ORIGINAL ARTICLE

DOI: 10.4274/nkmj.galenos.2023.58076
Nam Kem Med J 2023;11(1):72-79

The Relationship Between Depression and Inflammation Markers in Patients with Metastatic Lung Cancer

Metastatik Akciğer Kanseri Hastalarında Depresyon ile Enflamatuvar Belirteçler Arasındaki İlişki

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ABSTRACT

Aim: The role of systemic inflammation in lung cancer patients is known. Diagnosis and treatment of psychiatric disorders, especially depression, can increase patients' adherence to treatment and life quality. We aimed to investigate the relationship between inflammatory markers and depression in patients with *de novo* metastatic lung cancer.

Materials and Methods: Sixty-six patients newly diagnosed with *de novo* metastatic lung cancer between January and December 2021 were included in our study. Baseline characteristics, laboratory findings, and the Beck Depression Inventory (BDI) of patients were evaluated at the pre-chemotherapy visit.

Results: Neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and systemic inflammation response index (SII) were significantly higher in the group with depression. NLR, PLR, C-reactive protein to lymphocyte ratio and SII values showed a positive correlation with BDI scores, indicating depression. It was determined that the values of 3.63 for NLR, 173 for PLR and 1208 for SII could be used as cut-off values to detect depression.

Conclusion: Although the biopsychosocial approach is important in terms of disease prognosis during oncological evaluation, cancer remains the main life-threatening disease, making it difficult for clinicians to screen for depression unless the patient has an additional request. Predicting the possible risk of depression via common laboratory values measured at the time of diagnosis will significantly contribute to the treatment process of the patients.

Keywords: Depression, inflammation, lung cancer

ÖZ

Amaç: Akciğer kanseri hastalarında sistemik enflamasyonun rolü bilinmektedir. Kanser hastalarında depresyon başta olmak üzere psikiyatrik bozuklukların tanı ve tedavisi hastaların tedaviye uyumunu ve yaşam kalitesini artırabilmektedir. Bu çalışmada *de novo* metastatik akciğer kanserli hastalarda enflamatuvar belirteçler ile depresyon arasındaki ilişkinin araştırılması hedeflendi.

Gereç ve Yöntem: Ocak-Aralık 2021 tarihleri arasında yeni tanı alan *de novo* metastatik akciğer kanseri 66 hasta çalışmaya dahil edildi. Hastaların temel özellikleri, laboratuvar bulguları ve Beck Depresyon Envanteri (BDI) kemoterapi öncesi vizitte değerlendirildi.

Bulgular: Nötrofil lenfosit oranı (NLR), platelet lenfosit oranı (PLR) ve sistemik enflamasyon yanıt indeksi (SII) BDI'ye göre depresyon saptanan grupta anlamlı derecede yüksek bulundu. NLR, PLR, C-reaktif protein/lenfosit oranı ve SII değerleri, BDI puanları ile pozitif korelasyon gösterdi. NLR için 3,63, PLR için 173 ve SII için 1208 değerlerinin depresyonu saptamak için cut-off değer olarak kullanılabileceği saptandı.

Sonuç: Onkolojik değerlendirme sırasında biyopsikososyal yaklaşım hastalığın prognozu açısından önemli olmakla birlikte, kanserin yaşamı tehdit eden ana hastalık olması, hastanın ek bir isteği olmadıkça klinisyenlerin rutinde depresyon taraması yapmasını güçleştirmektedir. Tanı anında ölçülen rutin laboratuvar değerleri ile olası depresyon riskinin önceden tahmin edilmesi hastaların tedavi süreçlerine önemli katkı sağlayacaktır.

Anahtar Kelimeler: Depresyon, enflamasyon, akciğer kanseri

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Received: 16.01.2023 **Accepted:** 31.01.2023

INTRODUCTION

The second most common cancer in the world according to GLOBOCAN is lung cancer (11.4%), followed by breast cancer (11.7%). It has the first rank among cancers that cause death in the world (18%)[1]. In metastatic (Stage 4) lung cancer patients, the rate for 5-year survival is less than five percent[2]. In a meta-analysis, the frequency of major depression was found to be 15% in cancer patients, while anxiety rate was found to be 10%[3]. Although the frequency varies with the type of cancer, the highest rates of anxiety and depression are seen in lung cancer. Because metastatic patients have a poor prognosis, from the time of diagnosis, these patients tend to have anxiety and depression[4]. Diagnosis of cancer and initiation of treatment disrupt the physical, emotional, social and economic balances of the individual and family, prevent them from getting satisfaction from life and reduce their quality of life. Since the presence of depression predicts worse survival in patients with metastasis, unmanaged psychosocial difficulties may have important implications for cancer treatment[4-6].

