EJMI

DOI: 10.14744/ejmi.2024.38549
EJMI 2024;8(4):260–268

Research Article

Prognostic Factors in Extensive-Stage Small Cell Lung Cancer: An Evaluation of LIPI, mGPS, and PIV Scores

İrem Öner,[1] Mustafa Büyükkör,[1] Fatih Tay,[1] Muhammed Esad Durmuş,[2] Alper Türkel,[1] Necla Demir,[1] Necati Alkış,[1] Cengiz Karaçin[1]

[1]Department of Medical Oncology, Dr. Abdurrahman Yurtaslan Ankara Oncology Research and Training Hospital Ankara, Türkiye
[2]Department of Internal Medicine, Dr. Abdurrahman Yurtaslan Ankara Oncology Research and Training Hospital Ankara, Türkiye

Abstract

Objectives: This study investigated the prognostic significance of three systemic inflammation-based indices—the Lung Immune Prognostic Index (LIPI), the modified Glasgow Prognostic Score (mGPS), and the Pan-Immune-Inflammation Value (PIV)—in patients with extensive-stage small-cell lung cancer (ES-SCLC) receiving first-line platinum-based chemotherapy.

Methods: This retrospective study included 135 ES-SCLC patients. LIPI, mGPS, and PIV were calculated from pretreatment laboratory data. Kaplan-Meier and Cox regression analyses were used to evaluate the association of these indices with progression-free survival (PFS) and overall survival (OS).

Results: Patients with an LIPI score of 2 experienced significantly worse OS (p=0.002) and PFS (p=0.001) compared to those with a score of 0. No significant association was observed between mGPS or PIV and survival outcomes. Multivariate analysis identified LIPI, prophylactic cranial irradiation, and female sex as independent prognostic factors. A LIPI score two was associated with worse OS (HR: 2.18; p=0.016) and PFS (HR: 2.20; p=0.012), while PCI and female sex were favorable prognostic factors.

Conclusion: LIPI is an independent prognostic factor for ES-SCLC patients receiving first-line platinum-based chemotherapy. Incorporating LIPI into clinical practice may improve risk stratification and guide personalized treatment strategies.

Keywords: Small cell lung carcinoma; prognostic factors; lung immune prognostic index; modified glasgow prognostic score, pan-immune-inflammation value

Cite This Article: *Öner İ, Büyükkör M, Tay F, Durmuş ME, Türkel A, Demir N, et al. Prognostic Factors in Extensive-Stage Small Cell Lung Cancer: An Evaluation of LIPI, mGPS, and PIV Scores. EJMI 2024;8(4):260–268.*

Small cell lung cancer is an aggressive form of lung cancer, accounting for approximately 15% of all cases, characterized by rapid cell proliferation, a high growth rate, and a propensity for early metastasis.[1, 2] For most patients with extensive-stage small cell lung cancer (ES-SCLC), initial treatment typically consists of combination chemotherapy (CT) regimens based on cisplatin or carboplatin.[3] The addition of immunotherapy (IO) to standard first-line chemotherapy has led to a significant improvement in survival.[4] Despite initial sensitivity to these first-line combination therapies, widespread relapse with resistant disease is observed within a few months to a year in most patients. ES-SCLC survivors typically range from 8 to 13 months.[5] Identifying factors influencing prognosis and tailoring treatment strategies to individual needs are essential.

Address for correspondence: İrem Öner, MD. Department of Medical Oncology, Dr. Abdurrahman Yurtaslan Ankara Oncology Research and Training Hospital Ankara, Türkiye
Phone: +90 312 336 09 09 **E-mail:** dr_iremoner@hotmail.com

Submitted Date: November 03, 2024 **Revision Date:** December 18, 2024 **Accepted Date:** December 25, 2024 **Available Online Date:** November 16, 2025

Inflammation and immunity are critical in tumor development, progression, invasion, metastasis, and treatment response.[6] Numerous studies have demonstrated the association of various markers of systemic inflammation with poor prognosis in many solid malignancies.[7, 8] Several inflammation and immunity indices, such as the Diffuse Cancer Inflammation Index.[9, 10] Neutrophil-to-Lymphocyte Ratio[11, 12] Platelet-to-Lymphocyte Ratio,[11] Lymphocyte-to-Monocyte Ratio,[13] Systemic Immune-Inflammation Index,[14] Systemic Inflammation Response Index,[15] and the Prognostic Nutritional Index[16] are increasingly being utilized as prognostic factors in patients with advanced lung cancer.

Recent studies suggest the prognostic value of the Lung Immune Prognostic Index (LIPI), particularly in non-small cell lung cancer (NSCLC),[17] the Modified Glasgow Prognostic Score (mGPS),[18, 19] extensively studied in various solid tumors, and the Pan-Immune-Inflammation Value (PIV) [20, 21] in several cancer types, including colorectal, breast, esophageal, Merkel cell carcinoma, and malignant melanoma. These represent valuable markers for personalizing treatment and predicting outcomes. However, evidence regarding the efficacy of these inflammatory markers in SCLC remains limited and conflicting. Notably, studies in the literature have yet to evaluate these three parameters together in ES-SCLC.

Therefore, we aimed to evaluate the relationship between pre-treatment inflammatory markers, such as LIPI, mGPS, and PIV, and progression-free survival (PFS) and overall survival (OS) outcomes in patients diagnosed with ES-SCLC treated with platinum-based CT. By doing so, we seek to contribute to developing personalized treatment strategies for SCLC, an aggressive type of cancer.

