Original Study

Incorporation of the SUVmax Measured From FDG PET and Neutrophil-to-lymphocyte Ratio Improves Prediction of Clinical Outcomes in Patients With Locally Advanced Non–small-cell Lung Cancer

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Abstract

Approximately 20% to 25% of patients with non–small-cell lung cancer (NSCLC) are diagnosed with locally advanced disease. Despite carefully implemented treatment, the survival outcomes of these patients remain poor, with 5-year overall survival rates of 10% to 20%, and locoregional recurrence rates of 35% to 70%. This retrospective analysis of 138 patients with locally advanced NSCLC was conducted to find out the prognostic factors and to improve prediction of clinical outcomes. Incorporation of the maximum standardized uptake value and neutrophil-to-lymphocyte ratio improves prediction of clinical outcomes in patients with locally advanced NSCLC.

Introduction: The aim of the present study was to investigate the value of incorporation 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) maximum standardized uptake value (SUVmax) and neutrophil-to-lymphocyte ratio (NLR) for improving prediction of clinical outcomes of patients with locally advanced non–small-cell lung cancer (LA NSCLC). **Materials and Methods:** We retrospectively enrolled 138 patients with unresectable LA NSCLC at our institution from July 2010 to August 2017. Spearman correlation analyses were used to estimate the correlations between SUVmax and NLR level. The univariate and multivariate Cox survival analyses were used to evaluate the prognostic indicators, including the incorporation of SUVmax and NLR. We defined the SUVmax and NLR grade (SNG = 0, 1, or 2) score as the number of risk factors among (1) SUVmax > 11.95 and (2) NLR > 3.82. The SNG score prognostic value was evaluated for overall survival (OS) and progression-free survival (PFS). **Results:** Univariate analysis showed that tumor stage, SUVmax, SUVmean, NLR, and SNG score were significantly associated with OS and PFS in patients with LA NSCLC. Kaplan-Meier analysis and log-rank test demonstrated significant differences in both OS and PFS among patients in SNG score (OS, $P < .001$; PFS, $P < .001$). Spearman correlation analyses showed that SUVmax had a correlation with the NLR ($r = 0.237$; $P = .005$). In subgroup analyses for patients with tumor pathologic stage IIIA/IIIB, we found that the SNG score was significantly associated with OS and PFS in each subgroup ($P < .001$, $P < .001$ for OS and $P = .027$, $P < .001$ for PFS, respectively). Multivariate analysis showed that the SNG score was a significantly independent prognostic factor for OS (hazard ratio, 1.612; 95% confidence interval, 1.157-2.246; $P = .005$) and PFS (hazard ratio, 2.241; 95% confidence interval, 1.486-3.379; $P < .001$).

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Conclusion: Incorporation of the SUVmax and NLR improves prediction of clinical outcomes in patients with LA NSCLC.

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Introduction

Lung cancer remains the leading cause of cancer-related death worldwide, accounting for 1.3 million deaths each year.[1] Non−small-cell lung cancer (NSCLC) accounts for 85% of all primary lung cancers.[2] Approximately 20% to 25% of patients with NSCLC are diagnosed with locally advanced (LA) disease and have poor survival.[3] The majority of patients with LA NSCLC are not candidates for surgical resection owing to poor underlying lung function, comorbidities, poor tumor resectability, or mediastinal lymphadenopathy. The current standard treatment for these patients with good performance status is concurrent thoracic radiotherapy and platinum-based chemotherapy.[4,5] Despite carefully implemented treatment, the survival outcomes of these patients remain poor, with a median overall survival (OS) of 20 to 28 months, 5-year OS rates of 10% to 20%, and locoregional recurrence rates of 35% to 70%.[6-8] Biomarkers that indicate risk stratification for patients by clinicians could be used to tailor treatment intensity and type.

