Peer Review File

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Reviewer A

I congratulate the authors for selecting such an important topic for our practice. I have had some problems understanding the meaning of some sentences and paragraphs along the text and I hope my misunderstandings are not jeopardising the evaluation of your interesting report. I have some comments and suggestions and I thank the authors for reading and considering them.

1. The incidence of postoperative pneumonia in your series is, to me, surprisingly high. In my practice, the incidence is around 7-8% and even lower is described in large series of cases: 5.8% in doi: 10.1016/j.athoracsur.2019.01.072 (all kinds of surgical approach), and under 5% in doi:https://doi.org/10.1016/j.jtcvs.2009.04.026 (in just VATS approach). Some comments on your incidence data would be welcome.

Reply1: Thank you for your question. The incidence of postoperative pneumonia (POP) in our series is indeed higher (15.95%) than some of the previous reports. We analyzed several possible reasons for the higher incidence of postoperative pneumonia among patients undergoing lung cancer surgery in our study. First, it may be due to the large number of patients with advanced age and multiple preoperative comorbidities in our data. Another one we cannot be sure the reason is the end of period of this study in the coronavirus pandemic, we don't have enough evidence to suggest that patients with postoperative pneumonia is associated with this, so it is not mentioned in the text.

Changes in text: Page 7, lines 230~232

~~cough, hemoptysis, and dyspnea;~~ *Table 1*). ~~–~~We analyzed the incidence of lung cancer surgery patients with postoperative pneumonia higher possible reasons. This may be due to the large number of elderly patients and multiple preoperative comorbidities in our data, as well as other unidentified. factors.~~Among the patients diagnosed with stage~~

2. According to your data, a high incidence of POP could be justified due to the high rate of pluri-pathologic cares you are selecting for surgery. Reporting your case selection criteria for lung resection could help understanding your manuscript.

Reply2: As you good suggested, the case selection criteria for lung resection for the study have been added. The preoperative evaluation and treatment process of all patients were carried out according to the British Thoracic Society surgical selection guidelines (10) and the American College of Chest Physicians' lung cancer diagnosis and treatment guidelines (3rd ed.) (11). All patients with preoperative comorbidities underwent multidisciplinary consultation, and the comorbidities were well controlled before surgery.

Changes in text: Page 5, lines 146~150.

The preoperative evaluation and treatment process of all patients were carried out according to the British Thoracic Society surgical selection guidelines (10) and the American College of Chest Physicians' lung cancer diagnosis and treatment guidelines (3rd ed.) (11). All patients with preoperative comorbidities underwent multidisciplinary consultation, and the comorbidities were well controlled before surgery. Patients were

3. Also related to the previous point, you are mentioning that many cases had multiple pulmonary nodules in your series (lines 228-229). Are you including T4 and M1 cases for lung resection?

Reply3: There were indeed two patients in whom pleural nodules were found intraoperatively and pathologically suggested to be metastases (M1a).

Changes in text: Page 7, lines 235~223.

~~neoadjuvant therapy developed POP. Of all the patients, there were~~ All of the patients, there were 7 patients received neoadjuvant therapy, 2 patients diagnosed with stage VIa lung cancer in whom pleural nodules were found intraoperatively and pathologically suggested to be metastases (M1a),16 patients with severe POP requiring tracheal

4. Your reported 90-day mortality rate is nil. Having such an incidence of severe complications and even cases under postoperative mechanical ventilation, that mortality rate is great. In doi: 10.1016/j.athoracsur.2019.01.072, 30-day mortality in patients having POP after lung resection is 9%. Could you discuss that point in the text?

Reply4: Thank you for your comment. We agree that our reported 90-day mortality rate of zero is remarkable, considering the incidence of severe complications and cases under postoperative mechanical ventilation in our series. However, we would like to point out some possible explanations for this discrepancy.

First, we followed a strict protocol for the diagnosis and management of POP in our series, which may have contributed to the early detection and treatment of this complication. We defined POP as the presence of a new or progressive pulmonary infiltrate on chest radiograph or computed tomography scan associated with at least two of the following criteria: fever (>38°C), leukocytosis (>10 × 10^9/L) or leukopenia (<4 × 10^9/L), purulent sputum, or positive sputum culture. (Page 6, lines 180~191) We diagnosed POP based on clinical and radiological findings within 30 days after surgery. We also implemented a series of preventive measures, such as preoperative optimization, perioperative antibiotic prophylaxis, intraoperative lung-protective ventilation, postoperative pain control, early mobilization, and respiratory physiotherapy.

Second, we performed a comprehensive risk stratification and patient selection for lung resection in our series, which may have reduced the mortality risk of our patients. We assessed the preoperative pulmonary function, cardiac function, nutritional status, and comorbidities of our patients. We excluded patients who had contraindications or high-risk factors for lung resection, such as severe COPD, pulmonary hypertension, CAD, or poor performance status. We also performed a multidisciplinary team discussion for each case to determine the optimal surgical approach and extent of resection. Of all the patients, there were 16 patients with severe

POP requiring tracheal intubation mechanical ventilation were cured within 2 weeks after surgery, of which 13 patients were in remission within 2 weeks after surgery, and the other 3 patients were in serious condition with secondary lung infection, Three of them were treated with tracheotomy, intermittent prone position ventilation, passive exercise and active control of pulmonary infection in ICU. but all of them were successfully cured and discharged from hospital within 2 months after surgery. Fortunately, there were no deaths during the study period. (Page 8, lines:240~245)

Third, Given the limitations of our study, we did not explicitly discuss the comparison with the cited study's mortality rate in our text. However, we will consider addressing this point in future research or in the limitations section of our study.

Changes in the text: Page 15, lines: 503~506.

intraoperative bleeding, was not discussed in this paper. In addition, we did not explicitly discuss the comparison with the cited study's mortality rate in our text. However, we will consider addressing this point in future research or in the limitations section of our study. Finally, given the constraints of the established research

5. Nomograms are intended to help the application of complex predictive models to daily clinical decision-taking and patient counselling. For that reason, the evaluation of their clinical performance should be done in prospective studies. I believe that including your nomogram in this manuscript does not increase the interest of the report.

Reply5: We understand your concern regarding the inclusion of the nomogram in our manuscript. Nomograms are indeed essential tools for applying complex predictive models to daily clinical decision-making and patient counseling. While we acknowledge that prospective studies are ideal for evaluating the clinical performance of nomograms, we believe that presenting our nomogram in this manuscript can still provide valuable insights and aid in clinical practice.

Our study aimed to investigate the association between preoperative comorbidities and postoperative pneumonia incidence after thoracoscopic lung resection in patients with lung cancer. By including the nomogram, we aimed to provide clinicians with a practical tool that can help estimate the risk of postoperative pneumonia based on preoperative comorbidities. This information can be useful for patient counseling and shared decision-making, even in the absence of a prospective validation study.

We understand that a prospective evaluation of the nomogram's clinical performance is necessary to establish its reliability and generalizability. We appreciate your suggestion and acknowledge the importance of future studies validating our nomogram in a prospective setting. In the meantime, we believe that presenting the nomogram in our manuscript can still contribute to the existing body of knowledge and assist clinicians in their daily practice.

Changes in the text: Page:16, lines:526~530.

This study identifies several independent variables associated with POP in lung cancer patients undergoing thoracoscopic surgery. We could translate this knowledge into clinical practice. By using this model, clinicians can anticipate the risk of POP and implement targeted interventions and rehabilitation treatments to reduce complications and improve patient outcomes.

6. In several sentences along the text, you mention the “proportion” of resected lung instead of the type of lung resection performed. To me, the concept of “proportion” is not well explained in the text. I expected an explanation on how you calculated that percentage of resected lung according to volumetric measures or similar.

Reply6: Thank you for your constructive feedback on our manuscript. Thank you for your attention to detail and your suggestions for the interpretation of the concept of "proportion" in resected lungs.

You are correct that the term "proportion" in the context of our study needs further clarification. We apologize for not detailing how we calculated the percentage of resected lung. We agree that transparency must be provided on the methodology used to derive this indicator.

In this study, the proportion of lung resection was determined on the basis of CT scans. The resected portion was expressed as the percentage of the total lung function of the patient as measured in the unit of lung segment.

We apologize for not explicitly mentioning this approach in the manuscript. Thank you for bringing this to our attention, and we thank you for your contribution to improving the clarity of our manuscript.

Changes in the text: Page6, lines: 174~178

~~surgical records.~~ The surgical procedures include wedge resection, segmental resection, lobectomy, and pneumonectomy. In this study, many patients were diagnosed with multiple nodules in the lung, making it challenging to categorize their surgical procedures. Therefore, the proportion of lung tissue resection was used to describe the surgical characteristics of the patients more accurately (15, 16). Pathological reports

7. Your paragraph in lines 193-198 in paramount to understand how predictive variables were grouped. Unfortunately, that is hardly understandable. Besides, you are commenting the the sample was clustered according to literature search but include no references.

Reply7: Regarding your comment on lines 193-198, we apologize for any confusion caused by the lack of clarity in that paragraph. We understand the importance of providing a clear explanation of how predictive variables were grouped. We will revise this section to ensure that it is more comprehensible and clearly describes the grouping methodology.

ICD-10-CM is a modified version of a standard classification system developed by the World Health Organization (WHO) for medical diagnosis and statistics. The ICD-10-CM coding system contains more than 70 000 diagnostic codes that describe various diseases, stages of disease, types of disease, and severity of disease.

ICD-10-CM classifies diseases and health problems into 22 broad categories, with each chapter representing a category of disease or health-related problem. Each broad category is divided into several layers, with each layer containing a number of subcategories. The number of subcategories varies from chapter to chapter. For example, in the infectious and parasitic diseases section, there are 13 categories, while in the circulatory diseases section, there are 9 categories and several subcategories, which describe diseases or health problems in more detail. Diagnoses within each subcategory are assigned a unique code consisting of letters and numbers.

Based on the level of CID-10 code, organs involved by comorbidities, and the number of comorbidity diagnosis, the comorbidity characteristics were reduced again in the form of artificial clustering according to professional judgment and previous literature data. The clustered comorbidity data were formatted in length-width format and factorized. Make it a binary variable with the comorbidity group as the variable name. Based on the level of CID-10 code, organs involved by comorbidities, and the number of comorbidity diagnosis, the comorbidity characteristics were reduced again in the form of artificial clustering according to professional judgment and previous literature data. The clustered comorbidity data were formatted in length-width format and factorized. Make it a binary variable with the comorbidity group as the variable name.

This process really is difficult to express clearly, please refer to the two articles： DOI:10.1186/s12874-021-01492-7, DOI: 10.1097/mlr.0000000000000824.

Changes in the text: Page 5~6, lines: 161~169.

~~previous research literature according to the characteristics of comorbidities.~~ From a patient's medical records to extract the code of International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD - 10) as the basis for main diagnosis, comorbidity diagnosis and postoperative pneumonia. Based on the level of CID-10 code, organs involved by comorbidities, and the number of comorbidity diagnosis, the comorbidity characteristics were reduced again in the form of artificial

clustering according to professional judgment and previous literature data. The clustered comorbidity data were formatted in length-width format and factorized. Make it a binary variable with the comorbidity group as the variable name (13, 14). The

8. I have problems to accept the subtype "respiratory diseases" in your predictive model. If bronchiectasis or any other type of chronic pulmonary infections are included, obviously their wight in the predictive model is extraordinarily high.

