

Impact of preserved ratio impaired spirometry on postoperative outcomes of non-small cell lung cancer surgery

Received: 28 March 2025

Accepted: 27 February 2026

Published online: 11 March 2026

Cite this article as: Lee D., Lee G., Kong S. *et al.* Impact of preserved ratio impaired spirometry on postoperative outcomes of non-small cell lung cancer surgery. *Sci Rep* (2026). <https://doi.org/10.1038/s41598-026-42778-4>

Daeyeun Lee, Genehee Lee, Sunga Kong, Boksoon Chang, Yunjoo Im, Danbee Kang & Hye Yun Park

We are providing an unedited version of this manuscript to give early access to its findings. Before final publication, the manuscript will undergo further editing. Please note there may be errors present which affect the content, and all legal disclaimers apply.

If this paper is publishing under a Transparent Peer Review model then Peer Review reports will publish with the final article.

Impact of Preserved Ratio Impaired Spirometry on Postoperative Outcomes of Non-Small Cell Lung Cancer Surgery

Daegeun Lee^{1,*}, Genehee Lee^{2,3,*}, Sunga Kong^{2,3}, Boksoon Chang⁴, Yunjoo Im⁵, Danbee Kang^{2,3,6†}, Hye Yun Park^{7†}

¹Division of Pulmonary, Allergy and Critical Care Medicine, Chung-Ang University Gwangmyeong Hospital, Gwangmyeong, Republic of Korea.

²Department of Clinical Research Design and Evaluation, SAIHST, Sungkyunkwan University, Seoul, South Korea.

³Patient-Centered Outcomes Research Institute, Samsung Medical Center, Seoul, Republic of Korea.

⁴Department of Thoracic and Cardiovascular Surgery, Samsung Medical Center, Seoul, Republic of Korea

⁵Division of Pulmonology and Allergy, Department of Internal Medicine, Kyung Hee University Medical Center, Seoul, South Korea

⁶Center for Clinical Epidemiology, Samsung Medical Center, Seoul, Republic of Korea.

⁷Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

*These authors contributed equally to this work as the first authors.

†These authors contributed equally to this work as the corresponding authors.

Correspondence to

Hye Yun Park, MD, PhD, Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul, 06351, Republic of Korea

E-mail: hyeyunpark@skku.edu

or

Danbee Kang, PhD, Department of Clinical Research Design and Evaluation, SAIHST,
Sungkyunkwan University, 81 Irwon-ro, Gangnam-gu, Seoul, 06351, South Korea.

Email: dbee.kang@skku.edu

ARTICLE IN PRESS

ABSTRACT

Preserved ratio impaired spirometry (PRISm) is associated with increased morbidity and mortality. However, the impact of PRISm on the postoperative outcomes of non-small cell lung cancer (NSCLC) surgery remains poorly understood. We retrospectively analyzed data of 834 patients with NSCLC from the prospective CATCH-LUNG cohort who underwent curative lung resection between March 2016 and December 2020. The patients were categorized into four groups: normal, PRISm, mild obstructive lung disease (OLD), and moderate OLD. The primary outcomes were postoperative pulmonary complications (PPCs) and cardiac complications (PCCs) that occurred within 30 days post-surgery. The incidences of PPCs and PCCs were significantly higher in the PRISm group (PPC: 11.5%; PCC: 16.4%) than in the normal lung function group (PPC: 3.3%; PCC: 4.6%). Patients with PRISm had adjusted RRs of 2.62 (95% CI: 1.10–6.23) for PPCs and 2.67 (95% CI: 1.42–4.99) for PCCs. The adjusted RRs for PPCs were 2.32 in mild OLD and 3.25 in moderate OLD, whereas those for PCCs were 1.94 in mild OLD and 2.32 in moderate OLD. Notably, among patients with PRISm, those with low FVC (<80% predicted) had markedly higher risks of PPCs (adjusted RR = 3.41; 95% CI: 1.22–9.54) and PCCs (adjusted RR = 3.31; 95% CI: 1.74–6.31) compared to those with normal FVC. PRISm, like chronic obstructive pulmonary disease, substantially increases the risk of postoperative complications of NSCLC surgery and should be recognized as an important clinical category.

Keywords: PRISm, postoperative pulmonary complications, postoperative cardiac complications, NSCLC, lung cancer surgery

Short title: PRISm and Lung Cancer Surgery Outcomes

INTRODUCTION

Non-small cell lung cancer (NSCLC) is a major public health burden despite improvements in diagnostic techniques and treatment strategies¹. Surgical resection remains the mainstay of curative treatment for patients with early-stage NSCLC. However, postoperative complications are a major concern, adversely affecting patient outcomes, quality of life, and healthcare costs²⁻⁴. Therefore, identifying patients at a high risk of postoperative complications is crucial to improve surgical outcomes.

Preserved ratio impaired spirometry (PRISm), historically referred to as a “restrictive spirometric pattern”, is now recognized as a distinct spirometric phenotype. PRISm is characterized by a reduced forced expiratory volume in 1 second (FEV1) of <80%, with an FEV1/forced vital capacity (FVC) ratio of ≥ 0.7 ⁵. The prevalence of PRISm is estimated to range from 7% to 12%^{5,6} in the general population. The 2025 Global Initiative for Chronic Obstructive Lung Disease (GOLD) report describes PRISm as an abnormal spirometric pattern with a preserved FEV1/FVC ratio and impaired lung function. The report notes that individuals with PRISm, similar to those with other forms of pre-chronic obstructive pulmonary disease (pre-COPD), are at increased risk of developing airflow obstruction over time⁷. Longitudinal cohort studies suggest that roughly one-third of individuals with PRISm progress to COPD over 4–5 years, whereas a substantial proportion may revert to normal spirometry or remain stable^{8,9}. Unlike COPD, in which both FEV1 and FEV1/FVC ratio are compromised, PRISm is considered a heterogeneous spirometric pattern that was previously often labeled broadly as restrictive lung disease. It may reflect various underlying pathophysiologic conditions, including obesity-related hypoventilation, subclinical interstitial abnormalities, early airway disease, and incomplete lung development^{10,11}. PRISm can be classified into restrictive (FVC <80%) and non-restrictive (FVC $\geq$ 80%) subtypes. The two groups differ in their risk factors, CT findings, and how they progress over time¹². Several systematic reviews and meta-analyses

have reported that PRISm is associated with increased all-cause, cardiovascular, and respiratory mortality compared with normal spirometry^{8,9,13-17}. However, its implications in a perioperative setting, particularly in patients undergoing lung resection for NSCLC, remain poorly understood. Considering that lung function is a crucial factor for assessing surgical risk¹⁸, the impact of PRISm on postoperative outcomes requires further investigation.

