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Association of Inflammation-Based Indices With Short-, Mid-, and Long-Term Survival in Inoperable Non–Small Cell Lung Cancer

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Research Article

Keywords: Inoperable NSCLC, CRP albumin ratio, Neutrophil lymphocyte ratio, Modified glasgow prognostic score, Overall survival

Posted Date: May 25th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9706840/v1

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Additional Declarations: No competing interests reported.

Abstract

Background:

Systemic inflammation plays a key role in cancer progression and survival outcomes in non–small cell lung cancer (NSCLC). This study investigated the association between inflammation-based indices—including the C-reactive protein-to-albumin ratio (CAR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and modified Glasgow Prognostic Score (mGPS)—and short-term (1-year), mid-term (2-year), and long-term (5-year) survival outcomes in patients with inoperable NSCLC managed in routine clinical practice.

Methods:

This retrospective cohort study included patients with inoperable NSCLC diagnosed between 2010 and 2018 at a tertiary center. Baseline demographic, clinical, and laboratory data were collected. Survival status at 1, 2, and 5 years was assessed. Inflammation-based indices were calculated using baseline laboratory values. Group comparisons, Kaplan–Meier survival analyses, and multivariable logistic regression models were used to evaluate prognostic associations.

Results:

A total of 210 patients were analyzed (mean age 75.8 ± 11.0 years; 82.9% male). Median overall survival (OS) was 13.96 ± 16.18 months, while 1-, 2-, and 5-year survival rates were 42.4%, 21.4%, and 7.1%, respectively. Higher inflammatory marker levels, including CAR, NLR, and PLR, were consistently observed among non-survivors across all predefined follow-up periods (all $p < 0.05$). Kaplan–Meier analyses demonstrated significantly reduced OS in patients with elevated CAR and NLR, together with a clear stepwise decline in survival across increasing mGPS categories (all log-rank $p < 0.001$). In multivariable analyses, higher CAR independently associated with reduced 1-year survival (OR: 0.89, 95% CI: 0.86–0.93, $p < 0.001$), 2-year survival (OR: 0.80, 95% CI: 0.72–0.89, $p < 0.001$), and 5-year survival (OR: 0.65, 95% CI: 0.45–0.92, $p = 0.014$). Higher NLR was also independently associated with reduced 1- and 2-year survival.

Conclusions:

Inflammation-based indices, particularly CAR and NLR, were associated with survival outcomes in patients with inoperable NSCLC. These findings suggest that routinely available inflammatory biomarkers may contribute to prognostic evaluation in real-world clinical settings.

Background

Lung cancer remains the leading cause of cancer-related mortality worldwide and represents a major global health burden. According to the most recent global cancer statistics, approximately 2.5 million new lung cancer cases and 1.8 million deaths were reported in 2022, making it the most frequently diagnosed cancer and the leading cause of cancer-related death globally [1, 2]. Despite advances in early detection and treatment, the prognosis of lung cancer remains poor, particularly in patients diagnosed at advanced stages.

Non–small cell lung cancer (NSCLC) accounts for the majority of lung cancer cases and is characterized by substantial heterogeneity in clinical behavior and outcomes. Although therapeutic options such as chemotherapy, radiotherapy, targeted therapy, and immunotherapy have improved survival in selected patient groups, a considerable proportion of patients are ineligible for surgical resection and continue to have limited long-term survival [3]. Therefore, identification of reliable and easily accessible prognostic biomarkers remains a critical need in clinical practice.

Accumulating evidence suggests that systemic inflammation plays a central role in cancer development, progression, and treatment resistance. Chronic inflammatory processes contribute to tumor growth, angiogenesis, immune evasion, and metastatic spread through complex interactions within the tumor microenvironment [4, 5]. In particular, inflammatory mediators such as C-reactive protein (CRP) have been shown to promote tumor progression and are increasingly recognized as key components of cancer-related systemic responses [6].

In this context, several inflammation-based indices derived from routine laboratory parameters have emerged as practical prognostic tools in oncology. The modified Glasgow Prognostic Score (mGPS), which integrates CRP and albumin levels, has consistently demonstrated prognostic value across multiple malignancies, including lung cancer [7–9]. Similarly, other indices such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and C-reactive protein-to-albumin ratio (CAR) have been associated with survival outcomes in patients with NSCLC, reflecting the balance between pro-tumor inflammatory activity and host immune response [10–15].

Although inflammation-based biomarkers have been widely investigated in NSCLC, many previous studies focused on selected treatment populations or single survival endpoints. Data evaluating the relationship between baseline inflammatory indices and fixed-time survival outcomes across short-, mid-, and long-term follow-up in real-world inoperable NSCLC populations remain limited.

Therefore, the present study aimed to investigate the association between baseline inflammation-based indices, including mGPS, NLR, PLR, and CAR, and 1-, 2-, and 5-year survival outcomes in patients with inoperable NSCLC.

Methods

Study Design and Setting

This was a single-center retrospective cohort study conducted at Konya City Hospital. The study focused on patients diagnosed with NSCLC between 2010 and 2018 who were considered unsuitable for surgical treatment and were therefore managed with non-surgical approaches. Clinical, laboratory, pathological, treatment, and follow-up data were obtained from the hospital information system and laboratory information system through a structured data extraction framework prepared before analysis. Retrieved variables were cross-checked with source records when necessary to improve consistency and accuracy.