Methods

Patients

Between April 2014 and December 2021, patients with ES-SCLC were retrospectively enrolled in a study at Ankara Oncology Hospital. Patients with a pathologically confirmed diagnosis of SCLC were staged according to the Veterans Administration Lung Study Group staging system. Extensive-stage disease was defined as the development of distant metastases beyond the ipsilateral hemithorax and regional lymph nodes, malignant pericardial or pleural effusions, and contralateral supraclavicular and hilar lymph node involvement.

Inclusion criteria included a diagnosis of ES-SCLC, first-line treatment with carboplatin plus etoposide or cisplatin plus etoposide, receipt of at least two cycles of chemotherapy, and availability of laboratory and imaging results for follow-up. Limited-stage disease, unknown pre-treatment hemogram, biochemical parameters, a history of a known infectious disease within the last 4 weeks, prior use of steroid therapy for any reason, and receipt of non-platinum-based chemotherapy were the main exclusion criteria.

The study was conducted according to ethical standards and approved by the Non-Interventional Clinical Research Ethics Committee of the Ministry of Health of the Republic of Turkey, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital (Approval No: 2024-11/185). The review boards accepted the waiver of the informed consent requirement.

Data Collection

Patient characteristics, including age, sex, smoking status, Eastern Cooperative Oncology Group Performance Status (ECOG PS), CT regimen, presence of brain, liver, contralateral lung, bone, bone marrow, and adrenal gland metastases, presence of pleural effusion, receipt of prophylactic cranial irradiation (PCI), and pre-treatment hemogram and biochemistry parameters (serum neutrophil, monocyte, lymphocyte, platelet, hemoglobin, lactate dehydrogenase (LDH), sodium, C-reactive protein (CRP), and albumin levels) were recorded from patient files, archives, and hospital automation systems.

The CT regimens administered to the patients included 100 mg/m^2 etoposide (on days 1, 2, and 3) in combination with either carboplatin at an AUC of 5 (on day 1) or 75 mg/m^2 cisplatin (on day 1), with treatment cycles repeated every 21 days.[22, 23]

Selected patients who achieved a complete or partial response to chemotherapy and had no brain metastases at baseline received PCI (250 cGy x 10 fractions).

The LIPI score was a combination of the derived neutrophil-to-lymphocyte ratio (dNLR = neutrophil count / (white blood cell count - neutrophil count)) and LDH levels.[17]

LIPI was categorized as follows:

- LIPI 0 (good) = dNLR < 3 and LDH below the upper limit of normal
- LIPI 1 (intermediate) = dNLR ≥ 3 and LDH below the upper limit of normal or dNLR < 3 and LDH above the upper limit of normal
- LIPI 2 (poor) = dNLR ≥ 3 and LDH above the upper limit of normal.

The mGPS was defined as follows:

- mGPS 0 = albumin ≥ 3.5 g/dL and CRP ≤ 1 mg/dL
- mGPS 1 = albumin ≥ 3.5 g/dL and CRP > 1 mg/dL or albumin < 3.5 g/dL and CRP ≤ 1 mg/dL

- mGPS 2 = albumin < 3.5 g/dL and CRP > 1 mg/dL.[24]

The PIV was calculated using the formula: (neutrophil count × platelet count × monocyte count) / lymphocyte count, with counts obtained within 7 days before treatment initiation.[25] Patients were divided into two groups based on the median PIV value: low-PIV (≤ median) and high-PIV (> median).

Statistical Analysis

Descriptive statistics for parametric continuous variables are presented as mean±standard deviation, while non-parametric continuous variables are presented as median and interquartile range (IQR, Q1-Q3). Categorical data are presented as frequencies (percentages). For the parameters, independent samples t-tests or Mann-Whitney U tests were used for continuous variables, and Chi-square or Fisher's exact tests were used for categorical variables. PFS was defined as the time from treatment initiation to disease progression or death, and OS was defined as the time from diagnosis to death or last follow-up. These times were calculated using the Kaplan-Meier method. Kaplan-Meier curves and log-rank tests were used to compare PFS and OS between the two groups. A Cox regression model was constructed using factors found to be statistically significant in the Kaplan-Meier analysis to identify independent prognostic factors. All tests were two-sided; a p-value <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0.

Results

The study included 135 patients diagnosed with ES-SCLC. The median age was 60 (range 39–83). Of these patients, 43 (31.9%) received carboplatin plus etoposide, while 92 (68.1%) received cisplatin plus etoposide. Patient characteristics are summarized in Table 1.

Twenty-four patients (17.8%) had a LIPI score of 0, 52 patients (38.5%) had a score of 1, and 59 patients (43.7%) had a score of 2. Thirty-three patients (24.4%) had a mGPS of 0, 66 patients (48.9%) had a score of 1, and 36 patients (26.7%) had a score of 2. The cut-off value for PIV was determined as the median value of 619. PIV values of 619 or lower were considered low, while values above 619 were considered high. Sixty-four patients (47.4%) were in the low PIV group, and 71 patients (52.6%) were in the high PIV group (Table 1).

