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Lung Immune Prognostic Index (Lipi) As Prognostic Markers For Advanced Non-Small-Cell Lung Cancer (Nsclc) Treated With Immunotherapy: A Systematic Review And Meta-Analysis

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Abstract

The Lung Immune Prognostic Index (LIPI), based on the derived neutrophil-to-lymphocyte ratio (dNLR) and lactate dehydrogenase (LDH) levels, has been recognized as an important prognostic biomarker in lung cancer. However, its prognostic value in patients with non–small cell lung cancer (NSCLC) has not been extensively discussed. Objective: This systematic review and meta-analysis aimed to comprehensively evaluate the association between LIPI and survival outcomes in patients with advanced-stage NSCLC receiving immunotherapy. Systematic literature search was conducted across PubMed, ScienceDirect, Cochrane Library, SSRN, Epistemonikos, and Google Scholar databases up to January 10, 2025. Study quality was assessed using the Newcastle–Ottawa Scale (NOS). Data were extracted for qualitative and quantitative synthesis, including pooled analyses and subgroup analyses. Random-effects models were applied to pool hazard ratios (HRs) with 95% confidence intervals (CIs) to assess the association between LIPI and progression-free survival (PFS) and/or overall survival (OS) in patients with advanced NSCLC treated with immunotherapy. A total of 7,551 patients from 13 studies were included in the analysis. Pooled analysis demonstrated that patients with poor or intermediate LIPI scores, compared with those with good LIPI scores, had significantly shorter PFS (HR = 2.20, 95% CI: 1.83–2.63, P < 0.001; HR = 1.47, 95% CI: 1.31–1.65, P < 0.001) and worse OS (HR = 3.31, 95% CI: 2.70–4.06, P < 0.001; HR = 1.88, 95% CI: 1.58–2.23, P < 0.001). Subgroup analyses based on immunotherapy type (monotherapy versus combination therapy) yielded consistent results. This study demonstrates that poor and intermediate LIPI scores are significantly associated with worse prognosis in patients with advanced-stage NSCLC receiving immunotherapy. Therefore, LIPI may serve as a promising non-invasive prognostic biomarker for predicting survival outcomes in this patient population. Keywords: lung immune prognostic index, LIPI, non–small cell lung cancer, immunotherapy.

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INTRODUCTION

Lung cancer remains a major cause of cancer-related mortality globally in both men and women (Rojiani & Rojiani, 2024). It is broadly classified into two main subtypes: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC constitutes approximately 85% of all lung cancer cases and predominantly comprises lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC), which account for roughly 70% and 30% of cases, respectively(Rojiani & Rojiani, 2024). Nearly 53% of NSCLC cases are diagnosed at stage IV with distant metastases, while approximately 20–35% present at stage III. The 5-year survival rate for stage IV disease is about 8.9%, in contrast to 36%, 26%, and 13% for stages IIIA, IIIB, and IIIC, respectively. These marked differences in survival highlight the heterogeneity of NSCLC, with treatment strategies and prognostic outcomes varying substantially even among patients within the same disease stage (Asmara et al., 2024).

Immunotherapy, particularly immune checkpoint inhibitors (ICIs), has emerged as a safe, effective, and widely adopted treatment strategy for patients with non-small cell lung cancer (NSCLC). Compared with conventional chemotherapy, ICIs have significantly improved survival outcomes. However, primary and acquired resistance to immunotherapy remains common, limiting its long-term efficacy. Therefore, the identification of reliable predictive and prognostic biomarkers is essential to better stratify patients and optimize immunotherapy outcomes. With advances in molecular biology, genomic sequencing technologies, and a deeper understanding of the tumor immune microenvironment, ongoing and future studies are expected to validate promising biomarkers, ultimately expanding the clinical benefit of immunotherapy to a broader population of patients with lung cancer (Gauci et al., 2019; Li et al., 2023).

To optimize patient selection, biomarkers such as programmed death-ligand 1 (PD-L1) expression and tumor mutational burden (TMB) have been investigated, but their clinical use is limited by tumor heterogeneity, variability in testing methods, high cost, and limited availability in routine practice. There is therefore a growing need for simple, accessible, and non-invasive biomarkers to predict prognosis and guide immunotherapy in advanced NSCLC. Systemic inflammation plays an important role in cancer progression and prognosis, and inflammation- or immune-based biomarkers derived from peripheral blood have emerged as practical options because of their low cost, ease of assessment, and wide applicability in clinical settings (Hiam-Galvez et al., 2021; Restrepo et al., 2024).