Study Population

During the study period, 491 patients with a diagnosis of NSCLC were identified from hospital records. From this source population, patients who did not undergo resection of the primary tumor and had sufficient baseline laboratory and survival data were considered for inclusion. Patients were excluded if essential laboratory parameters were missing, survival status could not be confirmed, or records were incomplete for the calculation of inflammation-based indices. After applying these criteria, a total of 210 patients constituted the final study cohort (Fig. 1). Inoperability had been determined in routine clinical practice on the basis of advanced disease extent, medical comorbidity, poor pulmonary reserve, impaired functional status, or multidisciplinary tumor board assessment. The final cohort consisted of consecutively eligible patients meeting these criteria.

Patients were followed from the date of diagnosis until death or the last available follow-up entry. For patients with repeated admissions or multiple hospital encounters, only the initial diagnostic episode was used as the reference point in order to avoid repeated inclusion of the same individual.

Eligibility Criteria

Patients were included if they had histopathologically confirmed NSCLC, documented clinical stage at diagnosis, no surgical resection of the primary tumor, available pretreatment laboratory measurements including platelet count, neutrophil count, lymphocyte count, CRP, and albumin, and accessible survival follow-up data. Patients were excluded if key laboratory parameters were unavailable, survival status could not be verified, or the records were insufficient for construction of the inflammatory indices used in the analysis. Missing observations were not replaced statistically, and only patients with complete data for the primary analyses were retained.

Definition of Exposures and Covariates

Baseline inflammatory markers were defined using laboratory test results obtained nearest to the date of diagnosis and before initiation of oncologic treatment whenever available. The mGPS was derived from CRP and albumin values. Patients received a score of 0 when CRP was 10 mg/L or lower. A score of 1 was assigned when CRP was greater than 10 mg/L while albumin remained at or above 3.5 g/dL. A

score of 2 was assigned when CRP was greater than 10 mg/L and albumin was below 3.5 g/dL. This variable was evaluated categorically.

Other inflammation-based indices were also generated. The NLR was calculated by dividing neutrophil count by lymphocyte count. The PLR was calculated as platelet count divided by lymphocyte count. The PAR was obtained by dividing platelet count by albumin concentration. In addition, the CAR was calculated by dividing CRP by albumin.

Candidate covariates included age, sex, clinical stage category, histological subtype, and treatment-related variables. Clinical stage was grouped according to disease extent as locally advanced or metastatic. Treatment variables included receipt of systemic therapy and radiotherapy. Where relevant, systemic treatment modalities such as chemotherapy, immunotherapy, or targeted therapy were recorded according to the available clinical documentation. However, detailed treatment sequencing, regimen intensity, treatment duration, and molecular treatment selection criteria were not uniformly available because of the retrospective nature of the dataset. Consequently, the present analysis primarily focused on the association between baseline inflammatory burden and survival outcomes rather than treatment-specific effects, allowing a broader real-world evaluation relatively independent of individual treatment protocols.

Outcome Definitions

The principal endpoint of the study was overall survival (OS). OS was defined as the interval between the date of diagnosis and death from any cause. Patients who were alive at the end of follow-up were censored on the date of their last documented contact. Survival duration was expressed in months.

In addition to OS time, fixed-time survival outcomes were examined at 1, 2, and 5 years. For each of these landmarks, patients were classified as alive or deceased according to their survival status at 12, 24, and 60 months after diagnosis.

Bias and Confounding

To reduce selection-related distortion, all consecutive patients meeting the predefined eligibility criteria were considered for inclusion. Information bias was limited by using routinely recorded electronic data and predefined variable rules during extraction and analysis. Because of the retrospective design, unmeasured confounding cannot be ruled out entirely. To address this issue as much as possible, multivariable models were used to adjust for clinically relevant factors and variables associated with the outcomes of interest.

Study Size

The study sample was formed from all eligible inoperable NSCLC cases identified during the predefined study interval. No formal sample size or power calculation was performed in advance because the investigation was retrospective and based on the available institutional dataset.

Missing Data

A complete-case strategy was applied. Patients lacking essential exposure, covariate, or outcome information required for the planned analyses were excluded. No imputation or data replacement procedure was performed.

Statistical Analysis

All analyses were conducted using Wistats v3.0 (WisdomEra Corp., Istanbul, Turkey), a Python-based statistical platform integrating SciPy, scikit-learn, and statsmodels (https://wistats.wisdomera.io, accessed on 25 March 2026). The distribution of continuous variables was examined using skewness, kurtosis, and the Shapiro-Wilk test. Categorical variables were summarized as number and percentage. Continuous variables were reported as mean with standard deviation when they followed an approximately normal distribution.

Comparisons according to 1-year, 2-year, and 5-year survival status were performed using the chi-square test or Fisher's exact test for categorical data and the independent samples t-test or Mann-Whitney U test for continuous data, depending on distributional characteristics.

To explore factors associated with survival at 1, 2, and 5 years, univariable and multivariable logistic regression analyses were performed using survival status at each predefined time point as a binary outcome (alive = 1, deceased = 0).

Because the survival status of all individuals at 1, 2, and 5 years was fully ascertained (i.e., no censoring occurred and all patients either died within 5 years or were known to survive beyond 5 years), time-to-event modeling using Cox proportional hazards regression was not considered necessary.