Therefore, the aim of our study was to investigate the incidence and outcomes of postoperative cardiopulmonary complications in patients with PRISm who underwent lung resection for NSCLC. Specifically, we compared the incidence of postoperative complications among patients with PRISm, those with normal pulmonary function, and those with airflow limitation.

RESULTS

Patients

Among the participants, 582 (69.8%), 61 (7.3%), 94 (11.3%), and 97 (11.6%) had normal, PRISm, mild OLD, and moderate OLD before surgery, respectively. Participants with PRISm or OLD were more likely to be male, smokers, have more comorbidities, and have a more severe disease stage than those with normal lung function. Participants with PRISm or OLD also had a higher proportion of pneumonectomy or bilobectomy, and fewer VATS procedures, compared to the normal lung function group (**Table 1**).

Postoperative cardiopulmonary complications

The overall incidence of PPCs was 6.8% (n = 57). The incidence of PPCs was higher in the PRISm (11.5%), mild OLD (11.7%), and moderate OLD (20.6%) groups than in the normal group (**Table 2**). In the adjusted models, the relative risks (RRs) for PPCs were significantly higher in the PRISm (RR = 2.62; 95% confidence interval (CI) = 1.10–6.23), mild

OLD (RR = 2.32; 95% CI = 1.15–4.70), and moderate OLD (RR = 3.25; 95% CI = 1.69–6.27) groups than in the normal group. In the subgroup analysis, the PRISm group had a consistently higher incidence of PPCs than the normal group. However, the association between PRISm and PPC in lobectomy subgroup was stronger than in other surgical groups (p for interaction <0.01) (**Figure 2**). The overall incidence of PCCs was 7.9% ($n = 66$), with the highest incidence observed in the PRISm (16.4%), mild OLD (12.8%), and moderate OLD (17.5%) groups than in the normal group (**Table 2**). In the adjusted models, the RRs for PCCs were significantly increased in the PRISm (RR = 2.67; 95% CI = 1.42–4.99), mild OLD (RR = 1.94; 95% CI = 1.02–3.67), and moderate OLD (RR = 2.32; 95% CI = 1.20–4.48) groups than in the normal group.

Postoperative cardiopulmonary complications according to FVC

Among patients with PRISm, those with a low FVC had a significantly higher rate of PPCs (14.6%) compared to those with a normal FVC (5.0%) and normal lung function (3.3%). Similarly, the rate of PCCs was significantly higher in patients with a low FVC (22.0%) than in those with a normal FVC (5.0%) or normal lung function (4.6%). The adjusted RRs of PPCs (RR = 3.41; 95% CI = 1.22–9.54) and PCCs (RR = 3.31; 95% CI = 1.74–6.31) were markedly higher in patients with a low FVC than in those with a normal FVC (**Table 3**).

Mortality

In the 5-year mortality (median = 4.8; interquartile range = 2.7–5), the five-year survival rate was 94.7% in the normal group, 86.4% in the PRISm group, 86.8% in the mild OLD group and 81.6% in the moderate OLD group. In the Cox models, the adjusted HR were 1.19 (95% CI 0.51–2.82) in the PRISm group, 1.87 (95% CI 0.89–3.92) in the mild OLD group and 2.01 (95% CI 1.00–4.14) in the moderate OLD group compared with the normal group (**Table 4**).

DISCUSSION

We evaluated the perioperative outcomes in patients with PRISm in comparison with those with mild OLD, moderate OLD, and normal lung function after lung cancer surgery. The proportion of patients with PRISm in the current cohort (7.3%) was similar to that in previous reports, suggesting that the prevalence rate of PRISm was between 7% and 12% in the general population^{5,6}. The rates of PPCs in patients with PRISm, mild OLD, and moderate OLD were 11.5%, 11.7%, and 20.6%, respectively, compared to 3.3% in patients with normal lung function. The adjusted RRs for the PRISm, mild OLD, and moderate OLD groups were 2.62, 2.32, and 3.25, respectively. Furthermore, the incidence rates of PCCs were significantly higher in the PRISm, mild OLD, and moderate OLD groups than in the normal group. A subgroup analysis demonstrated a consistently higher risk ratio for PPCs in the PRISm group than in the normal group.

To our knowledge, only a few studies have evaluated the risk of PPCs in patients with PRISm. Some studies have highlighted an increased incidence of PPCs in patients with PRISm or restrictive spirometry patterns undergoing non-cardiothoracic surgery^{19,20}. Additionally, a study from Taiwan suggested that PRISm may be a risk factor for lung cancer and is associated with increased overall mortality¹⁷. A major strength of our study is that both PPCs and PCCs were prospectively assessed according to pre-defined, standardized definitions, thereby minimizing misclassification and outcome ascertainment bias. This rigorous outcome assessment enabled direct comparison of PPC rates among patients with PRISm, OLD, and normal lung function within a lung cancer surgery cohort.

Interestingly, in the present study, the moderate OLD group had the highest risk of PPCs, followed by the PRISm and mild OLD groups. These findings support those of previous studies demonstrating a direct relationship between the degree of airflow limitation and an

increased rate of postoperative complications after thoracic surgery^{21,22}. However, our study showed that patients with PRISm had a higher risk of PPCs compared to those with mild OLD. This suggests that patients with reduced lung function but preserved airflow limitation may have greater surgical vulnerability than those with mild airflow obstruction.