The Lung Immune Prognostic Index (LIPI) is calculated based on the derived neutrophil-to-lymphocyte ratio (dNLR) and lactate dehydrogenase (LDH) levels, allowing patients to be stratified into good, intermediate, and poor LIPI risk groups (Mezquita et al., 2018). LIPI has been evaluated across a wide range of tumor types treated with immune checkpoint inhibitors (ICIs), including melanoma, head and neck cancer, bladder cancer, triple-negative breast cancer, renal cell carcinoma, microsatellite instability–high solid tumors, and various malignancies included in phase I–II clinical trials. Accumulating evidence indicates that the prognostic value of LIPI is largely independent of tumor type. Patients with poor LIPI scores consistently demonstrate limited benefit from ICIs, suggesting that LIPI assessment may identify subgroups with reduced or absent response to immunotherapy. Current clinical evidence strongly supports the prognostic relevance of LIPI in advanced NSCLC, irrespective of the planned treatment strategy (Aldea et al., 2020). Therefore, in this systematic review and meta-analysis, we aimed to evaluate the prognostic value of the Lung Immune Prognostic Index (LIPI) in relation to progression-free survival (PFS) and overall survival (OS).

RESEARCH METHODS

Design Study & Search Strategy

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed in PubMed, ScienceDirect, Cochrane Library, SSRN, Epistemonikos, and Google Scholar to identify all relevant studies. Any discrepancies during the selection process were discussed and resolved through consensus among the authors. The search strategies applied to each database were as follows: PubMed: (“Carcinoma, Non-Small-Cell Lung” [MeSH]) AND (“lung immune prognostic index” OR “LIPI” [Title/Abstract]); ScienceDirect: “lung immune prognostic index LIPI”; Cochrane Library: (“non-small cell lung ca*” OR “NSCLC”) AND (“Lung Immune Prognostic Index” OR “LIPI”); SSRN: “lung immune prognostic index”; Epistemonikos: ((lung immune prognostic index) OR (LIPI)) AND ((NSCLC) OR (non-small cell lung ca*)); and Google Scholar: ((non-small cell lung) OR NSCLC) AND ((lung immune prognostic index) OR LIPI). The publication period was restricted to studies published between 2015 and 2025. Duplicate records were removed, and the remaining studies were screened based on predefined inclusion criteria.

Eligibility Criteria and Study Selection

The inclusion criteria for this review were as follows: (1) patients with a pathological diagnosis of non-small cell lung cancer (NSCLC) at TNM stage III–IV; (2) patients receiving immunotherapy as monotherapy, without combination with other treatment modalities; (3) retrospective or prospective cohort studies published between 2015 and 2025; (4) assessment of the Lung Immune Prognostic

Index (LIPI) based on derived neutrophil-to-lymphocyte ratio (dNLR) and lactate dehydrogenase (LDH) levels measured prior to immunotherapy initiation (pretreatment LIPI); (5) studies evaluating the association between LIPI and the effectiveness of immunotherapy, with outcomes including progression-free survival (PFS) and overall survival (OS); (6) studies providing sufficient data to estimate hazard ratios (HRs) with 95% confidence intervals (95% CIs); and (7) availability of full-text articles published in English.

The exclusion criteria were: (1) studies of low methodological quality; (2) studies in which human subjects were not the primary focus; (3) publication types including reviews, meeting abstracts, letters, editorials, case reports, systematic reviews, and meta-analyses; and (4) studies with insufficient or duplicate data.

All identified studies were independently screened and assessed for eligibility by two authors using the PRISMA flow diagram. The screening process began with title and abstract review, followed by full-text screening of potentially eligible studies. All included studies were subsequently validated to ensure eligibility for the next stage of analysis.

Data Extraction and Quality Assesment

Data were independently extracted using Microsoft Excel spreadsheets to compile information from all eligible studies. The extracted data included the first author, year of publication, study period, study location, sample size, study design, patient age, pathological subtype, TNM stage, type of immune checkpoint inhibitor (ICI), treatment regimen, study endpoints, and Newcastle–Ottawa Scale (NOS) score.

