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Ahmet Kucukarda, Burcu Gulbagci, Elif Yuce

Tekirdag Dr Ismail Fehmi Cumalioglu City Hospital, Suleymanpasa, Tekirdag, Türkiye

Gustave Roussy immune score is an independent prognostic factor for treatment response and survival in advanced non-small cell lung cancer treated with nivolumab at second-line therapy

Address for correspondence:
Associate Professor Ahmet Kucukarda
Tekirdag Dr Ismail Fehmi Cumalioglu City Hospital, Suleymanpasa, 59100 Tekirdag, Türkiye
e-mail: ahmetkucukarda22@gmail.com

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ABSTRACT

Introduction. This study aimed to determine the prognostic significance of the Gustave Roussy immune score (GRim score) for patients receiving nivolumab as second-line therapy for advanced non-small cell lung cancer (NSCLC).

Material and methods. We used serum albumin, lactate dehydrogenase (LDH), and the neutrophil-lymphocyte ratio (NLR) obtained 1 to 7 days before treatment to calculate GRim scores for 105 NSCLC patients.

Results. We evaluated the relationship between oncological outcomes and GRim scores. Of the 105 patients, 82 (78.1%) belonged to the low-score group, which had an objective response (OR) of 30 (36.6%), whereas 1 (4.3%) belonged to the high-score group ($p = 0.002$). In the low-score group, median PFS and OS were 4.7 months (95% CI 3.9–5.4) and 17.9 months (95% CI — NE), respectively, whereas in the high-score group, they were 1.8 months (95% CI 0.1–4.3) and 2.5 months (95% CI 0.1–2.5; $p < 0.001$), respectively. A low GRim score (HR = 0.30; $p = 0.003$) and the absence of brain metastases (HR = 0.42; $p = 0.02$) were essential indicators of PFS in multivariate analysis. From an OS perspective, having an ECOG performance score of 0 (HR = 0.45; $p = 0.04$), a low GRim score (HR = 0.21; $p = 0.001$), and a CPS score of ≥ 1 (HR = 0.33; $p = 0.01$) were independent predictors. Furthermore, there was no discernible relationship ($p = 0.73$) between the GRim score and the CPS.

Conclusions. The findings of our study demonstrate that the GRim score, which is derived from standard laboratory tests conducted on patients, is an affordable and simple prognostic indicator for treatment response and survival in patients with advanced NSCLC receiving nivolumab as second-line therapy.

Keywords: non-small cell lung cancer, nivolumab, Gustave Roussy immune score, objective response, and survival

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Introduction

In the world, 25% of cancer-related deaths are caused by lung cancer [1]. In over 85% of all cases, non-small cell lung cancer (NSCLC) is the most prevalent subtype [2]. While driver mutation-negative NSCLC has been successfully treated with checkpoint inhibitors (ICI), some patients are not amenable to immunotherapy and need platinum doublet treatment [3].

The programmed cell death protein 1 (PD-1) pathway-targeting inhibitor nivolumab (ICI) has demonstrated notable clinical benefits in patients with advanced NSCLC undergoing platinum-based chemotherapy. CheckMate-017 for squamous (SCC) and CheckMate 057 for adenocarcinoma (AC) subtypes supported the approval of this drug [4]. In clinical trials, nivolumab outperformed docetaxel in terms of objective response rate (ORR), progression-free survival (PFS), and overall survival (OS).

