EJMI

DOI: 10.14744/ejmi.2023.39651
EJMI 2024;8(1):54–57

Research Article

Can Pan-Immune Inflammation Value and Systemic Inflammatory Response Index be Used Clinically to Predict Inflammation in Patients with Non-Small Cell Lung Cancer?

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Abstract

Objectives: Lung cancer is one of the most cancer type with the highest rate of cancer-related deaths in worldwide. Chronic inflammation has been associated with many diseases, including cancer, and the immune inflammatory response plays an important role in cancer patients. The aim of the study is to investigate the role of whether the pan-immune-inflammation value (PIV) and the systemic inflammatory response index (SIRI) are effective in predicting non-small lung cancer patients.

Methods: In this retrospective case-control study, eighty-four patients and 71 healthy controls followed in Ordu State Hospital, Department of Medical Oncology from January 2020- to January 2023 were included.

Results: White Blood Cell, Neutrophil, Hemoglobin , RDW, CRP were statistically significant between the study groups ($p<0.05$). A statistically significant difference was found between SII, SIRI, PIV, NLR, LMR and dNLR indices between the case and healthy subjects ($p<0.05$). However, there was no significant difference in PLR levels between the groups ($p>0.05$).

Conclusion: We indicated that SIRI and PIV could be novel cost-effective biomarkers and treatment response precursors in patients with NSCLC.

Keywords: Non-small cell lung cancer, Inflammation, Systemic inflammatory response index, Pan-immune-inflammation value

Cite This Article: *Karaoglanoglu S, Erdal H, Karaoglanoglu Sonmez M. Can Pan-Immune Inflammation Value and Systemic Inflammatory Response Index be Used Clinically to Predict Inflammation in Patients with Non-Small Cell Lung Cancer? EJMI 2024;8(1):54–57.*

Lung cancer, is one of the most common and deadly types of cancer in the world.[1] There are two main types of lung cancer including Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC).[1, 2] NSCLC is the most common type of lung cancer, accounting for about 80-85% of all cases.[2] SCLC is a more aggressive form of lung cancer, accounting for about 10-15% of cases. It tends to grow quickly and is often already in an advanced stage at the time of diagnosis. The leading cause of lung cancer is tobacco smoking, including both active (smoking cigarettes) and passive smoking (being exposed to secondhand smoke).[3] Other risk factors for lung cancer include exposure to environmental pollutants a history of certain lung diseases, a family history of lung cancer, and genetic factors.[4, 5] Several studies reported that the levels of oxidative stress play an important role in the occurrence and progression of many different diseases, including cancer.[6-10]

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Submitted Date: August 21, 2023 **Revision Date:** September 17, 2023 **Accepted Date:** October 04, 2023 **Available Online Date:** October 26, 2023

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Inflammation is a complex biological response that involves the activation of the immune system to protect the body from harmful stimuli, such as pathogens, damaged cells, or irritants.[11] Chronic inflammation plays a vital role in the pathogenesis of many diseases, including cancer.[11, 13] In the context of lung cancer, chronic inflammation can play a pivotal role in the development and progression of the disease. Moreover, chemicals in tobacco smoke trigger chronic inflammation in the lungs, which contributes to the development of cancerous changes in lung cells over time.

The pan-immune-inflammation value (PIV) and the systemic inflammatory response index (SIRI) are a new comprehensive biomarker that has proven to be a powerful predictor of survival outcomes, outperforming other well-known markers. In the literature, recent studies state that SIRI and PIV are markers of systemic inflammatory conditions in several studies.[14-18] The objective of the study was the evaluate PIV, SII, SIRI, NLR, PLR together in patients with NSCLC.

Methods

This retrospective case-control study was conducted at the Ordu State Hospital from January 2020- to January 2023. A total of 84 patients with diagnosed with lung cancer were included in the present study. The control group consisted of 71 healthy control subjects. There was no significant difference between the groups in terms of age and gender. Retrospective data of the study groups were obtained from the hospital automation system. The current study was approved by the Ethics Committee of Ordu University (Date: 31.03.2023/No: 2023/90). The study was conducted in accordance with the Helsinki Declaration rules.

