 592: Use Roman numerals for GOLD stage.

Reply: We have double checked the whole text and tables and used Roman numerals for GOLD stage

Changes in the text: Whole text and tables.

8. Lastly, the authors should thoroughly review the manuscript for grammatical errors and formatting issues that detract from the overall quality of the manuscript.

Reply: We thank the Peer Reviewer for all these great and instructive comments. We apologize for these issues. We have had this manuscript revised by a native English speaker, and we have double-checked that all the written text is understandable and clear.

Changes in the text: Major English writing revision was performed in this whole submission.

Authors should pay attention to correct spelling throughout the manuscript. Errors such as "Lung" (line 50), "Smoking" (line 157), "Spirometry," "Contents" (line 160), "Least" (line 265), and others should be avoided.

Reply: We thank the Peer Reviewer for these suggestions and apologize for these issues. We have double-checked these and all related issues in the whole text.

Changes in the text: Major English writing revision was performed in this whole submission.

Reviewer D

The topic of COPD and lung cancer has been studied in multiple dimensions before. The advantage of this study is the large number of patients looked at and the study of COPD treatment rates in lung cancer patients. The authors investigate a topic with potential quality of life and prognosis implications on patients diagnosed with lung cancer.

Overall, the theme of the paper is easy to understand. However, I recommend the following:

Comment 1. Revise the paper for language. You can use an editing service to check for language accuracy or have the paper checked by a native English-speaking colleague.

Reply: We thank the Peer Reviewer for all these great and instructive comments. We apologize for these issues. We have had this manuscript revised by a native English speaker, and we have double-checked that all the written text is understandable and clear.

Changes in the text: Major English writing revision was performed in this whole submission.

Comment 2. The authors should clarify what the admission indications for the patients admitted to the two departments were. I assume patients were admitted to Thoracic Surgery for the purpose of lung cancer surgery. The indication of admission to Respiratory and Critical Care is less clear.

Reply: We have now clarified the inclusion and exclusion criteria of this study. However, the main criteria for inclusion were confirmed and accurately staged lung cancer and no specific indications were used for differentiating patient selection between these two departments to make this study applicable to real-world scenarios.

Changes in the text: Methods, section Patient selection: "The study inclusion criteria were: (1) patients with primary bronchopulmonary carcinoma confirmed by histopathology or cytopathology; ... (4) primary diagnosis of other diseases, such as the heart (i.e., congestive heart failure), lungs (i.e., active pulmonary tuberculosis), and others that may affect patients' lung function (i.e., abnormalities in large airways)." (lines: 150-161).

Comment 3. The authors use the term "COPD airway management" or "airway

management" at several points in the paper. I recommend to simplify it to "COPD management" or "management". Airway management is a term that is typically used for upper airway management in emergencies or elective procedures.

Reply: Thank you very much for this comment. We have now revised to COPD management in the whole text.

Changes in the text: Whole text.

Comment 4. Was the 3-monthly telephone follow-up done prospectively starting in 2019? If yes, the authors should mention this more explicitly.

Reply: We thank the Peer Reviewer for this comment. We apologize for this confusion. We have provided clearer details about the follow-up of the 300 patients in the Method section.

a) Method, section Follow-up

Changes in the text: "The LC patients with COPD undergo long-term follow-up every 3 months in our hospital. In this study, we followed up all the included spirometry-defined COPD LC patients until September 2022 to obtain information about whether they were aware of their underlying COPD condition (referred to as COPD awareness in this study) and adherence to COPD inhalation therapy after discharge. The longest follow-up time was 46 months." (please view the Yellow highlight, lines: 211-216)

b) Results, section Awareness of COPD and adherence to inhaled therapy

Changes in the text: "Follow-up was performed for all the 690 spirometry-defined COPD patients; however, only 300 were successfully contacted because 285 had died and 105 were lost to follow-up and their contacted patients' relatives could not provide accurate follow-up information."(lines 303-306).