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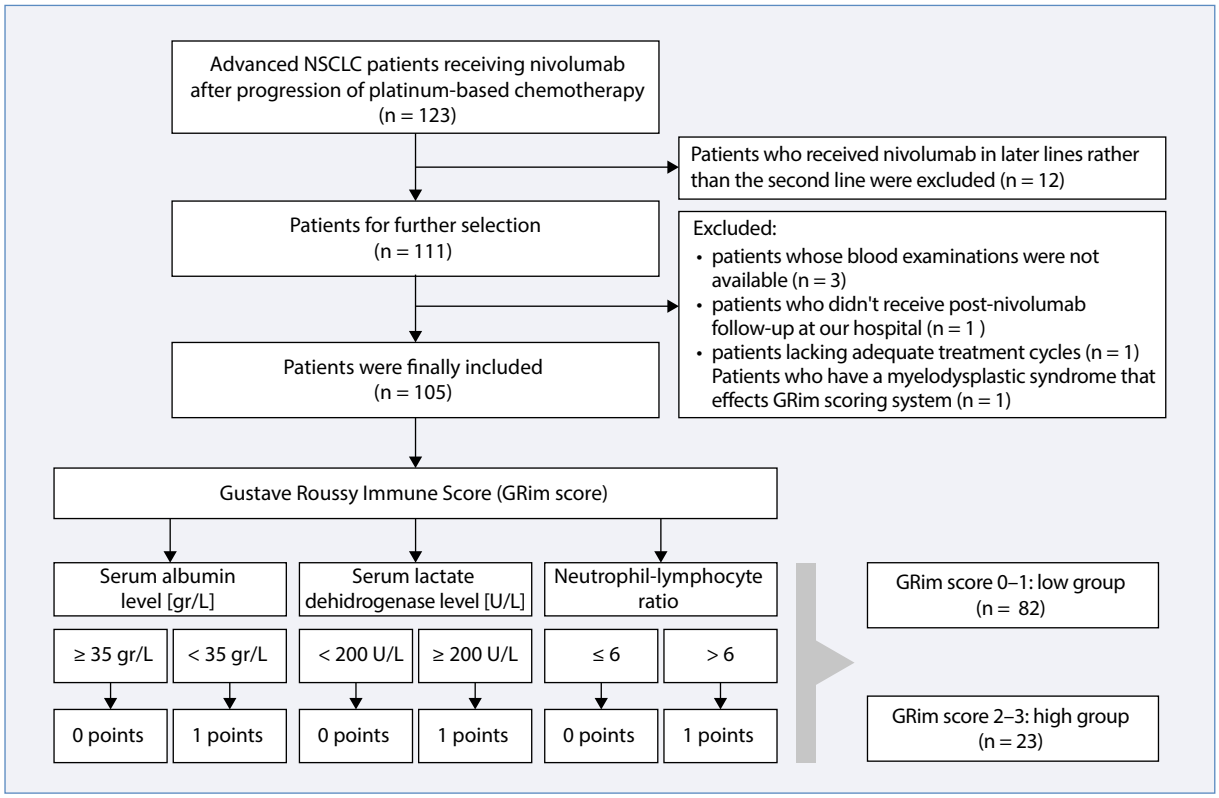


Figure 1. Consort diagram of the study population; NSCLC — non-small cell lung cancer

As a result, it is now the recommended second-line treatment for nearly all patients. The combined positive score (CPS), which quantifies the proportion of programmed cell death protein ligand 1 (PD-L1) positive tumor and immune system cells, has no bearing on its effectiveness [3, 4].

Although nivolumab has produced encouraging results, there are still issues with its clinical use. When it comes to patients who might benefit from nivolumab, predictive biomarkers are essential [5]. Traditional predictors include tumor stage, histology, age, smoking history, comorbidities, performance status, and CPS. Still, patient survival rates differ even in the same circumstances [6]. Objective data for prognostic prediction of ICI in lung cancer patients are provided by clinical risk scoring systems such as the lung immune prognostic index, systemic immune-inflammation index, and prognostic nutritional index [5, 6].

Developed by Frederic Bigot in 2017, the Gustave Roussy immune score (GRim score) uses serum albumin levels, lactate dehidrogenase (LDH), and the neutrophil-lymphocyte ratio (NLR) to predict survival in various cancer types, especially in patients treated with ICIs [7]. Research on the predictive utility of the GRim score in patients with advanced NSCLC is lacking, and there is no survey on second-line nivolumab treatment [8, 9].

In this study, we assessed GRim score values in patients with advanced NSCLC receiving nivolumab to see if the GTim score is a possible predictive biomarker for oncological outcomes.

Materials and methods

Patient characteristics and study design

This study involved NSCLC patients treated in the Department of Medical Oncology at Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital between 2022 and 2023. Complete clinical and laboratory data were available for the patients who were treated with nivolumab at the second line after progression with first-line platinum-based combination therapy, had a biopsy-confirmed NSCLC, and were over the age of 18. Individuals with severe systemic infections, confirmed renal and hepatic failure, or hematological diseases were not included (Fig. 1).