The hemogram parameters and serum C-reactive protein (CRP) levels were assessed. Neutrophil, lymphocyte, monocyte, platelet, hemoglobin, RDW, MPV levels of groups were used in the complete blood parameters. The NLR, PLR, LMR, SII, SIRI PIV and dNLR respectively, were calculated as follows: the ratio of neutrophils to lymphocytes, platelets to lymphocytes, lymphocytes to monocytes, that of platelets x (neutrophils / lymphocytes), (neutrophils x monocytes) / lymphocytes and (neutrophils x platelets x monocytes) / lymphocytes. The neutrophil count divided by the result of WBC count minus neutrophil count.

Exclusion Criteria

The exclusion criteria of the study were as follows: To be younger than than 18 years old and have diagnosed with another malignancy, having previously received treatment for malignancy, having previously known inflammatory, hematological, autoimmune disease, using anti-inflammatory, steroid, immunosuppressive treatment in the last 6 months and patients with liver and kidney dysfunction.

Statistical Analysis

SPPS 22 was used to carry out all data analysis. Data are reported as median±min-max. The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test. Variables that did not show normal distribution were compared with the Mann-Whitney U test. The chi-square test was used to compare categorical variables. Statistical significance was accepted as <0.05.

Results

The present study consisted of a total of 155 subjects and consists of 71 healthy controls with an average age of 66.7±3.7 and 84 NSCLC patients with an average age of 67.6±8.2. There was no statistically significant difference between the groups in terms of age and gender (Table 1).

The median (min-max) outcomes of the hemogram parameters and indexes between the groups are shown in Table 2.

White Blood Cell, Neutrophil, Hemoglobin, RDW, CRP were statistically significant betweeen the groups (p<0.05, Table 2). However, there was no statistically significant difference between Lymphocyte, Monocyte, Platelet, MPV among the groups. In addition, inflammatory indices were calculated for the case groups. A statistically significant difference was found between SII, SIRI, PIV, NLR, LMR and dNLR indices between the case and healthy groups (p<0.05). Table 2). However, there was no significant difference in PLR levels between the study and healthy controls (p>0.05, Table 2).

Discussion

In this retrospective case-control study, we demonstrated for the first time that SII, SIRI, PIV, NLR, LMR and dNLR indices together in patients with NSCLC. The current study was to examine whether systemic inflammatory indices play an important role in predicting prognosis of NSCLC. In the current study, we indicated that SII, SIRI, PIV, NLR, LMR and dNLR levels were higher and statistically signifi-

Table 1. Demographic information of the study groups

Parameters	NSCLC (n=84) Mean±SD	Control (n=71) Mean±SD	p
Gender, n (%)			
Male	22 (40)	28 (50.9)	0.625*
Female	33 (60)	27 (49.1)	
Age (year)	67.6±8.2	66.7±3.7	0.383¥

*Chi-Square test; ¥: Student t –test.

Table 2. Comparison of the blood parameters of the study and control groups

Parameters	NSCLC (n=84) Median (min-max)	Control (n=71) Median (min-max)	p*
White Blood Cell (10^3µL)	9.7 (3.8-29.5)	8.22 (3.8-29.5)	0.001
Neutrophil (10^3µL)	6.5 (0.62-25.6)	4.73 (2.4-25.6)	<0.001
Lymphocyte (10^3µL)	2.06 (0.43-4.9)	2.17 (0.75-3.95)	0.169
Monocyte (10^3µL)	0.75 (0.16-1.64)	0.56 (0.16-1.5)	0.530
Hemoglobin (g/dL)	13.2 (9.2-16.8)	13.0 (9.6-16.6)	<0.001
Platelet (10^3µL)	312.2 (109-880)	292.1 (153-880)	0.266
MPV (fL)	9.7 (7.7-12.1)	9.4 (5.9-12.1)	0.154
RDW	44.9 (38.5-59.3)	211.2 (40.2-438)	<0.001
CRP (mg/L)	35.2 (0.5-179)	1.71 (0.13-15.0)	<0.001
SII	1200. 1 (63.5-6175.8)	747.6 (230.1-6175.7)	<0.001
SIRI	2.91 (0.21–17.6)	1.56 (0.35-17.6)	<0.001
PIV	969.4 (72.5–7349.2)	523.4 (85.6-7349.1)	<0.001
NLR	3.83 (0.18-15.6)	2.39 (0.94-14.7)	<0.001
PLR	184.1 (56.7-1173.3)	150.6 (60.1-1173.3)	0.051
LMR	2.96 (0.93-8.6)	4.36 (1.2-10.2)	<0.001
dNLR	2.29 (0.05-7.3)	1.67 (0.32-11.3)	<0.001

