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ORIGINAL RESEARCH

The Construction of a Nomogram Using the Pan-Immune-Inflammation Value Combined with a PILE Score for Immunotherapy Prediction Prognosis in Advanced NSCLC

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Purpose: The purpose of this study was to investigate the predictive value of Pan-Immune-Inflammation Value (PIV) combined with the PILE score for immunotherapy in patients with advanced non-small cell lung cancer (NSCLC) and to construct a nomogram prediction model to provide reference for clinical work.

Patients and Methods: Patients with advanced NSCLC who received ICIs treatment in Qingdao Municipal Hospital from January 2019 to December 2021 were selected as the study subjects. The chi-square test, Kaplan-Meier survival analysis, and Cox proportional risk regression analysis were used to evaluate the prognosis. The results were visualized by a nomogram, and the performance of the model was judged by indicators such as the area under the subject operating characteristic curve (AUC) and C-index. The patients were divided into high- and low-risk groups by PILE score, and the prognosis of patients in different risk groups was evaluated.

Results: Multivariate Cox regression analysis showed that immune-related adverse events (irAEs) were prognostic factors for overall survival (OS) improvement, and ECOG PS score ≥2, bone metastases before treatment, and high PIV expression were independent risk factors for OS. The C index of OS predicted by the nomogram model is 0.750 (95% CI: 0.677–0.823), and the Calibration and ROC curves show that the model has good prediction performance. Compared with the low-risk group, patients in the high-risk group of PILE were associated with a higher inflammatory state and poorer physical condition, which often resulted in a poorer prognosis.

Conclusion: PIV can be used as a prognostic indicator for patients with advanced NSCLC treated with ICIs, and a nomogram prediction model can be constructed to evaluate the survival prediction of patients, thus contributing to better clinical decision-making and prognosis assessment.

Keywords: non-small cell lung cancer, immune checkpoint inhibitors, pan-immune-inflammation value, prognosis, nomogram

Introduction

In terms of the incidence of malignant tumors worldwide, lung cancer ranks second, accounting for 11.4% of all cases. Mortality ranks first, accounting for 18% of all cancer deaths.[1] Of these, 85% of lung cancers are characterized by non-small cell lung cancer (NSCLC), with poor 5-year survival.[2,3] In contrast to conventional chemotherapy utilizing cytotoxic drugs, immune checkpoint inhibitors (ICIs) remove the suppression of immune function caused by the immune checkpoint by blocking the binding of the immune checkpoint to its ligand, thereby reactivating immune cells to perform an anti-tumor role.[4,5] It has progressively become one of the treatment options for advanced NSCLC as a result of its considerable long-term survival benefits. But observed that only some patients benefited. Therefore, some predictive biomarkers are necessary to judge the prognosis. PD-L1 expression status on tumor cells is a known biomarker for predicting ICIs response, but due to its lack of specificity, it has not been possible to screen out the patient population for optimal benefit.[6,7] Inflammation plays a significant role in the occurrence and development of malignant tumors, according to studies.[8,9] C-reactive protein (CRP), neutrophil-lymphocyte ratio (NLR), and platelet-lymphocyte ratio (PLR) have been demonstrated to accurately predict

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prognosis in a variety of malignancies, including NSCLC.[10,11] However, due to the limitations of a single index, it cannot accurately reflect systemic inflammation. Similar inflammatory indicators and scores, such as the Lung Immune Prognostic Index (LIPI), are scored by combining the ratio of neutrophils to lymphocytes, ie, neutrophil count/[white blood cell count - neutrophil count] (dNLR) and LDH.[12] The systemic immune inflammation index (SII) is a complex index composed of peripheral blood platelet count × peripheral blood neutrophil count/peripheral blood lymphocyte count.[13] However, in TME, monocytes express inhibitory molecules through tumor-derived signals and/or release soluble inhibitory factors, which inhibit tumor-related immune defense functions and play an important role in the occurrence and development of malignant tumors.[14,15] However, neither LIPL nor SII included monocytes as an indicator. Pan-immune inflammatory value (PIV) is a multi-parameter inflammatory index composed of neutrophils, lymphocytes, monocytes, and platelets that has the potential to reflect systemic immune and inflammatory states and is considered to be a reliable predictor of the prognosis of cancer patients.[16,17] In addition, the composite prognostic score combined with several parameters also showed the prognostic ability of patients.[18] The PILE score is a multi-parameter prognostic score based on PIV value, LDH value, and Eastern Tumor Cooperative Group functional status (ECOG PS), which can effectively reflect the systemic status. In a study of advanced cancer patients receiving immunotherapy, a higher PILE was shown to be inversely associated with survival outcomes. The PILE score also shows a good prospect for evaluating the prognosis of immunotherapy.[19] Based on PIV, this study investigated prognostic markers associated with survival outcomes in advanced NSCLC patients receiving ICIs and established a prognostic model, presented in a more intuitive nomogram, to serve as a reference for individualized survival assessment of NSCLC patients. Immunotherapy-receiving NSCLC patients' prognostic ability was determined using the PILE index.