Clinical data collection

We analyzed the laboratory, pathological, and radiological examination results as well as patient histories. Using an automated chemistry analyzer (Roche Hitachi Cobas 8000, Rotkreuz, Switzerland), we measured LDH and albumin levels. We determined with a hematology analyzer (Sysmex SE-9000, Kobe, Japan), neutrophil and lymphocyte counts.

The following criteria were used to calculate the GRim scores: 1) albumin levels ≥ 35 gr/L gain 0 points while < 35 gr/L gain 1 point; 2) LDH within normal limits gains 0 points while upper normal limits (UNL)

gain 1 point (UNL for our hospital: 200 U/Lt); and 3) NLR levels ≤ 6 gain 0 points, while > 6 gain 1 point. The group with a score of 0 or 1 was classified as low, while the group with a score of 2 or 3 as high [7]. The GRim score was calculated using laboratory values obtained one to seven days before nivolumab treatment (Fig. 1).

Treatment protocol and follow-up procedure

As part of the treatment regimen, a dose of 3 mg/kg of nivolumab was administered every two weeks. The follow-up period for each patient was measured from the start of treatment until examination on the final day. Every six to twelve weeks, patients were monitored until they passed away using contrasted systemic imaging positron emission tomography (PET-CT), computerized tomography (CT), and cranial magnetic resonance imaging (MRI).

Definition of study endpoints and clinical outcomes

The primary endpoints were PFS and OS. PFS was defined as the time interval between the first dose of nivolumab administration and the confirmed progression of the disease or death from any cause. The duration of OS was calculated from the date of nivolumab initiation to the date of cancer-related death or loss to follow-up. The final date of follow-up was March 1, 2024.

The response to treatment was assessed using the Response Evaluation Criteria in Solid Tumors (RECIST). The four categories of tumor responses were complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). The disease-control rate (DCR) was defined as CR + PR + SD, and the ORR was defined as the total percentage of CR + PR per all patients.

Statistical analysis

Categorical variables like age, sex, histology, metastatic sides, and CPS scores in both groups were compared using chi-square and Fisher's exact tests. We ran the log-rank test to compare PFS and OS in both groups. The best predictor variables were determined by applying the proportional hazards regression model through univariate and multivariate analyses. The threshold for statistical significance was p-value < 0.05. The data were analyzed using IBM SPSS Statistics 23.0 (IBM Corp., Armonk, NY, USA).

Results

Patients characteristics

The median age of participants was 64 years (the range was 58–69.5). Ninety-three patients (88.6%) were male, and 67 (63.8%) had an ECOG performance score of 0. Fifty-four (51.4%) of the 105 patients had an adenocarcinoma pathology subtype. There were 26 (24.8%), 38 (36.2%), and 26 (24.8%) cases of brain, liver, and bone metastases, respectively. Of them, 28 (26.7%) had no CPS examination and 26 (24.8%) had a CPS score of less than 1%. Table 1 presents a summary of the patient's baseline laboratory parameters.

Table 1. Demographic and clinical characteristics of the study population

Parameters	All patients (n = 105)
Age [years]	
Median (IQR)	64 (58–69.5)
Sex, n (%)	
Female	12 (11.4)
Male	93 (88.6)
ECOG performance score, n (%)	
ECOG 0	67 (63.8)
ECOG 1	38 (36.2)
Histology, n (%)	
Adenocarcinoma	54 (51.4)
Squamous cell carcinoma	45 (42.9)
Other subtypes	6 (5.7)
Brain metastasis, n (%)	
No	79 (75.2)
Yes	26 (24.8)
Liver metastasis, n(%)	
No	79 (75.2)
Yes	26 (24.8)
Bone metastasis, n (%)	
No	67 (63.8)
Yes	38 (36.2)
CPS score, n (%)	
< 1%	26 (24.8)
1–5%	20 (19.0)
5–10%	16 (15.2)
10–50%	8 (7.6)
> 50%	7 (6.7)
Unknown	28 (26.7)
Albumine [gr/L]	
Median (IQR)	38.7 (35.0–42.4)
Lactate dehydrogenase [U/L]	
Median (IQR)	188 (158.5–235.5)
Neutrophil [per mm^3]	
Median (IQR)	4810 (4055–7485)
Lymphocyte [per mm^3]	
Median (IQR)	1540 (1045–1955)
Neutrophil lymphocyte ratio, n (%)	
Median (IQR)	3.40 (2.49–5.07)