Several pathophysiologic mechanisms may explain this finding. First, patients with PRISm in our cohort had a numerically higher BMI compared with those with normal lung function or mild OLD. PRISm is often accompanied by obesity, which can reduce lung volumes through mechanical compression and is linked to a systemic pro-inflammatory state with elevated interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and C-reactive protein (CRP)^{23,24}. These obesity-related mechanical and inflammatory effects may impair wound healing and increase susceptibility to postoperative infections and cardiovascular events²⁵. Second, cardiovascular disease was more frequent among patients with PRISm in our cohort and preoperative functional capacity was also lower in PRISm patients, as reflected by shorter 6-minute walk test distances compared with those with normal lung function or mild OLD, indicating reduced cardiopulmonary reserve, a well-established predictor of postoperative complications²⁶. Although these comorbidities and functional limitations were accounted for in multivariable analyses, PRISm remained independently associated with increased risks of postoperative pulmonary and cardiac complications. Notably, the adjusted relative risk for PCCs was highest in the PRISm group, supporting the contribution of systemic factors beyond pulmonary function alone. These findings are consistent with prior reports linking PRISm to increased cardiovascular mortality^{8,14,27}. Our results suggest that PRISm represents a distinct pathophysiologic entity rather than a mild COPD variant and should be explicitly considered in preoperative risk assessment.

There is growing recognition that PRISm is a heterogeneous entity driven by diverse underlying pathophysiologies¹⁰. Recent studies have proposed stratifying PRISm into

"restrictive PRISm" (FVC <80% predicted) and "non-restrictive PRISm" (FVC $\geq$ 80% predicted), which exhibit distinct risk factor profiles and clinical trajectories¹². To explore this heterogeneity, we performed a stratified analysis based on FVC levels within the PRISm group. Our data demonstrated that PRISm patients with low FVC had a markedly higher risk of both PPCs (adjusted RR = 3.41) and PCCs (adjusted RR = 3.31) compared to those with normal FVC. This "low FVC" phenotype within PRISm may reflect more severe restrictive physiology related to obesity-induced lung compression, subclinical interstitial lung abnormalities, neuromuscular weakness, or other mixed pathologies^{24,28-30}. This "low FVC" subgroup represents a clinically important phenotype that may benefit from preoperative optimization through pulmonary rehabilitation, smoking cessation, and metabolic control.

These findings have practical implications for perioperative care. Clinicians should carefully assess PRISm before lung resection, especially when accompanied by low FVC or multiple comorbidities. Preoperative optimization may include pulmonary rehabilitation, smoking cessation, and weight reduction in obese patients—approaches supported by data from COPD and thoracic surgery studies³¹⁻³³. Given that PRISm often accompanies hypertension, diabetes, and dyslipidemia, these conditions should be well managed before surgery. For PRISm patients with low FVC who are deemed high-risk, a multidisciplinary discussion among pulmonologists, surgeons, and anesthesiologists can help decide whether minimally invasive techniques or limited resection are preferable. Although prospective perioperative data specific to PRISm are lacking, existing evidence suggests that targeted interventions could mitigate risk.

Our study has several limitations. First, since our study population was recruited from a single tertiary center, generalizability to other populations or surgical settings may be limited. The clinical characteristics of PRISm appear to vary across regions and ethnic populations. In several Asian cohorts, PRISm has been reported more frequently in individuals in settings with higher burdens of tuberculosis or environmental exposures, whereas in many Western

populations PRISm is more commonly linked to obesity and metabolic syndrome^{13,14}. These differences may affect the relationship between PRISm and postoperative outcomes, and external validation in other ethnic populations is warranted. Second, our study included only patients with lung cancer who received curative surgical treatment; therefore, the results may not be generalizable to other types of patients undergoing thoracic or non-thoracic surgical procedures. Future studies with larger, multicenter cohorts are required to enhance our understanding of the risks associated with PRISm. Finally, despite rigorous statistical adjustment for BMI, smoking, and functional capacity, we cannot completely rule out the possibility of residual confounding from unmeasured variables.

CONCLUSION

In conclusion, PRISm, similar to COPD, is a significant and independent risk factor for postoperative cardiopulmonary complications in lung cancer surgery. Patients with low FVC within the PRISm spectrum should be recognized as high-risk candidates who may benefit from perioperative pulmonary rehabilitation, weight management, and optimization of cardiometabolic comorbidities to improve surgical outcomes.

MATERIALS AND METHODS

Participants

Data were obtained from a prospective cohort study, the Coordinate Approach to Cancer Patients' Health for Lung Cancer (CATCH-LUNG). Patients for the CATCH-LUNG study were recruited from a tertiary university-based cancer center between March 2016 and December 2020 in Seoul, Korea. The following patients were included in the CATCH-LUNG study: 1) those who were expected to undergo curative lung cancer surgery for suspected NSCLC, 2) those with an Eastern Cooperative Oncology Group Performance Status of 0 or 1,

3) those who did not have any problem in walking, and 4) those who understood the purpose of this study and agreed to participate. The following patients were excluded from the study: 1) those who had undergone neoadjuvant treatment prior to surgery, 2) those free of NSCLC after pathological examination, 3) those for whom the surgery was canceled, or 4) those who withdrew consent before baseline data collection. Finally, 834 patients were included in this study (**Figure 1**). The study protocol was approved by the Institutional Review Board of Samsung Medical Center (IRB no. 2015-11-025) and aligns with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Spirometry test

Spirometry and diffusing capacity for carbon monoxide (DLco) measurements were performed using a Vmax 22 (SensorMedics, OH, USA) according to the American Thoracic Society (ATS)/European Respiratory Society criteria^{34,35}. Absolute values of FEV₁, forced vital capacity (FVC), and DLco were obtained, and the percentages of the predicted values (% predicted) for FEV₁, FVC, and DLco were calculated using a reference equation obtained from the analysis of a representative Korean sample^{36,37}. The participants were categorized into four groups: normal (FEV₁/FVC $\geq$ 0.7 and FEV₁ $\geq$ 80%), PRISm (FEV₁/FVC $\geq$ 0.7 and FEV₁ <80%), mild obstructive lung disease (OLD) (FEV₁/FVC <0.7 and FEV₁ $\geq$ 80%) and moderate OLD (FEV₁/FVC <0.7 and FEV₁ <80%)²⁸.