Materials and Methods

Object of Study

The study subjects were selected from patients with advanced NSCLC treated with programmed cell death 1 receptor (PD-1) and its ligand (PD-L1) inhibitors in our hospital from January 2019 to December 2021.

Inclusion criteria: (1) age 18–90 years old; (2) pathological or cytological diagnosis of advanced NSCLC (TNM stage IIIB or IV); (3) receiving PD-1/PD-L1 inhibitor monotherapy or combination therapy from January 2019 to December 2021; (4) there is no primary malignant tumor of other organs and previous history (such as primary kidney cancer, colorectal cancer, etc).; (5) have complete pre-medication clinical data and ≥18 months of follow-up records, or although the follow-up records are not perfect, they can understand their treatment and survival through telephone; (6) liver and kidney function were normal before immunotherapy and relevant laboratory tests were basically normal.

Exclusion criteria: (1) small cell lung cancer; (2) accompanied by autoimmune diseases or immune deficiency diseases; (3) there are serious underlying diseases (such as heart function grade IV, liver and kidney failure, stroke with serious sequelae, etc). leading to unclear outcome indicators; (4) non-tumor progressive death; (5) incomplete clinical data or incomplete follow-up records.

Data Collection

By consulting patients' medical records, including outpatient and inpatient electronic medical records, patients' age, gender, smoking history, pathological type, pathological stage, PD-L1 expression, EGFR mutation status, ECOG PS score, and tumor metastasis (lung metastasis, bone metastasis, and brain metastasis) were collected. Treatment regimen (including PD-1/PD-L1 inhibitor monotherapy or combination therapy, combination therapy including combination chemotherapy, radiation therapy, targeted therapy, and antiangiogenesis therapy), adverse events during ICIs treatment, and patient survival status. Prior to initiating initial ICIs treatment, we collected indicators of inflammation by reviewing laboratory tests, including neutrophils, lymphocytes, monocytes, platelets, and lactate dehydrogenase (LDH). The pan-immune inflammatory value was calculated by the formula (PIV = neutrophils × monocytes × platelets/lymphocytes). The PILE score is a composite score based on PIV, LDH levels, and ECOG PS, which is calculated as the sum of individual values (PIV < median = 0, PIV≥ median =1; LDH≤ Upper normal limit (ULN) = 0, >ULN = 1; ECOG PS <2 = 0, ≥2 = 1).

Evaluation of Efficacy and Toxicity

The patients were assessed every 4–6 weeks using computed tomography (CT) or magnetic resonance imaging (MRI). The therapy efficacy was evaluated using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. According to consensus guidelines for the management of toxicity associated with immune checkpoint inhibitors[20,21] and previously mentioned by Weber et al,[22] irAEs are defined as adverse events with underlying immune causes that require frequent monitoring and potential intervention with immunosuppression and/or endocrine replacement therapy. irAEs during treatment were evaluated according to CTCAE version 5.0 of common adverse event evaluation criteria. In order to reduce the bias, this study only focused on objective irAEs identified by laboratory or imaging assistive tests.

Follow Up

Patients were followed up by means of an electronic medical record system, outpatient records, and telephone, and the main clinical outcomes of concern were overall survival (OS). OS is defined as the time from the start of immunotherapy (day 1 of cycle 1) to death or the end of the study (December 2022).

Statistical Method

We used SPSS 27.0 software and R4.2.1 software to process and analyze the data. We used the Kolmogorov–Smirnov method to test the normality of the measurement data. Those who met the normal distribution were represented by the positive and negative standard deviation of the mean, and a *t*-test was used for comparison between groups. Those who did not conform to the normal distribution were represented by M (Q1, Q3), and the Mann–Whitney *U*-test was used for comparison between groups. Counting data were represented by the number of cases (%), and a chi-square test was used for comparison between groups.

The best truncation value of PIV was obtained by the receiver operator characteristic curve (ROC), which was divided into two categorical variables. The Kaplan-Meier was used to establish the survival curve, and a Log rank test was used to compare the differences between groups. We used Cox proportional risk models to evaluate predictors in both univariate and multifactor analyses of OS. According to the results of the multivariate Cox proportional risk regression analysis, the variables with statistical significance were included in the nomogram model. The prediction performance of the nomogram model was verified by the Bootstrap method (repeated sampling 1000 times), and the concordance index (C-index) was used to represent the prediction performance of the nomogram model, and the calibration graph method was used to directly represent its prediction conformity. A two-tailed P value of <0.05 was considered statistically significant.