Comment 5. Line #190: "We performed to determine whether awareness of COPD differed between discharge diagnosis of COPD or not the diagnosis of COPD" should be rewritten for clarity.

Reply: We apologize for this issue. We have now revised to "In addition, we determined the difference in COPD awareness between patients with and without a COPD diagnosis at discharge."

Changes in the text: Method, section Statistical analysis, please view the Yellow highlight, lines: 224-226.

Comment 6. Line #200: Was the spirometry done in the inpatient for all the patients? Or was it done in the outpatient for the Respiratory and Critical Care patients? Typically, spirometry is not performed inpatient if patients are admitted for COPD exacerbation. Again, authors should clarify reason for admission to the Respiratory department. If the spirometry was done in the setting of recent COPD exacerbation, it would affect the severity of COPD as determined by the spirometry.

Reply: Thank you for this comment. This study included lung cancer patients. All patients were admitted to the hospital for diagnosis and treatment of lung cancer, and lung function tests were conducted after admission. Patients with acute exacerbation of COPD were not included.

Comment 7. Line # 230: Of the 369 undiagnosed, how many were respiratory medicine and how many were thoracic surgery patients? Although we can guess that more undiagnosed were thoracic surgery patients, it would be better to have the numbers.

Reply: We thank the Peer Reviewer for this comment.

First, we have provided a definition of "missed diagnosis" in the text (Changes in the text: Results, section Missed COPD diagnosis in LC patients at discharge, lines: 278-281): "Although COPD was confirmed in 690 patients by spirometry, patients who did not have COPD recorded in their hospital discharge diagnosis (i.e., LC only as discharge diagnosis rather than LC and COPD) were considered as missed COPD diagnosis in this study."

Second, we have clarified the rates in subsequent sentences as " Further, the missed COPD diagnosis rate in the Department of Respiratory and Critical Care Medicine was significantly lower than that in the Department of Thoracic Surgery (30.9% vs. 92.5%, χ^2 , 244.370, $P < 0.001$). [Changes in the text: please view the Yellow highlight, lines: 282-284]".

Third, we have revised Figure 1 and clarified all important rates differences between the two departments. Lastly, we have made sure to only use "Department of Respiratory and Critical Care Medicine" in the whole text to avoid any misunderstandings.

Comment 8. Line # 245 can be explained under discussion to say that this is likely due to the fact that patients admitted under thoracic were resectable/curable due to earlier stages.

Reply: We thank the Peer Reviewer for this comment. Among LC+ COPD patients in Respiratory Medicine group, the LC clinical stage and COPD GOLD stage were significantly later than those of the Thoracic Surgery 247 group ($P < 0.05$). In addition, We have provided some potential explanations and solutions in the Discussion section. Changes in the text: Several location in Discussion, but specifically at:

- Lines 352-359: "COPD may be undiagnosed in LC populations due to the following reasons: (1) the COPD symptoms might be mistakenly regarded as cancer presentations(36); (2) the primary treatment priority in LC patients is to treat the underlying cancer condition, which may have a greater threat to the patient's survival, leading to a lack of attention towards COPD management; (3) LC patients may have multiple coexisting conditions that can complicate the diagnosis and treatment of COPD; and (4) some surgeons may not always be aware of the high prevalence of COPD in LC patients, and may not have the necessary knowledge and training to diagnose and treat COPD appropriately."

- Lines 379-381: "The higher screening rate for COPD in the Department of Thoracic Surgery may be attributed to the preoperative routine lung function tests required for thoracic surgery.

- Lines 429-443: "Based on our study results, we propose that the following steps could be taken in the future to improve the diagnosis and treatment of COPD in LC patients: (1) more emphasis should be placed on Healthcare providers should take steps such as routine screening, increasing awareness and education about COPD, improving communication between departments and specialties, and providing access

to specialized pulmonary care.”