18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) has shown potential as a prognostic imaging biomarker[9] and has been widely used for staging, detecting recurrence, and predictive prognosis in NSCLC.[10-12] Maximum standardized uptake value (SUVmax) is the most frequently used parameter of PET/CT, and studies have been shown that the degree of FDG uptake by the tumor, as assessed with SUVmax, is a significant prognostic factor in NSCLC,[13,14] but this finding has not been duplicated by other studies.[15,16] Recent studies have revealed that cancer-related inflammation plays an important role in cancer progression in NSCLC.[17-19] Neutrophil-to-lymphocyte ratio (NLR), as a systemic inflammatory marker, has been shown to have prognostic value in NSCLC.[20-23] The incorporation of SUVmax and NLR (SNG score) in predicting survival in LA NSCLC, which may represent different pathophysiologic characteristics and biological behaviors, however, has not been evaluated.

Hence, in the present study, we first explored the prognostic value of the SNG score in patients with LA NSCLC in an attempt to provide accurate and reliable clues for better prediction of outcomes in patients with LA NSCLC.

Materials and Methods

Study Population

The retrospective study was approved by the Ethics Committee of Shandong Cancer Hospital and Institute, and written informed consent was obtained from all participants. A total of 138 patients with histopathologically confirmed unresectable LA NSCLC were enrolled in our study at the Shandong Cancer Hospital and Institute between July 2010 and August 2017. Patients were staged according to the TNM classification (TNM 7th edition). Patients were eligible for inclusion if they had no prior treatment; Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2; adequate liver and kidney function; tumor stage III (IIIA and IIIB); had no history of cancer in another organ; no infections, acute or chronic pneumonia, hematologic disease, or autoimmune disease/disorder. Major exclusion criterion was a previous reaction to intravenous contrast agent. Finally, a total of 138 patients with LA NSCLC were included in the present study**.** The variables analyzed included patient gender, age, ECOG score, smoking status, histologic subtype, differentiation, tumor stage, location, SUVmax, NLR and other PET parameters, and laboratory blood indicators**.** The last follow-up time was January 2018.

18F-FDG PET/CT Imaging Analysis

18F-FDG PET-CT images were obtained via an integrated PET-CT device (Discovery LS PET/CT system; General Electric Healthcare, Milwaukee, WI). Before FDG PET examination, all patients fasted for at least 6 hours and were checked to ensure their glucose level was within the normal range (80-120 mg/dL). After injecting with 370 MBq (10 mCi) of 18F-FDG, CT scanning from head to thigh was performed first, with 140 kV, 80 mA, a pitch of 6, a section thickness of 4.25 mm, a field of view of 50 cm, and a matrix size of 512 × 512. PET/CT images were obtained approximately 60 minutes after the injection. All patients were advised to keep normal shallow respiration during the PET and CT scans. Emission data sets were reconstructed iteratively using CT data for attenuation correction, and PET, CT, and fused PET/CT images were displayed on the Philips extended brilliance workstation.

All collected PET/CT images were assessed independently by 2 nuclear medicine radiologists (F.J. and B.Z.), and disagreement between their assessments were resolved by consensus through discussion. The median time of the 18F-FDG PET/CT scan before treatment was 10 days (range, 5-18 days). The PET metrics recorded were the SUVmax, mean standardized uptake value (SUVmean), and metabolic tumor volume (MTV) of the primary tumor. MTV represents the volume in mL of metabolically active cancer. The SUVmax and SUVmean of the MTV were obtained automatically through the manufacturer's software.

Definition of Inflammatory Markers

Peripheral blood samples (including neutrophil count, lymphocyte count, platelet count, and monocyte count) were obtained from routine blood tests between 7 am and 10 am within a week before treatment. The NLR was determined from the differential count by dividing the absolute neutrophil count by the absolute lymphocyte count. The PLR was determined from the differential count by dividing

Table 1 Patient Baseline Characteristics

Characteristics	n (%)
Patients	138 (100)
Gender	
Male	77 (55.8)
Female	61 (44.2)
Age, y	
Range	36-84
Median	61
≥60	89 (64.5)
<60	49 (35.5)
ECOG score	
0-1	66 (47.8)
2	72 (52.2)
Smoking status	
Current or former	68 (49.3)
Never	70(50.7)
Histological subtype	
SCC	60 (43.5)
Adenocarcinoma	78 (56.5)
Differentiation	
Well/moderate	85 (61.6)
Poor	53 (38.4)
Tumor stage	
IIIA	56 (40.6)
IIIB	82 (59.4)
Location	
Right	77 (55.8)
Left	61 (44.2)
Treatment modality	
CCRT	79 (57.2)
SCRT	59 (42.8)
Albumin	
>41.15	33 (23.9)
≤41.15	105 (76.1)