The median overall survival (mOS) for all patients (n=135) was 7.56 months (95% CI: 6.21–8.90), and the median progression-free survival (mPFS) was 5.36 months (95% CI: 4.16–6.55). The mOS was 6.44 months (95% CI: 4.69–8.19) for male patients and 11.93 months (95% CI: 7.77–16.08) for

Table 1. Characteristics of patients with ES-SCLC

Characteristics	No of patients (n=135)	Percentage (%)
Age (year) median (Range)	60 (39-83)	
≤60 y	65	48.1%
> 60 y	70	51.9%
Gender		
Male	118	87.4%
Female	17	12.6%
Smoking history		
No smoke	3	2.2%
Smoke	131	97.0%
ECOG-PS		
0-1	93	68.9%
≥ 2	40	29.6%
Chemotherapy		
Cisplatin plus etoposide	92	68.1%
Carboplatin plus etoposid	43	31.9%
Brain metastasis		
Yes	45	33.3%
No	90	66.7%
Liver metastasis		
Yes	68	50.4%
No	67	49.6%
Bone metastasis		
Yes	86	63.7%
No	49	36.3%
Pleural effusion		
Yes	40	29.6%
No	95	70.4%
PCI		
Yes	21	15.6%
No	69	51.1%
Hyponatremia		
Yes	33	24.4%
No	102	75.6%
LIPI score		
0 (good)	24	17.8%
1 (intermediate)	52	38.5%
2 (poor)	59	43.7%
mGPS score		
0	33	24.4%
1	66	48.9%
2	36	26.7%
PIV score		
Low	64	47.4%
High	71	52.6%

ES-SCLC: extensive stage small cell lung cancer, ECOG-PS: Eastern Cooperative Oncology Group Performance Status, PCI: prophylactic cranial irradiation, LIPI: lung immune prognostic index, mGPS: modified Glasgow Prognostic Score, PIV: Pan-Immune-Inflammation Value.

female patients (p<0.001). The mPFS was 4.6 months (95% CI: 3.23–5.97) for male patients and 5.98 months (95% CI: 2.18–9.78) for female patients (p=0.010).

The median overall survival (mOS) was 9.33 months (95% CI: 5.78–12.88) for patients with a LIPI score of 0, 7.89 months (95% CI: 5.87–9.90) for those with a LIPI score of 1, and 5.45 months (95% CI: 4.04–6.87) for those with a LIPI score of 2 (p=0.002) (Fig. 1). The median progression-free survival (mPFS) was 8.08 months (95% CI: 7.10–9.07) for patients with a LIPI score of 0, 6.01 months (95% CI: 4.66–7.37) for those with a LIPI score of 1, and 4.11 months (95% CI: 3.37–4.85) for those with a LIPI score of 2 (p=0.001) (Fig. 2).

mOS was 9.33 months (95% CI: 4.71-13.95) in patients who underwent PCI and 6.01 months (95% CI: 4.56-7.46) in those who did not (p=0.001). Median PFS was 7.92 months (95% CI: 5.22-10.62) in patients with PCI and 4.40 months (95% CI: 3.10-5.70) in those without (p=0.004) (Table 2).

mOS was 6.47 months (95% CI: 3.44-9.50) in patients with an mGPS of 0, 7.56 months (95% CI: 5.89-9.22) in those with an mGPS of 1, and 7.46 months (95% CI: 3.06-11.85) in those with an mGPS of 2 (p=0.844). Median PFS was 4.40 months (95% CI: 2.55-6.25) in patients with an mGPS of 0, 5.52 months (95% CI: 4.08-6.96) in those with an mGPS of 1, and 5.26 months (95% CI: 2.36-8.15) in those with an mGPS of 2 (p=0.663) (Table 2).

The median PIV was 619 (IQR: 347.0-1118.5). Patients were divided into two groups based on the median PIV: low-PIV (≤619) and high-PIV (>619). Median OS was 7.62 months (95% CI: 6.01-9.23) in the low-PIV group and 6.54 months (95% CI: 4.49-8.59) in the high-PIV group (p=0.709). Median PFS was 5.36 months (95% CI: 3.81-6.90) in the low-PIV group and 5.26 months (95% CI: 3.75-6.76) in the high-PIV group (p=0.974) (Table 2).

Multivariate analysis showed that LIPI score, PCI, and sex were independent prognostic factors for OS and PFS. A LIPI score of 2 was associated with worse OS (HR: 2.18; 95% CI: 1.16-4.10; p=0.016) and PFS (HR: 2.20; 95% CI: 1.19-4.08; p=0.012), while a LIPI score of 1 was not associated with OS (HR: 1.19; 95% CI: 0.65-2.18; p=0.572) or PFS (HR: 1.55; 95% CI: 0.85-2.83; p=0.151). PCI and female sex were favorable prognostic factors for OS (HR: 0.47; 95% CI: 0.28-0.81; p=0.006 and HR: 0.28; 95% CI: 0.13-0.59; p=0.001, respectively) and PFS (HR: 0.53; 95% CI: 0.32-0.89; p=0.015 and HR: 0.44; 95% CI: 0.22-0.90; p=0.025, respectively) (Table 3).