CPS — combined positive score; ECOG — Eastern-Cooperative Oncology Group; IQR — Inter-quartile range

Table 2. Comparison of patient characteristics between the two Gustave Roussy immune score (GRim score) groups

Parameters	Low group (n = 82)	High group (n = 23)	p-value
Age [years], n (%)			
< 65	48 (58.5)	7 (30.4)	0.02
≥ 65	34 (41.5)	16 (69.6)	
Sex, n (%)			
Female	11 (13.4)	1 (4.3)	0.46
Male	71 (86.6)	22 (95.7)	
ECOG performance score, n (%)			
ECOG 0	52 (63.4)	15 (65.2)	0.99
ECOG 1	30 (36.6)	8 (34.8)	
Histology, n (%)			
Adenocarcinoma	45 (54.9)	9 (39.1)	0.09
Squamous cell carcinoma	31 (37.8)	14 (60.9)	
Other subtypes	6 (7.3)	0 (0)	
Brain metastasis, n (%)			
No	61 (74.4)	18 (78.3)	0.79
Yes	21 (25.6)	5 (21.7)	
Liver metastasis, n (%)			
No	61 (74.4)	18 (60.9)	0.79
Yes	21 (25.6)	5 (39.1)	
Bone metastasis, n (%)			
No	53 (64.6)	14 (37.5)	0.81
Yes	29 (35.4)	9 (62.5)	
CPS score, n (%)			
< 1%	21 (25.6)	5 (21.7)	
1–5%	16 (19.5)	4 (17.4)	
5–10%	14 (17.1)	2 (8.7)	0.14
10–50%	7 (8.5)	1 (4.3)	
> 50%	7 (8.5)	0 (0)	
Unknown	17 (20.7)	11 (47.8)	

CPS — combined positive score; ECOG — Eastern-Cooperative Oncology Group

Based on the GRim score, we allocated the patients into two groups: 82 (78.1%) belonged to the low-score group and 23 (21.9%) to the high-score group. Table 2 illustrates no statistically significant difference in the patient characteristics between the two groups, except in age distribution.

The follow-up period was 7.5 months on average (3.4–13.5 months). Fifty-three (50.5%) patients died, and 71 (67.6%) patients had radiologically confirmed progression diagnosed on the last day of follow-up.

Comparison of treatment response according to GRim score groups

Of the total 105 patients, 5 (4.8%) had a CR to nivolumab treatment, whereas 26 (24.8%) and 41 (30.9%) had PR and SD, respectively. A total of 31 patients (29.5%) experienced an OR, and 72 patients (68.6%) achieved disease control (DC) (Tab. 3).

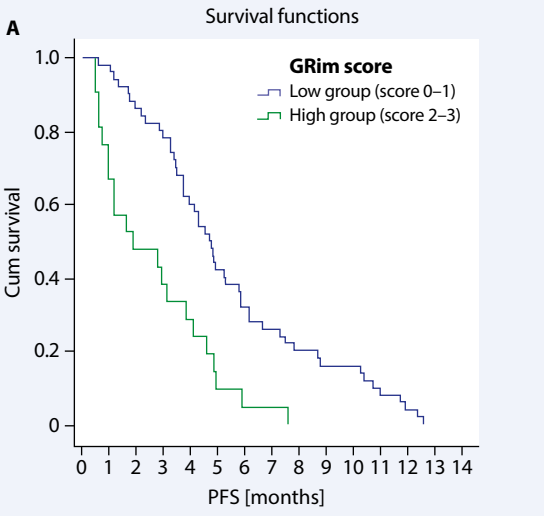
In the low-score group (82 patients), 5 (6.1%) had a CR and 25 (30.5%) PR, whereas in the high-score group (23 patients), there was no CR, and just 1 patient (4.3%) had a PR ($p = 0.001$). Similarly, Table 3 shows that ORRs and DCRs were significantly higher in the low-score group compared to the high-score group ($p = 0.002$ and $p < 0.001$, respectively).