Abbreviations: CCRT = concurrent chemoradiotherapy; ECOG = Eastern Cooperative Oncology Group; SCC = squamous cell carcinoma; SCRT = sequential chemoradiotherapy.

the absolute platelet count by the absolute lymphocyte count. The LMR was determined from the differential count by dividing the absolute lymphocyte count by the absolute monocyte count.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics version 20 (IBM Corporation, Armonk, NY) and GraphPad Prism 5.0 (GraphPad Software, Inc, La Jolla, CA). OS was defined as the interval between the treatment and death or the last follow-up. Progression-free survival (PFS) was defined as the interval between the treatment and the first incidence of detectable recurrence. The cut-off values of the SUVmax, SUVmean, MTV, NLR, PLR, and LMR were determined by receiver operating characteristic curve analysis. The Spearman correlation coefficient test was used to estimate the correlations between SUVmax and NLR level. Survival analysis was performed using the Kaplan-Meier method and Cox proportional hazard model. Variables that showed significant associations in the univariate analysis ($P < .05$) were included in a multivariate Cox regression model to validate their independent prognostic values. A *P*-value less than .05 was regarded as indicating statistical significance.

Table 2 FDG-PET Parameters and Inflammation Markers

Variables	Median (Range)
PET/CT parameters	
SUVmax	12.5 (5.9-20.7)
SUVmean	8.9 (3.8-21.8)
MTV	14.60 (1.9-179.6)
Inflammation markers	
NLR	3.57 (1.44-11.89)
PLR	115.3 (38.98-285.18)
MLR	2.69 (1.01-8.758)

Abbreviations: FDG-PET = fluorodeoxyglucose-positron emission tomography; LMR = lymphocyte-to-monocyte ratio; MTV = metabolic tumor volume; NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio; SUVmax = maximum standardized uptake value; SUVmean = mean standardized uptake value