Results

Baseline Characteristics

We comprehensively reviewed patients with NSCLC who received ICI treatment in our hospital from January 2019 to December 2021. After applying the inclusion and exclusion criteria, we included a total of 161 patients in the analysis. Table 1 displays the baseline characteristics of the patients. The median age of the patients was 65±8.7 years, including 127 males and 34 females. There were 90 patients with a smoking history and 71 patients without a smoking history. The pathological classification of NSCLC was adenocarcinoma in 113 cases and non-adenocarcinoma in 48 cases. There were 33 patients in stage IIIB and 128 patients in stage IV. PD-L1 expression was ≥50% in 24 patients, <50% in 31 patients, EGFR gene mutation in 30 patients, and no EGFR gene mutation in 131 patients. 48 cases received monotherapy, while 113 cases received combined immunotherapy. The ECOG PS score was 0–1 in 75 cases and ≥2 in 86 cases. irAEs occurred in 81 cases and none in 80 cases. By December 2022, there had been 86 deaths.

We divided the patients into two groups based on whether death occurred and drew the ROC curve. The optimal cutoff value for PIV was 250.51. The best truncation value divides PIV into two categorical variables. 82 patients (50.9%) had PIV levels below the cutoff value, and 79 patients (49.1%) had PIV levels above the cutoff value. Patients with low PIV levels had a higher proportion of irAEs (P = 0.041). There were no statistical differences in other demographic and clinical characteristics between the two groups (Table 1).

Table 1 Patient Characteristics [Cases (%)]

Characteristic	Total (n=161)	Low PIV (<250.51) (n=82)	High PIV (≥250.51) (n=79)	*P*
Age (years)	65 ± 8.7			
<65	74 (46.0)	38 (46.3)	36 (45.6)	1.000
≥65	87 (54.0)	44 (53.7)	43 (54.4)	
Gender				
Male	127 (78.9)	69 (84.1)	58 (73.4)	0.122
Female	34 (21.1)	13 (15.9)	21 (26.6)	
Smoking status				
No	71 (44.1)	36 (43.9)	35 (44.3)	1.000
Yes	90 (55.9)	46 (56.1)	44 (55.7)	
Pathological pattern				
Adenocarcinoma	113 (70.2)	57 (70.7)	56 (70.9)	1.000
Non-adenocarcinoma	48 (29.8)	24 (29.3)	23 (29.1)	
Pathological stage				
IIIB	33 (20.5)	15 (18.3)	18 (22.8)	0.560
IV	128 (79.5)	67 (81.7)	61 (77.2)	
PD-L1 expression				
≥ 50%	24 (14.9)	11 (13.4)	13 (16.5)	0.863
< 50%	31 (19.3)	16 (19.5)	15 (19.0)	
NA	106 (65.8)	55 (67.1)	51 (64.5)	
EGFR				0.420
No	131 (81.4)	69 (84.1)	62 (78.5)	
Yes	30 (18.6)	13 (15.9)	17 (21.5)	
Immunotherapy regimen				
Monotherapy	48 (29.8)	24 (29.3)	24 (30.4)	1.000
Combination therapy	113 (70.2)	58 (79.7)	55 (69.6)	
ECOG PS score				
0–1	75 (46.6)	41 (50.0)	34 (43.0)	0.430
≥2	86 (53.4)	41 (50.0)	45 (57.0)	
Metastatic site				
<2	81 (50.3)	47 (57.3)	34 (43.0)	0.084
≥2	80 (49.7)	35 (42.7)	45 (57.0)	
Pulmonary metastasis				
No	44 (27.3)	27 (32.9)	17 (21.5)	0.115
Yes	117 (72.7)	55 (67.1)	62 (78.5)	
Brain metastases				
No	113 (70.2)	62 (75.6)	51 (64.6)	0.168
Yes	48 (29.8)	20 (24.4)	28 (35.4)	
Osseous metastasis				
No	105 (65.2)	59 (72.0)	46 (58.2)	0.072
Yes	56 (34.8)	23 (28.0)	33 (41.8)	
Whether irAEs occurs				
No	80 (49.7)	34 (41.5)	46 (58.2)	0.041
Yes	81 (50.3)	48 (58.5)	33 (41.8)	
LDH				
≤ULN	134 (83.2)	68 (82.9)	66 (83.5)	1.000
>ULN	27 (16.8)	14 (17.1)	13 (16.5)	

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group Performance Status; irAEs, immune-related adverse events.