Postoperative cardiopulmonary complications

The primary endpoint of this study was the incidence of postoperative cardiopulmonary complications within the first 30 postoperative days. Data on postoperative pulmonary complications (PPCs) and postoperative cardiac complications (PCCs) were collected prospectively, following pre-agreed-upon definitions³⁸. A PPC was defined as any of the

following conditions: 1) atelectasis requiring bronchoscopic toileting; 2) pneumonia characterized by at least three of the following criteria: leukocytosis, pulmonary infiltrate or consolidation, fever ($>38^{\circ}\text{C}$), positive culture, or use of antibiotics; 3) acute lung injury or acute respiratory distress syndrome (rate of arterial oxygen partial pressure to fractional inspired oxygen <300 and bilateral infiltrate seen on chest radiograph without an evidence of congestive heart failure or volume overload); or 4) acute exacerbation of chronic obstructive pulmonary disease²¹. A PCC was defined as any of the following events: acute myocardial infarction, ventricular tachycardia/fibrillation, primary cardiac arrest, complete heart block, cardiac-related death, or atrial arrhythmia requiring the use of anti-arrhythmic drugs or anti-coagulants^{39,40}. All postoperative cardiopulmonary complications were assessed using Clavien–Dindo classification⁴¹. In this study, PPCs and PCC were defined as newly developed postoperative conditions of $\geq$ grade 2 according to the Clavien–Dindo classification; for arrhythmia, new or different postoperative rhythms distinct from any pre-existing abnormalities were classified as PCC.

Mortality

Overall survival (OS) was calculated from the date at operation to death from any cause. Vital status and date of death until May 23, 2023, were obtained from death certification collected from the Ministry of the Interior and Safety.

Other factors

Sociodemographic and behavioral information including age, sex, body mass index, smoking status, the presence of comorbidities, pulmonary function, and laboratory findings were recorded. The participants performed the 6-minute walk test (6MWT) according to the ATS guidelines⁴². Each participant was asked to walk (not run) back and forth along the

corridor as briskly as possible so that the longest possible distance was covered in 6 minutes. Data on the type of surgical approach, pathologic type of lung cancer, and pathological stage were collected after surgery.

Statistical analysis

Descriptive statistics were used to summarize the characteristics of the participants stratified by groups. Continuous and categorical variables were compared among the groups using analysis of variance and Fisher's exact test, respectively. We estimated the marginally adjusted proportions of postoperative cardiopulmonary complications in each group and calculated their relative risks (RRs) using Poisson regression with a robust variance. We selected covariates based on prior evidence and clinical relevance. The final multivariable models included age, sex, body mass index, smoking status, 6-minute walk test, history of cardiovascular disease, pathological stage, histological type, and type of surgery. In addition, we conducted an exploratory subgroup analysis within the PRISm cohort, comparing patients with low and normal FVC using the same multivariable adjustment to evaluate the association between low FVC and postoperative risk. For overall survival, we calculated the incidence rate of mortality per year and estimated the five-year cumulative survival rate using Kaplan Meier methods. We then performed Cox regression to estimate hazard ratios with 95% CIs for each lung function group. The covariates were identical to those used in the postoperative cardiopulmonary complication models. We calculated p-values for interactions to test whether the association between lung function and postoperative cardiopulmonary complications differed according to these factors. Statistical significance was set at P-value <0.05. All analyses were performed using STATA version 18 (StataCorp LP, College Station, TX, USA).

Declarations

Ethics approval and consent to participate: The study protocol was approved by the Institutional Review Board of Samsung Medical Center (IRB no. 2015-11-025) and aligns with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests: The authors declare no competing interests.

Funding: This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (RS-2025-00519997, NRF-2020R1F1A1075388).

Clinical trial number: Not applicable

Authors' contributions: **DL:** Writing – original draft; Writing – review & editing. **GL:** Data curation, Writing – review & editing. **SK:** Data curation; Resources; Writing – review & editing. **BC:** Writing – review & editing. **YI:** Writing – review & editing. **DK:** Formal analysis; Methodology, Visualization, Writing – review & editing. **HYP:** Conceptualization; Writing – review & editing. All authors reviewed the manuscript.