Based on the characteristics of the included studies, methodological quality was assessed using the Newcastle–Ottawa Quality Assessment Scale (NOS). This assessment evaluates three key domains: selection of study groups, comparability of populations, and assessment of exposure or outcomes for potential risk of bias. Studies with a NOS score ≥ 6 were considered high quality and were included in the final analysis.

Pooled Analysis

Statistical analyses were performed using Review Manager (RevMan) version 5.4.1. Hazard ratios (HRs) with 95% confidence intervals (95% CIs) were pooled to evaluate the association between pretreatment Lung Immune Prognostic Index (LIPI) and overall survival (OS) and/or progression-free survival (PFS) in patients with advanced-stage non-small cell lung cancer (NSCLC) receiving immunotherapy. All pooled results were presented using forest plots and funnel plots. Heterogeneity among studies was assessed using Cochran's Q (χ^2) test, I^2 statistic, and τ^2. Heterogeneity was considered statistically significant when $I^2 > 50\%$ and/or $p < 0.05$. Given the presence of inherent clinical heterogeneity among the included studies, a random-effects model was applied.

Subgroup analyses were conducted based on LIPI score comparisons (LIPI 1 vs. 0 and LIPI 2 vs. 0) and type of therapy administration (monotherapy vs. combination therapy) to account for variability across the included studies.

RESULTS AND DISCUSSION

Search Results

The literature search process is illustrated in **Figure 1.** Through database searching, 293 studies were identified. After removing 59 duplicate records, 234 studies underwent title and abstract screening, and 39 articles were retrieved for full-text assessment. We further excluded 26 studies due to ineligible outcomes and insufficient data. As a result, 13 studies were included in this systematic review, all of which were subsequently analyzed quantitatively in the meta-analysis.

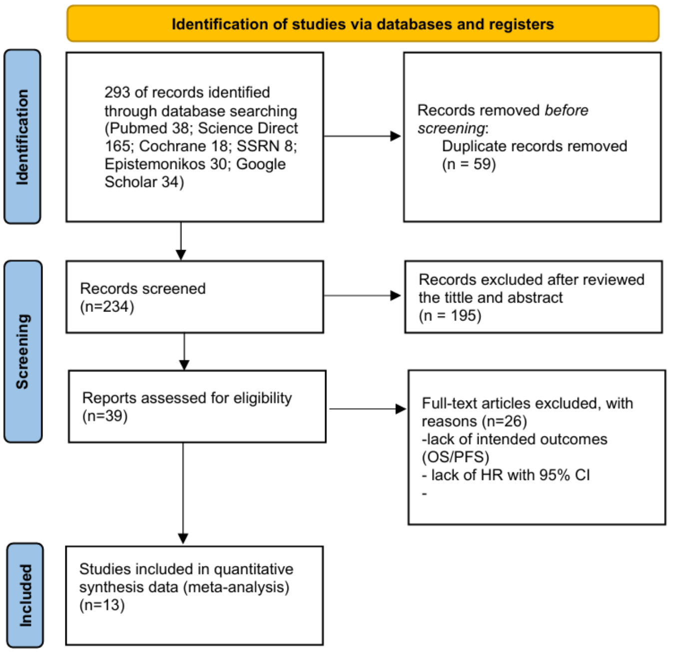

Figure 1. PRISMA flow diagram

Characteristic of Included Study and Critical Appraisal

The characteristics of the included studies are summarized in **Table 1**. All included studies were cohort studies, predominantly retrospective in design, and were published between 2018 and 2024, with study periods ranging from 2012 to 2023. Of the 13 included studies, six were conducted in Asia, four in Europe, two in Australia, and one in the United States. A total of 6,630 patients with advanced non-small cell lung cancer (NSCLC) were included, with median ages ranging from 61 to 70 years. Most patients had stage III–IV disease, and the predominant pathological subtypes were adenocarcinoma and squamous cell carcinoma. All patients received immune checkpoint inhibitor (ICI)–based immunotherapy, either as monotherapy or in combination regimens. The primary outcomes assessed across studies were overall survival (OS) and/or progression-free survival (PFS). Methodological quality assessment using the Newcastle–Ottawa Scale (NOS) indicated that all included studies were of moderate to high quality, with NOS scores ranging from 6 to 8, and all studies were therefore considered eligible for inclusion in the meta-analysis.