Results

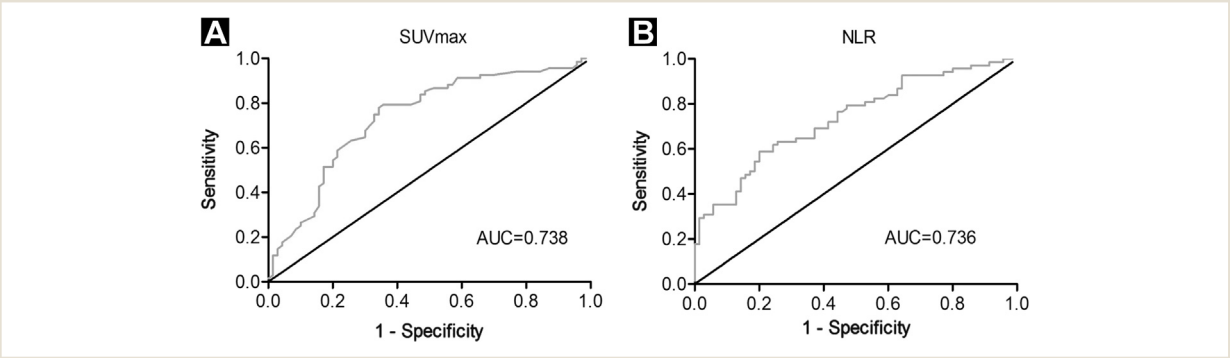
Patient Characteristics

The study population included 138 patients who were retrospectively analyzed. The patients' clinical characteristics have been summarized in Table 1. Male gender (n = 77; 55.8%), stage IIIB (n = 82; 59.4%), adenocarcinoma (n = 78; 56.5%), and well/moderate differentiation (n = 85; 61.6%) were relatively predominant. Slightly more patients in our sample presented with never-smoking (50.7%) than current or former smoking status. For these patients, an acceptable standard treatment consisted of a combination of chemotherapy and radiotherapy, administered either sequentially or concomitantly. Patients with good tolerance received concurrent chemoradiotherapy, whereas patients with poor tolerance received sequential chemoradiotherapy. Seventy-nine patients received concurrent chemoradiotherapy, and 59 received sequential chemoradiotherapy. Radiotherapy was given in 1.8 to 2 Gy fractions, with a total of 60 to 66 Gy. Five fractions a week were usually applied. The chemotherapy regimens used in our study were cisplatin/gemcitabine, cisplatin/pemetrexed, cisplatin/vinorelbine, and cisplatin/docetaxel.

Determination of Cutoff Value and SNG Score

The patients had a median SUVmax of 12.5 (range, 5.9-20.7) and NLR of 3.57 (range, 1.44-11.89). All of the parameters that were calculated from PET/CT, and peripheral blood cell counts are summarized in Table 2. On receiver operating characteristic analysis, the SUVmax and NLR were found to have the largest area under the curve (AUC = 0.738; 95% confidence interval [CI], 0.654-0.822; $P < .001$ and AUC = 0.736; 95% CI, 0.654-0.818; $P < .001$, respectively) (Figure 1). The optimal cutoff value for the SUVmax was 11.95 (sensitivity, 77.9%; specificity, 65.7%), and an optimal cutoff value for the NLR was 3.82 (sensitivity, 58.8%; specificity, 80%). In addition, the optimal cutoff value for the

Figure 1 ROC Curve of SUVmax (A) and NLR (B) for Recurrence Prediction



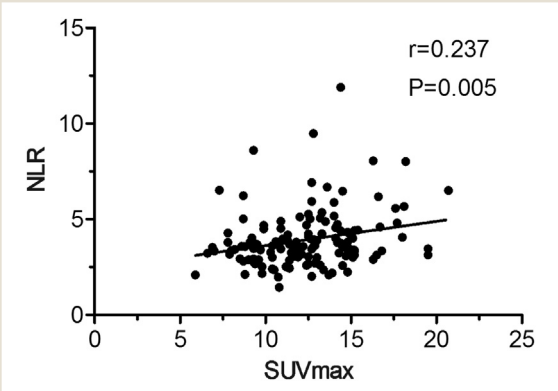
Abbreviations: AUC = area under the curve; NLR = neutrophil-to-lymphocyte ratio; ROC = receiver operating characteristic; SUVmax = maximum standardized uptake value.

SUVmean, MTV, PLR, and LMR were 8.05, 13.45, 101.54, and 1.84, respectively. There was a significant correlation between the SUVmax and NLR (r = 0.237; $P = .005$) (Figure 2). Based on the optimal cutoff values of the SUVmax and NLR, patients with both an increased SUVmax (> 11.95) and an elevated NLR (> 3.82) were SNG score 2, patients showing one or the other (SUVmax > 11.95 or NLR > 3.82) were SNG score 1, and patients showing neither (SUVmax ≤ 11.95 and NLR ≤ 3.82) were SNG score 0.

Univariate Survival Analysis

We performed the Kaplan-Meier analysis and log-rank test to determine the survival differences among the 3 SNG scores. The median OS in patients with SNG score 2 was significantly lower than the OS in patients with SNG score 1 and SNG score 0 (18.5 vs. 19 vs. 23 months; $P < .001$) (Figure 3A). The median PFSs were 8.5, 9, and 14 months for patients with SNG scores 0, 1, and 2, respectively ($P < .001$) (Figure 3B). When the stages (IIIA and IIIB) were analyzed separately, the OS and PFS of patients with SNG scores 0, 1, and 2 had significant differences in stage IIIA ($P < .001$ for OS; $P = .027$ for PFS) (Figure 4A and 4B). Thus, we came to the same conclusion for stage IIIB ($P < .001$ for OS; $P < .001$ for PFS) (Figure 4C and 4D).

Figure 2 Spearman Correlation Analyses Indicating a Significant Correlation Between that SUVmax and NLR (r = 0.237; $P = .005$)



Abbreviations: NLR = neutrophil-to-lymphocyte ratio; SUVmax = maximum standardized uptake value.