In this cohort, the vast majority of patients died during follow-up. Survival status at 1, 2, and 5 years was completely observed for all individuals, with no loss to follow-up and negligible censoring, as all patients either died within 5 years or were known to survive beyond this time point. Under these conditions, time-to-event modeling using Cox proportional hazards regression was considered suboptimal, as the near absence of censoring and the highly unbalanced event distribution may compromise the stability and interpretability of hazard ratio estimates.

Therefore, a landmark analysis framework based on logistic regression at predefined time points (1, 2, and 5 years) was adopted, providing a more robust and interpretable approach for estimating time-specific survival probabilities in this dataset.

Variables considered clinically relevant or showing association in univariable analysis were entered into the multivariable models. Effect estimates were presented as odds ratios with 95% confidence intervals. All significance tests were two-sided, and a p value below 0.05 was accepted as statistically significant.

OS was also examined using the Kaplan-Meier method. Survival curves were constructed according to mGPS categories and according to median-based grouping of the CAR and NLR. Differences between survival distributions were assessed using the log-rank test.

Results

A total of 210 patients with inoperable NSCLC were included in the final analysis. The mean age of the cohort was 75.79 ± 11.04 years, and the majority were male (82.9%). Most patients received chemotherapy (93.3%) and/or radiotherapy (64.8%), with chemoradiotherapy being the most common treatment modality (64.3%). Adenocarcinoma (51.4%) and squamous cell carcinoma (42.9%) were the predominant histological subtypes. More than half of the patients were diagnosed at stage IV disease (56.2%). During follow-up, 95.2% of patients died, with a mean OS of 13.96 ± 16.18 months among deceased cases. One-, two-, and five-year survival rates were 42.4%, 21.4%, and 7.1%, respectively (Table 1).

Table 1
Baseline Demographic and Clinical Characteristics of the Study Cohort

Variables	**cases** **Mean ± SD, N (%)**
Cases	210 (100%)
Gender	
female	36 (17.1%)
male	174 (82.9%)
Age	75.79 ± 11.04
Chemotherapy	
no	14 (6.7%)
yes	196 (93.3%)
Radiotherapy	
no	74 (35.2%)
yes	136 (64.8%)
Treatment Type	
chemoradiotherapy	135 (64.3%)
only chemotherapy	61 (29.0%)
only radiotherapy	1 (0.5%)
treatment refused	13 (6.2%)
Histopathology	
adenocarcinoma	108 (51.4%)
large cell carcinoma	12 (5.7%)
squamous cell carcinoma	90 (42.9%)
Clinical Stage	
IIIA	28 (13.3%)
IIIB	39 (18.6%)
IIIC	25 (11.9%)

NLR, neutrophil-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; mGPS, modified Glasgow prognostic score; CAR, crp-to-albumin ratio; N: Number of cases.

Variables	cases Mean ± SD, N (%)
IVA	73 (34.8%)
IVB	45 (21.4%)
Clinical Stage Group	
stage 3	92 (43.8%)
stage 4	118 (56.2%)
Vital Status	
alive	10 (4.8%)
deceased	200 (95.2%)
Overall Survival Exitus Cases (months)	13.96 ± 16.18
1-Year Survival Status	
deceased	121 (57.6%)
alive	89 (42.4%)
2-Year Survival Status	
deceased	165 (78.6%)
alive	45 (21.4%)
5-Year Survival Status	
deceased	195 (92.9%)
alive	15 (7.1%)
PLR	219.59 ± 133.59
PAR	89.07 ± 36.70
NLR	4.94 ± 3.63
CAR	16.57 ± 19.66
mGPS	
0	40 (19.0%)
1	119 (56.7%)

NLR, neutrophil-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; mGPS, modified Glasgow prognostic score; CAR, crp-to-albumin ratio; N: Number of cases.

Variables	cases Mean ± SD, N (%)
2	51 (24.3%)
Wbc (K/uL)	10.08 ± 4.36
Rbc (M/uL)	4.83 ± 0.64
Hgb (gr/dL)	13.59 ± 1.81
Hct (%)	41.16 ± 5.00
Plt (K/uL)	323.96 ± 109.17
Neu (K/UL)	7.25 ± 4.03
Lym (K/UL)	1.77 ± 0.78
Ast (U/L)	29.18 ± 31.51
Alt (U/L)	26.96 ± 46.74
Ldh (U/L)	295.10 ± 141.16
Crp (mg/L)	57.17 ± 60.95
Albumin (g/dL)	3.74 ± 0.49
NLR, neutrophil-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; mGPS, modified Glasgow prognostic score; CAR, crp-to-albumin ratio; N: Number of cases.	

When patients were stratified according to 1-year survival status, several significant differences were observed. Patients who survived beyond one year were younger compared to those who did not (73.53 ± 10.13 vs. 77.45 ± 11.43 years, $p = 0.014$). Receipt of chemotherapy and radiotherapy was significantly more frequent among survivors ($p = 0.004$ and $p < 0.001$, respectively), and chemoradiotherapy was more commonly administered in this group (79.8% vs. 52.9%, $p < 0.001$). Advanced disease stage was strongly associated with mortality, as stage IV disease was more prevalent among patients who died within one year (68.6% vs. 39.3%, $p < 0.001$). Inflammatory markers also differed markedly: patients who died had higher PLR, NLR, and CAR values (all $p < 0.001$). In addition, higher mGPS scores were significantly associated with increased mortality ($p < 0.001$) (Table 2).