We performed survival analysis based on PIV levels and observed a significant difference in survival between the two groups, as shown by the Kaplan-Meier survival curve (Figure 1). The survival rate of the low PIV group was significantly higher than that of the high PIV group ($P<0.0001$).

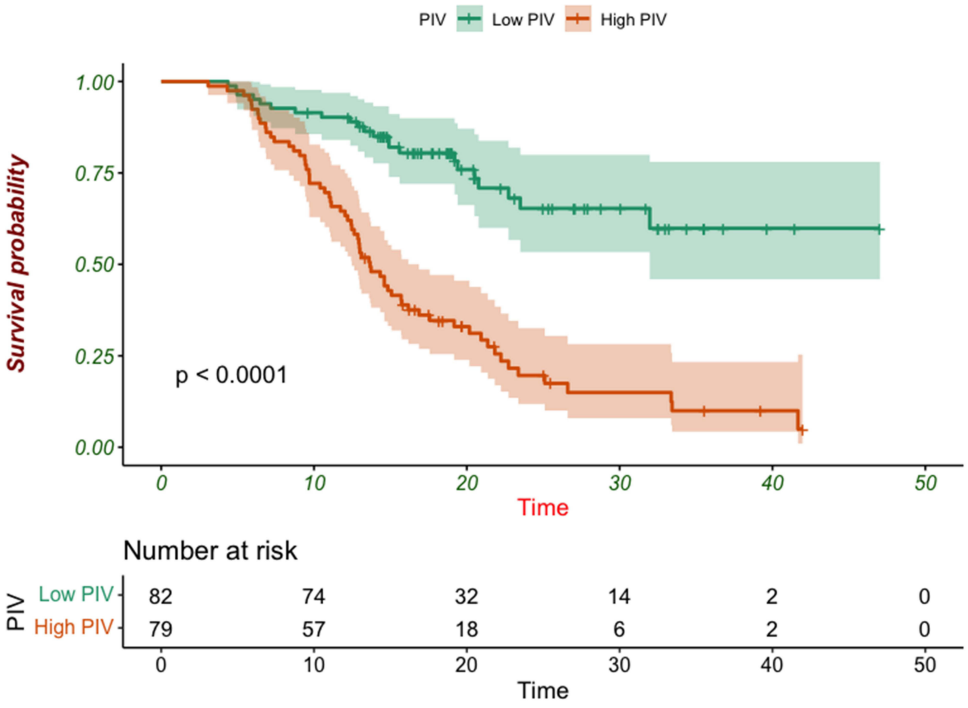

Figure 1 Kaplan-Meier survival curves of patients with different levels of PIV.

Univariate and Multivariate Regression Analysis of Clinical Features and the Relationship Between PIV and OS

Potential independent predictors were evaluated using Cox proportional risk models. Advanced NSCLC patients receiving immunotherapy showed a correlation between the prognosis and factors such as the ECOG PS score, the number of tumor metastasis sites before immunotherapy, brain metastasis and bone metastasis, irAEs, and PIV level during treatment ($P < 0.05$). The above statistically significant factors were included in the multivariate Cox regression model, and the analysis Results showed that irAEs (HR=0.321, 95% CI: 0.198–0.519, $P<0.001$) was a prognostic factor for overall survival improvement; however, ECOG PS score ≥2 points (HR=1.567, 95% CI: 1.003 ~ 2.447, $P=0.048$), bone metastases (HR=3.380, 95% CI: 1.784–6.404, $P<0.001$), and high PIV expression (HR= 3.752, 95% CI: 2.281 ~ 6.171, $P<0.001$) were independent risk factors for overall survival. As shown in Table 2.

Establishment and Verification of Nomogram

Using R software, a nomogram model was drawn based on statistically significant variables in Cox regression analysis (ECOG PS score, presence or absence of bone metastases, presence or absence of irAEs, and PIV levels). We used the model to assess individualized prognostic predictions in patients with advanced NSCLC treated with ICIs. We added the score of the first row corresponding to the vertical of each indicator to obtain the total score, which allowed us to determine the estimated survival probability of patients at 6 months, 12 months, and 18 months by positioning the total score. The higher the score, the worse the predicted prognosis. As shown in Figure 2A.