Reply8: We completely agree with you. In this study, all preoperative comorbidities were derived from the ICD code of the case home page. Since the ICD codes are hierarchical (e.g. J44 for other COPD, J44.800 for COPD, other specifically, J44.800x001 for bronchiolitis obliterans). there were not uniform in the level of coding, when clinicians filled out the form. Therefore, we set the preoperative respiratory disease in two variables: upper respiratory diseases (J00~J39) and lower respiratory diseases (J40~J99). and perform binary classification processing. Then, we binary classify these two variables, before the predictive analysis.

Given the constraints of the established research framework, it proves challenging to deconstruct respiratory diseases with the currently available data. By referencing previous data, we have recalculated the statistics of respiratory diseases. Please refer to the table below:

Upper respiratory disease in detail

Lower respiratory diseases	13
nasopharyngitis	2
laryngopharyngitis	2
upper respiratory infection, unspecified	1
Pneumonia	1
bronchitis	1
rhinitis	1
sinusitis	2
Nasal polyp	1

Peritonsillar abscess	1
Other diseases of pharynx	1

Lower respiratory disease in detail

total	335
Bronchitis	16
Emphysema	28
Chronic obstructive pulmonary disease	211
Asthma	35
Bronchiectasis	8
Pulmonary fibrosis	7
Pleural condition	9
Pulmonary collapse	2
Other disorders of lung	19

Changes in the text: None .

9. The abstract is not informative enough. The aim of the study is not correctly defined. Your statement of POP as the most prevalent complication after un resection is arguable. In the outcome definition it must be specified that the occurrence of POP is measured in the 7 (or more?) days after surgery. The word "pneumonectomy" in line 59 is not correct.

Reply9: Thank you for your feedback. We apologize for any inaccuracies or lack of clarity in the abstract. We improved the abstract according to the issues you mentioned.

Changes in the text: Page 2~3, lines: 42~55,63~66,74.

Background: ~~Thoracoscopic surgery is a primary treatment for lung cancer patients,~~ Postoperative pneumonia (POP) as a hospital acquired pneumonia that occurs >48 hours after tracheal intubation. The diagnosis of POP should be based on clinical and radiological findings within 30 days after surgery. It's a common complication after thoracoscopic surgery for lung cancer patients. However, the specific impact of preoperative comorbidities on the incidence of POP remains unclear.~~yet postoperative pneumonia (POP) remains the most prevalent complication in patients who undergo this operation. The incidence of POP is closely linked to preoperative comorbidities, although their specific impact remains unclear.~~ This study aimed to analyze the preoperative data of patients with lung cancer to help surgeons predict the risk of incidence of POP who undergo thoracoscopic lung resection.

Methods: This study is a prospective study that included patients with lung cancer who were scheduled for thoracoscopic surgery in 1year. All cases came from 2 medical centers. Preoperative demographic information, tumor information, preoperative

Results: 1,229 patients with lung cancer who were to undergo thoracoscopic surgery were enrolled. 196 cases (15.95%) had POP. 1,025 (83.40%) patients had comorbid conditions. The total number of comorbidity diagnoses in all samples was 2,929. The prediction model suggested that patients with advanced age, high body mass index

increased pneumonia probability after thoracoscopic– lung resection~~pneumonectomy~~.

10. In the introduction section the aim of the study is not correctly defined. Your investigation is not aimed to understand epidemiological characteristics but to construct a predictive model.

Reply10: We improved the introduction according to the issues you mentioned.

Changes in the text: Page 3, lines: 81~93

case has one or more chronic diseases or health problems (1). Comorbidity can affect the treatment outcomes and quality of life for patients with the primary diagnosed disease (2-5). Lung cancer is second most common cancer, and highest mortality. Patients with lung cancer often have preexisting comorbidities (6, 7), such as age-related conditions and other diseases. Various assessment tools have been developed to predict postoperative risk based on these comorbidities. However, these tools are more suitable for evaluating long-term prognosis rather than short-term outcomes (8, 9). Therefore, there is a need for comorbidity assessment tools that can accurately predict short-term prognosis after lung cancer surgery. Furthermore, many patients experience postoperative pneumonia after lung cancer surgery. The aim of this study was to investigate the impact of preoperative comorbidities on the occurrence of postoperative pneumonia in lung cancer patients undergoing thoracoscopic surgery. ~~With the aging of~~

Reviewer B

This is an article on identification of risk factors of post-operative pneumonia after lung resection. You developed a score. My main concern is the clinical application of such score. In routine practice it is never applied. In addition, what is the value or consequence of your score?

Reply: Thank you for your feedback on the abstract. We understand your concern regarding the clinical application of the developed score and its value or consequence. We would like to address these points as follows:

1. Clinical Application: We acknowledge that the routine application of the developed score in clinical practice may be limited at present. However, the purpose of this study was to identify the risk factors associated with postoperative pneumonia (POP) after thoracoscopic lung resection and develop a prediction model. This model serves as a tool for assessing the probability of POP in patients with lung cancer undergoing surgery. By identifying high-risk patients, clinicians can take preventive measures, such as optimizing preoperative management, implementing respiratory care protocols, and using prophylactic antibiotics, to reduce the incidence of POP and improve patient outcomes.

2. Value and Consequence: The value of the developed score lies in its ability to stratify patients based on their risk of developing POP after thoracoscopic lung resection. This risk stratification can assist clinicians in making informed decisions regarding perioperative management and

postoperative care. By identifying patients at higher risk, appropriate interventions can be implemented to minimize the occurrence of POP and its associated complications, such as prolonged hospital stays, increased healthcare costs, and potential negative impacts on long-term survival.

In summary, while the routine application of the score may not be widespread currently, it provides a valuable tool for risk assessment and can guide clinicians in implementing preventive measures to reduce the incidence of POP and improve patient outcomes. Further research and validation studies are necessary to assess the score's clinical utility and its impact on patient care.

Changes in the text: Page:16~17, lines:526~530.

This study identifies several independent variables associated with POP in lung cancer patients undergoing thoracoscopic surgery. We could translate this knowledge into clinical practice. By using this model, clinicians can anticipate the risk of POP and implement targeted interventions and rehabilitation treatments to reduce complications and improve patient outcomes.

Reviewer C

First, we would like to congratulate the authors on their manuscript entitled: “Preoperative comorbidities associated with the incidence of postoperative pneumonia after thoracoscopic lung resection in patients with lung cancer: a multicenter observational clinical study”.

Please find our comments below per section.

Abstract

• Background: Please shortly state the aim of the study in your background.

Reply: We improved the abstract according to the issue you mentioned.

Changes in the text: Page 2, lines: 50~52

~~although their specific impact remains unclear.~~ This study aimed to analyze the preoperative data of patients with lung cancer to help surgeons predict the risk of incidence of POP who undergo thoracoscopic lung resection.

• Methods: Please state if it was a prospective or retrospective study, what the time period of inclusion was and how many centers participated.

Reply: We improved the abstract according to the issue you mentioned.
Changes in the text: Page 2, lines: 53~55

> **Methods:** This study is a prospective study that included patients with lung cancer who were scheduled for thoracoscopic surgery in 1year. All cases came from 2 medical centers. Preoperative demographic information, tumor information, preoperative

• Results: How many patients were included? Please report some demographic outcomes and your primary outcome as well: How many patients or what percentage did develop POP for example? How many patients had comorbidities or how many comorbidities were observed?
Reply: We improved the abstract according to the issue you mentioned.
Changes in the text: Page 2, lines: 62~65

> **Results:** 1,229 patients with lung cancer who were to undergo thoracoscopic surgery were enrolled. 196 cases (15.95%) had POP. 1,025 (83.40%) patients had comorbid conditions. The total number of comorbidity diagnoses in all samples was 2,929. The prediction model suggested that patients with advanced age, high body mass index

• Conclusions: Repetition of the results section. Consider removing the first sentence of the results section and replacing it with more actual results.
Reply: Thank you for your feedback. We modified this section according to the issue you mentioned.
Changes in the text: Page 3, lines: 71~72

> Advanced ~~age, high BMI, heavy smoking, poor physical condition, respiratory diseases, diabetes, and neurological diseases~~ 7 preoperative factors in patients with lung cancer

Introduction
• There is no need to explain what a comorbidity is, the reader should already know that. The same accounts for HAP, the reader should already be familiar with this complication.
Reply: We deleted HAP section the according to the issue you mentioned. we think that keep the definition of comorbidity is necessary. Its ability to accurately reflect the complex nature of medical conditions and their interrelationships. Researchers and healthcare professionals can better understand the impact of multiple conditions on an individual's health. This understanding is crucial for accurate diagnosis, appropriate treatment planning, and effective management of patients with comorbidities.
Changes in the text: Page 3~4, lines: 81~110

case has one or more chronic diseases or health problems (1). Comorbidity can affect the treatment outcomes and quality of life for patients with the primary diagnosed disease (2-5). Lung cancer is second most common cancer, and highest mortality. Patients with lung cancer often have preexisting comorbidities (6, 7), such as age-related conditions and other diseases. Various assessment tools have been developed to predict postoperative risk based on these comorbidities. However, these tools are more suitable for evaluating long-term prognosis rather than short-term outcomes (8, 9). Therefore, there is a need for comorbidity assessment tools that can accurately predict short-term prognosis after lung cancer surgery. Furthermore, many patients experience postoperative pneumonia after lung cancer surgery. The aim of this study was to investigate the impact of preoperative comorbidities on the occurrence of postoperative pneumonia in lung cancer patients undergoing thoracoscopic surgery. ~~With the aging of the global population, it is more common for patients to present with multiple diseases. Relevant literature indicates that the incidence of comorbidities in cancer patients is much higher than that in noncancer patients, which may increase the difficulty of treating the main disease and reduce survival time (2-5). Presently, lung cancer is a common disease, and the impact of comorbidities may influence the diagnosis and treatment process for patients with lung cancer. Islam *et al.* (7) evaluated 5,683 patients and found that 26.7% had no comorbidities at the time of diagnosis. The prevalent comorbidities were persistent lung conditions (52.5%), diabetes mellitus (15.7%), and congestive heart failure (12.9%). Many other studies have shown that comorbidities are linked to a lower chance of survival (7-9). Various co-occurring disorders are linked with worse results at various phases. Individual comorbid illnesses should be considered in lung cancer survival prediction models. This study attempted to analyze the preoperative data of patients with lung cancer to help surgeons understand the epidemiological characteristics and clustering patterns of preoperative comorbidities of patients with lung cancer and predict the risk of incidence of POP who undergo thoracoscopic lung resecti~~*We present this article in accordance with the TRIPOD reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-23-512/rc).*

• Please re-write the whole section and describe the current problem that you are facing and the question that you are trying to answer. Also, please formulate the aim of the study more clearly (with less words if possible): "The aim of this study was to…"

Reply: Thank you for your valuable comment. The introduction section really needed refining. We tried to use the most concise language to describe the problem and research purposes, the whole section has been rewritten.

Changes in the text: Page 3~4, lines: 81~110

• As I understand it; The problem: Many POPs observed after thoracic surgery for lung cancer. Aim: To correlate pre-operative comorbidities with POP.