Acknowledgements: None

ORCID IDs

Daegun Lee: 0000-0001-5843-8927

Genehee Lee: 0000-0002-6361-4822

Sunga Kong: 0000-0001-7313-7786

Boksoon Chang: 0000-0003-1623-2685

Yunjoo Im: 0000-0002-0892-334X

Danbee Kang: 0000-0003-0244-7714

Hye Yun Park: 0000-0002-5937-9671

ARTICLE IN PRESS

REFERENCES

- 1 Sung, H. *et al.* Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* **71**, 209-249, doi:10.3322/caac.21660 (2021).
- 2 Nojiri, T. *et al.* Impact of cardiopulmonary complications of lung cancer surgery on long-term outcomes. *Surg Today* **45**, 740-745, doi:10.1007/s00595-014-1032-z (2015).
- 3 Shin, S. *et al.* Longitudinal changes in pulmonary function and patient-reported outcomes after lung cancer surgery. *Respir Res* **23**, 224, doi:10.1186/s12931-022-02149-9 (2022).
- 4 Ludbrook, G. L. The Hidden Pandemic: the Cost of Postoperative Complications. *Curr Anesthesiol Rep* **12**, 1-9, doi:10.1007/s40140-021-00493-y (2022).
- 5 Wan, E. S. *et al.* Epidemiology, genetics, and subtyping of preserved ratio impaired spirometry (PRISm) in COPDGene. *Respir Res* **15**, 89, doi:10.1186/s12931-014-0089-y (2014).
- 6 Schwartz, A. *et al.* Preserved Ratio Impaired Spirometry in a Spirometry Database. *Respir Care* **66**, 58-65, doi:10.4187/respcare.07712 (2021).
- 7 Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for Prevention, Diagnosis and Management of COPD: 2025 Report. (2025).
- 8 Wijnant, S. R. A. *et al.* Trajectory and mortality of preserved ratio impaired spirometry: the Rotterdam Study. *European Respiratory Journal* **55**, 1901217, doi:10.1183/13993003.01217-2019 (2020).
- 9 Higbee, D. H., Granell, R., Davey Smith, G. & Dodd, J. W. Prevalence, risk factors, and clinical implications of preserved ratio impaired spirometry: a UK Biobank cohort analysis. *Lancet Respir Med* **10**, 149-157, doi:10.1016/S2213-2600(21)00369-6 (2022).
- 10 Wan, E. S. The Clinical Spectrum of PRISm. *Am J Respir Crit Care Med* **206**, 524-525, doi:10.1164/rccm.202205-0965ED (2022).
- 11 Lu, J. *et al.* Subtyping preserved ratio impaired spirometry (PRISm) by using quantitative HRCT imaging characteristics. *Respir Res* **23**, 309, doi:10.1186/s12931-022-02113-7 (2022).
- 12 Miura, S. *et al.* Preserved ratio impaired spirometry with or without restrictive spirometric abnormality. *Sci Rep* **13**, 2988, doi:10.1038/s41598-023-29922-0 (2023).
- 13 Wan, E. S. *et al.* Association Between Preserved Ratio Impaired Spirometry and Clinical Outcomes in US Adults. *JAMA* **326**, 2287-2298, doi:10.1001/jama.2021.20939 (2021).
- 14 Wade, R. C. & Wells, J. M. Preserved Ratio With Impaired Spirometry: The Lung's Contribution to Metabolic Syndrome. *CHEST* **164**, 1075-1076, doi:10.1016/j.chest.2023.06.030 (2023).
- 15 Heo, I. R. *et al.* Impact of coexistent preserved ratio impaired spirometry on the survival of patients with lung cancer: Analysis of data from the Korean Association for Lung Cancer Registry. *Thorac Cancer* **12**, 2478-2486, doi:10.1111/1759-7714.14095 (2021).
- 16 Yang, S., Liao, G. & Tse, L. A. Association of preserved ratio impaired spirometry with mortality: a systematic review and meta-analysis. *European Respiratory Review* **32**, 230135, doi:10.1183/16000617.0135-2023 (2023).

- 17 Thu Win, K. *et al.* Impaired lung function and lung cancer risk in 461 healthy individuals: a cohort study. *BMJ Open Respiratory Research* **11**, e001936, doi:10.1136/bmjresp-2023-001936 (2024).
- 18 Kearney, D. J., Lee, T. H., Reilly, J. J., DeCamp, M. M. & Sugarbaker, D. J. Assessment of operative risk in patients undergoing lung resection. Importance of predicted pulmonary function. *Chest* **105**, 753-759, doi:10.1378/chest.105.3.753 (1994).
- 19 Shin, S. H. *et al.* Restrictive Spirometric Pattern and Postoperative Pulmonary Complications Following Non-cardiothoracic Surgery. *Sci Rep* **9**, 12750, doi:10.1038/s41598-019-49158-1 (2019).
- 20 Gong, J. *et al.* Increased postoperative complications after laparoscopic gastrectomy in patients with preserved ratio impaired spirometry. *J Gastrointest Surg* **28**, 889-895, doi:10.1016/j.gassur.2024.03.022 (2024).
- 21 Shin, S. *et al.* Joint effect of airflow limitation and emphysema on postoperative outcomes in early-stage nonsmall cell lung cancer. *Eur Respir J* **48**, 1743-1750, doi:10.1183/13993003.01148-2016 (2016).
- 22 Yoshimi, K. *et al.* Impact of Airflow Limitation on Comorbidities and Postoperative Complications in Patients Undergoing Thoracic Surgery: A Retrospective Observational Study. *Annals of Thoracic and Cardiovascular Surgery* **22**, 146-152, doi:10.5761/atcs.oa.15-00301 (2016).
- 23 Poirier, P. *et al.* Obesity and cardiovascular disease. pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation* **113**, 898-918, doi:10.1161/circulationaha.106.171016 (2006).
- 24 Leone, N. *et al.* Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. *Am J Respir Crit Care Med* **179**, 509-516, doi:10.1164/rccm.200807-1195OC (2009).
- 25 Powell-Wiley, T. M. *et al.* Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation* **143**, e984-e1010, doi:10.1161/cir.0000000000000973 (2021).
- 26 Silvapulle, E. & Darvall, J. Objective methods for preoperative assessment of functional capacity. *BJA Educ* **22**, 312-320, doi:10.1016/j.bjae.2022.03.003 (2022).
- 27 Im, Y. *et al.* Association of Preserved Ratio Impaired Spirometry (PRISm) with All-Cause Mortality: A Longitudinal Cohort Study. *Ann Am Thorac Soc*, doi:10.1513/AnnalsATS.202403-250OC (2024).
- 28 Godfrey, M. S. & Jankowich, M. D. The Vital Capacity Is Vital: Epidemiology and Clinical Significance of the Restrictive Spirometry Pattern. *Chest* **149**, 238-251, doi:10.1378/chest.15-1045 (2016).
- 29 Shah, N. M. & Kaltsakas, G. Respiratory complications of obesity: from early changes to respiratory failure. *Breathe (Sheff)* **19**, 220263, doi:10.1183/20734735.0263-2022 (2023).
- 30 Guerra, S. *et al.* Morbidity and mortality associated with the restrictive spirometric pattern: a longitudinal study. *Thorax* **65**, 499-504, doi:10.1136/thx.2009.126052 (2010).
- 31 Bolton, C. E. *et al.* British Thoracic Society guideline on pulmonary rehabilitation in adults: accredited by NICE. *Thorax* **68**, ii1-ii30, doi:10.1136/thoraxjnl-2013-203808 (2013).