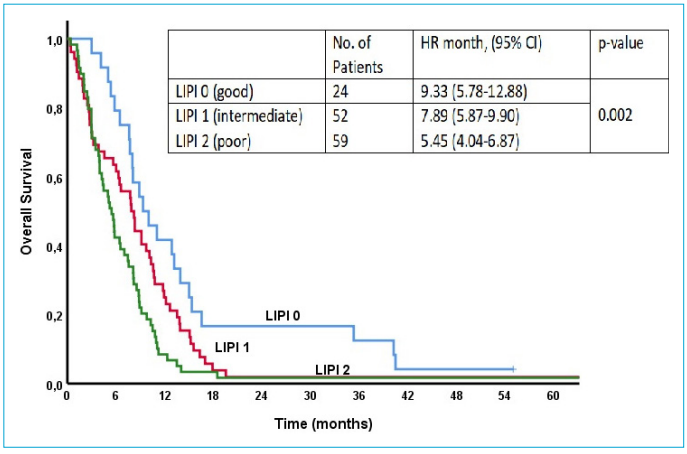

Figure 1. Median OS curve based on LIPI in ES-SCLC patients.

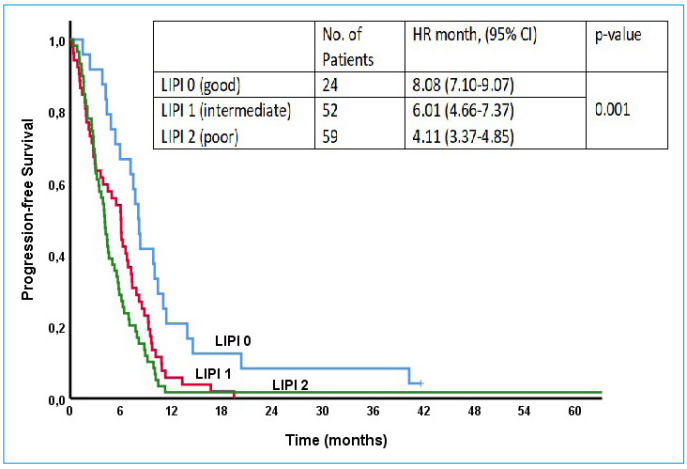

Figure 2. Median PFS curve based on LIPI in ES-SCLC patients.

Discussion

This study demonstrates that the LIPI is an independent prognostic marker for PFS and OS in patients with ES-SCLC receiving first-line platinum-based CT. In contrast to LIPI, neither the mGPS nor the PIV showed a statistically significant association with PFS or OS. This finding supports the potential value of LIPI as a prognostic tool in this patient population.

Numerous studies have demonstrated the prognostic potential of LIPI in SCLC. One study revealed that the low-risk LIPI 0 group had a significantly longer mOS than other risk groups (21.0 vs. 11.6 months, p<0.001), although no difference was observed in mPFS. Conversely, the LIPI 2 group exhibited significantly shorter mOS and mPFS compared to the LIPI 0 group (p=0.006 and p<0.001, respectively).[26] This study was the first to highlight the potential use of LIPI as a prognostic biomarker for SCLC patients. Similarly, another study found a significant difference in mOS among LIPI groups (12, 10.1, and 7.7 months for LIPI 0, 1, and 2, respectively; p=0.02), but no difference in mPFS (8.9, 8, and 5.6 months, respectively; p=0.1). However, LIPI 2 was shown to be an independent prognostic factor for both OS (HR: 1.757, p=0.04) and PFS (HR: 1.839, p=0.02).[27] In a study conducted on patients with extensive-stage pulmonary neuroendocrine carcinoma, the impact of LIPI on OS

Table 2. OS and PFS rates in patients with ES-SCLC

	OS Median (95%CI)	p	PFS Median (95%CI)	p
Age (year), median (range)		0.212		0.057
≤60 y	8.12 (7.45-8.78)		6.05 (4.93-7.16)	
> 60 y	5.82 (4.33-7.30)		4.34 (2.62-6.05)	
Gender		<0.001*		0.010*
Male	6.44 (4.69-8.19)		4.60 (3.23-5.97)	
Female	11.93 (7.77-16.08)		5.98 (2.18-9.78)	
Smoking history		0.853		0.242
Never smoke	5.36 (4.83-5.88)		4.34 (1.81-6.86)	
Smoke	7.56 (6.23-8.88)		5.52 (4.41-6.63)	
ECOG-PS		0.279		0.216
0-1	7.89 (6.87-8.90)		5.98 (5.44-6.52)	
≥ 2	5.22 (3.29-7.16)		3.81 (3.35-4.27)	
Chemotherapy		0.259		0.335
Cisplatin plus etoposide	7.82 (7.09-8.55)		5.82 (4.80-6.83)	
Carboplatin plus etoposid	5.03 (3.47-6.59)		3.91 (2.22-5.60)	
Brain metastasis		0.801		0.631
Yes	7.62 (6.03-9.21)		4.60 (3.09-6.11)	
No	6.54 (3.95-9.13)		5.75 (4.39-7.11)	
Liver metastasis		0.654		0.406
Yes	7.72 (6.10-9.45)		4.83 (3.50-6.16)	
No	6.60 (4.30-8.91)		5.98 (4.10-7.86)	
Bone metastasis		0.085		0.629
Yes	6.54 (4.99-8.09)		5.45 (3.99-6.92)	
No	7.89 (6.91-8.86)		4.93 (2.95-6.91)	
Pleural effusion		0.762		0.993
Yes	8.15 (4.85-8.10)		6.08 (3.89-8.27)	
No	6.47 (4.85-8.10)		4.83 (3.69-5.97)	
PCI		0.001*		0.004*
Yes	9.33 (4.71-13.95)		7.92 (5.22-10.62)	
No	6.01 (4.56-7.46)		4.40 (3.10-5.70)	
Hyponatremia		0.484		0.814
Yes	5.36 (3.84-6.87)		4.21 (2.95-5.46)	
No	7.75 (6.45-9.05)		5.65 (4.65-6.66)	
LIPI score		0.002*		0.001*
0 (good)	9.33 (5.78-12.88)		8.08 (7.10-9.07)	
1 (intermediate)	7.89 (5.87-9.90)		6.01 (4.66-7.37)	
2 (poor)	5.45 (4.04-6.87)		4.11 (3.37-4.85)	
mGPS		0.844		0.663
0	6.47 (3.44-9.50)		4.40 (2.55-6.25)	
1	7.56 (5.89-9.22)		5.52 (4.08-6.96)	
2	7.46 (3.06-11.85)		5.26 (2.36-8.15)	
PIV		0.709		0.974
Low	7.62 (6.01-9.23)		5.36 (3.81-6.90)	
High	6.54 (4.49-8.59)		5.26 (3.75-6.76)	