It is known that cancer and inflammation are related to each other and the cellular immune system plays a significant role in inflammation[7]. In literature, the studies have also underlined that inflammation response may alter neurotransmission and neuroendocrine pathways that play a role in depression. In addition, recent studies have revealed that rheumatological diseases and increase in proinflammatory markers are related to a higher risk of depression[8,9].

Neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), C-reactive protein to lymphocyte ratio (CRP/L), neutrophil to lymphocyte, platelet ratio (NLPR), and systemic inflammation response index (SII) are biomarkers that can be obtained from the complete blood count test. As depression is a psychiatric disorder related to inflammation, the relationship between inflammation markers such as NLR, PLR and depression has also been explored by numerous studies, but the results showing the relationship between depression and NLR and PLR are controversial[10,11]. Studies have shown that depression is associated with inflammation in patients with cancer and other chronic medical diseases[12,13]. The importance of identification of depression in lung cancer patients may be essential to improve disease outcome. In spite of all efforts to screen for depression, depression is still inadequately treated[14].

The meanings that patients attribute to cancer and the way they perceive the disease affect the response to cancer, impair treatment adherence, increase the length of hospital stay and treatment costs, and may adversely affect the course of the disease. We aimed to investigate the relationship between inflammatory markers and depression in patients with de novo diagnosed metastatic lung cancer, which causes one of the highest rates of depression among all cancer types (16-29%)[4,15,16].

MATERIALS AND METHODS

Study Population and Sample

Sixty-six patients newly diagnosed with metastatic (Stage 4) lung cancer were included in our study (Figure 1). Cancer patients were recruited from the Medical Oncology Clinic of University Hospital between January and December 2021. Inclusion criteria included age of 18≥ years, willingness and ability to provide written informed consent. Patients with a history of psychiatric disorder prior to their cancer diagnosis, with a history of dementia or any other organic neurological disorders, with Eastern Cooperative Oncology Group >2 were excluded. Baseline characteristics, clinical and laboratory findings, and the Beck Depression Inventory (BDI) of patients with newly diagnosed *de novo* metastatic lung cancer were evaluated at the pre-chemotherapy visit.

The Ethics Committee of the Bezmialem Vakıf University approved this cross-sectional study with reference number 16/330 on date 22.09.2020. It was performed in accordance with the Declaration of Helsinki. All patients provided written informed consent for attendance.

The Beck Depression Inventory

It consists of 21 questions and a scoring system between 0 and 3. The severity of depression experienced by individuals is determined by the high scores obtained from the scale. Each question is scored in the range of 0-3 points and results ranging from 0 to 63 are obtained[17]. Validity and reliability studies of BDI for adaptation to the Turkish language have been conducted[18]. In the Turkish reliability and validity study, the cut-off point was 17. It was determined that scores of 17 and above on the scale might require treatment. It has been stated that it can distinguish over 90% of depressive disorders[19]. In our study, the cut-off point was 17 based on Hisli's[18] recommended cut-off scores.

Laboratory Findings and Inflammation Markers

The results of blood tests, which were routinely requested from cancer patients for treatment evaluation, were obtained from the laboratory findings. Blood tests before the chemotherapy were examined.

They were calculated as follows: NLR=Neutrophil/lymphocyte count, PLR=Platelet/lymphocyte count, NLPR=Neutrophil/(lymphocyte × platelet count), CRP/L=C-reactive protein levels/lymphocyte count, SII=Platelet × neutrophil/lymphocyte count.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) 22 software (SPSS, IBM Inc. IL, USA) was used to analyze the study. The normal distribution was evaluated with the Kolmogorov-Smirnov test and Skewness-Kurtosis values. Normally distributed data are presented with mean and standard deviations in analytical evaluation; Non-normally distributed data are presented with median and minimum-maximum values. The Mann-Whitney U test was used for the comparison of the independent groups without normal distribution. The Student's t-test was employed to compare two independent groups with normal distribution. The chi-square tests were employed to compare categorical data. The Spearman correlation test was performed for correlation analysis of non-normally distributed data. Moreover, the univariate logistic regression analysis was used to determine factors predicting depression in lung cancer patients. With receiver operating characteristic (ROC) analysis, cut off values for NLR, PLR, NLPR, CRP/L and SII for depressive symptoms in cancer patients were investigated. A p value <0.05 was considered statistically significant.