Table 1. Baseline Characteristics

Author, Year	**Study Period**	**Location**	**Sample Size (M/F)**	**Study Design**	**Median Age (years)**	**Pathological Type (Ad/NSq)**	**TNM Stage**	**ICIs**	**Regimen**	**End Point**	**NOS**
Mezquita, 2018	2012–2017	Europe	466 (301/165)	R	62	415/307	IIIB–IV	N, P, A, D, I	Mono	OS, PFS	7
Kazandjian, 2019	2013–2017	USA	1368 (834/534)	R	65	363/1005	IV	NR	Mono	OS, PFS	8
Sorich, 2019	NR	Australia	1489 (1347/873)	R	65	618/1602	III–IV	A	Mono	OS, PFS	7
Hopkins, 2020	NR	Australia	1548 (NR)	P	NR	NR	III–IV	A	Mono	OS	7
Wang, 2020	2016–2019	China	330 (277/53)	R	65	158/172	IIIB–IV	N, P, A	Mono, Mixed	OS, PFS	8
Hopkins, 2021	NR	Australia	1202 (720/482)	R	63	0/1202	III–IV	A, B	Mixed	OS, PFS	6
Huang, 2021	2017–2019	China	91 (67/24)	R	62.4	33/58	III–IV	NR	Mono	OS, PFS	7

Diker, 2023	2017–2022	Cyprus	150 (131/19)	R	68	54/96	IV	P, N, I	Mixed	OS, PFS	7
Olgun, 2023	2017–2021	Cyprus	83 (73/10)	R	66	32/51	IIIB–IV	P, N, I	Mono	PFS, OS	7
Hirata, 2024	2018–2022	Japan	82 (67/15)	R	69	33/49	III	D	Mixed	OS, PFS	7
Zhi, 2024	2015–2019	China	305 (233/72)	R	61	113/192	III–IV	N, P, A, D	Mixed	OS, PFS	7
Nelli, 2024	2016–2023	Italy	345 (173/76)	R	70	84/261	IV	P, N, A	Mono, Mixed	OS, PFS	7
Xiong, 2023	2019–2021	China	146 (118/28)	R	65	78/68	IIIB–IV	P, S, T	Mixed	PFS	7

M/F indicates male/female; R retrospective and P prospective cohort study; Ad adenocarcinoma; NSq non-squamous carcinoma; NR not reported. ICI includes N (nivolumab), P (pembrolizumab), A (atezolizumab), D (durvalumab), I (ipilimumab), B (bevacizumab), S (sintilimab), and T (toripalimab). Mono denotes immunotherapy monotherapy and Mixed combination regimens. Outcomes were OS (overall survival) and PFS (progression-free survival). Study quality was assessed using the Newcastle–Ottawa Scale (NOS), with scores ≥6 indicating moderate to high quality.

Study Outcome

Progression-free Survival (PFS) of LIPI

A total of 12 studies investigated the association between LIPI and progression-free survival (PFS) in patients with advanced-stage NSCLC receiving immunotherapy (**Figure 2**). The pooled analysis demonstrated that patients with poor or intermediate LIPI scores, compared with those with good LIPI scores, had a significantly shorter PFS (HR = 2.20, 95% CI: 1.83–2.63, P < 0.001 and HR = 1.47, 95% CI: 1.31–1.65, P < 0.001, respectively). Subgroup analyses were further performed according to treatment modality (immunotherapy monotherapy versus combination therapy). Publication bias was assessed using funnel plots (**Figure 3**). Both plots (A and B) showed minor asymmetry, with all included studies falling within the triangular region, indicating a low likelihood of publication bias.