The nomogram model's prediction performance was evaluated using C-index and calibration curve, revealing a C-index of 0.750 (95% CI: 0.677–0.823) for predicting OS. We internally verified the prediction model using the Bootstrap self-sampling method (B = 1000). We took the predicted survival rate as the abscissa and the actual survival rate as the ordinate. The calibration curve showed that there was good agreement between the 6-month, 12-month, and 18-month predicted survival rates and the actual observed probability of advanced NSCLC patients treated with ICIs, indicating a good fit of the model. As shown in Figure 2B–D.

We plotted the ROC curves for 6-month, 12-month, and 18-month survival rates based on independent factors to assess the model's accuracy. The results showed that the area under curve (AUC) of the model was 0.755 (95% CI:

Table 2 Univariate and Multivariate Analysis of Overall Survival in NSCLC Patients

Characteristic	Overall Survival	
	Univariate Analysis	Multivariate Analysis
	HR (95% CI) *P* - value	HR (95% CI) *P* - value
Age (years)		
<65 vs ≥ 65	1.405 (0.914–2.158) *P*=0.269	-
Gender		
Male vs Female	1.189 (0.726–1.946) *P*=0.492	-
Smoking status		
No vs Yes	1.494 (0.968–2.307) *P*=0.070	-
Pathological pattern		
Adenocarcinoma vs Non-adenocarcinoma	1.204 (0.757–1.913) *P*=0.433	-
Pathological stage		
IIIB vs IV	1.031 (0.624–1.703) *P*=0.905	-
Immunotherapy regimen		
Monotherapy vs Combination therapy	0.981 (0.621–1.550) *P*=0.934	-
ECOG PS score		
0–1 vs ≥2	1.862 (1.202–2.883) *P*=0.005	1.567 (1.003–2.447) *P*=0.048
Metastatic site		
<2 vs ≥2	1.770 (1.153–2.719) *P*=0.009	0.667 (0.337–1.319) *P*=0.244
Pulmonary metastasis		
No vs Yes	1.665 (0.965–2.871) *P*=0.067	-
Brain metastases		
No vs Yes	1.903 (1.231–2.941) *P*=0.004	1.250 (0.763–2.048) *P*=0.376
Osseous metastasis		
No vs Yes	2.690 (1.757–4.117) *P*<0.001	3.380 (1.784–6.404) *P*<0.001
Whether irAEs occurs		
No vs Yes	0.291 (0.182–0.465) *P*<0.001	0.321 (0.198–0.519) *P*<0.001
PIV		
<250.51 vs ≥250.51	4.241 (2.605–6.904) *P*<0.001	3.752 (2.281–6.171) *P*<0.001

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group Performance Status; irAEs, immune-related adverse events; PIV, Pan-Immune-Inflammation Value.

0.5777–0.934), 0.788 (95% CI: 0.701–0.875), and 0.797 (95% CI: 0.724–0.869). The model showed good differentiation (Figure 3A). Decision curve analysis (DCA) was used to evaluate the application value of the model, and the results showed that when the threshold probability was greater than 0.05, the threshold probability was positively correlated with the net benefit level of the model, as shown in Figure 3B.

Kaplan-Meier Survival Curve Analysis of Patients with Different Risk Stratification Based on PILE

The PILE score is based on the compound score of PIV (PIV< median = 0, ≥ median =1), LDH level (LDH≤ upper normal limit (ULN) = 0, >ULN = 1), and ECOG PS (ECOG PS score <2 = 0, ≥2 =1). According to the total score, the patients were divided into a low-risk group (0–1 score, 104 cases) and a high-risk group (≥2 points, 57 cases). Kaplan-Meier survival curve analysis showed a significant difference in OS between the low-risk and high-risk groups (median OS: 23.50 vs 13.10 months, P<0.001), suggesting poor prognosis for patients in the high-risk group with immunotherapy (Figure 4).

Discussion

With the development of anti-tumor drugs, immunotherapy has shown good efficacy and safety in patients with various advanced tumors, such as NSCLC.[23,24] However, not all patients benefited from ICIs treatment. Therefore, biomarkers that accurately predict the treatment outcome and survival prognosis of patients with accepted ICIs are required. Patients'