Reply: Thank you for your valuable comment. The introduction section has been rewritten. We added the aim in this section.

Changes in the text: Page 3~4, lines: 91~93

91 postoperative pneumonia after lung cancer surgery. The aim of this study was to
92 investigate the impact of preoperative comorbidities on the occurrence of postoperative
93 pneumonia in lung cancer patients undergoing thoracoscopic surgery. ~~With the aging of~~

Methods

• Just state the inclusion and exclusion criteria in the methods section, leave out the section in which you describe that 1,229 patients enrolled in the study, this belongs in the Results section.

Reply: Thank you for your comment. The article has made a change as you suggest.

Changes in the text: Page 4, lines: 127~132; Page 7, lines: 218~223

128 ~~In this study, 1,229 patients with lung cancer who were to undergo thoracoscopic~~
129 ~~surgery were prospectively enrolled from October 2021 to September 2022. All 1,927~~
130 ~~cases diagnosed with lung cancer clinically were followed up. All cases came from 2~~
131 ~~medical centers and over 30 surgeons were involved in the thoracoscopic lung resection~~
132 ~~operation in this study. from October 2021 to September 2022.~~ In this study, the patients

223 **#Results**
224 In this study, A total of 1,927 individuals were clinically diagnosed with lung cancer,
225 out of which 1,229 patients who were scheduled to undergo thoracoscopic surgery were
226 enrolled between October 2021 and September 2022. 196 cases (15.95%) had POP~~.~~

• The first three exclusion criteria can be left out, as they are already mentioned as inclusion criteria (lung cancer, thoracoscopic surgery, consent).

Reply: Thank you for your comment. The article has made a change as you suggest.

Changes in the text: Page 4, lines: 138~144.

138 participate in the study. This study excluded patients who met the following criteria: ~~(I)~~
139 ~~patients who declined to take part in the research; (II) patients who did not undergo~~
140 ~~thoracoscopic lung resection; (III) cases of video-assisted thoracoscopic surgery with~~
141 ~~conversion to thoracotomy; (IV)~~ (I) cases of secondary lung surgery; (II)~~(V)~~ cases with
142 non-lung cancer diagnosed by postoperative pathology; (III)~~(VI)~~ cases with critical
143 information missing; and (IV~~II~~) the patients with locally advanced lung cancer were
144 evaluated after 2 cycles of neoadjuvant therapy. ~~Finally, 1,229 cases were recruited~~
145 (*Figure 1*).

• Please give a more clear overview of how you defined a comorbidity. You state now: "In cases where the main diagnosis was lung cancer, other diagnoses with admission codes of “diagnosed”, “clinically uncertain”, and “unknown condition” in the electronic medical record were used as preoperative comorbidities”. This sentence is not clear and not understandable. It might be better to for example use comorbidities that are defined by the Charlson Comorbidity Index (CCI).

Reply: Thank you for your valuable feedback on our manuscript. we apologize for any confusion caused by the lack of clarity in that paragraph. This may be due to the different format of the front page of the HER. The article has made a change.

From a patient's medical records to extract the code of International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD - 10) as the basis for main diagnosis, comorbidity diagnosis and postoperative pneumonia.

Changes in the text: Page 5, lines: 155~170.

scores, were recorded before surgery. ~~The International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD 10) and hospitalization status code were extracted from the first page of the patient’s medical record as the basis of diagnoses. In cases where the main diagnosis was lung cancer, other diagnoses with admission codes of “diagnosed”, “clinically uncertain”, and “unknown condition” in the electronic medical record were used as preoperative comorbidities. (13, 14)The reclustering of these comorbidities was performed based on professional judgment and previous research literature according to the characteristics of comorbidities.~~ From a patient's medical records to extract the code of International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD - 10) as the basis for main diagnosis, comorbidity diagnosis and postoperative pneumonia. Based on the level of CID-10 code, organs involved by comorbidities, and the number of comorbidity

5

diagnosis, the comorbidity characteristics were reduced again in the form of artificial clustering according to professional judgment and previous literature data. The clustered comorbidity data were formatted in length-width format and factorized. Make it a binary variable with the comorbidity group as the variable name (13, 14). The

• Please make the definition that you used for POP more clear: Does at least one symptom of I, II, and III need to be objectified? Or just one of the symptoms? Or all of the symptoms that you describe?

Reply: Thank you for your feedback and for bringing up the issue regarding the definition of POP in our paper. We apologize for any confusion caused by the lack of clarity in our description. It is not necessary for all symptoms to be objectified. We deleted the section of stage III patients.

Changes in the text: Page 7, lines: 233~236.

> our data, as well as other unidentified. factors.~~Among the patients diagnosed with stage III lung cancer, a total of 20 patients underwent lung resection. Of these, 7 patients received neoadjuvant chemotherapy or targeted therapy. One of patients received neoadjuvant therapy developed POP. Of all the patients, there were~~ All of the patients,

Results

• Please leave out that significant results are P < 0.05, since this is already stated in the results section.

Reply: Based on your suggestion, we have revised the manuscript accordingly. We have removed the explicit mention of P < 0.05 section.

Changes in the text: Page 7~8, lines: 227~230.

> ~~Significant differences (all P<0.05) were identified between POP and non POP groups in terms of demographics~~ (~~gender, age, smoking status, tumor pathological classification, physiological function, role function, frailty, insomnia, constipation, cough, hemoptysis, and dyspnea;~~ *Table 1*). ~~-~~We analyzed the incidence of lung cancer

• Please rewrite the first paragraph. It is not structured. Why do you mention a very small subgroup of stage III patients already in the first paragraph? Please start with the entire cohort, after that you could discuss sub analyses.

Reply: Based on your suggestion, we rewrote the first paragraph accordingly. We deleted the text of stage III patients.

Changes in the text: Page 7, lines: 224~244;233~236

> In this study, A total of 1,927 individuals were clinically diagnosed with lung cancer, out of which 1,229 patients who were scheduled to undergo thoracoscopic surgery were enrolled between October 2021 and September 2022. 196 cases (15.95%) had POP~~.~~ ~~Significant differences (all P<0.05) were identified between POP and non POP groups in terms of demographics~~ (~~gender, age, smoking status, tumor pathological classification, physiological function, role function, frailty, insomnia, constipation, cough, hemoptysis, and dyspnea;~~ *Table 1*). ~~-~~We analyzed the incidence of lung cancer surgery patients with postoperative pneumonia higher possible reasons. This may be due to the large number of elderly patients and multiple preoperative comorbidities in

our data, as well as other unidentified. factors.~~Among the patients diagnosed with stage III lung cancer, a total of 20 patients underwent lung resection. Of these, 7 patients received neoadjuvant chemotherapy or targeted therapy. One of patients received neoadjuvant therapy developed POP. Of all the patients, there were~~ All of the patients, there were 7 patients received neoadjuvant therapy, 2 patients diagnosed with stage VIa lung cancer in whom pleural nodules were found intraoperatively and pathologically suggested to be metastases (M1a),16 patients with severe POP requiring tracheal intubation mechanical ventilation were cured within 2 weeks after surgery, of which 13 patients were in remission within 2 weeks after surgery, and the other 3 patients were in serious condition with secondary lung infection, but all of them were successfully cured and discharged from hospital within 2 months after surgery. Fortunately, there were no deaths during the study period.

• Please explain the “comorbidity burden” in your methods section; does a comorbidity burden mean 14 comorbidities? Or does it mean a CCI of 14? Please elaborate.

Reply: In our study, the term "comorbidity burden" refers to the overall burden or presence of comorbidities in the study population. It does not specifically indicate the number of comorbidities or a specific comorbidity index, such as the Charlson Comorbidity Index (CCI). We want to find a more specific predictive tool than CCI. Based on your suggestion, we have revised the manuscript accordingly.

Changes in the text: Page 8, lines: 247~263

In addition, 1,025 (83.40%) patients had comorbid conditions. The total number of comorbidity diagnoses in all samples was 2,929. ~~The number of comorbid diagnoses in each sample was counted as the "comorbidity burden" of the sample. The maximum comorbidity burden of all samples was 14, and the minimum comorbidity burden was 0. Based on professional judgment and previous literature research, the sample was reclustered into 22 comorbidity groups according to the characteristics of comorbidities.~~ We clustered over 700 comorbidities into 22 groups based on onset frequency, characteristics, and systemic organs involved. This subgrouping helps screen variables clearly and ensures clinical significance, sufficient sample size, and appropriate confidence intervals for each comorbidity group. Using comorbidity groups as predictors simplifies and expedites the prediction of postoperative risk. The number of comorbid diagnoses in each sample was counted as the "comorbidity burden" of the sample. The maximum comorbidity burden of all samples was 14 (Patients had 14 of the 22 comorbidity groups), and the minimum comorbidity burden was 0 (Patient had no comorbid diagnoses). ~~Significant differences (all P<0.05) were identified between POP and non-POP groups in preoperative comorbidities~~ (~~respiratory diseases, hypertension, neurological diseases, diabetes, digestive and abdominal diseases, abnormal clinical manifestations, and comorbidity burden;~~ *Table 2*).

• Please elaborate further on the 22 comorbidity groups, this is not explained in the methods section and not entirely understandable in the results section.

Reply: ICD-10-CM classifies diseases and health problems into 22 broad categories, with each chapter representing a category of disease or health-related problem. There are several layers of classification of each of the categories below, each layer classification contains several child categories, the classification of the specific amount owing to the different sections, such as infection and parasitic diseases in the chapter, which is divided into 13 categories, and chapters in the circulatory system disease, which is divided into nine categories and the number of child category, a more detailed description of disease or health problems. Diagnoses within each subcategory are assigned a unique code consisting of letters and numbers.

Based on the level of CID-10 code, organs involved by comorbidities, and the number of comorbidity diagnosis, the comorbidity characteristics were reduced again in the form of artificial clustering according to professional judgment and previous literature data. The clustered comorbidity data were formatted in length-width format and factorized. Make it a binary variable with the comorbidity group as the variable name. Based on the level of CID-10 code, organs involved by comorbidities, and the number of comorbidity diagnosis, the comorbidity characteristics were reduced again in the form of artificial clustering according to professional judgment and previous literature data. The clustered comorbidity data were formatted in length-width format and factorized. Make it a binary variable with the comorbidity group as the variable name.

Changes in the text: Page 8, lines: 252~263.

We clustered over 700 comorbidities into 22 groups based on onset frequency, characteristics, and systemic organs involved. This subgrouping helps screen variables clearly and ensures clinical significance, sufficient sample size, and appropriate confidence intervals for each comorbidity group. Using comorbidity groups as predictors simplifies and expedites the prediction of postoperative risk. The number of comorbid diagnoses in each sample was counted as the "comorbidity burden" of the sample. The maximum comorbidity burden of all samples was 14 (Patients had 14 of the 22 comorbidity groups), and the minimum comorbidity burden was 0 (Patient had no comorbid diagnoses). ~~Significant differences (all P<0.05) were identified between POP and non-POP groups in preoperative comorbidities~~ (~~respiratory diseases, hypertension, neurological diseases, diabetes, digestive and abdominal diseases, abnormal clinical manifestations, and comorbidity burden;~~ *Table 2*).