RESULTS

Our study group consisted of 66 *de novo* metastatic lung cancer patients (mean age 61.97±10.74 years). Male/female (M/F) ratio was 55/11. When the education levels of the individuals were examined, it was determined that 61 (92.4%) were primary, secondary or high school graduates and 5 (7.6%) were university graduates or had PhD. Furthermore, it was determined that 8 (12.1%) patients lived in the countryside, whereas 58 (87.9%) patients lived in the city center. Forty-three of the patients (65.2%) had a previously known chronic disease, and there were 13 (19.7%) patients with polypharmacy. Clinically significant depression was endorsed by 45.5% (BDI ≥17) with a mean BDI score of 17.14±9.52. Regarding the histological type, 20 (30.3%) patients had small-cell lung carcinoma and 46 (69.7%) patients had non-small cell lung cancer. 60 (90.9%) patients were smokers, whereas 23 (34.8%) patients had a history of alcohol consumption. Descriptive characteristics of the study population are presented in Table 1.

Sixty-six patients were divided into two subgroups with the scores of BDI <17 and ≥17 as patients with depression. Patients with depression had significantly higher NLR [2.88 (1.13-14.12) vs. 4.37 (1.29-23.51), p=0.006], PLR [0.15 (0.06-0.71) vs. 0.21 (0.07-1.12), p=0.007] and SII [962 (205-3650) vs. 1510 (344-6173), p=0.002] levels compared to patients without depression (Table 1).

Spearman correlation analysis revealed that there was a significant positive relationship between BDI scores and NLR (r=0.298, p=0.015), PLR (r=0.308, p=0.012), CRP/L (r=0.254, p=0.039) and SII (r=0.353, p=0.004) (Table 2).

Since there is no shared and approved NLR cut-off value for depression in cancer patients in the literature, we consider the value of 3.5 close to the median NLR considering our study data. The univariate analysis results revealed that a statistically significant relationship was found between depression and