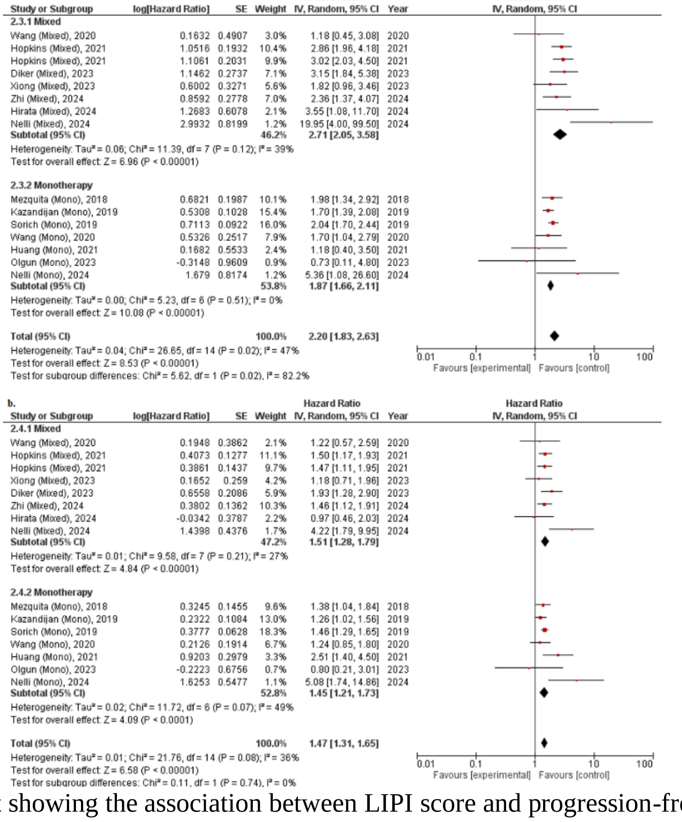

Figure 2. Forest plot showing the association between LIPI score and progression-free survival (PFS): (a) poor vs. good, and (b) intermediate vs. good

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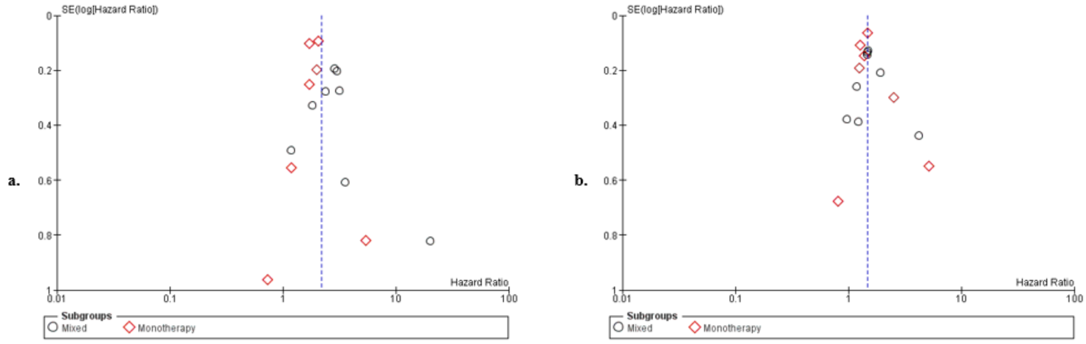

Figure 3. Funnel plot for the association between LIPI and progression-free survival (PFS): (a) poor vs. good, and (b) intermediate vs. good

Overall Survival (OS) of LIPI

A total of 12 studies examined the association between LIPI and overall survival (OS) in patients with advanced-stage NSCLC receiving immunotherapy (**Figure 4**). The pooled analysis showed that patients with poor or intermediate LIPI scores, compared with those with good LIPI scores, had significantly shorter OS (HR = 3.31, 95% CI: 2.70–4.06, P < 0.001 and HR = 1.88, 95% CI: 1.58–2.23, P < 0.001, respectively). Subsequent subgroup analyses were conducted according to the type of immunotherapy administration. The funnel plot illustrates the assessment of publication bias for overall survival (OS) according to LIPI (**Figure 5**). The plot shows minor asymmetry, with all included studies distributed within the triangular region, suggesting a low risk of publication bias.