Discussion

• Again, please rewrite this section in better understandable English and more importantly, a more logical structure.

Reply: Thank you for your comment. We appreciate your feedback and understand your concerns regarding the clarity and logical structure of this section. We will make every effort to improve the English and logical flow of the content. However, please note that rewriting this particular section is proving to be quite challenging for us. Nevertheless, we assure you that we will do our best to address these issues and modify according to your subsequent suggestions.

• The first paragraph of the discussion rather belongs in the "Methods" section in stead of the "Discussion" section, since you explain why you used "pulmonary resection ratio" instead of thoracic surgery procedures.

Reply: Based on your suggestion, we have revised the manuscript accordingly.

Changes in the text: Page 9, lines: 291~296; Page 5~6, lines: 173~179.

~~Thoracoscopic lung resection is the main surgical treatment for patients with lung cancer (17, 18). Surgical procedures include wedge resection, segmental resection, lobectomy, and pneumonectomy. In this study, many patients were diagnosed with multiple nodules in the lung. Multiple procedures are common in surgery. It is difficult to categorize the surgical procedures of patients. Therefore, the pulmonary resection ratio is more suitable to describe the surgical characteristics of the patients.~~

by thoracoscopy under general anesthesia with a double-lumen endotracheal tube. ~~The proportion of lung tissue resection was determined according to the description of surgical records.~~ The surgical procedures include wedge resection, segmental resection, lobectomy, and pneumonectomy. In this study, many patients were diagnosed with multiple nodules in the lung, making it challenging to categorize their surgical procedures. Therefore, the proportion of lung tissue resection was used to describe the surgical characteristics of the patients more accurately (15, 16). Pathological reports

• The second paragraph about CCI and ECI could be brought forward to the "Introduction" section, since you state here the problem that you are researching, and consequently, what the aim of your study was. This was not clear up until this point.

Reply: Based on your suggestion, we have revised the manuscript accordingly.

Changes in the text: Page 9~10, lines: 298~311; Page 3, lines: 82~91.

~~Most patients with lung cancer who are candidates for surgery are admitted with one or more preoperative comorbidities. Older age, the heavier burdens of comorbidities, and poor physical status have become common characteristics of patients with lung cancer today. Many assessment tools that use preoperative comorbidities to predict postoperative risk have been proposed, improved, and widely used in previous studies. A large number of studies have validated the Charlson comorbidity index (19) and Elixhauser comorbidity index (20), which have universal applicability and are related to disability, death, readmission, length of hospital stay, quality of life, and long term health outcomes of patients. However, such comorbidity tools are more suitable for evaluating patients' long term prognosis, but short term evaluation results are not ideal in fitting with the actual results. There is a lack of correlation between short- and long-term prognosis in postoperative risk assessment and other aspects. Therefore, the development and validation of comorbidity assessment tools for different diseases and the short term prognosis of surgery have become hotspots in clinical research.~~

case has one or more chronic diseases or health problems (1). Comorbidity can affect the treatment outcomes and quality of life for patients with the primary diagnosed disease (2-5). Lung cancer is second most common cancer, and highest mortality. Patients with lung cancer often have preexisting comorbidities (6, 7), such as age-related conditions and other diseases. Various assessment tools have been developed to predict postoperative risk based on these comorbidities. However, these tools are more suitable for evaluating long-term prognosis rather than short-term outcomes (8, 9). Therefore, there is a need for comorbidity assessment tools that can accurately predict short-term prognosis after lung cancer surgery. Furthermore, many patients experience postoperative pneumonia after lung cancer surgery. The aim of this study was to

• Please shorten the third paragraph about lung function and grouping of 700 comorbidites into 22 comorbidity groups. Please bring forward the explanation of the 22 comorbidity groups to your "methods" section, because up until now, it was not clear how and why these 22 groups were defined.

Reply: Thank you for your feedback. We have considered your suggestion and have made the following changes to the manuscript. We have shortened the third paragraph about lung function and the grouping of 700 comorbidities into 22 comorbidity groups. Additionally, we decided to move the explanation of the 22 comorbidity groups to the "results" section for two reasons. Firstly, the "Methods" section already contains a substantial amount of content, and adding the explanation of the comorbidity groups would make it overly long and complex. Secondly, the clustering of the 700 comorbidities into 22 groups can also be considered a significant research outcome.

We believe that these changes improve the clarity and flow of the manuscript. Thank you for your valuable input, and we hope that you find the revised version satisfactory.

Changes in the text: Page 10~11, lines: 313~349; Page 10~11, lines: 252~263.

The diagnostic basis and manifestations of comorbidity mainly come from the clinical manifestations and laboratory tests of patients. To avoid the interaction of predictor variables and the influence of collinearity, only demographic characteristics, comorbidity diagnosis information, and lung resection proportion were used as predictors when including patients' hospitalization information. For example, Poor lung function before surgery was indeed associated with a higher rate of postoperative respiratory complications. We also included preoperative forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC) indicators of some patients at the beginning of the study. However, in the design of the study, we recognized that there might be strong collinearity between preoperative pulmonary function measures and whether patients had preoperative respiratory comorbidities. If there is strong multicollinearity, it may lead to instability and inaccuracy of multiple linear regression models. Moreover, in this study, preoperative call system comorbidity was an important characteristic variable. In order to focus more on the study of preoperative comorbidity and save time and cost, we abandoned the collection of pulmonary function indicators. Based on the treatment experience and understanding of the disease, comorbidities were clustered according to the onset frequency, their characteristics, and the systemic organs involved. More than 700 kinds of comorbidities were divided into 22 comorbidity groups. This subgrouping helped to screen variables more clearly in the complex examination results and comorbidity diagnosis and ensures that each comorbidity group has appropriate clinical significance, sufficient sample size, and appropriate CI. From the patient's symptoms and signs to the laboratory examination report, diagnosing any disease needs a large number of clinical data support. Using the comorbidity group as a predictor can predict the postoperative risk more simply and quickly. The diagnostic basis and manifestations of comorbidity mainly come from clinical manifestations and laboratory tests. To avoid predictor variable interaction and collinearity, we only used demographic characteristics, comorbidity diagnosis information, and lung resection proportion as predictors. For instance, poor lung function before surgery was associated with a higher rate of postoperative respiratory complications. Although we initially included preoperative pulmonary function indicators, we recognized the potential collinearity with preoperative respiratory comorbidities. To focus on preoperative comorbidity and save time and cost, we omitted the collection of pulmonary function indicators. We clustered over 700 comorbidities into 22 groups based on onset frequency, characteristics, and systemic organs involved. This subgrouping helps screen variables clearly and ensures clinical significance, sufficient sample size, and appropriate confidence intervals for each comorbidity group. Using comorbidity groups as predictors simplifies and expedites the prediction of postoperative risk.

~~models. Moreover, in this study, preoperative call system comorbidity was an important characteristic variable. In order to focus more on the study of preoperative comorbidity and save time and cost, we abandoned the collection of pulmonary function indicators. Based on the treatment experience and understanding of the disease, comorbidities were clustered according to the onset frequency, their characteristics, and the systemic organs involved. More than 700 kinds of comorbidities were divided into 22 comorbidity groups. This subgrouping helped to screen variables more clearly in the complex~~

10

~~examination results and comorbidity diagnosis and ensures that each comorbidity group has appropriate clinical significance, sufficient sample size, and appropriate CI. From the patient's symptoms and signs to the laboratory examination report, diagnosing any disease needs a large number of clinical data support. Using the comorbidity group as a predictor can predict the postoperative risk more simply and quickly.~~ The diagnostic

We clustered over 700 comorbidities into 22 groups based on onset frequency, characteristics, and systemic organs involved. This subgrouping helps screen variables clearly and ensures clinical significance, sufficient sample size, and appropriate confidence intervals for each comorbidity group. Using comorbidity groups as predictors simplifies and expedites the prediction of postoperative risk. The number of comorbid diagnoses in each sample was counted as the "comorbidity burden" of the sample. The maximum comorbidity burden of all samples was 14 (Patients had 14 of the 22 comorbidity groups), and the minimum comorbidity burden was 0 (Patient had no comorbid diagnoses). ~~Significant differences (all P<0.05) were identified between POP and non-POP groups in preoperative comorbidities~~ (~~respiratory diseases, hypertension, neurological diseases, diabetes, digestive and abdominal diseases, abnormal clinical manifestations, and comorbidity burden;~~ *Table 2*).

• In the fourth paragraph you can leave out that Thoracoscopic surgery has been implemented for most patients in lung cancer, since this is already stated throughout your manuscript, and widely known.

Reply: Thank you for your valuable feedback on our manuscript. We appreciate your suggestion regarding the fourth paragraph. We made the necessary revisions to remove this redundant statement and ensure that the paragraph flows smoothly without any repetition.

Changes in the text: Page 11, lines: 351~352.

~~Thoracoscopic surgery has been implemented for most patients with lung cancer in major medical centers, and postoperative death has been rare (21, 22). With the~~

• Please explain why you think that POP is a better representation of postoperative outcomes when compared to other postoperative complications of lung cancer.

Reply: Thank you for your comment. While there are various postoperative complications that can occur in patients with lung cancer, postoperative pneumonia (POP) is often considered a significant and relevant outcome to assess. Here are a few reasons why POP is commonly used as a representation of postoperative outcomes:

POP is one of the most common complications following lung cancer surgery. Its high occurrence rate makes it an important consideration when evaluating postoperative outcomes.

POP can lead to significant morbidity rates. It can prolong hospital stays, increase healthcare costs, and potentially result in respiratory failure or even death, making it a crucial outcome to monitor.

While not all complications can be prevented, there are various strategies available to reduce the risk of POP. By focusing on preventing this specific complication, healthcare providers can potentially improve overall postoperative outcomes.

POP is often linked with other postoperative complications, such as atelectasis or respiratory failure. By monitoring and managing POP, healthcare providers can indirectly address and potentially prevent other related complications.

Changes in the text: Page 11~12, lines: 362~374.

~~acute respiratory distress syndrome.~~ While there are various postoperative complications that can occur in patients with lung cancer, POP is often considered a significant and relevant outcome to assess. POP is one of the most common

complications following lung cancer surgery. Its high occurrence rate makes it an important consideration when evaluating postoperative outcomes. POP can lead to significant morbidity rates. It can prolong hospital stays, increase healthcare costs, and potentially result in respiratory failure or even death (19-23), making it a crucial outcome to monitor. While not all complications can be prevented, there are various strategies available to reduce the risk of POP. By focusing on preventing this specific complication, healthcare providers can potentially improve overall postoperative outcomes. POP is often linked with other postoperative complications, such as atelectasis or respiratory failure. By monitoring and managing POP, healthcare providers can indirectly address and potentially prevent other related complications.

• The goal of this fourth paragraph is not entirely clear; do you want to state that POP is the most important complication after lung surgery? Do you want to explain why that is the case? Or do you want to explain different manifestations of POP (infectious, non-infectious, mild fever, imaging changes etc.)?

Reply: Based on your advice, we have rewritten the fourth paragraph. The purpose of this paragraph is to highlight that postoperative pneumonia is the most significant complication following lung surgery.

Changes in the text: Page 11~12, lines: 362~374.