- 32 Bobbio, A. *et al.* Preoperative pulmonary rehabilitation in patients undergoing lung resection for non-small cell lung cancer. *Eur J Cardiothorac Surg* **33**, 95-98, doi:10.1016/j.ejcts.2007.10.003 (2008).
- 33 Benzo, R. *et al.* Preoperative pulmonary rehabilitation before lung cancer resection: results from two randomized studies. *Lung Cancer* **74**, 441-445, doi:10.1016/j.lungcan.2011.05.011 (2011).
- 34 Miller, M. R. *et al.* Standardisation of spirometry. *Eur Respir J* **26**, 319-338, doi:10.1183/09031936.05.00034805 (2005).
- 35 American Thoracic Society. Single-breath carbon monoxide diffusing capacity (transfer factor). Recommendations for a standard technique--1995 update. *Am J Respir Crit Care Med* **152**, 2185-2198, doi:10.1164/ajrccm.152.6.8520796 (1995).
- 36 Choi, J. K., Paek, D. & Lee, J. O. Normal Predictive Values of Spirometry in Korean Population. *trd* **58**, 230-242, doi:10.4046/trd.2005.58.3.230 (2005).
- 37 Park, J. O., Choi, I. S. & Park, K. O. Normal predicted values of single-breath diffusing capacity of the lung in healthy nonsmoking adults. *Korean J Intern Med* **1**, 178-184, doi:10.3904/kjim.1986.1.2.178 (1986).
- 38 The Society of Thoracic Surgeons. *The Society of Thoracic Surgeons. STS General Thoracic Surgery Database Data Specifications, Version 2.3*, <https://www.sts.org/sites/default/files/documents/STSThoracicDataSpecsV2_3.pdf> (2014).
- 39 Brunelli, A. *et al.* Recalibration of the revised cardiac risk index in lung resection candidates. *Ann Thorac Surg* **90**, 199-203, doi:10.1016/j.athoracsur.2010.03.042 (2010).
- 40 Brunelli, A. *et al.* External validation of the recalibrated thoracic revised cardiac risk index for predicting the risk of major cardiac complications after lung resection. *Ann Thorac Surg* **92**, 445-448, doi:10.1016/j.athoracsur.2011.03.095 (2011).
- 41 Dindo, D., Demartines, N. & Clavien, P. A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* **240**, 205-213, doi:10.1097/01.sla.0000133083.54934.ae (2004).
- 42 Laboratories, A. T. S. C. o. P. S. f. C. P. F. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* **166**, 111-117, doi:10.1164/ajrccm.166.1.at1102 (2002).

FIGURE LEGENDS

Figure 1. Flowchart of study patients' selection process

NSCLC, non-small cell lung cancer; 6MWT, 6-minute walk test

Figure 2. Subgroup analysis (adjusted relative risk for PPC)

CVD, cardiovascular disease; RR, relative risk; PPC, postoperative pulmonary complications

ARTICLE IN PRESS

TABLES

Table 1. Characteristics of the patients in the pulmonary function groups (n = 834)

Characteristics	Normal (n=582)	PRISm (n = 61)	Mild OLD (n = 94)	Moderate OLD (n = 97)	<i>P values</i>
Age, years	60.3 (9.3)	60.9 (8.7)	65.2 (8)	67.4 (6.8)	<0.001
Sex, male	266 (45.7)	38 (62.3)	78 (83.0)	85 (87.6)	<0.001
BMI, kg/m²	23.9 (2.7)	24.8 (4.2)	24 (2.4)	23.7 (2.7)	0.14
Smoking status					<0.001
Never smoker	269 (46.2)	23 (37.7)	19 (20.2)	12 (12.4)	
Ever smoker	181 (31.1)	28 (45.9)	56 (59.6)	59 (60.8)	
Unknown	132 (22.7)	10 (16.4)	19 (20.2)	26 (26.8)	
Comorbidities					
Pulmonary	49 (8.4)	13 (21.3)	8 (8.5)	35 (36.1)	<0.001
Hypertension	198 (34)	26 (42.6)	33 (35.1)	40 (41.2)	0.35
Diabetes mellitus	71 (12.2)	15 (24.6)	17 (18.1)	17 (17.5)	0.03
Cardiovascular disease	47 (8.1)	11 (18.0)	9 (9.6)	16 (16.5)	0.010
Pathologic stage					0.03
I	446 (76.6)	37 (60.7)	67 (71.3)	67 (69.1)	
II	80 (13.7)	15 (24.6)	15 (16)	23 (23.7)	
III/IV	56 (9.6)	9 (14.8)	12 (12.8)	7 (7.2)	
Histologic type					<0.001
Squamous cell carcinoma	40 (6.9)	14 (23)	18 (19.1)	41 (42.3)	
Adenocarcinoma	526 (90.4)	43 (70.5)	72 (76.6)	50 (51.5)	
Others	16 (2.7)	4 (6.6)	4 (4.3)	6 (6.2)	
Type of surgery					0.001
Pneumonectomy	5 (0.9)	3 (0.5)	0 (0)	2 (0.3)	

Bilobectomy	4 (0.7)	5 (0.9)	3 (0.5)	4 (0.7)	
Lobectomy	452 (77.7)	47 (77.1)	74 (78.7)	73 (75.3)	
Segmentectomy	73 (12.5)	3 (0.5)	11 (1.9)	9 (1.5)	
Wedge resection	48 (8.2)	3 (0.5)	6 (1)	9 (1.5)	
Type of surgical approach, VATs	512 (88)	38 (6.5)	61 (10.5)	56 (9.6)	<0.001
Pulmonary function					
FVC, L	3.6 (0.8)	2.9 (0.6)	4.2 (0.8)	3.3 (0.7)	<0.001
FVC, % predicted	95.4 (10)	73.2 (8.1)	100.5 (10.4)	81.3 (9.8)	<0.001
FEV ₁ , L	2.8 (0.6)	2.2 (0.4)	2.8 (0.5)	1.9 (0.5)	<0.001
FEV ₁ , % predicted	96.6 (10.1)	72.4 (5.7)	89.8 (8.8)	65.5 (9.1)	<0.001
FEV ₁ /FVC	77.7 (4.8)	75.7 (4.3)	65.2 (3.4)	58.4 (8.1)	<0.001
DLco, % predicted	92.8 (14.7)	79.6 (16)	90.5 (18.5)	78.7 (15.3)	<0.001
6MWT, m	519.4 (81)	479.8 (92.4)	524 (72.6)	497.8 (63.2)	<0.001

Values are number of patients (%) or mean (standard deviation).

BMI, body mass index; PRISm, preserved ratio impaired spirometry; OLD, obstructive lung disease; 6MWT, 6-minute walk test; COPD, chronic obstructive pulmonary disease; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s; DLco, diffusing capacity of carbon monoxide; VATS, video-assisted thoracoscopic surgery; ppoFEV₁, predicted postoperative forced expiratory volume in 1 s; ppoDLco, predicted postoperative diffusing capacity of carbon monoxide.