Table 2
Comparative Outcomes Between Alive and Deceased Groups According to 1-Year Survival

Cases	**alive**	**deceased**	**p**
	Mean ± SD, N (%)	**Mean ± SD, N (%)**	
	89 (42.4%)	**121 (57.6%)**	
Gender			0.259
female	13 (14.6%)	23 (19.0%)	
male	76 (85.4%)	98 (81.0%)	
Age	73.53 ± 10.13	77.45 ± 11.43	0.014
Chemotherapy			0.004
no	1 (1.1%)	13 (10.7%)	
yes	88 (98.9%)	108 (89.3%)	
Radiotherapy			< 0.001
no	18 (20.2%)	56 (46.3%)	
yes	71 (79.8%)	65 (53.7%)	
Treatment Type			< 0.001
chemoradiotherapy	71 (79.8%)	64 (52.9%)	
only chemotherapy	17 (19.1%)	44 (36.4%)	
only radiotherapy	0 (0.0%)	1 (0.8%)	
treatment refused	1 (1.1%)	12 (9.9%)	
Histopathology			0.391
adenocarcinoma	45 (50.6%)	63 (52.1%)	
large cell carcinoma	3 (3.4%)	9 (7.4%)	
squamous cell carcinoma	41 (46.1%)	49 (40.5%)	
Clinical Stage			< 0.001
IIIA	21 (23.6%)	7 (5.8%)	
IIIB	25 (28.1%)	14 (11.6%)	
IIIC	8 (9.0%)	17 (14.0%)	

NLR, neutrophil-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; mGPS, modified Glasgow prognostic score; CAR, crp-to-albumin ratio; N: Number of cases.

Cases	alive	deceased	p
	Mean ± SD, N (%)	Mean ± SD, N (%)	
	89 (42.4%)	**121 (57.6%)**	
IVA	25 (28.1%)	48 (39.7%)	
IVB	10 (11.2%)	35 (28.9%)	
Clinical Stage Group			< 0.001
stage 3	54 (60.7%)	38 (31.4%)	
stage 4	35 (39.3%)	83 (68.6%)	
PLR	187.56 ± 121.10	243.15 ± 137.86	< 0.001
PAR	84.06 ± 32.49	92.76 ± 39.24	0.069
NLR	3.38 ± 1.82	6.09 ± 4.16	< 0.001
CAR	6.79 ± 7.78	23.77 ± 22.49	< 0.001
mGPS			< 0.001
0	33 (37.1%)	7 (5.8%)	
1	49 (55.1%)	70 (57.9%)	
2	7 (7.9%)	44 (36.4%)	

NLR, neutrophil-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; mGPS, modified Glasgow prognostic score; CAR, crp-to-albumin ratio; N: Number of cases.

Similar patterns were observed in the 2-year survival analysis. Patients alive at two years more frequently received radiotherapy and chemoradiotherapy ($p < 0.001$ and $p = 0.001$, respectively), and were more often in stage III disease (64.4% vs. 38.2%, $p = 0.001$). Elevated inflammatory indices were again associated with mortality. Specifically, PLR, NLR, and CAR values were significantly higher in patients who died within two years ($p = 0.009$, $p < 0.001$, and $p < 0.001$, respectively). Higher mGPS categories were also more common among non-survivors ($p < 0.001$) (Table 3).

Table 3
Comparative Outcomes Between Alive and Deceased Groups According to 2-Year Survival

Variables	**alive**	**deceased**	**p**
	Mean ± SD, N (%)	**Mean ± SD, N (%)**	
Cases	45 (21.4%)	165 (78.6%)	
Gender			0.473
female	7 (15.6%)	29 (17.6%)	
male	38 (84.4%)	136 (82.4%)	
Age	73.51 ± 9.74	76.41 ± 11.32	0.072
Chemotherapy			0.030
no	0 (0.0%)	14 (8.5%)	
yes	45 (100.0%)	151 (91.5%)	
Radiotherapy			< 0.001
no	5 (11.1%)	69 (41.8%)	
yes	40 (88.9%)	96 (58.2%)	
Treatment Type			0.001
chemoradiotherapy	40 (88.9%)	95 (57.6%)	
only chemotherapy	5 (11.1%)	56 (33.9%)	
only radiotherapy	0 (0.0%)	1 (0.6%)	
treatment refused	0 (0.0%)	13 (7.9%)	
Histopathology			0.174
adenocarcinoma	25 (55.6%)	83 (50.3%)	
large cell carcinoma	0 (0.0%)	12 (7.3%)	
squamous cell carcinoma	20 (44.4%)	70 (42.4%)	
Clinical Stage			< 0.001
IIIA	15 (33.3%)	13 (7.9%)	
IIIB	13 (28.9%)	26 (15.8%)	
IIIC	1 (2.2%)	24 (14.5%)	

NLR, neutrophil-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; mGPS, modified Glasgow prognostic score; CAR, crp-to-albumin ratio; N: Number of cases.

Variables	alive	deceased	p
	Mean ± SD, N (%)	Mean ± SD, N (%)	
IVA	11 (24.4%)	62 (37.6%)	
IVB	5 (11.1%)	40 (24.2%)	
Clinical Stage Group			0.001
stage 3	29 (64.4%)	63 (38.2%)	
stage 4	16 (35.6%)	102 (61.8%)	
PLR	174.67 ± 77.76	231.84 ± 142.88	0.009
PAR	85.42 ± 31.17	90.07 ± 38.10	0.567
NLR	3.12 ± 0.97	5.44 ± 3.92	< 0.001
CAR	3.80 ± 5.00	20.06 ± 20.71	< 0.001
mGPS			< 0.001
0	25 (55.6%)	15 (9.1%)	
1	16 (35.6%)	103 (62.4%)	
2	4 (8.9%)	47 (28.5%)	

NLR, neutrophil-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; mGPS, modified Glasgow prognostic score; CAR, crp-to-albumin ratio; N: Number of cases.