~~acute respiratory distress syndrome.~~ While there are various postoperative complications that can occur in patients with lung cancer, POP is often considered a significant and relevant outcome to assess. POP is one of the most common

complications following lung cancer surgery. Its high occurrence rate makes it an important consideration when evaluating postoperative outcomes. POP can lead to significant morbidity rates. It can prolong hospital stays, increase healthcare costs, and potentially result in respiratory failure or even death (19-23), making it a crucial outcome to monitor. While not all complications can be prevented, there are various strategies available to reduce the risk of POP. By focusing on preventing this specific complication, healthcare providers can potentially improve overall postoperative outcomes. POP is often linked with other postoperative complications, such as atelectasis or respiratory failure. By monitoring and managing POP, healthcare providers can indirectly address and potentially prevent other related complications.

• Paragraph 5 is clear, nothing to comment.

Reply: Thank you for your feedback on paragraph 5. If you have any further comments or questions, please let me know.

Changes in the text: None.

• Paragraphs 5,6,7, and 8 highlight age, BMI, smoking, and physical fitness status. Those are not comorbidities but demographic factors. It would be more interesting to discuss the impact of comorbidities first and why you believe they have that impact, before highlighting the impact of demographic factors on post-operative complications. Moreover, you discuss postoperative complications in general in these paragraphs, it would be better to focus on POP in these paragraphs, since this is your primary outcome.

Reply: Thank you for your valuable feedback on the article. I appreciate your insights regarding the content of paragraphs 5, 6, 7, and 8. I understand your point that age, BMI, smoking, and physical fitness status are demographic factors rather than comorbidities, and it would be more interesting to discuss the impact of comorbidities first.

I agree that it would be beneficial to prioritize the discussion of comorbidities and their impact before highlighting the influence of demographic factors on post-operative complications. By focusing on comorbidities initially, we can delve into their specific effects and provide a more comprehensive understanding of their contribution to the development of post-operative complications.

Additionally, your suggestion to concentrate on POP rather than post-operative complications in general is well-taken. In our opinion, there are few studies specifically investigating the correlation between demographic factors and POP in lung cancer patients, we can indirectly understand the association between age and postoperative pneumonia in lung cancer patients from a large body of literature discussing age and postoperative complications in this population.

Changes in the text: Page 12~13, lines: 376~414.

After screening the predictive variables of many participants, it was determined that respiratory diseases, diabetes, and nervous system diseases, age, BMI, smoking index, physiological function, ~~respiratory diseases, diabetes, and nervous system diseases~~ were independent risk factors for POP in patients with lung cancer undergoing thoracoscopic surgery. Dutkowska *et al.* (24), in their review of the comorbidity characteristics of patients with lung cancer, pointed out that age, chronic obstructive pulmonary disease (COPD), cardiovascular diseases, cerebrovascular diseases, and diabetes are all negative prognostic factors for lung cancer, consistent with this study.

Respiratory diseases, especially various lower respiratory tract diseases, are important risk factors for POP in patients with lung cancer. COPD is the most common comorbidity of lung cancer (25). Many studies have confirmed that COPD is an independent risk factor for perioperative lung cancer (26-29). Lin *et al.* (30) compared 24,109 surgical patients who had asthma before surgery to 24,109 non-asthmatic patients who underwent major surgery. Their results showed a significant increase in postoperative complications and mortality in patients with asthma. Nowadays, exacerbation of postoperative interstitial pneumonia in patients with interstitial lung disease and lung cancer has become a serious problem (31). Carr *et al.* (32) also confirmed that acute exacerbation of idiopathic interstitial pneumonia and POP are important postoperative complications in thoracic and nonthoracic surgery groups through their perioperative study of patients with idiopathic interstitial pneumonia. Hata *et al.* (33) performed a chart review of 250 patients with lung cancer who underwent lung resection to study the efficacy of radical surgery for lung cancer combined pulmonary fibrosis and emphysema (CPFE). Their results showed that the prognosis of CPFE patients identified on computed tomography scans was worse than that of patients with emphysema or normal lungs. When patients with lung cancer have CPFE before surgery, radical surgery should be carefully selected because of the associated poor prognosis.

Many studies have reported that diabetes significantly affects the survival of NSCLC patients (24, 34). However, the pathogenesis of POP ~~postoperative complications~~ of lung cancer caused by diabetes remains unclear. It may be related to complex complications of diabetes.

Lung cancer surgery in patients with neurological comorbidities is a major challenge in anesthesia and postoperative management, as cerebrovascular disease increases POP and mortality ~~to 20%~~ compared to patients with lung cancer without such comorbidities (34). Thoracic surgery for lung cancer in elderly patients is a very adverse prognostic factor. According to Dominguez-Ventura *et al.* (35), the risk of death increased 4-fold in patients aged ≥80 years with a history of stroke.

• So, consider bringing forward paragraphs 9, 10, and 11, since they actually discuss comorbitities like respiratory comorbidities, diabetes and neurological comorbidities. Again, try to focus on POP, instead of general complications if possible.

Reply: Thank you for your suggestion. To better address the topic of POP and its specific relation to comorbidities, I will make sure to emphasize paragraphs 9, 10, and 11. These paragraphs provide valuable information on respiratory comorbidities, diabetes, and neurological comorbidities, which are directly relevant to our focus on POP.

By highlighting these paragraphs, we can delve deeper into the specific impact of these comorbidities on POP and provide a more targeted analysis. I will ensure that the discussion remains centered on POP and its relationship with these comorbidities, rather than general complications.

Changes in the text: Page 13~15, lines: 416~466

• The limitations section is clear. No comments.

Reply: Thank you for your feedback on the limitations section. We appreciate your comment and are glad to hear that you found it clear. If you have any further questions or suggestions, please feel free to let us know.

Changes in the text: None.

Conclusions

• Please shorten the conclusion. You do not have to repeat the results that you found, just the conclusion that you draw from them.

Reply: Thank you for your feedback. Here's a revised, shorter version of the conclusion: "This study identifies several independent variables associated with postoperative pulmonary complications (POP) in lung cancer patients undergoing thoracoscopic surgery. These variables include age, BMI, smoking history, physiological function, respiratory diseases, diabetes, and neurological diseases. By using this model, clinicians can anticipate the risk of POP and implement targeted interventions and rehabilitation treatments to reduce complications and improve patient outcomes."

Changes in the text: Page 16, lines: 517~531

#Conclusions

~~The incidence rate of POP in this study was 15.95%. This study identified 7 independent variables associated with POP in patients with lung cancer undergoing thoracoscopic surgery, such as age, BMI, pack years of smoking, physiological function, respiratory diseases, diabetes, and neurological diseases. The evaluation shows that the model has a n acceptable AUC, Brier score. The utilization of this model offers clinicians a preliminary means to anticipate the risk of postoperative pulmonary complications in patients with lung cancer undergoing thoracoscopic surgery. This capability enables targeted preoperative interventions and rehabilitation treatments to mitigate potential postoperative complications, ultimately reducing their incidence. Such an approach holds significant promise for improving patient outcomes and avoiding adverse events.~~

This study identifies several independent variables associated with POP in lung cancer patients undergoing thoracoscopic surgery. We could translate this knowledge into clinical practice. By using this model, clinicians can anticipate the risk of POP and

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implement targeted interventions and rehabilitation treatments to reduce complications and improve patient outcomes.

Reviewer D

I scrupulously read the article. The authors demonstrated statistically confirmed data about 7 risk factors influencing postoperative pneumonia in thoracic surgery population.

The article is very well organized, including abstract, introduction including inclusion and exclusion criteria and all parts of the methods. Results support the conclusions and discussion is very clear. The table also are informative.

The manuscript is important for thoracic surgeons.

I don't have any comments and recommend accepting the manuscript for publication.

Reply: Thank you for your insightful comment on the article. We appreciate your thorough review of the manuscript.
Thank you once again for your valuable input.
Changes in the text: None.

Reviewer E

Thank you for this interesting article. I have some comments and questions:
1) In intro line 71, lung cancer is second most common cancer, and highest mortality,
Reply: According to your advice, we have added this section.
Changes in the text: Page 3, lines: 84.

> disease (2-5). Lung cancer is second most common cancer, and highest mortality.

2) in your abstract conclusion change it to thoracoscopic lung resections, since you didn't just look at thoracoscopic pneumonectomies, correct?
Reply: Thank you for your valuable feedback on our manuscript. We appreciate your suggestion regarding the abstract conclusion. You are absolutely correct that our study encompassed more than just thoracoscopic pneumonectomies. We have made the necessary changes to the abstract to reflect this clarification. We believe this modification will improve the accuracy and clarity of our findings.
Changes in the text: Page 3, lines: 73.

> were associated with increased pneumonia probability after thoracoscopic lung resection~~pneumonectomy~~. This model can help predict the incidence of POP after

3) please explain further line 193 what previous literature and what do you mean by professional judgement?
Reply: Thank you for your valuable feedback on our manuscript. The purpose of citing the references before line 193 in the article is to provide an overview of the current research status and background knowledge related to the parameters of this study. We have made appropriate revisions to the article to make the timeline more coherent.
Changes in the text: None.

4) Line 252 to 260 is too descriptive and is more shoudl be in methods section not in discussion.
Reply: Thank you for your feedback. We appreciate your suggestion regarding lines 252 to 260 being more suitable for the methods section rather than the discussion. We modified this in method section.
Changes in the text: Page 9, lines: 307~343; Page 6, lines: 175~179.

~~Thoracoscopic lung resection is the main surgical treatment for patients with lung cancer (17, 18). Surgical procedures include wedge resection, segmental resection, lobectomy, and pneumonectomy. In this study, many patients were diagnosed with multiple nodules in the lung. Multiple procedures are common in surgery. It is difficult to categorize the surgical procedures of patients. Therefore, the pulmonary resection ratio is more suitable to describe the surgical characteristics of the patients.~~

~~surgical records.~~ The surgical procedures include wedge resection, segmental resection, lobectomy, and pneumonectomy. In this study, many patients were diagnosed with multiple nodules in the lung, making it challenging to categorize their surgical procedures. Therefore, the proportion of lung tissue resection was used to describe the surgical characteristics of the patients more accurately (15, 16). Pathological reports

5) I think even lines 265 to 270 is more of a methods section area.

Reply: Thank you for your feedback. We appreciate your suggestion regarding lines 265 to 270. we decided to move the explanation of the 22 comorbidity groups to the "results" section for two reasons. Firstly, the "Methods" section already contains a substantial amount of content, and adding the explanation of the comorbidity groups would make it overly long and complex. Secondly, the clustering of the 700 comorbidities into 22 groups can also be considered a significant research outcome.

We believe that these changes improve the clarity and flow of the manuscript. Thank you for your valuable input, and we hope that you find the revised version satisfactory.