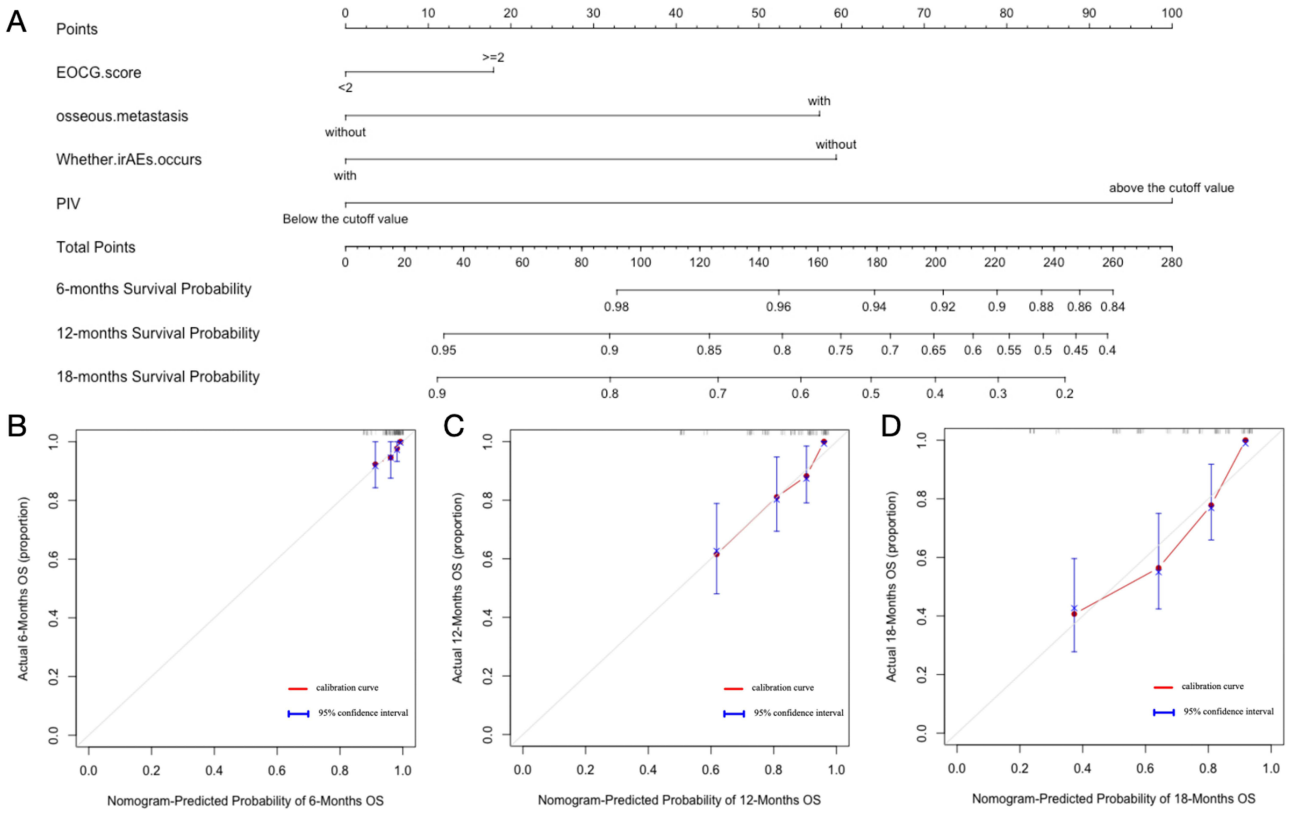

Figure 2 A nomogram and calibration curve for predicting overall survival in NSCLC patients treated with ICIs.
Notes: Nomogram model (**A**); Calibration curves for 6-month (**B**), 12-month (**C**), and 18-month (**D**) survival rates.

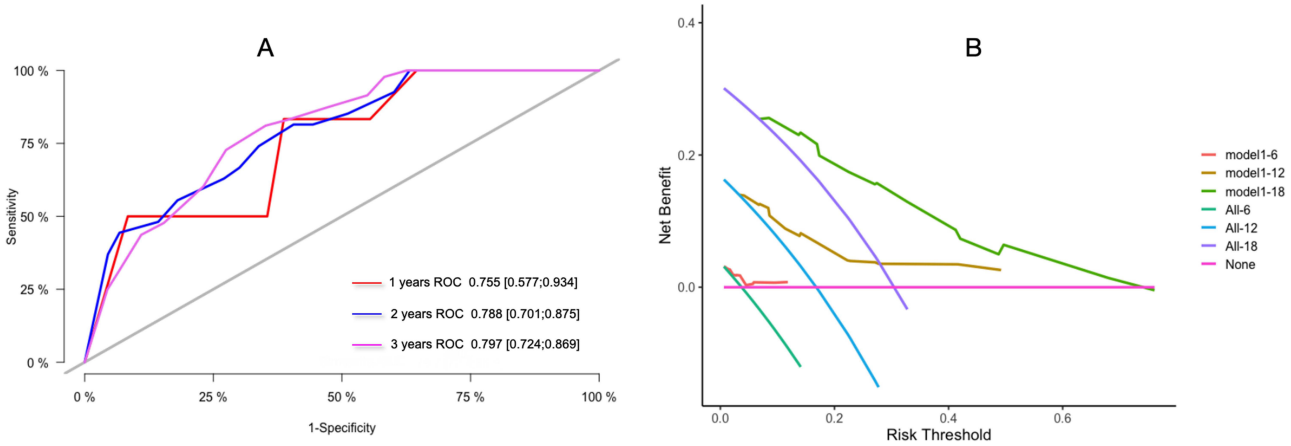

Figure 3 ROC curve and DCA curve of prediction model.
Notes: (**A**) ROC curves for survival predictions at 6, 12, and 18 months; (**B**) 6-, 12-, and 18-month DCA curves.