PFS: progression-free survival, OS: overall survival, ES-SCLC: extensive stage small cell lung cancer, ECOG-PS: Eastern Cooperative Oncology Group Performance Status, PCI: prophylactic cranial irradiation, LIPI: lung immune prognostic index, mGPS: modified Glasgow Prognostic Score, PIV: Pan-Immune-Inflammation Value, *Significant.

Table 3. Cox regression analysis for OS and PFS

	OS HR (95%CI)	p	PFS HR (95%CI)	p
LIPI score 0	Ref		Ref	
LIPI score 1	1.19 (0.65-2.18)	0.572	1.55 (0.85-2.83)	0.151
LIPI score 2	2.18 (1.16-4.10)	0.016*	2.20 (1.19-4.08)	0.012*
PCI	0.47 (0.28-0.81)	0.006*	0.53 (0.32-0.89)	0.015*
Gender	0.28 (0.13-0.59)	0.001*	0.44 (0.22-0.90)	0.025*

LIPI: lung immune prognostic index, PCI: prophylactic cranial irradiation, PFS: progression-free survival, OS: Overall survival, HR: Hazard ratio, CI: Confidence interval, *significant.

showed numerical differences but did not reach statistical significance (mOS for LIPI 0, 1, and 2: 15, 11, and 9 months, respectively; p=0.091).[28] A study conducted in Northern China demonstrated shorter mOS (7.9 months) and mPFS (4.1 months) in ES-SCLC patients with LIPI 2, associating a LIPI score of 2 with a significantly higher risk of poor prognosis (HR = 8.79; p<0.001).[29] Another Chinese study similarly linked LIPI 2 with shorter OS (HR=2.372, p<0.001) and PFS (HR=1.752, p=0.002).[30] Our study also found significant differences in mOS (9.33, 7.89, and 5.45 months for LIPI 0, 1, and 2, respectively; p=0.001) and mPFS (8.08, 6.01, and 4.11 months, respectively; p=0.001) among LIPI groups. Similar to other studies, patients with LIPI 2 in our study experienced worse outcomes for both OS (HR: 2.18; p=0.016) and PFS (HR: 2.20; p=0.012). However, our study found no difference between LIPI 1 and LIPI 2 for OS (HR: 1.19; p=0.572) or PFS (HR: 1.55; p=0.151). Another study consistent with our findings showed that in ES-SCLC patients, LIPI 2 was associated with shorter OS (HR: 1.35; p=0.012) and PFS (HR: 1.81; p<0.001), while there was no OS difference between LIPI 1 and LIPI 2 groups (HR: 1.01; p=0.82).[31]

Of the studies that have evaluated LIPI in LS-SCLC, a small number have also considered the impact of PCI on survival. One study showed that while univariate analysis indicated PCI improved overall survival (OS; p=0.031), PCI was not an independent prognostic factor in multivariate analysis (HR: 2.801; p=0.06).[32] Another study observed significant improvement in both OS (HR: 0.45; p<0.001) and PFS (HR: 0.55; p<0.001) in patients who received PCI.[33] Conversely, another study reported no significant effect of PCI on OS (HR: 1.73; p=0.16) or PFS (HR: 1.95; p=0.07).[34] Our study identified PCI as a favorable prognostic factor for both OS (HR: 0.47; p=0.006) and PFS (HR: 0.53; p=0.015). The prognostic significance of PCI has yet to be investigated in other studies evaluating LIPI in ES-SCLC. In this context, our study, which evaluates the prognostic significance of PCI, provides a unique contribution to the literature. However, potential selection bias due to patient selection criteria for PCI and the characteristics of the study population should be considered. These varying results suggest that the use of PCI in SCLC patients warrants further evaluation with a more comprehensive and personalized approach.