Changes in the text: Page 10~11, lines: 330~336; Page 8, lines: 252~263

~~involved. More than 700 kinds of comorbidities were divided into 22 comorbidity groups. This subgrouping helped to screen variables more clearly in the complex~~

10

~~examination results and comorbidity diagnosis and ensures that each comorbidity group has appropriate clinical significance, sufficient sample size, and appropriate CI. From the patient's symptoms and signs to the laboratory examination report, diagnosing any disease needs a large number of clinical data support. Using the comorbidity group as a predictor can predict the postoperative risk more simply and quickly.~~ The diagnostic

We clustered over 700 comorbidities into 22 groups based on onset frequency, characteristics, and systemic organs involved. This subgrouping helps screen variables clearly and ensures clinical significance, sufficient sample size, and appropriate confidence intervals for each comorbidity group. Using comorbidity groups as predictors simplifies and expedites the prediction of postoperative risk. The number of comorbid diagnoses in each sample was counted as the "comorbidity burden" of the sample. The maximum comorbidity burden of all samples was 14 (Patients had 14 of the 22 comorbidity groups), and the minimum comorbidity burden was 0 (Patient had no comorbid diagnoses). Significant differences (all $P<0.05$) were identified between POP and non POP groups in preoperative comorbidities (respiratory diseases, hypertension, neurological diseases, diabetes, digestive and abdominal diseases, abnormal clinical manifestations, and comorbidity burden; *Table 2*).

6) The conclusion was nicely written, however, what do the authors do differently now that they know this prediction model of 7 things that increase POP? do they advise patients differently? do they share this witih anesthesia and periop mediciine? how do they mitigate these factors to make less of a PNA?

Reply: Thank you for your insightful feedback on our paper. We appreciate your positive comments on the conclusion. Your questions regarding the practical implications of our findings are indeed important to address.

Now that we have developed a prediction model for identifying seven factors that increase the risk of POP, we could translate this knowledge into clinical practice. By using this model, clinicians can anticipate the risk of POP and implement targeted interventions and rehabilitation treatments to reduce complications and improve patient outcomes.

Changes in the text: Page 16, lines: 517~531.

#Conclusions

~~The incidence rate of POP in this study was 15.95%. This study identified 7 independent variables associated with POP in patients with lung cancer undergoing thoracoscopic surgery, such as age, BMI, pack years of smoking, physiological function, respiratory diseases, diabetes, and neurological diseases. The evaluation shows that the model has a n acceptable AUC, Brier score. The utilization of this model offers clinicians a preliminary means to anticipate the risk of postoperative pulmonary complications in patients with lung cancer undergoing thoracoscopic surgery. This capability enables targeted preoperative interventions and rehabilitation treatments to mitigate potential postoperative complications, ultimately reducing their incidence. Such an approach holds significant promise for improving patient outcomes and avoiding adverse events.~~

This study identifies several independent variables associated with POP in lung cancer patients undergoing thoracoscopic surgery. We could translate this knowledge into clinical practice. By using this model, clinicians can anticipate the risk of POP and

implement targeted interventions and rehabilitation treatments to reduce complications and improve patient outcomes.

Reviewer F

Dear authors, It has been interesting reading the manuscript however it is difficult to read and contains certain aspects that need a deep rework.

Comments for improvement:

Title: my suggestion is presenting the results of the logistic regresión model instead of leaving the title open to what is going to happen.

Reply: Thank you for your feedback on our paper. We agree that providing the results of the logistic regression model will enhance the clarity and specificity of our paper. By including these results in the title, readers will have a better understanding of the focus and outcomes of our study.

Changes in the text: Page 1, lines: 2~6.

~~**Preoperative comorbidities associated with the incidence of postoperative pneumonia after thoracoscopic lung resection in patients with lung cancer: a multicenter observational clinical study**~~**Seven preoperative factors have strong predictive value for postoperative pneumonia in patients undergoing thoracoscopic lung cancer surgery**

Abstract: please modify:

- Introduction: state which is the aim of the study

Reply: Thank you for your feedback on our paper. We improved the abstract according to the issues you mentioned.

Changes in the text: Page 2, lines: 50~52.

~~although their specific impact remains unclear.~~ This study aimed to analyze the preoperative data of patients with lung cancer to help surgeons predict the risk of incidence of POP who undergo thoracoscopic lung resection.

- Methods: describe the type of study and the population included

Reply: Thank you for your feedback on our paper. We improved the abstract according to the issues you mentioned.

Changes in the text: Page 2, lines: 53~55.

Methods: This study is a prospective study that included patients with lung cancer who were scheduled for thoracoscopic surgery in 1year. All cases came from 2 medical centers. Preoperative demographic information, tumor information, preoperative

- Results: present the objective data that support your model

Reply: Thank you for your feedback on our paper. We improved the abstract according to the issues you mentioned.

Changes in the text: Page 2, lines: 62~65.

Results: 1,229 patients with lung cancer who were to undergo thoracoscopic surgery were enrolled. 196 cases (15.95%) had POP. 1,025 (83.40%) patients had comorbid conditions. The total number of comorbidity diagnoses in all samples was 2,929. The prediction model suggested that patients with advanced age, high body mass index

Key words: you have up to 6 key words. Use them all. They will increase the probability of finding your paper within the corps of knowledge.

Reply: Thank you for your valuable feedback on my paper. We understand that including keywords can enhance the discoverability of my paper within the existing body of knowledge. We have taken your advice into consideration and have decided to stick with the four keywords originally chosen for my paper. I believe these keywords accurately represent the core themes and concepts discussed in my research.

Changes in the text: None.

Introduction: Please define the relationship between the HAP and POP. Otherwise, the sentence has no meaning. Please summarize why you think this is an important issue to analyze apart from saying there is no consensus.

Reply: Thank you for your feedback. We have deleted HAP section.

Changes in the text: Page 4, lines: 102~107.

pneumonia in lung cancer patients undergoing thoracoscopic surgery. ~~With the aging of the global population, it is more common for patients to present with multiple diseases. Relevant literature indicates that the incidence of comorbidities in cancer patients is much higher than that in noncancer patients, which may increase the difficulty of treating the main disease and reduce survival time (2-5). Presently, lung cancer is a common disease, and the impact of comorbidities may influence the diagnosis and treatment process for patients with lung cancer. Islam *et al.* (7) evaluated 5,683 patients~~

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~~and found that 26.7% had no comorbidities at the time of diagnosis. The prevalent comorbidities were persistent lung conditions (52.5%), diabetes mellitus (15.7%), and congestive heart failure (12.9%). Many other studies have shown that comorbidities are linked to a lower chance of survival (7-9). Various co-occurring disorders are linked with worse results at various phases. Individual comorbid illnesses should be considered in lung cancer survival prediction models. This study attempted to analyze the preoperative data of patients with lung cancer to help surgeons understand the epidemiological characteristics and clustering patterns of preoperative comorbidities of patients with lung cancer and predict the risk of incidence of POP who undergo thoracoscopic lung resecti~~*We present this article in accordance with the TRIPOD reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-23-512/rc).*

Methods:

- The amount of patients do not agree: 1229 or 1927 which one is the population of study? Please, clarify in the text

Reply: Thank you for your feedback on our paper. We improved the abstract according to the issues you mentioned. We decided to move it to the results section.

Changes in the text: Page 4, lines: 127~131; Page 7, lines: 224~226.

~~In this study, 1,229 patients with lung cancer who were to undergo thoracoscopic surgery were prospectively enrolled from October 2021 to September 2022. All 1,927 cases diagnosed with lung cancer clinically were followed up. All cases came from 2 medical centers and over 30 surgeons were involved in the thoracoscopic lung resection operation in this study. from October 2021 to September 2022.~~ In this study, the patients

In this study, A total of 1,927 individuals were clinically diagnosed with lung cancer, out of which 1,229 patients who were scheduled to undergo thoracoscopic surgery were enrolled between October 2021 and September 2022. 196 cases (15.95%) had POP.

Results:

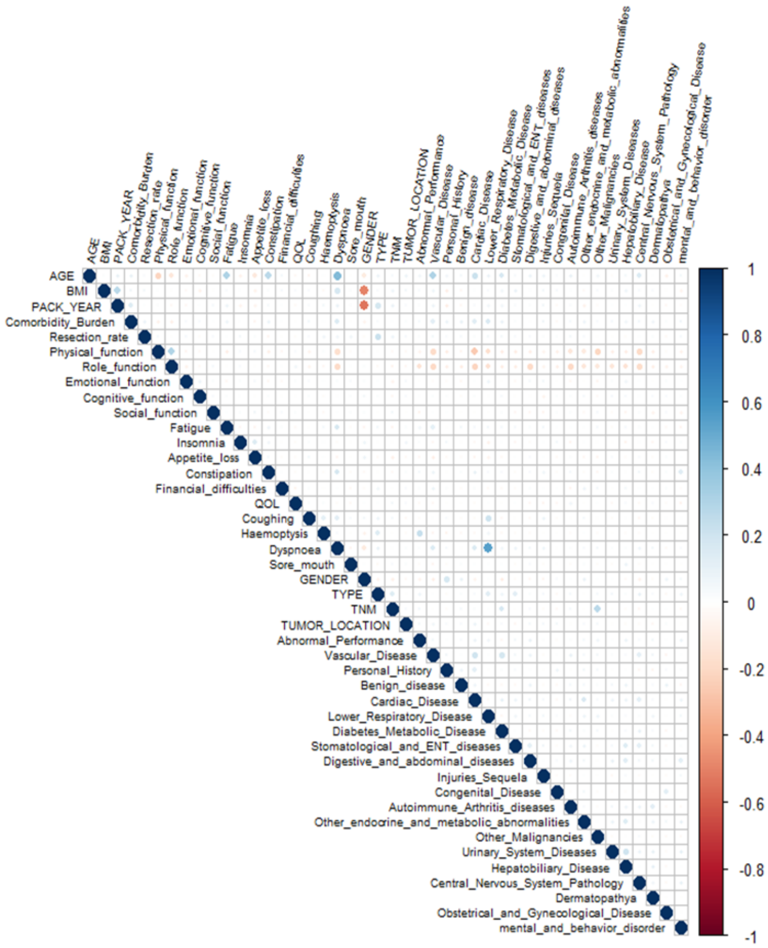
- Looking at the predictive model, I am not sure because it is not presented whether number of packs/year and pulmonary disease show or not collinearity. Please clarify. If collinearity exists, the model needs to be recalculated. Another example is Physical function and respiratory disease. Please, provide the data of the collinearity.

Reply: Thank you for your feedback on the predictive model. Before establishing the predictive model, we did conduct a correlation analysis on preoperative factors (Page 7, lines 202~203). The results can be seen in the correlation heatmap. However, we did not find any strongly correlated factors. Generally, when the absolute value of the correlation coefficient is less than 0.1, it can be considered that the two factors are not correlated; when the absolute value is between 0.1 and 0.4, it is considered to have a low degree of correlation; when it is between 0.5 and 0.7, it can be considered as a moderate degree of correlation; and if the correlation coefficient between two predictive factors is greater than 0.7, it can be considered that they have a high degree of correlation. In such cases, measures need to be taken to reduce the impact of multicollinearity. However, it is important to note that the strength of correlation between predictive factors is not only determined by the magnitude of the correlation coefficient but also by the reasons for its occurrence and its impact on the model, including the source of correlation, sample size, data distribution, and other factors. Even if the correlation coefficient between two variables is 0, there may still exist some nonlinear relationship between them. Therefore, when dealing with the issue of correlation between predictive factors, it is necessary to consider multiple factors to determine whether any action needs to be taken.