At 5 years, only 7.1% of patients remained alive. Although demographic and treatment-related variables were not significantly different between survivors and non-survivors, disease stage remained associated with long-term survival ($p = 0.011$). Inflammatory markers continued to show strong associations with mortality: PLR, NLR, and CAR values were significantly higher in patients who died within five years ($p = 0.003$, $p < 0.001$, and $p < 0.001$, respectively). Moreover, none of the patients with mGPS score of 2 survived to five years, whereas the majority of long-term survivors had an mGPS score of 0 (66.7%) (Table 4).

Table 4
Comparative Outcomes Between Alive and Deceased Groups According to 5-Year Survival

Variables	alive	deceased	p
	Mean ± SD, N (%)	Mean ± SD, N (%)	
Cases	15 (7.1%)	195 (92.9%)	
Gender			0.234
female	1 (6.7%)	35 (17.9%)	
male	14 (93.3%)	160 (82.1%)	
Age	74.73 ± 8.50	75.87 ± 11.23	0.562
Chemotherapy			0.283
no	0 (0.0%)	14 (7.2%)	
yes	15 (100.0%)	181 (92.8%)	
Radiotherapy			0.158
no	3 (20.0%)	71 (36.4%)	
yes	12 (80.0%)	124 (63.6%)	
Treatment Type			0.541
chemoradiotherapy	12 (80.0%)	123 (63.1%)	
only chemotherapy	3 (20.0%)	58 (29.7%)	
only radiotherapy	0 (0.0%)	1 (0.5%)	
treatment refused	0 (0.0%)	13 (6.7%)	
Histopathology			0.610
adenocarcinoma	8 (53.3%)	100 (51.3%)	
large cell carcinoma	0 (0.0%)	12 (6.2%)	
squamous cell carcinoma	7 (46.7%)	83 (42.6%)	
Clinical Stage			0.011
IIIA	6 (40.0%)	22 (11.3%)	
IIIB	4 (26.7%)	35 (17.9%)	
IIIC	0 (0.0%)	25 (12.8%)	

NLR, neutrophil-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; mGPS, modified Glasgow prognostic score; CAR, crp-to-albumin ratio; N: Number of cases.

Variables	alive	deceased	p
	Mean ± SD, N (%)	Mean ± SD, N (%)	
IVA	4 (26.7%)	69 (35.4%)	
IVB	1 (6.7%)	44 (22.6%)	
Clinical Stage Group			0.057
stage 3	10 (66.7%)	82 (42.1%)	
stage 4	5 (33.3%)	113 (57.9%)	
PLR	141.24 ± 54.38	225.62 ± 136.02	0.003
PAR	75.35 ± 28.79	90.13 ± 37.09	0.052
NLR	2.71 ± 0.68	5.11 ± 3.70	< 0.001
CAR	2.15 ± 1.69	17.68 ± 19.98	< 0.001
mGPS			< 0.001
0	10 (66.7%)	30 (15.4%)	
1	5 (33.3%)	114 (58.5%)	
2	0 (0.0%)	51 (26.2%)	

NLR, neutrophil-to-lymphocyte ratio; PAR, platelet-to-albumin ratio; PLR, platelet-to-lymphocyte ratio; mGPS, modified Glasgow prognostic score; CAR, crp-to-albumin ratio; N: Number of cases.

Kaplan–Meier survival analyses demonstrated a clear separation of survival curves according to inflammation-based indices. Patients with higher CAR values (above the median of 10.7) had markedly reduced OS compared with those with lower CAR levels (log-rank $p < 0.001$) (Fig. 2A). A similar pattern was observed for NLR, where patients with elevated NLR (above the median of 4) showed significantly poorer survival than those with lower values (log-rank $p < 0.001$) (Fig. 2B). Stratification by mGPS further revealed a stepwise decline in survival across increasing categories, with the best outcomes observed in patients with mGPS 0 and the worst in those with mGPS 2 (log-rank $p < 0.001$) (Fig. 2C). Overall, these findings indicate a strong and graded association between systemic inflammatory burden and OS.

Regression analyses further supported these findings. In the multivariable model for 1-year survival, higher CAR (OR: 0.89, 95% CI: 0.86–0.93, $p < 0.001$) and higher NLR (OR: 0.59, 95% CI: 0.43–0.80, $p < 0.001$) were independently associated with lower odds of surviving one year. Higher PLR (OR: 1.01, 95% CI: 1.00–1.01, $p = 0.026$) and advanced clinical stage (OR: 2.69, 95% CI: 1.26–5.76, $p = 0.011$) were also independently associated with 1-year survival status. For 2-year survival, CAR (OR: 0.80, 95% CI: 0.72–0.89, $p < 0.001$) and NLR (OR: 0.65, 95% CI: 0.44–0.97, $p = 0.033$) remained significantly associated with reduced survival probability, whereas radiotherapy (OR: 4.75, 95% CI: 1.52–14.82, $p = 0.007$) was associated with higher odds of survival. In the 5-year survival model, only CAR retained independent

prognostic significance (OR: 0.65, 95% CI: 0.45–0.92, p = 0.014), indicating a persistent association between systemic inflammation and decreased long-term survival (Table 5).