Table 2. Risk of postoperative cardiopulmonary complications (PPCs or PCCs) in patients with NSCLC

	Normal (n = 582)	PRISm (n = 61)	Mild OLD (n = 94)	Moderate OLD (n = 97)
Postoperative pulmonary complications				
N (%)	19 (3.3)	7 (11.5)	11 (11.7)	20 (20.6)
Crude RR (95% CI)	<i>Reference</i>	3.52 (1.54–8.02)	3.59 (1.76–7.29)	6.32 (3.50–11.40)
Adjusted RR (95% CI) *	<i>Reference</i>	2.62 (1.10–6.23)	2.32 (1.15–4.70)	3.25 (1.69–6.27)
Postoperative cardio complications				
N (%)	27 (4.6)	10 (16.4)	12 (12.8)	17 (17.5)
Crude RR (95% CI)	<i>Reference</i>	3.53 (1.80–6.95)	2.75 (1.44–5.24)	3.78 (2.14–6.67)
Adjusted RR (95% CI) *	<i>Reference</i>	2.67 (1.42–4.99)	1.94 (1.02–3.67)	2.32 (1.20–4.48)
Postoperative cardiopulmonary complications				
N (%)	44 (7.6)	16 (26.2)	18 (19.1)	32 (33.0)
Crude RR (95% CI)	<i>Reference</i>	3.47 (2.09–5.77)	2.53 (1.53–4.19)	4.36 (2.92–6.52)
Adjusted RR (95% CI) *	<i>Reference</i>	2.70 (1.63–4.49)	1.78 (1.07–2.97)	2.47 (1.55–3.94)

*Adjusted for age, sex, body mass index, smoking status, 6-minute walk test, history of cardiovascular disease, pathology stage, histologic type, and type of surgery

PPCs occurred as ALI/ARDS (n=14), ALI/ARDS with pneumonia (n=15), pneumonia alone (n=16), atelectasis requiring bronchoscopic toileting (n=9), and acute exacerbation of COPD (n=3); PCCs occurred as atrial arrhythmias (n=61), PSVT (n=1), sinus tachycardia (n=3), and myocardial infarction (n=1), with no ventricular arrhythmias, complete heart block, or cardiac arrest/death.

Reference refers to the normal lung function group set as the baseline (RR = 1.00)

PPCs, postoperative pulmonary complication; PCCs, postoperative cardiac complication; NSCLC, non-small cell lung cancer; PRISm, preserved ratio impaired spirometry; OLD, obstructive lung disease; CI, confidence interval; RR, relative risk; ALI, acute lung injury; ARDS, acute respiratory distress syndrome; PSVT, paroxysmal supraventricular tachycardia

ARTICLE IN PRESS

Table 3. Risk of postoperative cardiopulmonary complications (PPCs or PCCs) in patients with NSCLC: stratified by FVC

	Normal (n = 582)	PRISm with normal FVC (n = 20)	PRISm with low FVC (n = 41)
Postoperative pulmonary complications			
N (%)	19 (3.3)	1 (5.0)	6 (14.6)
Crude RR (95% CI)	<i>Reference</i>	1.53 (0.22–10.90)	4.48 (1.89–10.62)
Adjusted RR (95% CI) *	<i>Reference</i>	1.59 (0.20–12.81)	3.41 (1.22–9.54)
Postoperative cardio complications			
N (%)	27 (4.6)	1 (5.0)	9 (22.0)
Crude RR (95% CI)	<i>Reference</i>	1.08 (0.15–7.55)	4.73 (2.38–9.39)
Adjusted RR (95% CI) *	<i>Reference</i>	1.52 (0.20–11.43)	3.31 (1.74–6.31)
Postoperative cardiopulmonary complications			
N (%)	44 (7.6)	2 (10.0)	14 (34.2)
Crude RR (95% CI)	<i>Reference</i>	1.32 (0.34–5.08)	4.52 (2.71–7.53)
Adjusted RR (95% CI) *	<i>Reference</i>	1.56 (0.38–6.42)	3.37 (1.95–5.83)

*Adjusted for age, sex, body mass index, smoking status, 6-minute walk test, history of cardiovascular disease, pathology stage, histologic type, and type of surgery

Reference refers to the normal lung function group set as the baseline (RR = 1.00)

PPCs, postoperative pulmonary complication; PCCs, postoperative cardiac complication; NSCLC, non-small cell lung cancer; PRISm, preserved ratio impaired spirometry; OLD, obstructive lung disease; CI, confidence interval; RR, relative risk

Table 4. Hazard Ratio of mortality in patients with NSCLC

	Normal (n = 582)	PRISm (n = 61)	Mild OLD (n = 94)	Moderate OLD (n = 97)
Number of death (incidence rate per a year %)	28 (1.2)	8 (3.4)	11 (3.0)	16 (4.7)
5-years survival rate, %	94.7	86.4	86.8	81.6
Crude HR (95% CI)	<i>Reference</i>	2.81 (1.28–6.16)	2.47 (1.23–4.97)	3.89 (2.10–7.16)
Adjusted HR (95% CI) *	<i>Reference</i>	1.19 (0.51–2.82)	1.87 (0.89–3.92)	2.01 (1.00–4.14)

*Adjusted for age, sex, body mass index, smoking status, 6-minute walk test, history of cardiovascular disease, pathology stage, histologic type, and type of surgery

Reference refers to the normal lung function group set as the baseline (HR = 1.00)

NSCLC, non-small cell lung cancer; PRISm, preserved ratio impaired spirometry; OLD, obstructive lung disease; CI, confidence interval; HR, hazard ratio