In our study, the female sex was identified as a favorable prognostic factor for both OS (HR: 0.28; p=0.001) and PFS (HR: 0.44; p=0.025). However, a significant limitation of these findings is that female patients constituted only 12.6% of the total population, which may limit the generalizability of the results. The literature presents heterogeneous results regarding this issue. One study evaluating mGPS demonstrated, similar to our study, that female sex was an independent prognostic factor for OS (p=0.012).[35] However, another study evaluating the LIPI in LS-SCLC observed a correlation between OS and PFS in male patients, while this relationship was less pronounced in female patients.[33] Similarly, in another study with a comparable patient population, a difference in PFS (HR: 0.44; p<0.001) was found only in male patients, with no difference in OS [34] A study in ES-SCLC reported that male patients in the "good" LIPI group were associated with better OS (HR: 2.61; p=0.005) and PFS (HR: 1.87; p=0.020) compared to the "intermediate/poor" group, but this association was not observed in female patients.[36] Many other studies investigating the prognostic role of the LIPI score found no difference in survival between male and female patients.[27, 29, 31, 32]

The literature presents heterogeneous results regarding the prognostic value of mGPS and PIV in SCLC. Some studies have shown no significant impact of mGPS on OS or PFS,[37, 38] while others have reported an association between shorter OS in patients with an mGPS of 2 and worsening survival with higher mGPS values.[35, 39, 40] A limited number of studies on PIV have indicated that lower PIV values are associated with longer OS and PFS[41, 42], but this relationship is not consistent across all studies.[43] Although some studies suggest that mGPS and PIV may be prognostic markers in SCLC, our study did not observe this effect.

Our retrospective study design may have affected the va-

lidity of our results due to potential limitations such as selection and information bias. Furthermore, our study's single-center nature may limit our findings' generalizability. Our results need to be validated in different patient populations and treatment protocols. Factors such as differences in patient populations, treatment protocols, PIV measurement methods, and cutoff values may also contribute to consistency in results, potentially limiting the comparability of our study with other studies. Our study's sample size is relatively small. Larger sample sizes could provide more robust statistical analyses and more precise results. It may need to be clarified whether other factors not assessed in our study (such as comorbidities and nutritional status) were adequately controlled, which could affect the interpretation of the results. Despite these limitations, our study contributes to evaluating of prognostic markers in SCLC. Future studies addressing these limitations could yield more definitive results. In particular, multicenter, larger-scale, and prospective studies could significantly contribute to the knowledge base in this area.

Conclusion

This study demonstrates that the LIPI is an independent prognostic marker for OS and PFS in patients with ES-SCLC receiving first-line platinum-based CT. While the mGPS and PIV did not demonstrate significant associations with PFS or OS in our cohort, this result further highlights the relevance of LIPI in predicting patient outcomes. Furthermore, PCI and female sex were favorable prognostic factors for OS and PFS.

Overall, our results confirm the relevance of LIPI as a reliable prognostic tool in ES-SCLC while also underscoring the need for further investigation into the effects of gender, PCI, and other biomarkers to better personalize treatment strategies for this challenging patient group.

Disclosures

Ethics Committee Approval: Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Ethics Committee (Date: 12.12.2024 research code no: 2024-11/185).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – İ.Ö., M.B.; Design – İ.Ö.; Supervision – C.K., N.A.; Materials – F.T., M.B.; Data Collection and/or Processing – M.E.D., N.D., A.T.; Analysis and/or Interpretation – İ.Ö., C.K.; Literature Search – F.T., N.D., A.T.; Writing – İ.Ö.; Critical Review – C.K., N.A.

References

1. Govindan R, Page N, Morgensztern D, Read W, Tierney R, Vlahiotis A, Spitznagel EL, Piccirillo J: Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. J Clin Oncol 2006:24(28):4539-4544.
2. Oronsky B, Reid TR, Oronsky A, Carter CA: What's New in SCLC? A Review. Neoplasia 2017:19(10):842-847.
3. Rossi A, Di Maio M, Chiodini P, Rudd RM, Okamoto H, Skarlos DV, Früh M, Qian W, Tamura T, Samantas E et al: Carboplatin- or cisplatin-based chemotherapy in first-line treatment of small-cell lung cancer: the COCIS meta-analysis of individual patient data. J Clin Oncol 2012:30(14):1692-1698.
4. Chen HL, Tu YK, Chang HM, Lee TH, Wu KL, Tsai YC, Lee MH, Yang CJ, Hung JY, Chong IW: Systematic Review and Network Meta-Analysis of Immune Checkpoint Inhibitors in Combination with Chemotherapy as a First-Line Therapy for Extensive-Stage Small Cell Carcinoma. Cancers (Basel) 2020:12(12).
5. Dowlati A, Chiang A, Cervantes A, Babu S, Hamilton E, Wong S, Tazbirkova A, Sullivan I, van Marcke C, Italiano A: OA04. 04 Sacituzumab Govitecan as Second-Line Treatment in Patients with Extensive Stage Small Cell Lung Cancer. Journal of Thoracic Oncology 2024:19(10):S16.
6. Grivennikov SI, Greten FR, Karin M: Immunity, inflammation, and cancer. Cell 2010:140(6):883-899.
7. Lu Y, Jiang J, Ren C: The clinicopathological and prognostic value of the pretreatment neutrophil-to-lymphocyte ratio in small cell lung cancer: A meta-analysis. PLoS One 2020, 15(4):e0230979.
8. Banna GL, Cortellini A, Cortinovis DL, Tiseo M, Aerts J, Barbieri F, Giusti R, Bria E, Grossi F, Pizzutilo P et al: The lung immuno-oncology prognostic score (LIPS-3): a prognostic classification of patients receiving first-line pembrolizumab for PD-L1 ≥ 50% advanced non-small-cell lung cancer. ESMO Open 2021, 6(2):100078.
9. Mandaliya H, Jones M, Oldmeadow C, Nordman, II: Prognostic biomarkers in stage IV non-small cell lung cancer (NSCLC): neutrophil to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), platelet to lymphocyte ratio (PLR) and advanced lung cancer inflammation index (ALI). Transl Lung Cancer Res 2019, 8(6):886-894.
10. Kobayashi S, Karube Y, Inoue T, Araki O, Maeda S, Matsumura Y, Chida M: Advanced Lung Cancer Inflammation Index Predicts Outcomes of Patients with Pathological Stage IA Lung Adenocarcinoma Following Surgical Resection. Ann Thorac Cardiovasc Surg 2019, 25(2):87-94.
11. Zhang N, Jiang J, Tang S, Sun G: Predictive value of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in non-small cell lung cancer patients treated with immune checkpoint inhibitors: A meta-analysis. Int Immunopharmacol 2020, 85:106677.
12. Sebastian NT, Raj R, Prasad R, Barney C, Brownstein J, Grecula J, Haglund K, Xu-Welliver M, Williams TM, Bazan JG: Association of Pre- and Posttreatment Neutrophil-Lymphocyte Ratio With