Overall, inflammation-based indices—particularly CAR and NLR—showed significant associations with short-, mid-, and long-term survival outcomes in this retrospective real-world cohort, while mGPS demonstrated graded survival differences in unadjusted analyses.

Discussion

In this study, we evaluated the prognostic significance of inflammation-based indices in patients with inoperable NSCLC and demonstrated several key findings. First, systemic inflammatory markers, including CAR, NLR, and PLR, were significantly associated with survival outcomes at 1-, 2-, and 5-year time points. Second, mGPS exhibited a clear stepwise relationship with survival, with no patients surviving to five years in the mGPS 2 category. Third, among all evaluated indices, CAR emerged as the most consistent independent predictor, retaining its significance even in the 5-year multivariable model. Overall, these findings indicate that systemic inflammatory burden is strongly and consistently associated with both short- and long-term survival outcomes in patients with inoperable NSCLC.

The prognostic value of inflammation-based indices in NSCLC has been widely documented, and our results are in line with previous literature. In particular, the CAR has been identified as a robust predictor of survival in advanced NSCLC. Koh et al. reported that elevated CAR was independently associated with poorer OS in patients with stage IV disease receiving palliative chemotherapy [16]. Similarly, Ni et al. demonstrated that CAR not only served as an independent prognostic marker but also outperformed other indices such as NLR and PLR in predictive accuracy [17]. Consistent with these findings, our study showed that higher CAR levels were independently associated with reduced survival across all evaluated time horizons and remained the only parameter retaining significance in the long-term model, highlighting its potential as a durable prognostic indicator.

The association between NLR and survival in NSCLC has also been consistently supported by previous studies. Meta-analyses have demonstrated that elevated NLR is associated with worse overall and progression-free survival, irrespective of treatment modality [18, 19]. In our cohort, higher NLR values were significantly associated with reduced survival at 1- and 2-year time points and remained independently associated with survival probability in multivariable analyses. These findings further support the biological relevance of systemic inflammation, where neutrophil-mediated tumor promotion and lymphocyte suppression contribute to adverse clinical outcomes.

Similarly, PLR has been proposed as an accessible biomarker reflecting the balance between platelet-driven tumor progression and host immune response. Previous studies have reported that elevated PLR is associated with poorer survival, particularly in advanced-stage disease and in patients undergoing systemic therapies [20, 21]. In our study, PLR values were consistently higher among non-survivors across all time points, although its independent prognostic effect was less stable compared with CAR and NLR, suggesting a more limited but still clinically relevant role.

The mGPS represents one of the most widely validated inflammation-based prognostic tools in oncology. Prior studies and meta-analyses have demonstrated a strong association between increasing mGPS categories and worse survival outcomes in NSCLC [22]. Our findings extend this evidence by demonstrating a clear and graded survival pattern across mGPS categories, with a complete absence of long-term survival among patients with mGPS 2. This observation underscores the clinical utility of mGPS as a simple and effective risk stratification tool in inoperable disease settings.

A notable aspect of the present study is the simultaneous evaluation of multiple inflammation-based indices across predefined 1-, 2-, and 5-year survival outcomes within a real-world inoperable NSCLC cohort. While previous studies have frequently focused on specific treatment settings or single survival endpoints, our analysis explored the association between baseline inflammatory burden and survival status across different follow-up horizons using a landmark-based analytical framework. The survival rates observed in our cohort (42.4% at 1 year, 21.4% at 2 years, and 7.1% at 5 years) were broadly comparable to those reported in advanced and inoperable NSCLC populations.

In addition to inflammatory markers, clinical characteristics also influenced survival outcomes. Advanced disease stage was associated with worse survival, while receipt of radiotherapy and combined chemoradiotherapy was more frequent among patients who survived longer. These findings are consistent with prior evidence emphasizing the importance of disease burden and treatment intensity in determining prognosis [23, 24]. Importantly, even after adjustment for these clinical factors, inflammation-based indices remained independently associated with survival, highlighting their additive prognostic value beyond traditional clinical parameters.

Several important limitations should be acknowledged. First, this was a retrospective single-center study with a relatively limited sample size, which may restrict the generalizability of the findings. Second, the cohort was clinically heterogeneous with respect to disease stage, treatment exposure, and likely molecular characteristics. Important oncological variables including Eastern Cooperative Oncology Group performance status, driver oncogene status, PD-L1 expression, detailed comorbidity burden, and treatment sequencing were not consistently available in the retrospective dataset and therefore could not be fully adjusted for in the analyses. In current oncology practice, the presence of various molecular alterations in patients with inoperable metastatic NSCLC represents a major determinant of both prognosis and treatment decision-making. Therefore, larger studies incorporating comprehensive molecular profiling may provide a more accurate evaluation of the prognostic role of inflammation-based markers. Third, treatment strategies were not standardized and included heterogeneous combinations of chemotherapy, radiotherapy, and supportive care approaches over a prolonged study period. Fourth, inflammatory markers were evaluated at a single baseline time point and may not fully reflect dynamic inflammatory changes during treatment and disease progression. In addition, inflammation-based indices are nonspecific markers and may have been influenced by concurrent inflammatory or infectious conditions that were not systematically documented. The use of broad stage categories rather than detailed TNM classification may also have reduced prognostic precision. Finally, the findings were not

externally validated in an independent cohort and should therefore be interpreted as exploratory real-world associations rather than definitive prognostic estimates.

