INPLASY

The Impact of Comorbid COPD on Survival Outcomes in Lung Cancer Patients Treated with Immune Checkpoint Inhibitors: A Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 August 2025 and was last updated on 28 August 2025.

INTRODUCTION

Review question / Objective This study demonstrated that LC patients with COPD receiving ICIs exhibited significant OS improvements. Although statistically significant PFS benefits were observed, these results may be overestimated due to potential bias. Prospective studies integrating biomarker analyses are needed to elucidate COPD-ICIs synergism and optimize personalized strategies for this cohort.

Condition being studied Lung cancer (LC) remains the leading cause of cancer-related death worldwide. While immune checkpoint inhibitors (ICIs) have demonstrated survival benefits in advanced-stage disease, treatment responses exhibit significant heterogeneity across patients. The potential role of comorbid chronic obstructive pulmonary disease (COPD) in modulating survival outcomes from ICIs therapy remains controversial, with conflicting evidence regarding its synergistic or antagonistic effects. This meta-analysis systematically evaluates the impact of COPD on survival outcomes in lung cancer patients receiving ICIs, aiming to clarify its prognostic value and guide precision immunotherapy strategies.

METHODS

Participant or population Inclusion Criteria: (1)Lung cancer patients confirmed by histopathological diagnosis with comorbid COPD(diagnosed according to GOLD guidelines or pulmonary function tests);(2)Receiving ICIs monotherapy or combination regimens (e.g., ICIs combined with chemotherapy, radiotherapy);(3) Prospective or retrospective clinical studies investigating the impact of COPD on survival outcomes in patients treated with ICIs;(4)Direct or indirect reporting of survival endpoints, including but not limited to OS, PFS, hazard ratios (HR), and 95% confidence intervals (CI), or accessible Kaplan-Meier curve data for HR extraction.
Exclusion Criteria: (1)Studies that did not stratify lung cancer patients by COPD status or reported only systemic inflammatory markers (e.g., CRP, IL-6) without COPD-specific data;(2)Studies

including patients receiving non-ICIs therapies (e.g., targeted therapy, chemotherapy/radiotherapy alone) without subgroup analysis for ICIs-treated cohorts;(3)Case reports, conference abstracts, preclinical studies (e.g., animal experiments, cell models), reviews, or commentary articles; (4)Studies lacking sufficient data to extract HR and 95% CI for survival outcomes (even after contacting authors) or duplicate publications (retaining the most recent or largest cohort).

Intervention Inclusion Criteria: (1)Lung cancer patients confirmed by histopathological diagnosis with comorbid COPD(diagnosed according to GOLD guidelines or pulmonary function tests); (2)Receiving ICIs monotherapy or combination regimens (e.g., ICIs combined with chemotherapy, radiotherapy);(3) Prospective or retrospective clinical studies investigating the impact of COPD on survival outcomes in patients treated with ICIs; (4)Direct or indirect reporting of survival endpoints, including but not limited to OS, PFS, hazard ratios (HR), and 95% confidence intervals (CI), or accessible Kaplan-Meier curve data for HR extraction.
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Comparator Inclusion Criteria: (1)Lung cancer patients confirmed by histopathological diagnosis with comorbid COPD(diagnosed according to GOLD guidelines or pulmonary function tests); (2)Receiving ICIs monotherapy or combination regimens (e.g., ICIs combined with chemotherapy, radiotherapy);(3) Prospective or retrospective clinical studies investigating the impact of COPD on survival outcomes in patients treated with ICIs; (4)Direct or indirect reporting of survival endpoints, including but not limited to OS, PFS, hazard ratios (HR), and 95% confidence intervals (CI), or accessible Kaplan-Meier curve data for HR extraction.
Exclusion Criteria: (1)Studies that did not stratify lung cancer patients by COPD status or reported only systemic inflammatory markers (e.g., CRP, IL-6) without COPD-specific data;(2)Studies

including patients receiving non-ICIs therapies (e.g., targeted therapy, chemotherapy/radiotherapy alone) without subgroup analysis for ICIs-treated cohorts;(3)Case reports, conference abstracts, preclinical studies (e.g., animal experiments, cell models), reviews, or commentary articles; (4)Studies lacking sufficient data to extract HR and 95% CI for survival outcomes (even after contacting authors) or duplicate publications (retaining the most recent or largest cohort).

Study designs to be included OS and PFS/DF.

Eligibility criteria Inclusion Criteria: (1)Lung cancer patients confirmed by histopathological diagnosis with comorbid COPD(diagnosed according to GOLD guidelines or pulmonary function tests); (2)Receiving ICIs monotherapy or combination regimens (e.g., ICIs combined with chemotherapy, radiotherapy);(3) Prospective or retrospective clinical studies investigating the impact of COPD on survival outcomes in patients treated with ICIs; (4)Direct or indirect reporting of survival endpoints, including but not limited to OS, PFS, hazard ratios (HR), and 95% confidence intervals (CI), or accessible Kaplan-Meier curve data for HR extraction.
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Information sources PubMed, Cochrane Library, CNKI, and EMBASE.

Main outcome(s) This study demonstrated that LC patients with COPD receiving ICIs exhibited significant OS improvements. Although statistically significant PFS benefits were observed, these results may be overestimated due to potential bias. Prospective studies integrating biomarker analyses are needed to elucidate COPD-ICIs synergism and optimize personalized strategies for this cohort.

Quality assessment / Risk of bias analysis Publication bias was rigorously assessed using funnel plots, Egger's test, and Begg's test. The funnel plots for both OS and PFS demonstrated

high symmetry, indicating that the robustness of the pooled results was not significantly affected by bias.

Strategy of data synthesis This meta-analysis employed Stata SE (version 16.0; StataCorp, Texas, USA) to statistically evaluate the survival synergy between chronic obstructive pulmonary disease (COPD)-lung cancer immunoaxis interactions and clinical outcomes in patients receiving ICIs. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated through stratification. Heterogeneity across studies was assessed using Cochran's Q-test and I^2 statistics. A random-effects model was applied for pooled analysis when significant heterogeneity existed (I^2 > 50% or Q-test p-value < 0.10), while a fixed-effects model was used otherwise. Publication bias was preliminarily evaluated via funnel plot symmetry testing, further validated by Egger's regression analysis and Begg's rank correlation test (p-values < 0.05 indicated potential bias). To enhance methodological rigor, sensitivity analyses (iteratively excluding individual studies) were performed to test the stability of the pooled results, thereby confirming the robustness of the survival synergy between dynamic changes in the COPD-lung cancer immunoaxis and ICIs therapeutic efficacy.

Subgroup analysis Subgroup Analysis of OS in the COPD-Lung Cancer Immunoaxis Meta-Analysis of Patients Treated with ICIs.

Sensitivity analysis The sensitivity analysis revealed that omitting specific studies (e.g., Chan 2025 or Greib 2025 with HR=0.98) might significantly reduce the pooled HR for OS, suggesting a dilution effect of these studies on the overall results and potentially weakening the survival benefit conclusion of ICIs in the current meta-analysis.

Country(ies) involved China.

Keywords lung cancer; non-small cell lung cancer; immune checkpoint inhibitors; overall survival; progression-free survival; meta-analysis.

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