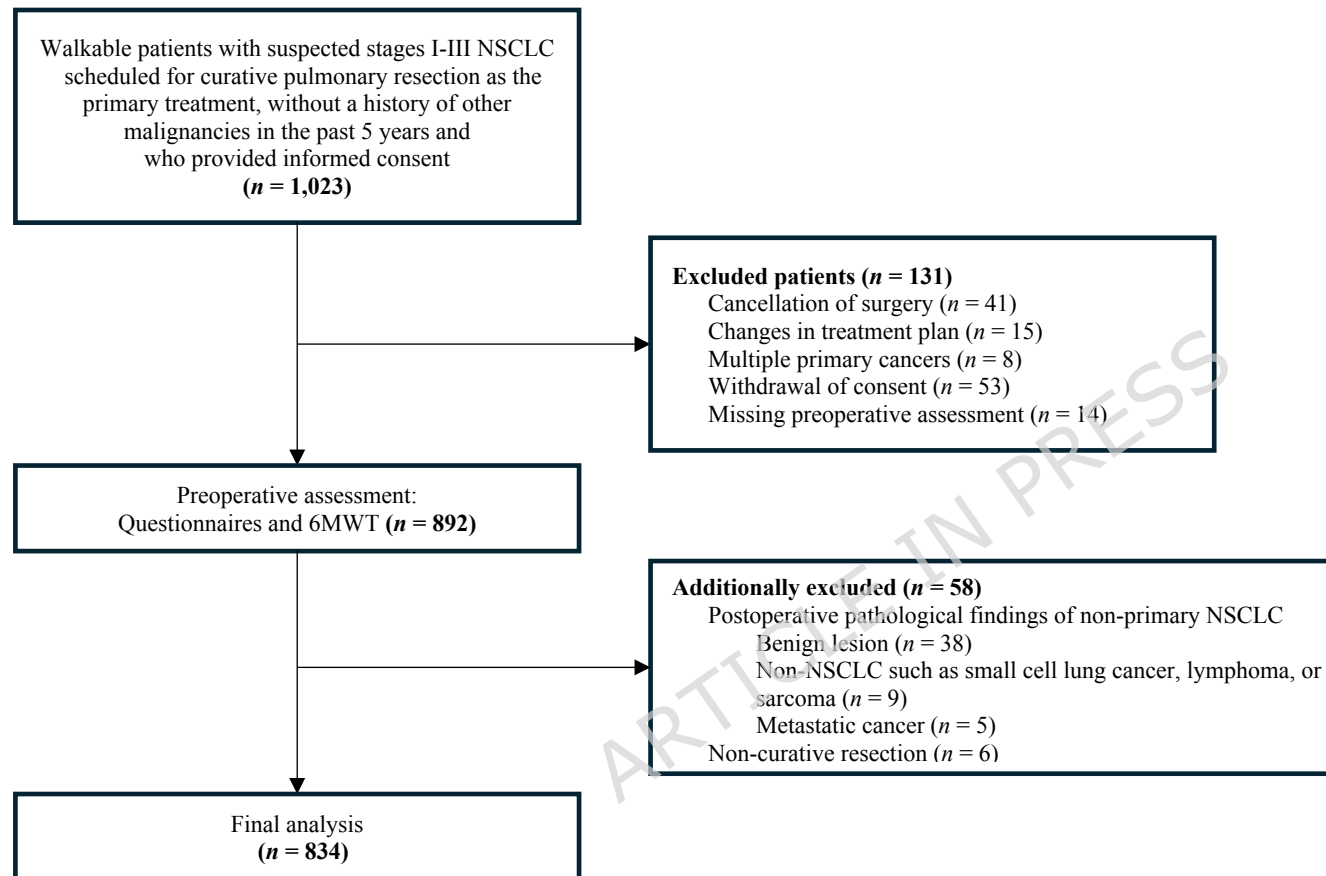


Figure 1.

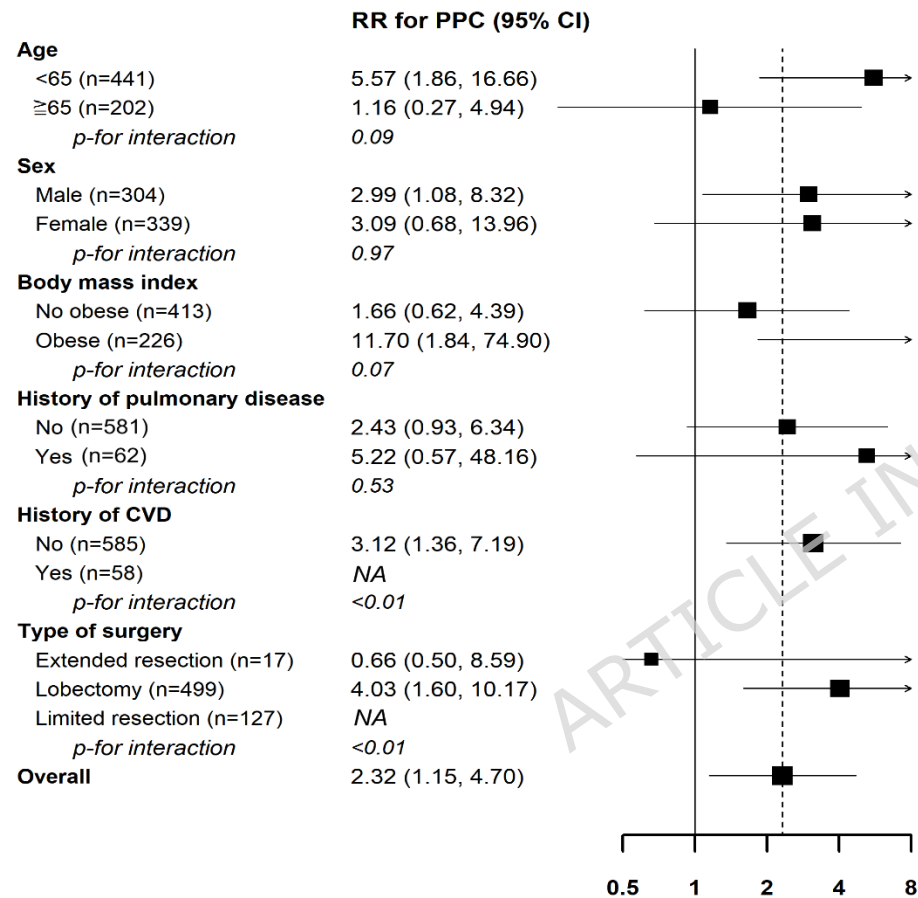


Figure 2.