Future research should focus on prospective validation of these findings in larger, multicenter cohorts and investigate the integration of inflammation-based indices with molecular, genomic, and radiological biomarkers. Additionally, longitudinal assessment of inflammatory markers may provide further insight into their role in treatment response and disease dynamics. Incorporating these indices into clinical decision-making frameworks may enhance individualized risk stratification and support more precise treatment planning in patients with inoperable NSCLC.

Conclusions

In conclusion, inflammation-based indices, particularly CAR and NLR, were significantly associated with survival outcomes in patients with inoperable NSCLC in this retrospective real-world cohort. The mGPS also demonstrated graded associations with survival outcomes across predefined follow-up periods. These findings support the potential relevance of systemic inflammatory burden in the clinical course of advanced NSCLC. However, given the retrospective design and clinical heterogeneity of the cohort, prospective multicenter studies with more detailed oncological characterization are necessary before these markers can be considered for routine prognostic implementation.

Abbreviations

NSCLC
Non–small cell lung cancer
CAR
C-reactive protein to albumin ratio
NLR
Neutrophil-to-lymphocyte ratio
PLR
Platelet-to-lymphocyte ratio
PAR
Platelet-to-albumin ratio
mGPS
Modified Glasgow Prognostic Score
CRP
C-reactive protein
OS
Overall survival
CI
Confidence interval.

Declarations

Ethics approval and consent to participate

This study was carried out in line with the ethical standards of the Declaration of Helsinki and its later revisions. Approval for the retrospective review of archived clinical and laboratory records was granted by the Institutional Review Board of Konya KTO Karatay University (approval number: 2025/050; approval date: December 25, 2025). Since the study used only retrospectively collected and fully anonymized data, the need for written informed consent was waived. All identifiable information was removed before analysis, and the dataset was handled in de-identified form throughout the study.

Consent for publication

The content of this manuscript has not been previously published and is not under consideration for publication elsewhere.

Availability of data and materials

The datasets generated and/or analysed during the current study are available in the Istinye University Dataset Sharing Platform repository, [https://dataset.istinye.edu.tr/dataset?did=90]

Competing interests

The authors declare no conflicts of interest.

Funding

No external funding was received.

Authors' contributions

MM: conceptualization, methodology, investigation, data curation, formal analysis, writing – original draft. HE: supervision, methodology, validation, writing – review and editing, resources. ÖB: validation, investigation, writing – review and editing, resources.

Acknowledgements

The authors would like to thank the Artificial Intelligence Research and Application Center of Istinye University (https://yzaum.istinye.edu.tr/, accessed on 25 March 2026) for providing technical support during manuscript preparation, including assistance with data validation processes and pre-submission similarity evaluation. The authors also acknowledge the Ditako Data Analytics Team (https://ditako.com, accessed on 25 March 2026) for their valuable contributions to the statistical analyses and methodological support provided for this study.

Clinical trial number: Not Applicable

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Table 5

Table 5 is available in the Supplementary Files section.