Comment 9. Line # 328: "reduce the effect of cancer therapy" is an incorrect statement to make. While unmanaged COPD in lung cancer patients has been associated with worse outcomes, it is likely due to the health effects of COPD itself, rather than COPD acting on the cancer therapy to make it less effective, as we do not have any literature to support the latter. If that was not the intention to say, rewrite for clarity.

Reply: We thank the Peer Reviewer for this comment. We have deleted such descriptions from the Discussion to avoid confusion.

Comment 10. Line #356-358: Do the lung cancer patients themselves need to submit a request for bronchodilation or their physician needs to?

Reply: We apologize for this issue. We have now revised to "patients with LC should undergo a bronchodilation test in addition to routine pulmonary function measurement after admission." In the Discussion, lines: 384-386.

Comment 11. Line #385: "were necessary for patients to whether known with COPD". Rewrite as hard to understand what the authors are trying to convey

Reply: We apologize for such an issue. We have deleted this description from the Discussion section

Comment 12. One of the shortcomings of the study also is that prognosis or even quality of life (QOL) assessment was not checked on follow up. That would have made the study more comprehensive. The importance of studying this topic lies in the effects on QOL and prognosis.

Reply: Indeed, we agree with the Peer Reviewer that survival rate analysis would be useful, however, since there are already literature on this topic, adding such would not improve the novelty of this study. Although the longest follow-up was 46 months, most patients have much shorter follow-up, we are waiting for data maturity for survival analysis as we want to conduct a 5-year survival assessment for these patients in our future studies.

Thus, due to the low proportion of these patients receiving clinical outcomes during the follow-up stage and the lack of data maturity, we are currently unable to conduct in-depth analysis of survival. We will continue to follow up and conduct further in-depth analysis when the data is mature.

Comment 13. Line #406-408: "The respiratory physicians and thoracic surgeons jointly discussed the development of airway disease management programs for LC patients to improve the prognosis of LC+COPD patients" - this has been written in past tense. Rewrite.

Reply: We have rewritten the whole Conclusion section and omitted this word.

Changes in the text: Conclusion: “Our study highlights the feasibility of screening for and treating COPD in LC patients ...to improve their treatment outcomes, quality of life and prognosis by more accurate and timely diagnosing COPD in LC patients and

implementing appropriate treatment.” (please view the Yellow highlight, lines: 460-466).

Comment 14. Lastly, do the authors have any explanation for why so many of the patients discharged from the Respiratory department were left undiagnosed or untreated? Although the numbers for diagnosis and treatment are better for Respiratory medicine than Thoracic surgery, one would expect these to be even better. Were there any patient related factors involved? For thoracic surgery, it may be an awareness issue and I agree with the proposal to involve respiratory physicians to make recommendations on COPD management.

Reply: We thank the Peer Reviewer for this very good comment. We have provided some potential explanations and solutions in the Discussion section.

Changes in the text: Several location in Discussion, but specifically at:

- Lines 352-359: “COPD may be undiagnosed in LC populations due to the following reasons: (1) the COPD symptoms might be mistakenly regarded as cancer presentations(36); (2) the primary treatment priority in LC patients is to treat the underlying cancer condition, which may have a greater threat to the patient's survival, leading to a lack of attention towards COPD management; (3) LC patients may have multiple coexisting conditions that can complicate the diagnosis and treatment of COPD; and (4) some surgeons may not always be aware of the high prevalence of COPD in LC patients, and may not have the necessary knowledge and training to diagnose and treat COPD appropriately.”
- Lines 379-381: “The higher screening rate for COPD in the Department of Thoracic Surgery may be attributed to the preoperative routine lung function tests required for thoracic surgery.”
- Lines 429-443: “Based on our study results, we propose that the following steps could be taken in the future to improve the diagnosis and treatment of COPD in LC patients: (1) more emphasis should be placed on healthcare providers should take steps such as routine screening, increasing awareness and education about COPD, improving communication between departments and specialties, and providing access to specialized pulmonary care.”