Mann- Whitney U test NLR: Neutrophil Lymphocyte Ratio; CRP: C-reactive protein; MPV: Mean Platelet Volume; PLR: Platelet Lymphocyte ratio; dNLR: Derived NLR ratio (neutrophil count divided by the result of WBC count minus neutrophil count); SII: Systemic inflammatory index (neutrophil x platelet / lymphocyte count); SIRI: Systemic inflammatory response index (neutrophil × monocyte / lymphocyte count) and PIV: Pan-immune inflammation value (neutrophil × platelet x monocyte /lymphocyte count). NSCLC: Non-Small Cell Lung Cancer.

cant in NSCLC patients with respect to the healthy subjects ($p<0.05$).

In the meta-analysis on cancer patients study conducted by Güven et al.[19] they concluded that PIV may be a prognostic biomarker in patients with cancer. Another study conducted by Karadag et al.[20] in hepatocellular cancer (HCC) patients they concluded that PIV and PILE score can be used as a prognostic biomarker at the time of diagnosis in patients with HCC.

In the meta-analysis study of Yang et al.[21] with 1879 participants in colorectal cancer and they concluded that PIV could be a valuable prognostic index in patients with colorectal cancer. In the present study, PIV levels were found higher in patients with NSCLC compared to the heathy subjects. We hypothesized that PIV may be a prognostic marker in patients with NSCLC. In addition, we also evaluated NLR and PLR values and found higher in patients with NSCLC with respect to the healthy subjects. Moreover, SII and SIRI levels were found higher and statistically significant in patients with NSCLC compared to the controls. We indicated that SIRI and PIV is a new and practical inflammatory index that can be used in the evaluation of patients with NSCLC.

In the literature, Huang et al.[22] evaluated the NLR , PLR and SII values in two independent cohort studies to predict the prognosis of patients with cervical cancer. They concluded that these index reflects the immune response and systemic inflammation. In another study, Ling et al.[23] in their study on surgical colorectal cancer (CRC) patients they indicated that NLR provide improved accuracy for predicting clinical outcomes in surgical CRC patients under surgery resection.

In this study, we indicated that PLR levels were not statistically significant in NSCLC patients compared to the control group. ($p>0.05$). Hovewer, we showed that LMR levels were found to be lower in the patient group compared to the control group.

Conclusion

As a result, SII, SIRI and PIV could be a prognostic biomarker in the evaluation of NSCLC patients. As known, inflammation emerges as a crirical player in the complex puzzle of NSCLC. These inflammatory indices can help the clinicians about the individual treatment process and strategies due to the practical, inexpensive and safe indicator of the inflammatory state of the NSCLC.

Disclosures

Limitations: The limitations of this study are the lack of pathological findings and survival information.

Ethics Committee Approval: This retrospective study was approved by the ethics committee of Ordu University (Date: 31.03.2023/No: 2023/90).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – H.E., SK., M.K.; Design – H.E., SK., MK.; Supervision – H.E.; Materials – MK ; Data collection &/or processing – SK., MK.; Analysis and/or interpretation – H.E.; Literature search – H.E., SK., MK.; Writing – H.E SK., MK; Critical review – H.E., SK., MK.

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