INPLASY

Prognostic Value of the C-Reactive Protein-Albumin-Lymphocyte (CALLY) Index in Lung Cancer: A Systematic Review and Meta-Analysis

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Jia, QQ; Shi, JY; Tong, X; Fan, H.

Corresponding author:
Qingqing Jia

qingqing_j@126.com

Author Affiliation:
West China Hospital of Sichuan University.

ADMINISTRATIVE INFORMATION

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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 12 January 2026 and was last updated on 12 January 2026.

INTRODUCTION

Review question / Objective Lung cancer imposes a severe global health burden, with prognosis heavily influenced by host systemic inflammation and nutritional status. The C-reactive protein-albumin-lymphocyte (CALLY) index, a novel composite biomarker integrating these key domains, has shown promising prognostic value in several solid tumors. However, evidence in lung cancer remains fragmented, and its overall prognostic significance has not been quantitatively synthesized. This study aims to systematically evaluate the association between the CALLY index and survival outcomes in lung cancer patients through a meta-analysis.

Condition being studied Lung cancer continues to be the leading cause of cancer-related mortality globally, imposing a severe and growing societal burden in terms of both lost disability-adjusted life years and substantial healthcare costs. While age-standardized incidence and mortality have improved in some regions, the absolute global burden remains high, with millions of new cases and deaths reported each year.

Accumulating research highlights the critical influence of host systemic inflammation and nutritional status on clinical outcomes in lung cancer, particularly in non-small cell lung cancer (NSCLC). Commonly used inflammatory markers, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII), are well-established indicators of aggressive disease and poor prognosis. However, composite biomarkers that integrate both inflammatory and nutritional dimensions have shown superior prognostic ability. For instance, the Advanced Lung Cancer Inflammation Index (ALI) and the Prognostic Nutritional Index (PNI)—which incorporate measures like body mass index, serum albumin,

and lymphocyte counts—have proven useful for risk stratification and guiding supportive care.
The C-reactive protein–Albumin–Lymphocyte (CALLY) index is a recently developed integrated score that simultaneously reflects systemic inflammation (via CRP), nutritional status (via albumin), and immune competence (via lymphocyte count). In several solid tumors, including colorectal, gastric, and breast cancers, a low CALLY index has consistently been associated with more advanced disease and worse survival. Preliminary studies in lung cancer also suggest its prognostic potential, with multiple retrospective cohorts reporting that low CALLY levels independently predict increased mortality risk. However, the existing evidence is fragmented, and no quantitative systematic synthesis has been conducted to evaluate its prognostic significance across studies.

METHODS

Participant or population Adults diagnosed with lung cancer (any histology or stage).

Intervention Exposure Metric: The baseline C-reactive protein-albumin-lymphocyte (CALLY) index.
Measurement Method: Studies using any assay method or reporting unit for CRP, albumin, and lymphocyte count were eligible. The specific formula for calculating the CALLY index could vary across studies.
Variable Format: The CALLY index could be analyzed as either a dichotomous variable (e.g., high vs. low, based on any study-specific cut-off) or a continuous variable.

Comparator For studies analyzing the CALLY index as a dichotomous variable, the required comparison is between patients classified as having a "high" index versus those with a "low" index (based on study-defined cut-offs).
For studies analyzing the CALLY index as a continuous variable, the comparison is defined as the change in hazard associated with a per-unit increase in the index score.

Study designs to be included Studies were included if they investigated the association between the baseline C-reactive protein-albumin-lymphocyte (CALLY) index and overall survival in patients with lung cancer, providing either hazard ratios or sufficient data to calculate an odds ratio.

Eligibility criteria We excluded reviews, case reports, conference abstracts, non-human studies, publications without extractable survival data, and studies with overlapping patient populations, retaining only the most comprehensive or recent report in cases of duplication. Exclusion criteria were: 1) reviews, case reports, conference abstracts, or non-human studies; 2) studies without extractable survival data (HRs or Kaplan-Meier curves); 3) studies with overlapping patient populations (only the most comprehensive or recent study was included).

Information sources PubMed/MEDLINE, Web of Science, Embase, Scopus, and the Cochrane Library
To ensure literature saturation, we also manually examined the reference lists of all included articles and relevant reviews.

Main outcome(s) Primary Outcome:
Overall Survival (OS), defined as the time from diagnosis or treatment initiation to death from any cause. No specific timing restriction was applied; studies with varying follow-up durations were included to assess the sustained prognostic effect of the CALLY index over time.

Additional outcome(s) Landmark survival at 5 years, analyzed as dichotomous (alive/dead) status at this fixed time point.

Quality assessment / Risk of bias analysis The Newcastle-Ottawa Scale (NOS).

Strategy of data synthesis For all pooled estimates, a two-tailed P-value < 0.05 was considered statistically significant, while a threshold of $P < 0.10$ was applied for tests of heterogeneity. All statistical analyses and meta-analyses were executed using Review Manager (RevMan) software, version 5.4.1 (The Cochrane Collaboration, 2020).

Subgroup analysis The pre-specified subgroup analysis was conducted by stratifying included studies based on the format of the CALLY index variable—specifically, comparing studies that analyzed the index as a dichotomous variable (high vs. low) versus those that treated it as a continuous variable (HR per unit increase).

Sensitivity analysis To assess the robustness of the pooled estimates, the following sensitivity analyses were performed:
1. Leave-one-out analysis: Sequentially excluding each individual study to evaluate its influence on the overall pooled hazard ratio (HR) and odds ratio (OR).
2. Analysis restricted to adjusted estimates: In the primary HR analysis, the dataset providing only a

univariable estimate was excluded to derive a pooled effect size based solely on multivariable-adjusted HRs, which resolved initial heterogeneity.

Language restriction English.

Country(ies) involved China.

Keywords Lung cancer; CALLY index; Prognosis; Meta-analysis; Survival.

Contributions of each author

Author 1 - Qingqing Jia.
Email: qingqing_j@126.com
Author 2 - Jingyu Shi.
Email: shijingyu@wchscu.edu.cn
Author 3 - Xiang Tong.
Email: tongxiang@scu.edu.cn
Author 4 - Hong Fan.
Email: fanhong@scu.edu.cn