prognosis and immunotherapy response are typically evaluated using tumor mutation burden (TMB), somatic cell copy number alteration (SCNA), and PD-L1 expression. However, due to numerous uncontrollable factors, such as expensive, time-consuming, and insufficient tumor specimens, they cannot be used as the most effective biomarkers.

The relationship between inflammation and cancer has been under study since Virchow hypothesized that cancer occurs at the site of chronic inflammation.[25] Neutrophils participate in tumor invasion and metastasis by producing interleukin (IL) and other tumor-related factors, such as IL-1β, which is involved in cell proliferation, differentiation, and apoptosis and promotes angiogenic factors produced by stromal cells in TME to induce tumor angiogenesis, endothelial cell activation, and

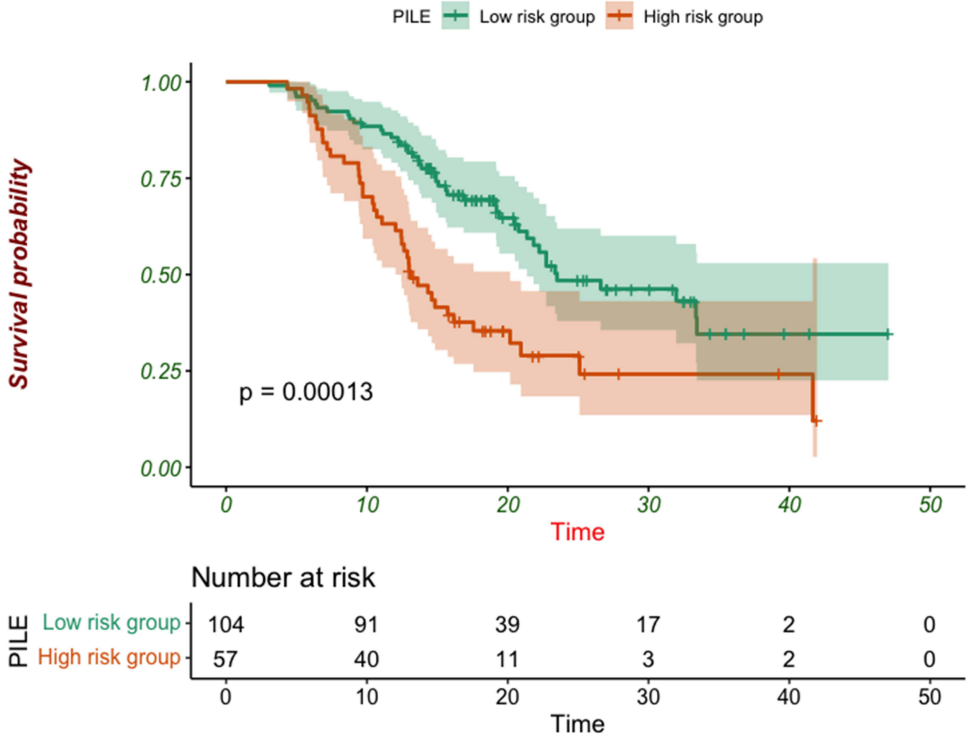

Figure 4 Kaplan-Meier survival curves of patients in low and high-risk groups based on PILE score.