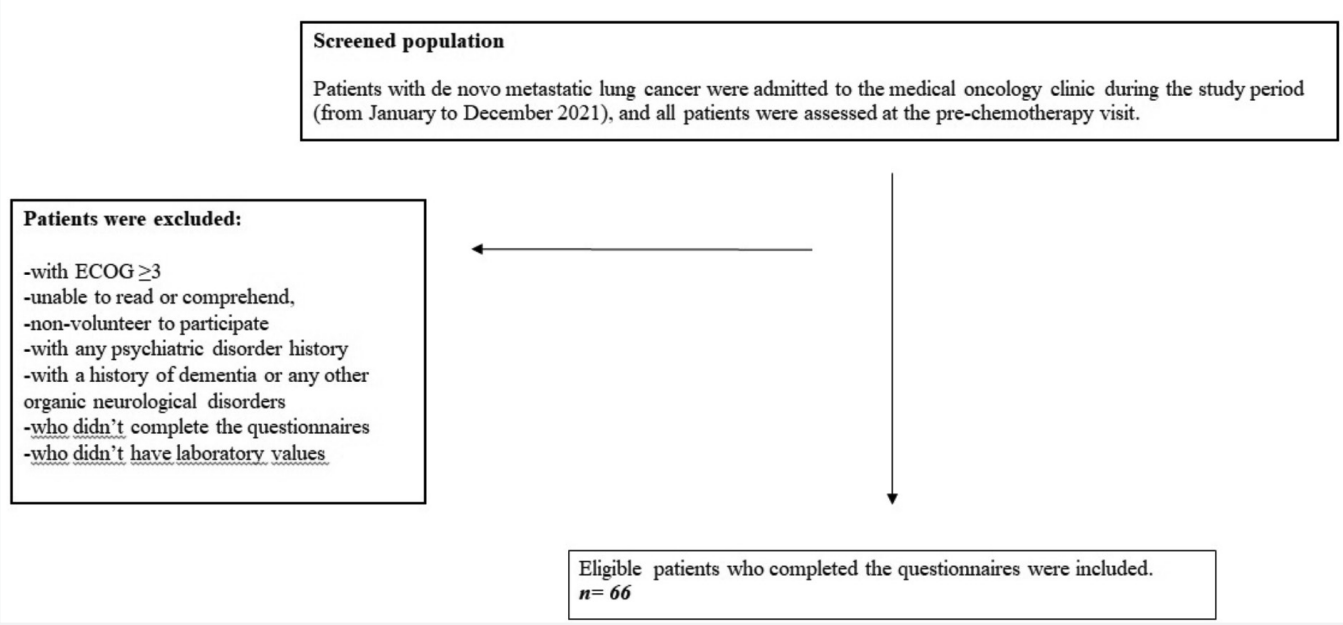

Figure 1. Flow chart of the patient selection process

ECOG: Eastern Cooperative Oncology Group

various risk factors, such as NLR >3.5 [odds ratio (OR): 3.06, 95% confidence interval: 1.12-8.37, p=0.030] and higher SII values (OR: 1.001, 95% confidence interval: 1.00-1.01, p=0.014) (Table 3).

In the ROC curve analysis performed in metastatic lung cancer patients, inflammation markers such as NLR, PLR, and SII were statistically significantly associated with depression (Figure 2). The cut-off, sensitivity, specificity and AUC values are shown in Table 4. SII had the highest AUC value for detecting depression (AUC=0.725, cut-off >1208.8, p=0.002, sensitivity 63.3%, specificity 63.9%).

Table 1. Demographic and clinical characteristics

		BDI <17	BDI ≥17	p
Age		62.7±10.92	61.1±10.7	0.56
Gender	Female Male	3 (8.3%) 33 (91.7%)	8 (26.7%) 22 (73.3%)	**0.04**
Marital status	Single Married	6 (16.7%) 30 (83.3%)	6 (20.0%) 24 (80.0%)	0.73
Education	Primary school or high school university or PhD	32 (88.9%) 4 (11.1%)	29 (96.7%) 1 (3.3%)	0.37
Smoking	Yes No	33 (91.7%) 3 (8.3%)	27 (90.0%) 3 (10.0%)	1.00
Alcohol	Yes No	15 (41.7%) 21 (58.3%)	8 (26.7%) 22 (73.3%)	0.20
Family history of lung cancer	Yes No	5 (13.9%) 31 (86.1%)	2 (6.7%) 28 (93.3%)	0.44
At least ≥1 comorbidity	Yes No	23 (63.9%) 13 (36.1%)	20 (66.7%) 10 (33.3%)	0.81
Polypharmacy	Yes No	8 (22.2%) 28 (77.8%)	5 (16.7%) 25 (83.3%)	0.57
Place of residence	Center Countryside city	33 (91.7%) 3 (8.3%)	25 (83.3%) 5 (16.7%)	0.45
Weight loss (>10%)	Yes No	14 (38.9%) 22 (61.1%)	16 (63.3%) 14 (46.7%)	0.24
Histologic classification	Small-cell Non-small cell	11 (30.6%) 25 (69.4%)	9 (30.0%) 21 (70.0%)	0.96
	All patients (n=66)	**BDI <17 (n=36)**	**BDI ≥17 (n=30)**	**p**
BDI	17.14±9.52	9.83±4.04	25.9±6.16	
Hb (g/dL)	12.90 (8.60-16.60)	13.10 (8.60-16.60)	12.80 (9.30-16.20)	0.49
TNC (×10³/µL)	6064 (2500-18100)	5550 (2500-16400)	6640 (3800-18100)	0.13
TPC (×10³/µL)	300 (95-484)	286 (124-482)	342 (95-484)	0.18
TLC (×10³/µL)	1800 (250-3800)	2200 (250-3700)	1500 (400-3800)	**0.03**
CRP (mg/L)	19.90 (0.20-150.00)	17.5 (0.20-150.0)	21.0 (0.20-149)	0.40
Albumin (mg/dL)	4.05 (3.10-5.00)	4.15 (3.10-5.00)	3.90 (3.20-5.00)	**0.09**
NLR	3.37 (1.13-23.51)	2.88 (1.13-14.12)	4.37 (1.29-23.51)	**0.006**
PLR	0.17 (0.06-1.12)	0.15 (0.06-0.71)	0.21 (0.07-1.12)	**0.007**
NLPR	0.01 (0-0,25)	0.01 (0-0.08)	0,01 (0.005-0.25)	0.06
CRP/L	0.01 (0-0.60)	0.01 (0-0.60)	0.01 (0-0.24)	0.21
SII	1177 (205-6173)	962 (205-3650)	1510 (344-6173)	**0.002**

Numbers indicate mean±standard deviation, median (minimum-maximum) or n (%).