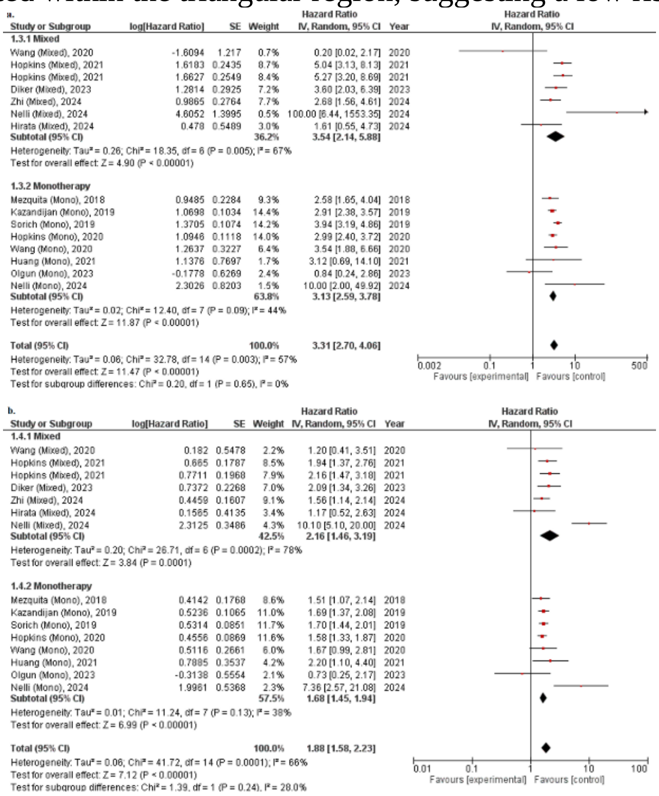

Figure 4. Forest plot showing the association between LIPI score and overall survival (OS): (a) poor vs. good, and (b) intermediate vs. good

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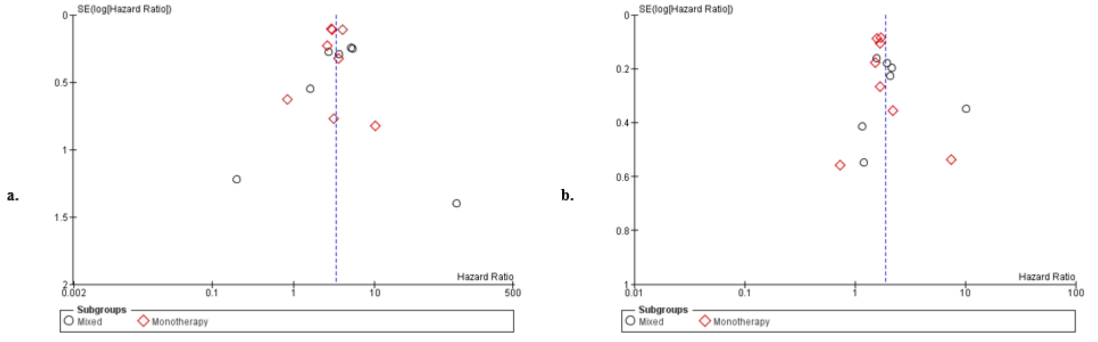

Figure 5. Funnel plot for the association between LIPI and overall survival (OS): (a) poor vs. good, and (b) intermediate vs. good

DISCUSSION

Non-small cell lung cancer (NSCLC) is a biologically and clinically heterogeneous disease, characterized by substantial variability in genetic alterations, histopathological features, and the tumor microenvironment, all of which play a pivotal role in influencing treatment response and overall prognosis (Restrepo et al., 2024). Until recently, the management of locally advanced or stage III NSCLC primarily relied on radical treatment approaches, including combinations of chemotherapy with surgery or radiotherapy (Asmara et al., 2024). Following the results of the PACIFIC trial, concurrent chemoradiotherapy (CRT) followed by adjuvant durvalumab emerged as the standard of care for patients with unresectable stage III NSCLC (Antonia et al., 2017). More recently, several clinical trials have expanded therapeutic options in this setting, including CheckMate 816, which investigated neoadjuvant immunotherapy, the ADAURA trial evaluating adjuvant tyrosine kinase inhibitors (TKIs), and IMpower010, which assessed adjuvant immunotherapy after definitive treatment (Felip et al., 2021; Forde et al., 2022; Wu et al., 2020).