Recurrence and Mortality in Locally Advanced Non-Small Cell Lung Cancer. Front Oncol 2020, 10:598873.
13. Luo H, Ge H, Cui Y, Zhang J, Fan R, Zheng A, Zheng X, Sun Y: Systemic Inflammation Biomarkers Predict Survival in Patients of Early Stage Non-Small Cell Lung Cancer Treated With Stereotactic Ablative Radiotherapy - A Single Center Experience. J Cancer 2018, 9(1):182-188.
14. Li X, Hu P, Liu J, Zhang J, Liu Q: Systemic immune-inflammation index predicted overall survival and radiosensitivity in advanced non-small-cell lung cancer. Future Oncol 2020, 16(5):103-115.
15. Zhang Y, Liu F, Wang Y: Evidence of the Prognostic Value of Pretreatment Systemic Inflammation Response Index in Cancer Patients: A Pooled Analysis of 19 Cohort Studies. Dis Markers 2020, 2020:8854267.
16. Jiang AM, Zhao R, Liu N, Ma YY, Ren MD, Tian T, Yao Y: The prognostic value of pretreatment prognostic nutritional index in patients with small cell lung cancer and it's influencing factors: a meta-analysis of observational studies. J Thorac Dis 2020, 12(10):5718-5728.
17. Mezquita L, Auclin E, Ferrara R, Charrier M, Remon J, Planchard D, Ponce S, Ares LP, Leroy L, Audigier-Valette C et al: Association of the Lung Immune Prognostic Index With Immune Checkpoint Inhibitor Outcomes in Patients With Advanced Non-Small Cell Lung Cancer. JAMA Oncol 2018, 4(3):351-357.
18. Laird BJ, Kaasa S, McMillan DC, Fallon MT, Hjermstad MJ, Fayers P, Klepstad P: Prognostic factors in patients with advanced cancer: a comparison of clinicopathological factors and the development of an inflammation-based prognostic system. Clin Cancer Res 2013, 19(19):5456-5464.
19. McMillan DC: An inflammation-based prognostic score and its role in the nutrition-based management of patients with cancer. Proc Nutr Soc 2008, 67(3):257-262.
20. Corti F, Lonardi S, Intini R, Salati M, Fenocchio E, Belli C, Borelli B, Brambilla M, Prete AA, Quarà V et al: The Pan-Immune-Inflammation Value in microsatellite instability-high metastatic colorectal cancer patients treated with immune checkpoint inhibitors. Eur J Cancer 2021, 150:155-167.
21. Sato S, Shimizu T, Ishizuka M, Suda K, Shibuya N, Hachiya H, Iso Y, Takagi K, Aoki T, Kubota K: The preoperative pan-immune-inflammation value is a novel prognostic predictor for with stage I-III colorectal cancer patients undergoing surgery. Surg Today 2022, 52(8):1160-1169.
22. Socinski MA, Smit EF, Lorigan P, Konduri K, Reck M, Szczesna A, Blakely J, Serwatowski P, Karaseva NA, Ciuleanu T et al: Phase III study of pemetrexed plus carboplatin compared with etoposide plus carboplatin in chemotherapy-naive patients with extensive-stage small-cell lung cancer. J Clin Oncol 2009, 27(28):4787-4792.
23. Reck M, Luft A, Szczesna A, Havel L, Kim SW, Akerley W, Pietanza MC, Wu YL, Zielinski C, Thomas M et al: Phase III Randomized Trial of Ipilimumab Plus Etoposide and Platinum Versus Placebo Plus Etoposide and Platinum in Extensive-Stage Small-Cell Lung Cancer. J Clin Oncol 2016, 34(31):3740-3748.
24. Forrest LM, McMillan DC, McArdle CS, Angerson WJ, Dunlop DJ: Evaluation of cumulative prognostic scores based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. Br J Cancer 2003, 89(6):1028-1030.
25. Zeng R, Liu F, Fang C, Yang J, Luo L, Yue P, Gao B, Dong Y, Xiang Y: PIV and PILE Score at Baseline Predict Clinical Outcome of Anti-PD-1/PD-L1 Inhibitor Combined With Chemotherapy in Extensive-Stage Small Cell Lung Cancer Patients. Front Immunol 2021, 12:724443.
26. Sonehara K, Tateishi K, Komatsu M, Yamamoto H, Hanaoka M: Lung immune prognostic index as a prognostic factor in patients with small cell lung cancer. Thorac Cancer 2020, 11(6):1578-1586.
27. Söyler Y, Kabalak PA, Kavurgacı S, Ayyürek M, Öztürk A, Yılmaz Ü: Lung immune prognostic index as a prognostic predictor in patients with advanced small cell lung cancer. Anatolian Current Medical Journal, 5(3):180-186.
28. Galvano A, Peri M, Guarini AA, Castiglia M, Grassadonia A, De Tursi M, Irtelli L, Rizzo S, Bertani A, Gristina V et al: Analysis of systemic inflammatory biomarkers in neuroendocrine carcinomas of the lung: prognostic and predictive significance of NLR, LDH, ALI, and LIPI score. Ther Adv Med Oncol 2020, 12:1758835920942378.
29. Dang J, Xu G, Guo G, Zhang H, Shang L: Construction of a prognostic model for extensive-stage small cell lung cancer patients undergoing immune therapy in northernmost China and prediction of treatment efficacy based on response status at different time points. J Cancer Res Clin Oncol 2024, 150(5):255.
30. Zhang M, Hao J, Wu Y, Gao Z, Wang M: Value of the lung immune prognostic index in patients with advanced small cell lung cancer treated with programmed death-ligand 1 and programmed death-1 inhibitors in the Chinese alpine region. Front Oncol 2024, 14:1411548.
31. Qi W, Zhao S, Chen J: Prognostic role of pretreatment lung immune prognostic index in extensive-stage small-cell lung cancer treated with platinum plus etoposide chemotherapy. Cancer Biomark 2021, 31(2):177-185.
32. SchnÖller L, KÄsmann L, Taugner J, Abdo R, Eze C, Manapov F: Prognostic Role of Lung Immune Scores for Prediction of Survival in Limited-stage Small Cell Lung Cancer. In Vivo 2021, 35(2):929-935.
33. Sun B, Hou Q, Liang Y, Xue S, Yao N, Wei L, Cao X, Li H, Si H, Cao J: Prognostic ability of lung immune prognostic index in limited-stage small cell lung cancer. BMC Cancer 2022, 22(1):1233.
34. Xie J, Xu K, Cai Z, Chen M, Jiang Y, Ye J, Lin X, Lv T, Zhan P: Efficacy and safety of first-line PD-L1/PD-1 inhibitors in limited-stage small cell lung cancer: a multicenter propensity score