CRP: C-reactive protein, CRP/L: C-reactive protein-to-lymphocyte ratio, Hb: Hemoglobin, NLR: Neutrophil-to-lymphocyte ratio, NLPR: Neutrophil-to-lymphocyte-platelet ratio, PLR: Platelet-to-lymphocyte ratio, TLC: Total lymphocyte count, TNC: Total neutrophil count, TPC: Total platelet count, SII: Systemic inflammation response index, BDI: Beck Depression Inventory

DISCUSSION

NLR, PLR and SII values were statistically significantly higher in the group with depression. NLR, PLR, CRP/L and SII values showed a positive correlation with BDI scores indicating depression. Considering the NLR value, it was determined that an NLR value above 3.5 was predictive of depression, and an increase in the SII value also predicted the presence of depression. Therefore, it has been determined that the values of 3.63 for NLR, 173 for PLR and 1208 for SII can be used as cut-off values to detect depression in patients with de novo metastatic lung cancer.

Our results showed no significant difference in neutrophil count between patients with and without depression, whereas the depressive patient group had significantly lower lymphocyte levels. In a study that emphasized the importance of NLR, similar to our results, lymphocyte count was significantly lower in patients with depression. On the other hand, neutrophil count was higher, controversial to our study[20]. Evaluating inflammation in relation to neutrophil or lymphocyte separately can be challenging, supporting the need to evaluate NLR, PLR, CRP/L or SII in inflammation.

Our results showed that higher depression scores were associated with increased inflammation, that can be detected by increased NLR, PLR, CRP/L and SII levels. Recently, there are some studies investigating the relationship between NLR and depression in cancer patients or other populations, which is an interesting area for clinicians nowadays. McFarland stated that there was a significant correlation between NLR and depression[21]. Besides, it has been shown that NLR and PLR levels were significantly higher in patients with major depressive disorders compared to the healthy individuals[22,23]. The PLR of patients with severe depression was found to be higher than that of patients with other types of depression (without psychotic features etc.), but there was no significant difference in NLRs among different types of depression[24]. Demir et al.[20] showed that NLR tended to be higher in patients with depression, and so they stated the fact that higher NLR values supported the approach that inflammation played critical role in the etiology of depression. A study found that after adjustment for values of hemoglobin, RDW and NLR, RDW and NLR were associated with depression independently of hemoglobin[25].

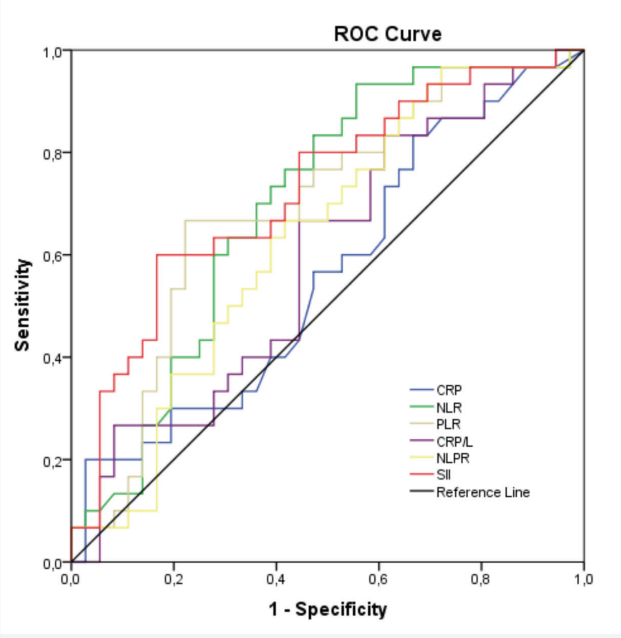

Figure 2. ROC curve analysis of inflammation markers for depression (Beck Depression Inventory ≥17)