When addressing the issue of high correlation between predictive factors, it is important to choose appropriate methods based on the specific circumstances and conduct proper validation and evaluation to ensure the accuracy and reliability of the model. In our study, we handled the high correlation between preoperative factors by removing highly correlated predictive factors and merging highly correlated ones. Among the preoperative factors in our study, Dyspnoea is an indicator of breathing difficulties derived from the QLQ-C30 and LC13 survival status questionnaires, respectively. Although these two indicators are derived using different scales and calculation formulas, they express the same meaning. In this study, we chose one of these factors for investigation. As for the other preoperative factors, the two variables with the highest correlation are gender and smoking index, with a correlation coefficient of -0.54, which does not reach an absolute value of 0.7, so they can be retained. If the correlation between two predictive factors is very high, it is possible to consider merging them into a new predictive factor to reduce the impact of multicollinearity. In the correlation coefficient heatmap of our study, it can be observed that the preoperative comorbidity burden is mildly correlated with various preoperative comorbidity classifications. This is because the comorbidity burden is the cumulative result of each patient's preoperative comorbidities. The comorbidity burden can to some extent reflect the overall effect of comorbidities on patients. However, the various comorbidity classifications can more specifically reflect the impact of different comorbidity types on patients.

However, we did not explicitly include it in the results section as we believe it has minimal impact on the study outcomes. If you believe it is essential to include the collinearity analysis in the results section, we can certainly provide additional information and revise the manuscript accordingly.

Thank you once again for your valuable feedback.



Changes in the text: None.

- The text is difficult to follow. I want to think that this is due to English that needs deep rework. Please redo paragraph number 1

Reply: Thank you for your feedback. I apologize for any confusion caused by the text, and I understand your concern regarding the difficulty in following it. I agree that it may require significant revisions, particularly in terms of the English language usage.

With that in mind, I will make sure to thoroughly rework paragraph number 1 to enhance its clarity and coherence. I appreciate your patience and understanding in this matter.

Changes in the text: Page 7~8, lines:224~244.

#Results

In this study, A total of 1,927 individuals were clinically diagnosed with lung cancer, out of which 1,229 patients who were scheduled to undergo thoracoscopic surgery were enrolled between October 2021 and September 2022. 196 cases (15.95%) had POP~~. Significant differences (all P<0.05) were identified between POP and non-POP groups in terms of demographics~~ (~~gender, age, smoking status, tumor pathological classification, physiological function, role function, frailty, insomnia, constipation, cough, hemoptysis, and dyspnea;~~ *Table 1*). ~~–~~We analyzed the incidence of lung cancer surgery patients with postoperative pneumonia higher possible reasons. This may be due to the large number of elderly patients and multiple preoperative comorbidities in our data, as well as other unidentified. factors.~~Among the patients diagnosed with stage III lung cancer, a total of 20 patients underwent lung resection. Of these, 7 patients received neoadjuvant chemotherapy or targeted therapy. One of patients received neoadjuvant therapy developed POP. Of all the patients, there were~~ All of the patients, there were 7 patients received neoadjuvant therapy, 2 patients diagnosed with stage VIa lung cancer in whom pleural nodules were found intraoperatively and pathologically suggested to be metastases (M1a), 16 patients with severe POP requiring tracheal intubation mechanical ventilation were cured within 2 weeks after surgery, of which 13 patients were in remission within 2 weeks after surgery, and the other 3 patients were in serious condition with secondary lung infection, but all of them were successfully cured and discharged from hospital within 2 months after surgery. Fortunately, there were no deaths during the study period.

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- I was not expecting that patients with comorbidities have a comorbidity burden of 0. Please clarify exactly which patients are included in this analysis.

Reply: Thank you for your feedback. We apologize for any confusion caused by the statement regarding the comorbidity burden of 0 in patients with comorbidities. I understand your concern and would like to provide clarification on the inclusion criteria for this analysis.

In our study, we defined patients with comorbidities as individuals who had been diagnosed with at least one additional medical condition, in addition to the primary condition under investigation. However, the comorbidity burden of 0 refers to the absence of any additional comorbid conditions beyond the primary condition.

Changes in the text: Page 8, lines:252~263.

We clustered over 700 comorbidities into 22 groups based on onset frequency, characteristics, and systemic organs involved. This subgrouping helps screen variables clearly and ensures clinical significance, sufficient sample size, and appropriate confidence intervals for each comorbidity group. Using comorbidity groups as predictors simplifies and expedites the prediction of postoperative risk. The number of comorbid diagnoses in each sample was counted as the "comorbidity burden" of the sample. The maximum comorbidity burden of all samples was 14 (Patients had 14 of the 22 comorbidity groups), and the minimum comorbidity burden was 0 (Patient had no comorbid diagnoses). ~~Significant differences (all P<0.05) were identified between POP and non POP groups in preoperative comorbidities (respiratory diseases, hypertension, neurological diseases, diabetes, digestive and abdominal diseases, abnormal clinical manifestations, and comorbidity burden;~~ *Table 2*).

- Most data of the figures have to be in the text. Figures complete the information.

Reply: Thank you for your feedback. We appreciate your suggestion to include more data from the figures in the text. We will make sure to appropriately incorporate the figures' information into the text.

Changes in the text:

In this study, A total of 1,927 individuals were clinically diagnosed with lung cancer, out of which 1,229 patients who were scheduled to undergo thoracoscopic surgery were enrolled between October 2021 and September 2022. 196 cases (15.95%) had POP. ~~Significant differences (all P<0.05) were identified between POP and non POP groups in terms of demographics~~ (~~gender, age, smoking status, tumor pathological classification, physiological function, role function, frailty, insomnia, constipation, cough, hemoptysis, and dyspnea;~~ *Table 1*). –We analyzed the incidence of lung cancer

- Table 1. There are impossible data: 376 pack-year?

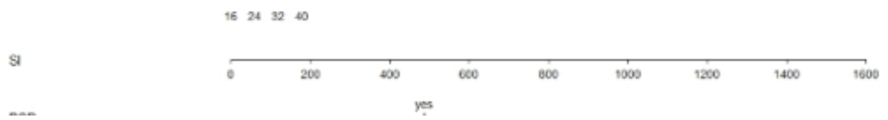
Reply: Thank you very much for your attention to our research and pointing out the error. We did indeed make a mistake, and the data in Table 1 should not be "pack-years" but rather "smoking index". Smoking index calculation formula: Number of cigarettes smoked per day x number of years smoked. We sincerely apologize for this and have already corrected the error. Please rest assured that we will make sure to avoid similar mistakes in future studies. Thank you again for your correction and support.

Changes in the text: Page 8, lines:268; Page 9, lines:272; Page 9, lines:277; Page 26, Figure 2; Page 26, lines: 798; Page 29, Table 1; Page 32, Table 3; Page 35, Table 4.

1.025–1.065; P<0.001], ~~pack years of smoking~~smoke index (OR, 1.004; 95% CI:

in patients with advanced age, high smoke index ~~pack years of smoking~~, poor physical

diabetes were further included in the final model. Age, BMI, smoke index~~pack years~~,



likelihood of POP could be calculated. BMI, body mass index; SI, smoke index; PF,

~~Pack-years~~Smoke index	75.30 (178.60)	376.58 (396.80)	<0.001
Pathological type			0.001

Smoke index~~Pack-years~~	1.004 (1.004–1.005)	<0.001

Smoke index~~Pack-years~~	1.005 (1.004–1.007)	<0.001	1.004 (1.003–1.005)	<0.001

- It is surprising how young is the series of patients; only 18.98% (6.78) and 19.83% (6.72) of the series (suffering or not POP) underwent lung resection? Following the same doubt, I cannot understand why lung resection is included in the regression analysis.

Reply: Thank you very much for your attention to our research and pointing out the error. We did indeed make a mistake. We apologize for the error in our English expression. It should not be "lung resection ratio." What we meant to convey is the proportion of lung function that is removed through lung tissue resection in relation to the total lung function of the patients. Thank you for pointing out the confusion.

Changes in the text: Page 6, lines:174~179.

~~proportion of lung tissue resection was determined according to the description of surgical records.~~ The surgical procedures include wedge resection, segmental resection, lobectomy, and pneumonectomy. In this study, many patients were diagnosed with multiple nodules in the lung, making it challenging to categorize their surgical procedures. Therefore, the proportion of lung tissue resection was used to describe the surgical characteristics of the patients more accurately (15, 16). Pathological reports

- I have not seen length of stay in any initial table/analysis and suddenly it appears in table 4. But not only appears it is also statistically significant. This is useless. Of course, patients having a POP have longer LOS.

Reply: Thank you for pointing out our oversight. The inclusion of length of stay (LOS) in table 4 was an error caused by a module that was left in our program script. We acknowledge that LOS is not meaningful in this study. We appreciate your attention to detail and thank you for bringing this to our attention.

Changes in the text: Page 35, table4.

~~Length of stay (days)~~	~~1.043 (1.011–1.077)~~	~~0.009~~	~~1.046 (1.015–1.078)~~	~~0.005~~

Discussion:

- Can you please explain what is “lung resection ratio”? Can you explain why you cannot aggregate patients according to the surgical procedure?

Reply: Thank you very much for your attention to our research and pointing out the error. We did indeed make a mistake. We apologize again for the error in our English expression. It should not be "lung resection ratio." What we meant to convey is the proportion of lung function that is removed through lung tissue resection in relation to the total lung function of the patients. Thank you for pointing out the confusion.

Changes in the text: Page 6, lines:174~179.

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- 2 paragraph, can you provide objective data to support your statement that well-known comorbidity index do not help in the short time?

Reply: Thank you for your feedback on our study. We apologize for any confusion caused by our previous statement. We really meant that the majority of well-known comorbidity indexes have limited effectiveness in predicting short-term outcomes. While these indexes have proven valuable in assessing long-term prognosis and risk stratification, their ability to accurately predict short-term outcomes is often limited.

We appreciate your input and have revised our statement accordingly. Thank you for bringing this to our attention, as it allows us to provide a more accurate representation of our meaning. If you have any further questions or require additional information, please do not hesitate to reach out.

We changed the expression way and move this part to the introduction part

Changes in the text: Page 9~10, lines:298~311; Page 3, lines:86~88.

~~Most patients with lung cancer who are candidates for surgery are admitted with one or~~

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~~more preoperative comorbidities. Older age, the heavier burdens of comorbidities, and poor physical status have become common characteristics of patients with lung cancer today. Many assessment tools that use preoperative comorbidities to predict postoperative risk have been proposed, improved, and widely used in previous studies. A large number of studies have validated the Charlson comorbidity index (19) and Elixhauser comorbidity index (20), which have universal applicability and are related to disability, death, readmission, length of hospital stay, quality of life, and long term health outcomes of patients. However, such comorbidity tools are more suitable for evaluating patients' long term prognosis, but short term evaluation results are not ideal in fitting with the actual results. There is a lack of correlation between short- and long-term prognosis in postoperative risk assessment and other aspects. Therefore, the development and validation of comorbidity assessment tools for different diseases and the short term prognosis of surgery have become hotspots in clinical research.~~

Patients with lung cancer often have preexisting comorbidities (6, 7), such as age-related conditions and other diseases. Various assessment tools have been developed to predict postoperative risk based on these comorbidities. However, these tools are more suitable for evaluating long-term prognosis rather than short-term outcomes (8, 9). Therefore, there is a need for comorbidity assessment tools that can accurately predict short-term prognosis after lung cancer surgery. Furthermore, many patients experience postoperative pneumonia after lung cancer surgery. The aim of this study was to

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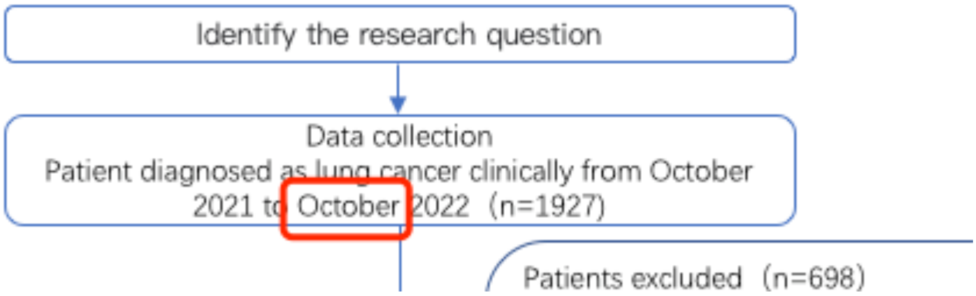
Reviewer G

1. Figure 1

The month is inconsistent. Please check and revise.