Immunotherapy, particularly the use of immune checkpoint inhibitors (ICIs), has been shown to be safe and effective and provides important alternative treatment options for patients with NSCLC, while combination strategies integrating ICIs with other treatment modalities may further enhance therapeutic efficacy in selected clinical settings (Li et al., 2023). In the context of ICIs, immune signaling pathways are closely linked to the circulatory phase of the immune response, such that alterations in peripheral blood parameters may influence treatment outcomes. Inflammation is widely acknowledged as a critical factor in cancer initiation and progression and is closely associated with tumor microenvironment heterogeneity and prognosis, as it promotes angiogenesis, tumor proliferation, metastasis, immune tolerance, and activation of oncogenic signaling pathways. Chronic inflammation further drives tumor progression through immune escape, matrix remodeling, and genomic instability by activating M2 macrophages, regulatory T cells, and myeloid-derived suppressor cells, as well as through local and systemic inflammatory signals that disrupt key pathways such as STAT3 and NF-κB (Lv et al., 2019). Accordingly, blood-based inflammatory biomarkers have gained increasing attention due to their consistent prognostic value and greater accessibility compared with tissue-based markers such as PD-L1 and tumor mutational burden (TMB). Compared with single indicators, integrating multiple peripheral blood parameters improves prognostic accuracy; for instance, the LIPI is a predictive scoring system that combines LDH levels and the dNLR (Zhou et al., 2025).

Lung Immune Prognostic Index (LIPI), as a circulating biomarker, reflects the status of the systemic immune response, which plays a crucial role in tumor development and progression. The derived neutrophil-to-lymphocyte ratio (dNLR), calculated from neutrophil and lymphocyte counts, serves as an indicator of systemic inflammation and potential resistance to immune checkpoint inhibitors (ICIs) (Lv et al., 2019). Neutrophils promote tumor angiogenesis through the secretion of vascular endothelial growth factor, enhance tumor proliferation by activating the PI3K signaling pathway, and suppress antitumor immune responses. Recruitment of neutrophils via IL-17–mediated signaling has been linked to resistance to immune checkpoint inhibitors, supporting the association between elevated dNLR and reduced immunotherapy efficacy. In contrast, lymphocytes inhibit tumor progression through cytotoxic activity and immune surveillance. Accordingly, dNLR reflects the balance between pro-tumorigenic neutrophils and antitumor immune cells within the tumor microenvironment. Unlike the conventional neutrophil-to-lymphocyte ratio, which uses lymphocytes alone as the denominator, dNLR incorporates both lymphocytes and monocytes, providing a more comprehensive representation of systemic immune status. This distinction is particularly relevant in cancer, where lymphopenia and monocytosis are common and monocytes contribute to angiogenesis and immunosuppression through differentiation into tumor-associated macrophages (Coffelt et al., 2016; Yang et al., 2016).

Meanwhile, lactate dehydrogenase (LDH) levels, which are involved in the conversion of lactate and pyruvate, reflect increased tumor burden and tumor necrosis associated with enhanced glycolysis and tumor hypoxia, conditions that can impair immune function and reduce the effectiveness of ICIs (Lv et al., 2019). Lactate dehydrogenase (LDH) catalyzes the reversible conversion of lactic acid and pyruvic acid, and elevated serum LDH levels reflect cellular damage, inflammation, and necrosis. In cancer, metabolic reprogramming is a hallmark of tumor development, and LDH serves as a key indicator of enhanced glycolytic activity and proliferative potential. Increased LDH levels correlate with tumor burden, invasiveness, and hypoxia-driven necrosis, even under aerobic conditions, as tumor cells preferentially rely on glycolysis to meet their energy demands. LDH-mediated lactate accumulation leads to acidification of the tumor microenvironment, which suppresses immune cell function and promotes immunosuppression. Tumor hypoxia further activates hypoxia-inducible factor-1 (HIF-1), resulting in upregulation of vascular endothelial growth factor (VEGF) and the formation of abnormal, dysfunctional tumor vasculature. Together, these metabolic and microenvironmental alterations impair immune cell infiltration and reduce the effectiveness of immune checkpoint inhibitor therapy, supporting the prognostic relevance of LDH in cancer immunotherapy (Petrelli et al., 2015; Shao et al., 2022; Zhao et al., 2024).