matched retrospective study. Transl Lung Cancer Res 2024, 13(3):526-539.
35. Zhou T, Hong S, Hu Z, Hou X, Huang Y, Zhao H, Liang W, Zhao Y, Fang W, Wu X et al: A systemic inflammation-based prognostic scores (mGPS) predicts overall survival of patients with small-cell lung cancer. Tumour Biol 2015, 36(1):337-343.
36. Li L, Pi C, Yan X, Lu J, Yang X, Wang C, Li X, Zhang S, Zhang Z, Sun Y et al: Prognostic Value of the Pretreatment Lung Immune Prognostic Index in Advanced Small Cell Lung Cancer Patients Treated With First-Line PD-1/PD-L1 Inhibitors Plus Chemotherapy. Front Oncol 2021, 11:697865.
37. Oyman A, Çil İ, Özçelik M, Özyükseler DT, Başak M, Gökyer A, Ökten İN: Evaluation of LIPI and mGPS as prognostic factors in extensive-stage small-cell lung cancer. Journal of Surgery and Medicine 2022, 6(2):115-119.
38. Sonehara K, Tateishi K, Komatsu M, Yamamoto H, Hanaoka M, Kanda S, Koizumi T: Modified Glasgow Prognostic Score as a Prognostic Factor in Patients with Extensive Disease-Small-Cell Lung Cancer: A Retrospective Study in a Single Institute. Chemotherapy 2019, 64(3):129-137.
39. Zhou T, Zhao Y, Zhao S, Yang Y, Huang Y, Hou X, Zhao H, Zhang L: Comparison of the Prognostic Value of Systemic Inflammation Response Markers in Small Cell Lung Cancer Patients. J Cancer 2019, 10(7):1685-1692.
40. Xie Y, Li H, Hu Y: Prognostic value of pretreatment modified Glasgow Prognostic Score in small cell lung cancer: A meta-analysis. Medicine (Baltimore) 2023, 102(45):e35962.
41. Chen X, Hong X, Chen G, Xue J, Huang J, Wang F, Ali W, Li J, Zhang L: The Pan-Immune-Inflammation Value predicts the survival of patients with anaplastic lymphoma kinase-positive non-small cell lung cancer treated with first-line ALK inhibitor. Transl Oncol 2022, 17:101338.
42. Kucuk A, Topkan E, Ozkan EE, Ozturk D, Pehlivan B, Selek U: A high pan-immune-inflammation value before chemo-radiotherapy indicates poor outcomes in patients with small-cell lung cancer. Int J Immunopathol Pharmacol 2023, 37:3946320231187759.
43. Aydın AA, Acun M: The prognostic impact of the pan-immune-inflammation value (PIV) on the efficacy of treatment and clinical outcomes in patients with extensive-stage small cell lung cancer (ES-SCLC). Journal of Health Sciences and Medicine 2024, 7(5):494-499.