Univariate analyses of baseline characteristics are shown in Table 3, and we can see the results of univariate analyses of FDG PET parameters and inflammation markers in Table 4. Univariate analysis demonstrated that the tumor stage ($P = .004$), SUVmax ($P < .001$), SUVmean ($P = .022$), MTV ($P = .043$), NLR ($P = .003$), LMR ($P = .010$), and SNG score ($P < .001$) were correlated with OS, and the tumor stage ($P = .005$), SUVmax ($P < .001$), SUVmean ($P = .027$), NLR ($P < .001$), PLR ($P = .018$), and SNG score ($P < .001$) were significantly associated with PFS.

Multivariate Analysis of Independent Prognostic Indicators

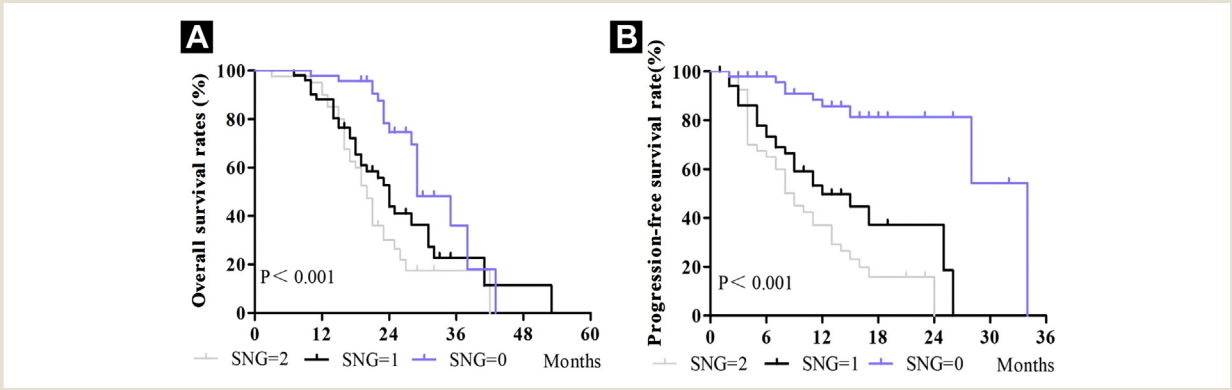
To determine the independent predictive indicators, Cox multivariate analysis, which included the variables mentioned above, was performed. As shown in Table 5, multivariate analysis revealed that SNG score was significantly related to PFS (hazard ratio, 2.241; 95% confidence interval, 1.486-3.379; $P < .001$) and OS (hazard ratio, 1.612; 95% confidence interval, 1.157-2.246; $P = .005$) along with tumor stage ($P = .030$) and LMR ($P = .041$).Therefore, multivariate analysis demonstrated that SNG score was considered an independent prognostic indicator for OS and PFS.

Discussion

In the present study, the results showed that SNG scores are independent predictors of OS and PFS among patients with LA NSCLC. In addition, to the best of our knowledge, our study was the first to combine the SUVmax and NLR as a variable and demonstrated that the SNG score was a more effective candidate prognostic biomarker than the SUVmax or NLR alone in LA NSCLC.

Abnormal glucose metabolism is one of the core features of tumor cell function metabolism. It is considered to be an important indicator of tumor diagnosis and evaluation of tumor biological behavior. In recent years, semi-quantitative 18F-FDG PET parameters can reflect the glucose metabolism of primary tumors

Figure 3 Survival Curves for Overall Survival (A) and Progression-free Survival (B) in SNG Score 2, 1, and 0 in Patients With Locally Advanced Non–small-cell Lung Cancer