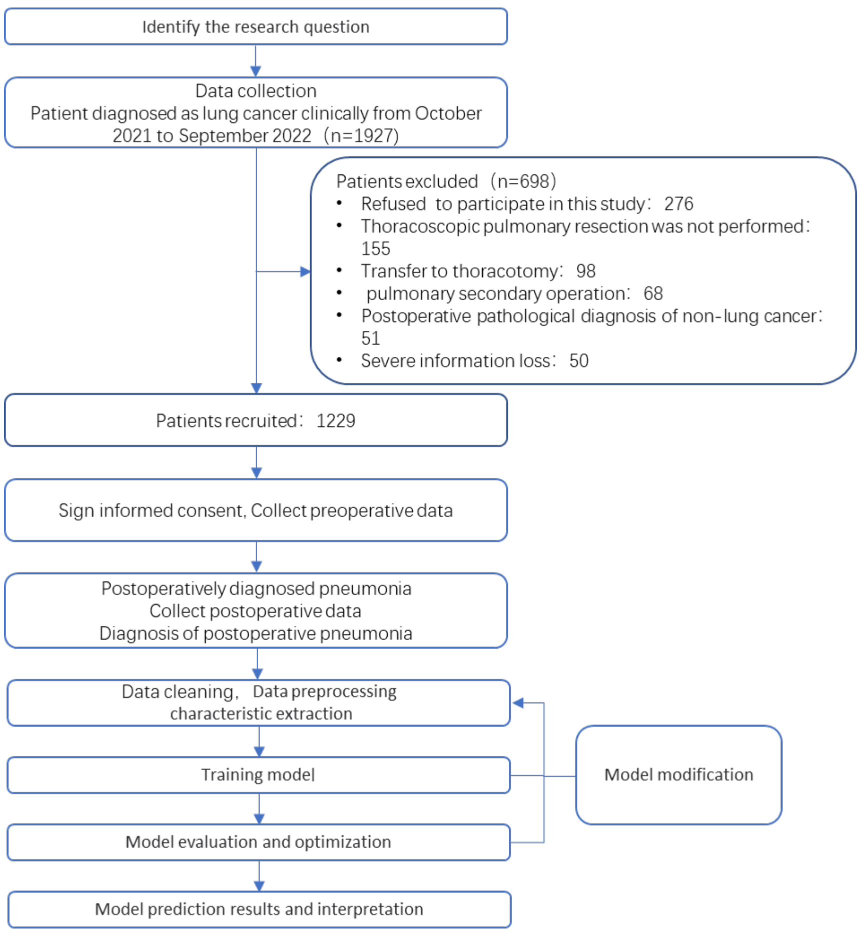
In this study, the patients with lung cancer who were to undergo thoracoscopic surgery were prospectively enrolled from 2 medical centers from Octoer 2021 to September 2022. Inclusion criteria in this trial include (I) patients with suspected or diagnosed lung

#Results

In this study, A total of 1,927 individuals were clinically diagnosed with lung cancer, out of which 1,229 patients who were scheduled to undergo thoracoscopic surgery were enrolled between October 2021 and September 2022. 196 cases (15.95%) had POP

R8: Thank you for your feedback. We revised Figure 1, according your comment. Once again, we apologize for any confusion caused and appreciate your assistance in improving the quality of our paper.

We have corrected this as follows (Page25, line: 786)



2. The author's name does not match the citation. Please check and revise.

according to Teresa *et al.* (18). Pneumonia occurred in postoperative patients within 30 days after surgery: (I) at least 2 chest imaging examinations were performed within 30

18. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008;36:309-32.

R9: Thank you for your feedback. We revised this, according your comment. We have corrected this as follows (Page6, line: 186)

"…, according to Horan et al."

3. The first author of citation 39 should also be mentioned here. Please revise.

BMI has different effects on short- and long-term prognosis after lung cancer surgery. Benker *et al*. (38, 39) recruited 1,219 patients who underwent NSCLC resection between 2000 and 2015. They concluded that high age, low BMI, and low FEV1 could

38. Benker M, Citak N, Neuer T,et al. Impact of preoperative comorbidities on postoperative complication rate and outcome in surgically resected non-small cell lung cancer patients [J]. Gen Thorac Cardiovasc Surg, 2022, 70(3): 248-256.

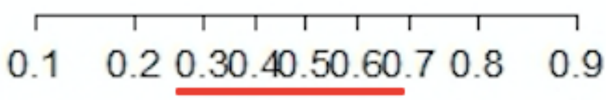
39. Seigneurin A, Delafosse P, Trétarre B, et al. Are comorbidities associated with long-term survival of lung cancer? A population-based cohort study from French cancer registries. BMC Cancer 2018;18:1091.

R10: Thank you for your feedback. We revised this, according your comment. We have corrected this as follows (Page14, line: 439)

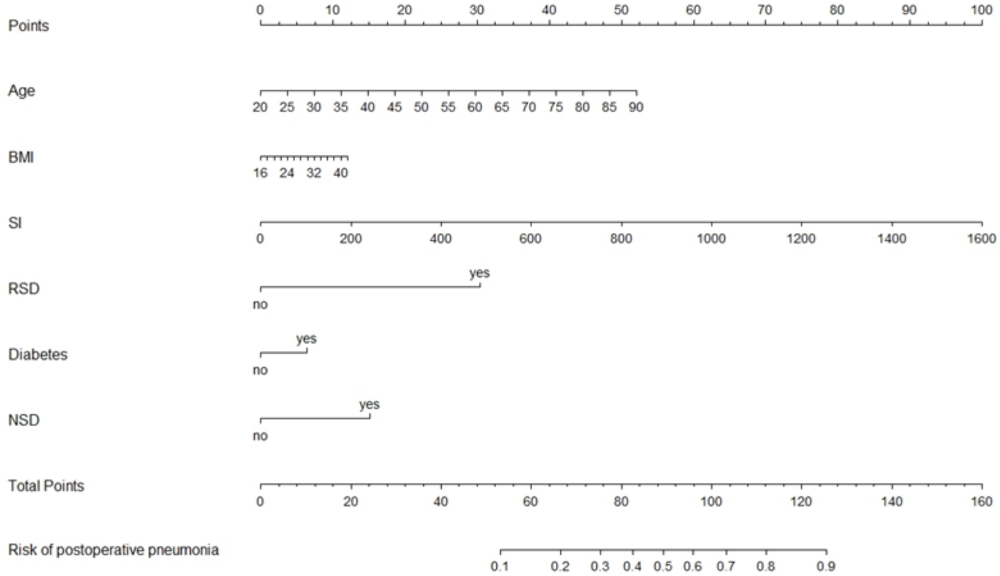
"Benker and Seigneurin et al. (38, 39) recruited 1,219 patients who underwent NSCLC resection between 2000 and 2015."

4. Figure 2

These numbers are too close. Please revise.



R11: Thank you for your feedback. We revised this, according your comment. We have corrected this as follows (Page27, line: 791).



5. Figure 3

Please check which data is correct: 1.755 or -1.755.

Figure 3 Model ROC curve. Maximum Youden index: 0.545. Corresponding diagnostic cutoff value: 1.755, Sensitivity: 74.4%, Specificity: 80.1%. AUC, area under the curve; ROC, receiver operating characteristic.

R12: Thank you for your feedback. -1.755 is correct. We revised this, according your comment. We have corrected this as follows (Page87, line: 804).

6. Table 3

Please check if data are missing here.

No	Ref.	
Yes	0.875 (0.637–1.195)	0.404
Comorbidities burden	1.268 (1.180–1.363)	<0.001

POP, postoperative pneumonia; OR, odds ratio; CI, confidence interval; Ref., reference;
BMI, body mass index; A, adenocarcinoma; S, squamous carcinoma; O, other types of

R13: Thank you for your feedback. We have carefully reviewed and confirmed that there are no missing data in our Table 3.

If you have any further questions or concerns, please don't hesitate to let us know. We appreciate your attention to detail and thank you for your time.

7. The below sentence is confusing. Ref. 39 does not seem to match the information "recruited 1,219 patients who underwent NSCLC resection between 2000 and 2015". Please check carefully and revise.

"Benker and Seigneurin et al. (38, 39) recruited 1,219 patients who underwent NSCLC resection between 2000 and 2015."

Reply: Thank you for your feedback. According to your suggestions, we revised this. Reference 39 was deleted.

Change in text: Page14~15, lines: 440, 443, 446, 452, 458, 465, 466; Page: 22, lines:720~722.

Benker and Seigneurin *et al.* (38~~39~~) recruited 1,219 patients who underwent NSCLC

et al. (39, 40~~40, 41~~) had similar results, showing that obesity has beneficial effects on

al.(41~~2~~) and Kaw *et al.*(42~~3~~) had another conclusion that obese patients have an

for POP (43~~4~~). The detrimental effects of smoking extend beyond lung cancer. It is a

11, 23, 44~~5~~) and is also deeply ingrained among physicians.

the impact of quality of life on postoperative lung cancer (45~~6~~, 46~~7~~) and proposed that optimizing preoperative functional status can improve postoperative status (47~~8~~, 48~~9~~).

~~Seigneurin A, Delafosse P, Trétarre B, et al. Are comorbidities associated with long-term survival of lung cancer? A population-based cohort study from French cancer registries. BMC Cancer 2018;18:1091.~~

8. Ref. 9 and Ref. 16 are the same.

Ref. 8 and Ref. 15 are the same.

Please revise.

Reply: Thank you for your feedback. We revised this, according your suggestion.

Changes in text: Page: 6, lines: 179, 186, 187; Page: 12, line: 368, 380, 386, 387, 392, 393, 396; Page: 13, lines: 405, 412, 413, 423, 427; Page: 14, lines: 440, 443, 446, 452, 458; Page:15, lines: 465,466.

9. Please check and confirm whether any information is missing here.

Lung cancer surgery in patients with neurological comorbidities is a major challenge in anesthesia and postoperative management, as cerebrovascular disease increases POP and mortality compared to patients with lung cancer without such comorbidities ().

Reply: Thank you for your feedback. We confirmed that nothing was missing here, and we have made changes according to your suggestions

Change in text: Page13, line:412