Several studies have demonstrated that Lung Immune Prognostic Index (LIPI) is closely associated with prognosis across various cancer types. Zhang et al. (2024) evaluated the potential added value of LIPI in patients with small cell lung cancer (SCLC) treated with programmed death-1 (PD-1)/programmed death-ligand 1 (PD-L1) inhibitors in a Chinese alpine population and reported that multivariate analysis confirmed worse LIPI scores were significantly correlated with shorter overall survival (OS) and progression-free survival (PFS), although dNLR, rather than LIPI, was associated with the occurrence of immune-related adverse events. Similarly, a meta-analysis study by.Liu et al. (2021) reported that LIPI scores may serve as a promising predictive biomarker for therapeutic outcomes in patients with solid tumors treated with immune checkpoint inhibitors (ICIs) or chemotherapy. In addition, Carrril-Ajuria et al. (2024) demonstrated that pretreatment LIPI was significantly associated with worse survival outcomes in patients with metastatic renal cell carcinoma (mRCC) treated with either ICIs or antiangiogenic therapy, confirming the prognostic relevance of LIPI regardless of systemic treatment modality. Furthermore, a meta-analysis by Zhou et al, (2025) showed that baseline LIPI represents a potent and novel prognostic factor in patients with extensive-stage SCLC (ES-SCLC) receiving ICIs, with higher LIPI scores significantly associated with poorer OS and PFS, underscoring its clinical utility in immunotherapy settings. Although the individual components LDH and dNLR are each associated with survival outcomes, LIPI integrates these parameters to provide a more comprehensive and superior prognostic assessment. Consistent with these findings, the present study demonstrated that patients with advanced-stage NSCLC who had poor or intermediate LIPI scores experienced significantly worse clinical outcomes. Specifically, poorer LIPI categories were associated with shorter progression-free survival (PFS) (HR = 2.20, 95% CI: 1.83–2.63, $P < 0.001$; HR = 1.47, 95% CI: 1.31–1.65, $P < 0.001$) and inferior overall survival (OS) (HR = 3.31, 95% CI: 2.70–4.06, $P < 0.001$; HR = 1.88, 95% CI: 1.58–2.23, $P < 0.001$). Furthermore, subgroup analyses according to immunotherapy modality (monotherapy versus combination therapy) yielded consistent results, supporting the robustness of LIPI as a prognostic indicator across different treatment strategies.

Prognostic evaluation is essential to support clinical decision-making and guide treatment strategies in patients with advanced NSCLC receiving immunotherapy, and the Lung Immune Prognostic Index (LIPI) may represent a practical tool for risk stratification and early identification of poor treatment outcomes. However, this study has several limitations that should be acknowledged. Most included studies were retrospective in design, which may introduce selection bias and limit causal inference. In addition, heterogeneity in patient populations, immunotherapy regimens, follow-up duration, and LIPI assessment across studies may have influenced the pooled results, despite the application of random-effects models and subgroup analyses. The absence of individual patient-level data also precluded adjustment for potential confounders and evaluation of dynamic changes in LIPI during treatment. Future research should focus on prospective, well-designed studies with standardized LIPI evaluation and longer follow-up, as well as integration of LIPI with established biomarkers, molecular characteristics, and clinical factors to improve prognostic accuracy and optimize personalized immunotherapy strategies in advanced NSCLC.

CONCLUSION

In conclusion, this systematic review and meta-analysis demonstrates that the Lung Immune Prognostic Index (LIPI) is a promising prognostic biomarker in patients with advanced-stage non-small cell lung cancer (NSCLC) treated with immune checkpoint inhibitors (ICIs). Patients with poor and intermediate LIPI scores consistently showed significantly worse progression-free survival (PFS) and overall survival (OS) compared with those with good LIPI scores. Given that LIPI is derived from simple and widely available blood-based parameters, it represents a practical and non-invasive tool for risk stratification in routine clinical practice. However, variability in LIPI assessment and study design across the included studies highlights the need for standardized LIPI cut-off values to improve comparability and clinical applicability. Future prospective studies with more homogeneous patient populations and treatment strategies are warranted to further validate the prognostic role of LIPI and to support its potential incorporation into clinical decision-making and prognostic guidelines for immunotherapy-treated NSCLC patients.

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