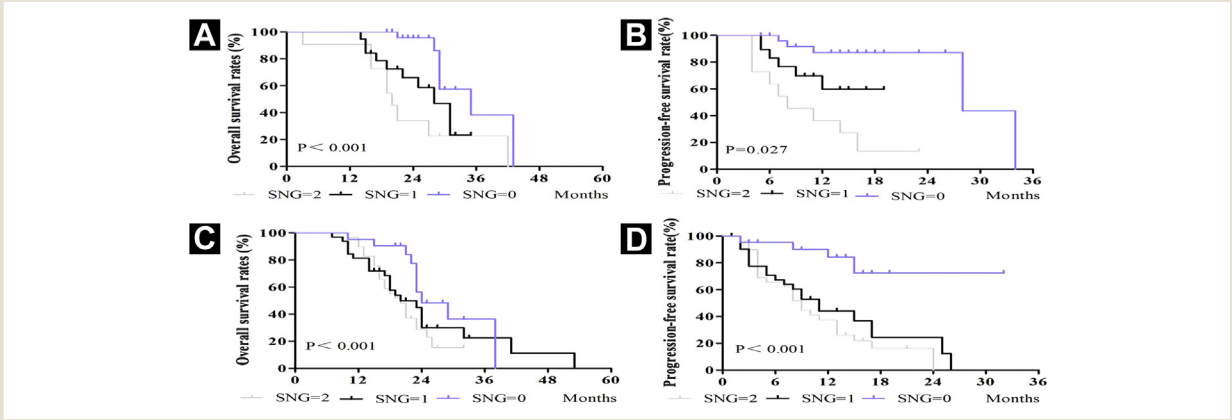


Abbreviation: SNG = SUVmax and NLR grade.

and can provide valuable prognostic information in NSCLC.[13,24,25] The accumulation of 18FDG uptake is associated with the increased rate of glycolysis and glucose transport in malignant cells,[26,27] and increased 18FDG uptake is related to the tumor cell proliferation rate in patients with lung cancer.[28] This potential mechanism might explain why patients with increased 18FDG uptake have a significantly poorer prognosis. A widely accepted functional metabolism biomarker derived from 18F-FDG PET is standardized uptake value (SUV); moreover, unlike immunohistochemistry, the SUVmax can be used to estimate the survival value even if no surgical specimen is available. Previous studies had demonstrated that SUVmax of the primary tumor is a valuable prognostic factor in patients with NSCLC.[24,25,29-31] However, Machtay et al[32] had carried out a large prospective study, including 226 patients for evaluating the pretreatment SUVmax, and demonstrated that the pretreatment SUVmax, as either a continuous or categorical variable, was not associated with survival on univariate or multivariable analyses in patients with advanced NSCLC. Our results are consistent with this prospective study that found that the SUVmax of the primary tumor is not an independent prognostic factor ($P = .186$ for OS and $P = .367$ for PFS). These discrepancies may reflect the heterogeneity of patients in each clinical study.

The NLR as an inflammatory-immunological marker of the whole body has been evaluated as an indicator for prognosis in malignant tumors. Recent clinical studies revealed that elevated NLR has been shown to be a poor prognostic indicator in various cancers,[23,33-38] including LA NSCLC. However, there is no fixed cutoff value of NLR yet. The differences between using cutoff values varying from 2.5 to 5.0 might be owing to the patients included and methodology chosen. However, the optimal cutoff value of NLR is not well-understood. In the present study, using the discriminatory value of 3.82, it was possible to differentiate clearly

Figure 4 Survival Curves for Overall Survival (A) and Progression-free Survival (B) in SNG Score 2, 1, and 0 in Patients With Stage IIIA Non–small-cell Lung Cancer, and Overall Survival (C) and Progression-free Survival (D) in SNG Score 2, 1, and 0 in Patients With Stage IIIB Non–small-cell Lung Cancer



Abbreviation: SNG = SUVmax and NLR grade.