Comparison of survival in the GRim score groups

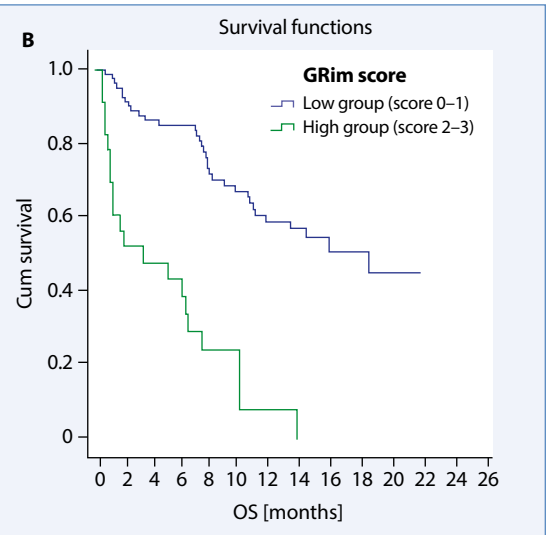
In the whole study population, median OS was 10.5 months [95% confidence interval (CI) 7.1–14.0], and median PFS was 4.1 months (95% CI 3.2–5.0). Median PFS and OS for the low-score group were 4.7 months (95% CI 3.9–5.4) and 17.9 months (95% CI

Table 3. Response evaluation between the two Gustave Roussy immune score (GRim score) score groups and the entire population

Response, n (%)	Total (n = 105)	Low group (n = 82)	High group (n = 23)	p-value
Complete response (CR)	5 (4.8)	5 (6.1)	0 (0)	**0.001**
Partial response (PR)	26 (24.8)	25 (30.5)	1 (4.3)	
Stable disease (SD)	41 (39.0)	34 (41.5)	7 (30.4)	
Progressive disease (PD)	33 (31.4)	18 (22.0)	15 (65.2)	
Objective response rate (ORR)	31 (29.5)	30 (36.6)	1 (4.3)	0.002
Disease control rate (DCR)	72 (68.6)	64 (78)	8 (34.8)	< 0.001



	Low group (n = 82)	High group (n = 23)
Events, no. (%)	50 (61.0)	21 (91.3)
Median PFS [months] (95% CI)	4.7 (3.9 to 5.4)	1.8 (0.1 to 4.3)
Hazard ratio (HR), (95% CI)	0.36 (0.21–0.62), p < 0.001	



	Low group (n = 82)	High group (n = 23)
Events, no. (%)	33 (40.2)	20 (87.0)
Median PFS [months] (95% CI)	17.9 (NE)	2.5 (0.1 to 2.5)
Hazard ratio (HR), (95% CI)	0.18 (0.10–0.33), p < 0.001	

Figure 2. A. Kaplan Meier progression-free survival analysis according to the Gustave Roussy immune score (GRim score) groups; B. Kaplan-Meier overall survival analysis according to GRim score groups; CI — confidence interval; HR — hazard ratio; OS — overall survival; PFS — progression-free survival

— NE), respectively. For the high-score group, the corresponding values were 1.8 months (95% CI 0.1–4.3) and 2.5 months (95% CI 0.1–2.5), respectively, ($p < 0.001$, for both groups). Figure 2 shows the GRim score group's Kaplan-Meier survival analysis.

Comparison of survival according to CPS level and correlation with GRim score groups

Of 105 patients, 77 (73.3%) had CPS information. For CPS > 50%, median OS was not reached; for CPS 10–50%, 5–10%, 1–5%, and < 1%, respectively, median OS was 15.4 months (95% CI 12.4–18.4), 10.5 months (95% CI 9.1–11.9), 8.5 months (95% CI 6.8–10.2), and 6.8 months (95% CI 6.3–7.3), respectively.

The CPS and GRim score groups did not significantly correlate with one another (The Pearson Chi-Square value was 2.025; $p = 0.73$).