immunosuppressive cells.[26,27] Secondly, some neutrophils can also promote epithelial mesenchymal transformation through TGF-β/Smad signaling pathway, which is also considered to be a key factor in tumor occurrence and development.[28] Cytokines produced in the systemic inflammatory response promote an increase in Platelet count and release platelet-derived growth factor (PDGF), thrombospondin (TSP), and platelet factor 4 (PF4), which are closely related to the proliferation and migration of tumor cells.[29] In TME, monocytes continuously enter the tumor site to express inhibitory molecules and/or release soluble inhibitory factors through tumor-derived signaling, suppressing tumor-related immune defense functions. And in mouse models of cancer, monocytes have been shown to be associated with tumor progression and metastasis.[14,15,30] Lymphocytes, by secreting cytokines, inhibit the proliferation and migration of tumor cells and play an important role in tumor defense and immune surveillance.[31] Multiple studies have demonstrated that the inflammatory response is a significant prognostic factor for tumor progression and survival. So, immune-based inflammatory indices like neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and monocyte/lymphocyte ratio (MLR) have been used to predict the prognosis of different cancers and have a high predictive value.[11,32] However, a single indicator of inflammation has limited predictive value. PIV is an inflammatory complex index composed of multiple parameters that more comprehensively reflect the inflammatory response and immune status of the body. It showed good predictive value in patients with extensive-stage small cell lung cancer, melanoma, and metastatic renal cell carcinoma treated with ICIs.[16,33,34] In this study, the optimal cutoff value of PIV was determined by the ROC curve, and Kaplan-Meier survival curve analysis showed that patients in the low PIV group had better OS ($p<0.0001$). When PIV was included in the multivariate analysis, the results were still significant. PIV may be a strong predictor of prognosis in NSCLC patients receiving immunotherapy.

With the increasing understanding of ICIs, immune-related adverse events (irAEs) can occur in some organ systems while the immune system is highly activated.[35] Studies have demonstrated that the occurrence of irAEs is substantially associated with melanoma prognosis, and this association makes monitoring these side effects essential.[36] The presence of irAEs was found to be a prognostic factor for OS improvement in this study. Because irAEs are caused by the activation of self-reactive T cells, patients who respond to ICIs are at a higher risk of developing irAEs, which may be a key reason why irAEs are able to enhance patient outcomes. Second, the ECOG PS score reflects the systemic status of patients and also serves as a predictor of overall survival. Patients with an ECOG PS score ≥2 tend to have a lower individual survival rate than

those with scores 0–1; this is due to poor physiological reserve, which limits patients' ability to tolerate anti-tumor drug therapy and is associated with treatment-related side effects that result in treatment interruption.[37]

In this study, a Cox model incorporating body condition and immune status was established based on age, ECOG PS score, and variables screened in multivariate analysis (P<0.05). In the modeling group and verification group, the model was evaluated using the C-index and calibration curve, and the results indicated that the degree of fitting and accuracy of the nomogram graph were satisfactory. It has significant clinical applicability. The nomogram is more practical and accurate than the traditional TNM stage prognosis assessment system, as it can incorporate a greater number of predictive indicators to assess the prognosis and survival of patients. In addition, various risk groups of patients were stratified based on their PILE score in order to evaluate the correlation between risk groups and prognosis. In comparison to The Scottish Inflammatory Prognostic Score (SIPS) and The Glasgow Prognostic Score (GPS), By combining LDH and PIV, which reflect systemic immune inflammation, and supplementing them with the ECOG PS score, PILE is able to more accurately reflect the systemic conditions of patients. In this study, patients were divided into low- and high-risk groups based on their PILE score for evaluation purposes. As a consequence of the association between the high-risk group and a high inflammatory state and poor physical condition, the prognosis was frequently poor. The results suggested that the PILE score was effective at predicting the prognosis of immunotherapy-treated NSCLC patients. However, further studies are needed to confirm this.

This study has some limitations. First, it is a retrospective, single-center study, and selection bias is inevitable. Secondly, due to the loss of PD-L1 expression and other gene expression in some patients, this factor could not be further studied. Third, the sample size of this study is relatively small, and the optimal cut-off value of PIV still needs to be further verified in large-sample and multi-center studies. In addition, external validation was not possible due to the lack of external data in our study. Despite the limitations, this study comprehensively considered age, physical status, systemic immune inflammation status, metastatic sites affecting prognosis, and whether there were side effects affecting efficacy and survival prognosis during ICIs treatment. The relationship between patients and survival outcomes can be accurately estimated by establishing a Nomogram graph for the reference of both doctors and patients. The PILE score was used to evaluate the prognosis of patients in different risk groups and had good predictive value. It can provide a reference for predicting the prognosis of NSCLC patients.

Conclusion

PIV can be used as a prognostic indicator for patients with advanced NSCLC treated with ICIs, and a Nomogram prediction model can be constructed to evaluate the survival prediction of patients, thus contributing to better clinical decision-making and prognosis assessment.

Data Sharing Statement

The data used to support the findings of this study are included within the article.

Ethics Approval and Consent to Participate

This study was reviewed and approved by Institutional Review Board of Qingdao Municipal Hospital (ethical approval NO.2023-111), which waived the informed consent requirement due to the retrospective design of the study. This study complied with the Declaration of Helsinki. The patient data was maintained with confidentiality.

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Disclosure

The authors declare that there are no conflicts of interest in this work.

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