Table 3 Univariate Analysis for OS and PFS According to Baseline Characteristics

Variables	OS			PFS		
	P Value	HR	95% CI	*P* Value	HR	95% CI
Gender						
Female/male	.421	1.202	0.769-1.878	.847	1.049	0.647-1.699
Age, y						
≥ 60/< 60	.114	0.686	0.429-1.095	.865	0.957	0.579-1.582
ECOG score						
2/0-1	.146	0.716	0.456-1.123	.184	0.721	0.445-1.168
Smoking status						
Never/current or former	.127	0.703	0.447-1.106	.133	0.689	0.425-1.119
Histologic subtype						
SCC/adenocarcinoma	.735	0.925	0.591-1.449	.428	1.216	0.750-1.971
Differentiation						
Well, moderate/poor	.068	0.632	0.386-1.035	.099	0.644	0.381-1.087
Tumor stage						
IIIB/IIIA	.004	1.988	1.238-3.191	.005	2.129	1.249-3.629
Location, %						
Right/left	.530	1.156	0.736-1.815	.792	0.937	0.578-1.519
Treatment modality						
CCRT/SCRT	.730	1.083	0.690-1.699	.477	1.202	0.723-1.99
Albumin						
> 46.5/≤ 46.5	.530	1.172	0.714-1.925	.445	1.235	0.718-2.124

Abbreviations: CCRT = concurrent chemoradiotherapy; CI = confidence interval; ECOG = Eastern Cooperative Oncology Group; HR = hazard ratio; OS = overall survival; PFS = progression-free survival; SCC = squamous cell carcinoma; SCRT = sequential chemoradiotherapy.

between the 2 prognostic groups. As shown by our study analysis, the prognostic value of the NLR in LA NSCLS was consistent with the results of previous literature. The complex mechanisms whereby a poor prognosis is associated with elevated NLR in patients with cancer remain unclear and unproven. The view is that tumor development is associated with inflammatory-immunological processes. On the one hand, neutrophils have been demonstrated to secrete a large number of proangiogenic chemokines to promote tumor vascular formation, which is thought to play an integral role in tumor development.[39] In addition, neutrophils can secrete matrix

Table 4 Univariate Analysis for OS and PFS According to FDG-PET Parameters and Inflammation Markers

Variables	OS			PFS		
	P Value	HR	95% CI	*P* Value	HR	95% CI
SUVmax						
>11.95/≤11.95	<.001	2.547	1.569-4.133	<.001	4.387	2.373-8.111
SUVmean						
>8.05/≤8.05	.022	1.091	1.088-3.146	.027	1.915	1.076-3.407
MTV						
>13.45/≤13.45	.043	1.669	1.016-2.742	.144	1.489	0.873-2.539
NLR						
>3.82/≤3.82	.003	1.982	1.266-3.103	<.001	3.034	1.847-4.958
PLR						
>101.54/≤101.54	.914	1.026	0.639-1.650	.018	1.974	1.123-3.470
LMR						
>1.84/≤1.84	.010	2.636	1.263-5.501	.076	2.039	0.929-4.478
SUVmax-NLR						
Group A, B, C	<.001	1.851	1.393-2.460	<.001	2.557	1.837-3.559

Abbreviations: CI = confidence interval; FDG-PET = fluorodeoxyglucose-positron emission tomography; HR = hazard ratio; LMR = lymphocyte-to-monocyte ratio; MTV = metabolic tumor volume; NLR = neutrophil-to-lymphocyte ratio; OS = overall survival; PFS = progression-free survival; PLR = platelet-to-lymphocyte ratio; SUVmax = maximum standardized uptake value; SUVmean = mean standardized uptake value.

Table 5 Multivariable Analysis for OS and PFS

Variables	OS			PFS		
	P Value	HR	95% CI	*P* Value	HR	95% CI
Tumor stage						
IIIB/IIIA	.03	1.729	1.054-2.836	.144	1.513	0.868-2.640
SUVmean						
>8.05/≤8.05	.923	1.031	0.554-1.920	.696	1.138	0.595-2.179
MTV						
>13.45/≤13.45	.673	1.128	0.646-1.970			
PLR						
>101.54/≤101.54				.579	1.197	0.635-2.256
LMR						
>1.84/≤1.84	.041	2.260	1.033-4.944			
SNG score						
2, 1, 0	.005	1.612	1.157-2.246	<.001	2.241	1.486-3.379

Abbreviations: CI = confidence interval; HR = hazard ratio; NLR = neutrophil-to-lymphocyte ratio; OS = overall survival; PFS = progression-free survival; SUVmax = maximum standardized uptake value.

metalloproteinases (MMPs) and produce numerous ligands, which can induce tumor cell metastatic and proliferation.[40] On the other hand, lymphocytes possess anti-cancer activities that could affect growth and metastasis in the malignant cells of the tumor. In view of the role of tumor promoting of neutrophils and anti-tumor effect of lymphocytes, elevated NLR may reflect a strong pro-tumor activity or weak anti-tumor efficacy, consequently leading to poorer survival of patients.