Clinical features and their accuracy in predicting survival

In univariate analyses, only the GRim score was a statistically significant predictor of PFS. Table 4 shows that the CPS and GRim scores were important predictors of OS survival.

The absence of brain metastases [hazard ratio (HR) = 0.42; p = 0.02] and having a low GRim score (HR = 0.30; p = 0.003) were essential predictors of PFS in multivariate analysis with variables with a p-value less than 0.50. Regarding OS, the multivariate analyses also showed that an ECOG performance score of 0 (HR = 0.45; p = 0.04), a CPS score of ≥ 1 (HR = 0.33; p = 0.01), and a low GRim score (HR = 0.21; p = 0.001) were independent predictors of OS (Tab. 4).

Discussion

This study examined the predictive value of the GRim score in patients with advanced NSCLC receiving nivolumab as a second-line treatment. Our research findings imply that PFS, OS, and treatment response can all be predicted using the GRim score. After analyzing the data of 105 patients, we found that a higher GRim score may have prognostic significance for unfavorable oncological outcomes, which is consistent with other research on the effects of ICI treatment on different types of cancer. The score is a good, non-invasive, and reasonably priced discriminator.

In patients who progressed during or after platinum-based chemotherapy, ICIs have become the standard of care due to durable responses, favorable safety profiles, and clinically meaningful survival benefits. After two phase III trials (CheckMate 017, CheckMate 057), nivolumab emerged as the first PD-1 inhibitor to show clinically meaningful activity in NSCLC in second-line treatment. It was also associated with a favorable safety profile. Median PFS and OS of the trials were 2.5 months (95% CI 2.2–3.5) and 11.1 months (95% CI 9.2–13.1), respectively, based on the most recent pooled analysis conducted in 2021. In the pooled population, the ORR was 19.7%, with 1.4% CR and 18.3% PR [4]. According to our analysis, median PFS and OS were, respectively, 4.1 months (95% CI 3.2–5.0) and 10.5 months (95% CI 7.1–14.0). With 4.8% CR and 24.8% PR, the ORR was also 29.5%. The outcomes were strikingly alike. OS remained the same even though median PFS was found to be longer due to an improved ORR. This circumstance is crucial in representing the findings of our study that was conducted on on a broader population [10, 11].

In contrast, not every patient responds to therapy in the same way despite nivolumab's positive effects. Finding predictive biomarkers can assist us in selecting the right patient who will most benefit from treatment [5, 6]. CPS is among the most significant indicators of response and survival in ICI therapy. Median OS in patients with CPS < 1% was 9.6 months (95% CI 7.6–13.3), progressively rising to 20.5 months (95% CI 15.1–29.7) with CPS > 50%, according to data from a pooled analysis of CheckMate trials [12]. In our study, the group with CPS < 1% had median OS of 6.8 months (95% CI 6.3–7.3), but this group did not reach the median (above 17 months) with CPS > 50% of patients. Despite being a significant biomarker, patients with comparable CPS levels occasionally have different survival outcomes [12]. CPS evaluation is also costly and time-consuming. These factors prompt the ongoing search for novel prognostic markers.

Critical traits of cancer patients include malnourishment and uncontrolled inflammation, which can worsen long-term prognoses and reduce response to treatment [13, 14]. Numerous studies have shown peripheral blood parameters to be valuable biomarkers for evaluating cancer patients' inflammatory and nutritional status. The quest for clinically useful biomarkers is driving an increasing number of studies; complete blood count-based biomarkers are particularly attractive to clinicians because of their low cost, minimally invasive collection, and objectivity [5–9, 13, 14]. For example, the Lung Immune Prognostic Index (LIPI) was developed by the association between the derived neutrophil-lymphocyte ratio (dNLR), and LDH levels in the blood. In a retrospective analysis of 466 patients with advanced NSCLC treated with ICI or chemotherapy, patients were assigned into three groups according to their LIPI values: good, intermediate, and poor LIPI, with the values based on the dNLR and LDH levels. In the ICI cohort, the DCR, PFS, and OS were significantly different for patients with poor, intermediate, and good LIPI, respectively, with the poorest outcomes reported for the poor LIPI subgroup. Thus, for the poor, intermediate, and good LIPI groups, median OS was 4.8 months (95% CI 3.6–7.7), 10.0 months (95% CI 7.3–12.6), and 16.5 months (95% CI 11.4–34.0) respectively, while median PFS was 2.0 months (95% CI 1.7–4.0), 3.7 months (95% CI 3.0–4.8), and 6.3 months (95% CI 5.0–8.0), respectively. The strong correlation between clinical outcomes and LIPI subsets indicated the prognostic role of LIPI in pretreated advanced NSCLC receiving ICI therapies. Following this first report, the predictive role of LIPI has been investigated in other studies, but it has not been confirmed [15].