CRP: C-reactive protein, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, CRP/L: C-reactive protein to lymphocyte ratio, NLPR: Neutrophil to lymphocyte-platelet ratio, SII: Systemic inflammation response index

The NLR is calculated by two types of cell counts mediating two different immune pathways. Having a phagocytic and apoptotic function neutrophil plays role at the first line of immunity[26]. As specific inflammation mediators, lymphocytes play an important role in host defense mechanisms with regulatory or protective effects. Since NLR covers both immune responses, it is expected to be more predictive and valuable than neutrophil and lymphocyte counts alone[24]. Increased neutrophil levels and decreased lymphocyte levels by production of pro-inflammatory cytokines cause elevated NLR values in different kinds of inflammatory processes. PLR is another potential and easy to measure parameter[27]. In the first-line immune response, the platelets regulate permeability of endothelium, migration of neutrophils, macrophages and other mediators. Glutamate

Table 2. Spearman correlation analysis between Beck Depression Inventory scores and laboratory findings

	r	p value
Hb (g/dL)	-0.212	0.087
Albumin (mg/dL)	-0.249*	0.044
TLC (×10³/µL)	-0.233	0.060
TNC (×10³/µL)	0.144	0.248
TPC (×10³/µL)	0.167	0.181
CRP (mg/L)	0.239	0.054
NLR	**0.298***	0.015
PLR	**0.308***	0.012
CRP/L	**0.254***	0.039
NLPR	0.193	0.121
SII	**0.353****	0.004

r: Spearman's Rho, *p<0.05, **p<0.01.

CRP/L: C-reactive protein-to-lymphocyte ratio, Hb: Hemoglobin, NLR: Neutrophil-to-lymphocyte ratio, NLPR: Neutrophil- to-lymphocyte-platelet ratio, PLR: Platelet-to-lymphocyte ratio, TLC: Total lymphocyte count, TNC: Total neutrophil count, TPC: Total platelet count, SII: Systemic inflammation response index

and serotonin pathways and other proinflammatory molecules have originated from the activated thrombocytes and so, the function of thrombocytes is modulated, resulting in alterations in pathophysiology ending up with mood disorders[28,29]. A meta-analysis mentioned above has also demonstrated that NLR and PLR levels are significantly higher in major depression and patients with mood disorders than in healthy individuals[26]. In another study it has been revealed that high NLR levels are found to be independently related to depressive symptoms in female group, but not in males[30].

The potential usage of the newly discovered CRP/L ratio as a biomarker has attracted our attention[31]. So, as an important study presenting real-life data, we examined the relationship between CRP/L ratio and depression, we found a positive

Table 3. Univariate analysis of the potential associations between patient characteristics and depression (Beck Depression Inventory ≥17) in *de novo* metastatic lung cancer patients

	Univariate regression analysis			
	OR	Lower	Upper	p value
Gender male vs female	4.00	0.95	16.7	0.06
Age	0.99	0.94	1.03	0.56
Marital status (single vs. married)	1.25	0.36	4.37	0.73
Education (primary school or high school vs. university or PhD)	3.62	0.38	34.3	0.26
Place of residency (countryside vs. city center)	0.45	0.09	2.08	0.31
Weight loss (>10%) (yes vs. no)	1.80	0.67	4.79	0.24
Smoking (ever vs. never)	0.82	0.15	4.39	0.82
Alcohol (yes vs. no)	0.51	0.18	1.45	0.21
Family history of lung cancer	0.44	0.08	2.47	0.35
At least ≥1 comorbidity (yes vs. no)	1.13	0.41	3.12	0.81
Polypharmacy (yes vs. no)	0.70	0.20	2.42	0.57
Histologic classification (small-cell vs. non-small cell)	1.02	0.35	2.94	0.96
HB (g/dL)	0.092	0.71	1.19	0.52
TNC ($\times10^3$/µL)	1.00	1.00	1.05	0.15
TPC ($\times10^3$/µL)	1.01	0.99	1.01	0.21
TLC ($\times10^3$/µL)	0.99	0.99	1.00	0.039
CRP (mg/L)	1.01	0.99	1.02	0.43
Albumin (mg/dL)	0.37	0.12	1.11	0.08
NLR (>3.5 vs. <3.5)	3.06	1.12	8.37	0.030
PLR	1.00	0.99	1.01	0.11
CRP/L	0.58	0.01	195.0	0.86
NLPR	0.66	0.00	1.12	0.19
SII	1.001	1.00	1.01	0.014