Based on the above theory, SUVmax reflects tumor cell function metabolism, and can be used to evaluate the biological behavior of the tumor. NLR represents an inflammatory-immunological marker of the whole body, which can show the balance between pro-tumor activity and anti-tumor activity. SUVmax or NLR alone may exert a limited effect on tumor characteristics and host immune status. Recently, some studies reported that combining 2 peripheral blood serum indexes, such as a combination of circulating tumor cells with serum carcinoembryonic antigen,[41] or a combination of platelet count and NLR,[42] can be considered useful independent prognostic markers in NSCLC. However, their studies take into account only 2 peripheral blood serum indexes, which represent only inflammatory-immunological markers of the whole body without reflecting the biological behavior of the tumor itself. Hence, incorporation of the SUVmax and NLR presents a good prognostic indicator for patients with LA NSCLC. SNG score increases the unfavorable effect of SUVmax and NLR, which eventually increases the predicted significance for patients with LA NSCLC. According to the results of the Kaplan-Meier analysis and log-rank test, our study revealed that patients with an SNG score of 2 (SUVmax > 11.95 and NLR > 3.82) exhibited a poorer prognosis than those with SNG score 1 (SUVmax > 11.95 or NLR > 3.82) or in SNG score 0 (SUVmax ≤ 11.95 and NLR ≤ 3.82). In the present study, multivariate analysis using the characteristics selected in univariate analysis revealed that SNG score was significantly correlated with OS ($P = .005$) and PFS ($P < .001$). Moreover, when the patients with different stages were analyzed separately, the OS and PFS in the patients with SNG score 2 (SUVmax > 11.95 and NLR > 3.82) were lower than those with SNG score 1 (SUVmax > 11.95 or NLR > 3.82) and with SNG score 0 (SUVmax ≤ 11.95 and NLR ≤ 3.82) in stage IIIA ($P < .001$ for OS; $P = .027$ for PFS) and IIIB ($P < .001$ for OS; $P < .001$ for PFS). Therefore, the advantage of the SNG score based on the SUVmax and NLR more accurately reflects tumor biological behavior and host immune status to improve the reliability of the prediction.

We acknowledge several limitations to our study, including the limited number of enrolled patients from a single center and its retrospective nature, which can be associated with inherent unavoidable biases. In addition, although we restricted the influence of other factors, blood cell counts can be influenced by a variety of factors. Further analysis and validation with large-scale samples and prospective and multicenter studies will be necessary to translate these results to the clinic. Although these limitations exist, we cannot ignore the value of this study, which suggests that the SNG score is a potentially effective factor to predict clinical outcomes of patients with LA NSCLC.

Conclusion

Incorporating the SUVmax and NLR as an indicator in our study, we found that the SNG score was superior to the SUVmax or NLR alone in predicting OS and PFS. The SNG score may serve as a novel predictor of clinical outcomes in patients with unresectable LA NSCLC and may help to further identify high-risk patients for close surveillance. In addition, the SNG score may optimize patients for intensified treatments with higher radiation dose, newer concurrent drugs, or maintenance immunotherapy in the future.

Clinical Practice Points

- The survival outcomes of patients with LA NSCLC remain poor. Abnormal glucose metabolism is one of the core features of tumor cell function metabolism. The NLR as an inflammatory-immunological marker of the whole body has been evaluated as an indicator for prognosis in NSCLC.
- The incorporation of SUVmax and NLR (SNG score) in predicting survival in LA NSCLC, which may represent different

pathophysiologic characteristics and biological behaviors, however, has not been evaluated.

- We confirmed that incorporation of the SUVmax and NLR improves prediction of clinical outcomes in patients with LA NSCLC.

Acknowledgments

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Disclosure

The authors have stated that they have no conflicts of interest.

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