Using three parameters (serum LDH, serum albumin, and NLR), Bigot et al. (2017) [7] developed the GRIm score as a potential prognostic assessment tool in this context. The GRIm score's high discriminatory value may be explained by combining these three critical markers. The first, LDH, is critical for tumor growth, metastasis, and the energy metabolism of tumors under hypoxic conditions [16]. Additionally, by stimulating inflammatory cytokines and blocking the activation of CD8 T lymphocytes and natural killer cells, LDH creates an inflammatory environment within the tumor microenvironment, which allows cancer cells to evade the immune system [17]. High LDH plasma level

Table 4. Univariate and multivariate analyses of clinical features for progression-free survival and overall survival

	Progression-free survival analyses				Overall survival analyses			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95% CI; Lower–upper)	p-value	HR (95% CI; Lower–upper)	p-value	HR (95% CI; Lower–upper)	p-value	HR (95% CI, Lower–upper)	p-value
Age								
<65 *vs.* ≥ 65 years	0.90 (0.53–1.55)	0.71			0.90 (0.53–1.55)	0.71		
Sex								
Female *vs.* male	1.03 (0.49–2.16)	0.94			0.86 (0.34–2.17)	0.76		
ECOG								
0 *vs.* 1	0.76 (0.47–1.24)	0.27	0.59 (0.29–1.19)	0.14	0.64 (0.37–1.11)	0.11	**0.45 (0.20–0.99)**	**0.04**
Histology								
Adenocarcinoma *vs.* SCC	1.22 (0.75–1.98)	0.43	1.31 (0.71–2.42)	0.38	0.76 (0.44–1.32)	0.33	0.89 (0.41–1.89)	0.75
Brain metastasis								
No *vs.* yes	0.69 (0.39–1.22)	0.20	**0.42 (0.20–0.88)**	**0.02**	0.87 (0.48–1.57)	0.65		
Liver metastasis								
No *vs.* yes	0.91 (0.54–1.52)	0.72			0.58 (0.33–1.02)	0.06	0.70 (0.29–1.65)	0.41
Bone metastasis								
No *vs.* yes	0.83 (0.51–1.35)	0.46	0.85 (0.45–1.60)	0.62	0.64 (0.37–1.10)	0.10	0.80 (0.35–1.85)	0.61
CPS score								
≥ 1 *vs.* < 1	0.80 (0.43–1.51)	0.49	0.69 (0.33–1.44)	0.32	**0.43 (0.21–0.90)**	**0.02**	**0.33 (0.14–0.78)**	**0.01**
GRim score								
Low *vs.* high	**0.36 (0.21–0.62)**	**<0.001**	**0.30 (0.13–0.67)**	**0.003**	**0.18 (0.10–0.33)**	**<0.001**	**0.21 (0.09–0.52)**	**0.001**

CPS — combined positive score; ECOG — Eastern-Cooperative Oncology Group; SCC — squamous cell carcinoma

was found to be substantially correlated with shorter PFS and OS in cancer patients, according to a recent meta-analysis comprising 76 papers [18]. In a study with NSCLC patients receiving atezolizumab or docetaxel, high LDH levels indicated poor OS; an increased pretreatment LDH level was significantly associated with worse outcomes [19]. The second parameter, NLR, has been extensively demonstrated to forecast unfavorable outcomes in solid tumors [20]. Neutrophils facilitate the growth and invasion of tumor cells by creating an environment conducive to their proliferation [21]. Conversely, a decrease in lymphocyte counts inhibits the immune system's reaction to cancer [22]. A study found that NLR was a crucial prognostic marker in patients with advanced NSCLC receiving nivolumab at baseline [23]. Finally, albumin is a biomarker that indicates the level of nourishment in cancer patients. Low serum albumin levels have been linked to increased infection risk, slowed wound healing, and decreased patient survival, according to studies. Additionally, proinflammatory cytokine production and immunosuppression are closely linked to hypoalbuminemia [24]. For instance, serum albumin levels may be an excellent clinical biomarker of survival in patients with NSCLC receiving nivolumab therapy [25].