Figures

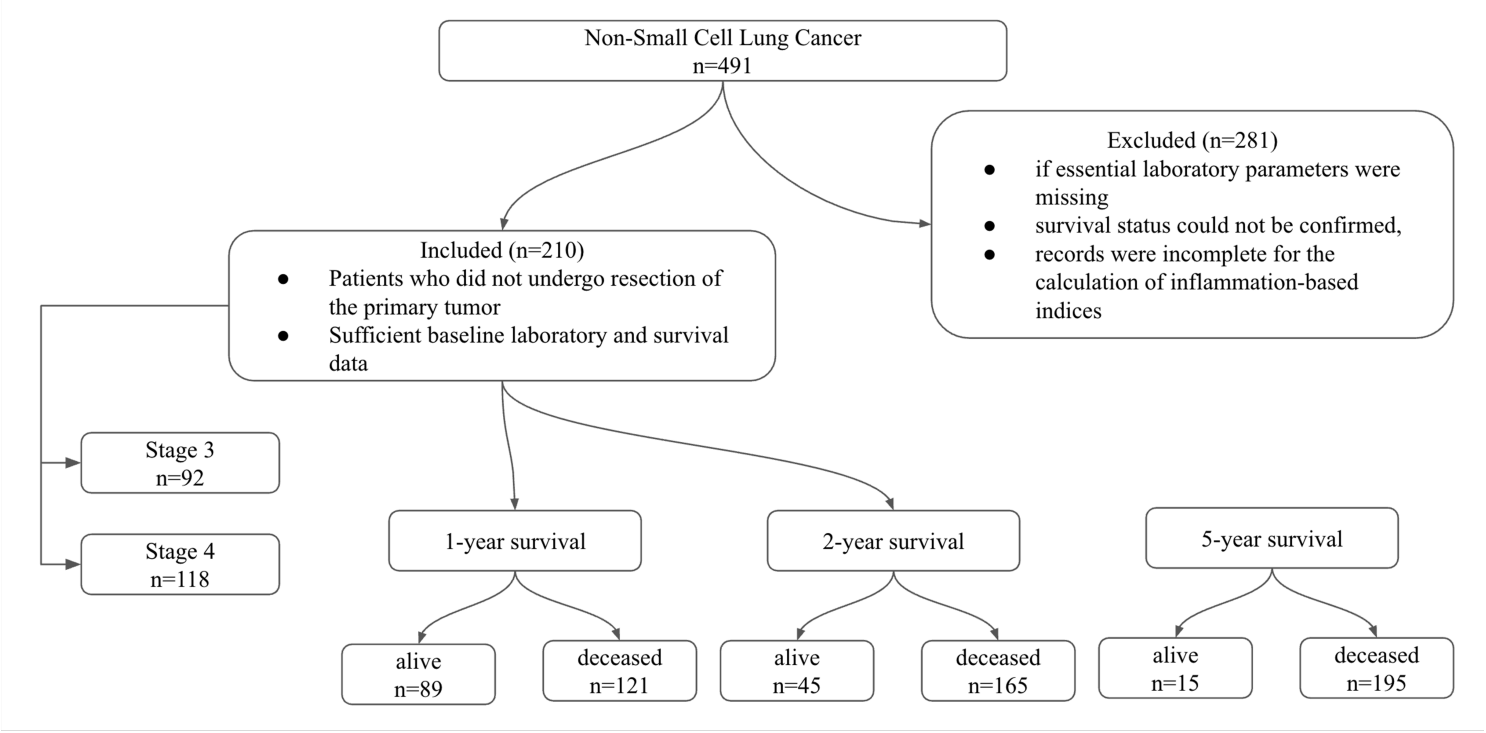


Figure 1

Study flow diagram and survival outcomes in patients with inoperable non–small cell lung cancer (NSCLC).

A total of 491 patients with NSCLC were initially identified. After applying exclusion criteria (missing essential laboratory parameters, unconfirmed survival status, or incomplete records for inflammation-based indices), 210 patients were included in the final analysis. The cohort consisted of stage III (n=92) and stage IV (n=118) patients who did not undergo surgical resection and had sufficient baseline laboratory and survival data. Survival status was evaluated at 1, 2, and 5 years. At 1 year, 89 patients were alive and 121 had died; at 2 years, 45 were alive and 165 had died; and at 5 years, 15 were alive and 195 had died.

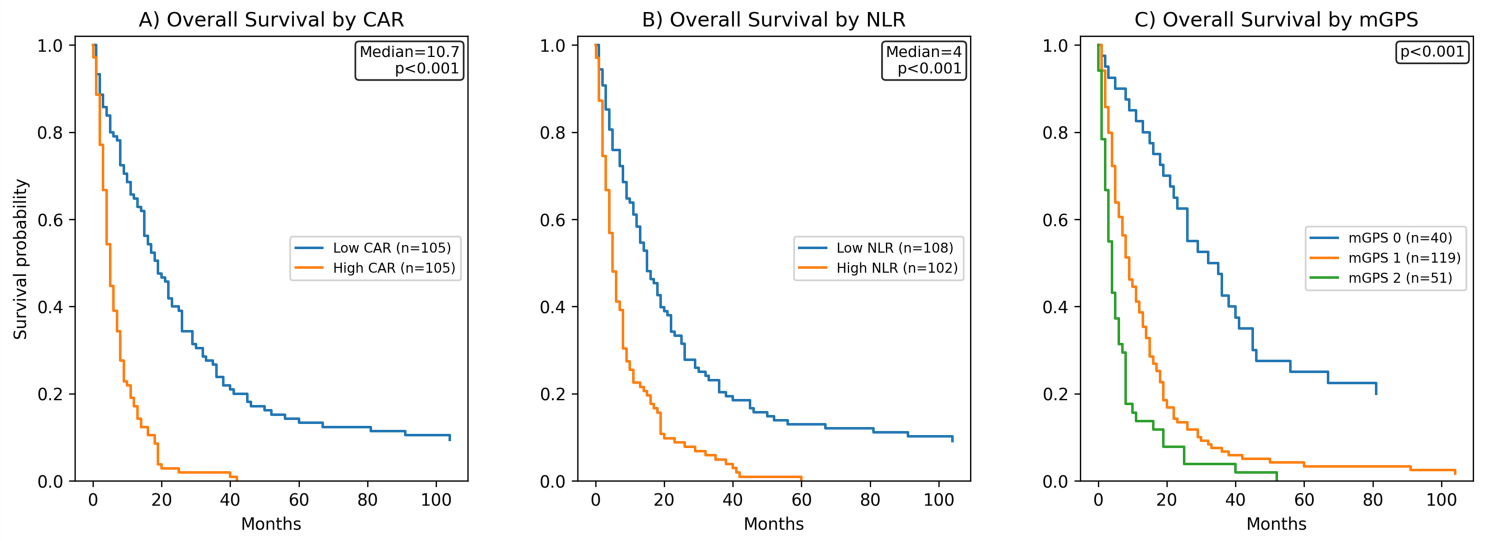


Figure 2

Kaplan–Meier overall survival curves according to baseline inflammation-based indices. Panel A illustrates overall survival stratified by the C-reactive protein-to-albumin ratio (CAR), dichotomized according to the median value (low vs high). Panel B shows survival curves according to the neutrophil-to-lymphocyte ratio (NLR), also categorized based on the median. Panel C presents overall survival across modified Glasgow Prognostic Score (mGPS) categories (0, 1, and 2). In all panels, survival differences between groups were assessed using the log-rank test. Higher levels of inflammation-based indices were consistently associated with reduced overall survival.

Supplementary Files

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- Table5.docx