OR: Odds ratio, CRP: C-reactive protein, CRP/L: C-reactive protein to lymphocyte ratio, Hb: Hemoglobin, NLR: Neutrophil to lymphocyte ratio, NLPR: Neutrophil to lymphocyte-platelet ratio, PLR: Platelet to lymphocyte ratio, TLC: Total lymphocyte count, TNC: Total neutrophil count, TPC: Total platelet count, SII: Systemic inflammation response index

Table 4. Evaluation of depression (Beck Depression Inventory ≥17) in *de novo* metastatic lung cancer patients with ROC curve analysis

	AUC	p value	Lower bound	Upper bound	Cut-off point	Sensitivity %	Specificity %
CRP	0.56	0.403	0.42	0.700			
NLR	0.696	**0.006**	0.568	0.824	>3.63	63.3	63.9
PLR	0.693	**0.007**	0.563	0.822	>173	66.7	66.7
CRPL	0.59	0.212	0.452	0.728			
NLPR	0.632	0.066	0.498	0.767			
SII	**0.725**	**0.002**	0.601	0.849	>1208.8	63.3	63.9

AUC: Area under curve, CRP: C-reactive protein, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, CRP/L: C-reactive protein to lymphocyte ratio, NLPR: Neutrophil to lymphocyte-platelet ratio, SII: Systemic inflammation response index

correlation between CRP/L levels and the severity of depression in our study. However, according to univariate analysis results, CRP/L was not found to be a risk factor for depression, or a cut-off value that would shed light on the presence of depression risk could not be reached according to the ROC analysis results. Comprehensive studies are needed to clarify the relationship.

In our study, high SII values were found to be a risk factor for depression, consistent with the recent studies. Wang et al.[32] stated that after adjusting for socio-demographic and clinical features, high SII levels were found to be a risk factor for depression in patients with diabetes.

Clinical Implications

NLR, PLR, CRP/L and SII can be calculated easily and cheaply via routinely used laboratory findings. Although the biopsychosocial approach is important in terms of disease prognosis during oncological evaluation, the fact that cancer remains the main life-threatening disease makes it difficult for clinicians to screen for depression unless the patient has an additional request. Predicting the possible risk of depression via routine laboratory values measured at the time of diagnosis will greatly contribute to the treatment process of the patients. Since the diagnosis and treatment process and quality of life of patients are negatively affected by depression levels, it is important to determine the need for support in the early period to be able to screen individuals under cancer treatment for depression and to intervene in the psychosocial problems of patients at risk.

Study Limitations

This study was an important research presenting real-life data, investigating the relationship among NLR, PLR, NLPR, CRP/L and SII and depression in metastatic lung cancer patients. However, we had some limitations in our study. Patients admitted to a single center were included. This study had a small sample size. While providing valuable information for this area, reaching more patients could help us draw precise conclusions. Finally, the study's cross-sectional design could not explain causal relations well. Patients' socio-demographic, clinical characteristics, and cancer status can affect depression and inflammation processes in patients with *de novo* metastatic lung cancer; therefore, we believe these factors may not be considered independently. Longitudinal studies with larger clinical samples could provide more comprehensive findings.

CONCLUSION

Our study revealed that a high NLR, PLR, CRP/L and SII might be a predictive factor for higher depression levels in patients with metastatic cancer. Our results may underline the importance of an altered inflammation process in set of causes of depression. The current study was an important study with real-life data that evaluated the diagnostic power of inflammatory markers such as NLR, PLR, CRP/L and SII for indicating depression in cancer patients. As the management of cancer patients should also focus on providing patients with psychological support regarding its improving effect on treatment response, detecting the presence of depression or identifying patients at high risk of depression is of great importance, promisingly done easily by clinicians via inflammatory markers screening.

Acknowledgments

The authors sincerely thank Dr. Ayşe İrem YASİN and Dr. Zehra SUCUOĞLU İŞLEYEN for their help during the study period.

Ethics

Ethics Committee Approval: The Ethics Committee of the Bezmialem Vakıf University approved this cross-sectional study with reference number 16/330 on date 22.09.2020.

Informed Consent: All patients provided written informed consent for attendance.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices - Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: İ.Ö.Ü., A.T.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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