Because of its availability and quick computation, the GRIm score has been more and more often used to assess prognosis in different cancers. Patients in the high GRim score group had worse OS (HR = 2.07; 95% CI 1.73–2.48; $p < 0.0001$; I2 = 62%) and PFS (HR = 1.42; 95% CI 1.22–1.66; $p < 0.0001$; I2 = 36%), according to a meta-analysis involving 4997 cancer patients. The predictive value of the GRim score on assessing OS and PFSl has been noted for various tumor types and stages [13].

A few research articles examine the predictive capabilities of the GRim score in patients with advanced NSCLC receiving immunotherapy. There was no discernible difference in OS or PFS between patients with low and high GRim scores in a study with 135 patients undergoing first-line pembrolizumab treatment (low *vs.* high: median OS 17.0 *vs.* 11.2 months; $p = 0.32$; median PFS 9.0 *vs.* 5.9 months; $p = 0.60$). Furthermore, there was no discernible difference in the ORR by GRim scores (46.7% *vs.* 40%; $p = 0.60$) [8]. A second study looked at 76 patients who were given pembrolizumab, atezolizumab, or nivolumab in later lines. While there was no significant difference in PFS (2.6 *vs.* 2.1 months; $p = 0.13$), OS in the high GRim score group was significantly shorter than that in the low group (median 19.9 *vs.* 3.2 months; $p < 0.01$). This article contained no statistical information regarding the ORR [9]. In our research, in the low GRim score group, median PFS was statistically significantly longer (4.7 *vs.* 1.8 months; HR = 0.36; $p < 0.001$) than in the high-score group. Similar to PFS, the low GRim score group has significantly better median OS (17.9 *vs.* 2.5 months; HR = 0.18; $p < 0.001$). The GRim score was a predictive marker for both PFS and OS in multivariate analysis. Additionally, the low-score group's ORR was 36.6% with 6.1% CR and 30.5% PR, while the high-score group's ORR was 4.3% with no CR and only 4.3% PR.

There were certain limitations to our study. Initially, it was a retrospective study in a single oncology facility. Secondly, before starting therapy, we only evaluated one score. We did not examine the dynamic prediction function of the GRim score. Third, the accuracy of our results may be limited by the comparatively short follow-up period. Therefore, to confirm the predictive value of the GRim score in patients with advanced NSCLC treated with nivolumab as a second-line therapy, a more extensive, multi-center prospective study is needed.

Conclusions

Our study showed that the GRim score is a useful, independent prognostic marker for treatment response and survival in patients with advanced NSCLC receiving nivolumab as a second-line therapy. Additionally, it is inexpensive and simple to assess using laboratory tests regularly administered to patients. For patients with advanced NSCLC, the GRim score may be useful in predicting survival and determining whether to administer nivolumab.

Article information and declarations

Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

Ethical statement

This study was conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki (version 2008). The Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital's Scientific Research Ethics Committee approved this study, which adheres to the Declaration of Helsinki's postulates.

Author contributions

A.K.: conceptualization, methodology, writing — review and editing, supervision; B.G.: data curation, investigation, writing — original draft; E.Y.: investigation, data curation, visualization, writing — original draft; A.K., B.G.: data curation, writing — review and editing; B.G., E.Y.: software, validation, formal analysis, writing — review and editing; A.K.: resources, project administration, funding acquisition, writing — review and editing; B.G.: data curation, formal analysis, writing — original draft, writing — review and editing; A.K., B.G., E.Y.: methodology, validation, writing — review and editing,

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Conflict of interest

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Supplementary material

None.

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