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Value of prognostic nutritional index in patients with non-small cell lung cancer

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Abstract:

BACKGROUND AND AIM: The systemic inflammatory response plays a crucial role in the development and progression of many cancer types. In our study, we investigated the association of prognostic nutritional index (PNI) with progression-free survival (PFS) and overall survival (OS) in patients with non-small cell lung cancer (NSCLC).

METHODS: This was a retrospective cohort study. The data of patients who were followed up in the oncology clinic of our hospital between October 2011 and June 2014 were obtained from the hospital automation system records and patient files. A total of 240 patients with NSCLC diagnosis were included in the study, and their demographic and clinicopathological characteristics were recorded. PNI was calculated at the time of diagnosis based on albumin levels and lymphocyte counts.

RESULTS: In total, 231 patients were included in the study (205 [88.7%] men and 26 [11.3%] women), with a mean age of 59.97±9.44 years. We divided the patients into two groups, namely low (≤42.2) and high (>42.2) PNI groups, based on their median PNI values. The median OS of the low and high PNI groups were 380.00 (95% CI: 347.00–412.96) and 568.00 (95% CI: 515.52–620.48) days, respectively. The difference was statistically significant (p=0.009). Low PNI was associated with a poor OS, and the mortality rate of the low PNI group was 1.5 times higher than that of the high PNI group (hazard ratio: 1.50; 95% CI: 1.08–2.08). No statistically significant difference was observed between PNI values and PFS (p=0.328).

CONCLUSIONS: This study showed that PNI (≤42.2) at diagnosis is an independent biomarker of poor prognosis in patients with NSCLC. Therefore, PNI can be used as a biomarker of NSCLC prognosis because it is simple, inexpensive, and easily available.

Keywords:

Non-small cell lung cancer, prognostic nutritional index, survival, prognosis

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Introduction

Lung cancer ranks among the leading cancers based on the 2020 global cancer statistics, accounting for 11.4% of new cases and causing 18% of deaths.[1] According to the Türkiye 2017 cancer statistics report, 56.7 per 100 000 men and 11.1 per 100 000 women have lung cancer. Considering all age groups, lung cancer incidence ranks first in men (21.7%) and fourth in women (6.4%). Non-small cell lung cancer (NSCLC) accounts for 79.6% of lung cancers; adenocarcinoma is the most common subtype of NSCLC, with an incidence rate of 47.7%; and 56.5% of the patients were in the advanced stage.[2]

The 5-year relative survival rate of NSCLC is approximately 25% for all stages. Advanced stage, advanced performance score, and weight loss are considered poor prognostic factors in NSCLC.[3] However, easily accessible parameters are needed for predicting survival and identifying high-risk individuals. Recent studies have shown that the patient's systemic inflammatory response status, nutritional status, and immunological status have crucial roles in cancer development. Several indices containing various inflammatory parameters are used to determine the prognosis of patients with cancer. The prognostic nutritional index (PNI) is a simple scale that involves the combination of the serum albumin level and lymphocyte count in the peripheral blood. PNI was found to be an effective biomarker in the prognosis of patients who underwent surgery for esophageal, colorectal, and gastrointestinal cancers.[4,5] Furthermore, studies have shown that PNI has a prognostic value in patients with resectable lung cancer.[6,7]

Our study aimed to investigate the association of PNI with overall and progression-free survival (PFS) in NSCLC patients.

Materials and Methods

This was a retrospective cohort study. A total of 240 patients with a histopathological diagnosis of NSCLC who were followed in the oncology clinic of our hospital between October 2011 and June 2014 were included in the study. Demographic data, clinicopathological features, laboratory findings, and treatment methods of the patients were obtained from the hospital automation system records and patient files. Nine patients were excluded from the study because of comorbidities, such as malignancy of other organs, autoimmune and hematological diseases, and other diseases that could affect the blood lymphocyte count and serum albumin level. The study was approved by the ethics committee of (No.: 235-2021; Date: November 22, 2021), and it was conducted in accordance with the Declaration of Helsinki. All patients were staged using the seventh Tumour stage (TNM) system.[8] We analyzed biochemical (albumin, protein, lactate dehydrogenase, glucose, and calcium levels) and hematological (neutrophil, lymphocyte, hemoglobin, and thrombocyte counts) values in the blood samples collected at the time of diagnosis. PNI was calculated according to the following formula: (10 × albumin [g/dL]) + (0.005 × peripheral lymphocyte count per mm^3).[3] In our study, PFS was defined as the period from the date of initial pathological diagnosis to the date of disease progression, and overall survival (OS) was calculated from the time of pathological diagnosis to the date of death from any cause. The patients were divided into two groups, namely, high and low PNI groups, based on their median PNI values.

Statistical analysis

The normality of the data was tested using the Shapiro–Wilk test. Continuous variables were presented as mean ± standard deviation for normally distributed variables, and comparisons between the two independent groups were performed using an independent samples t-test, whereas they were presented as median (minimum–maximum) values for nonnormal variables, and comparisons between the two independent groups were performed using the Mann–Whitney U-test. Categorical variables were expressed as numbers and percentages, and comparisons between the groups were performed using Pearson's Chi-squared or the Fisher–Freeman–Halton test. The Kaplan–Meier analysis and log-rank test were used to compare survival times between the groups. Additionally, the Cox regression analysis was performed for the multivariate analysis of survival data. A p-value of 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 23.0 (IBM Corp., USA).

Results

In total, 231 patients were included in the study, 205 (88.7%) men and 26 (11.3%) women. The mean age of the patients was 59.9±9.4 years (range: min 34 max 82). In our study, smoking, a crucial risk factor for lung cancer, was 91.8% (n=212), and the most common histopathological subtype was adenocarcinoma (n=107, 46.3%). At diagnosis, 106 (45.9%) patients had stage 4 disease. The most common sites of metastasis were the brain (n=95, 41.1%) and the bone (n=55, 23.8%). The demographics and clinical characteristics of the patients are presented in Table 1. The median OS and PFS were found to be 444.00 days (95% CI: 366.75–521.25) and 288.00 days (95% CI: 250.76–325.14), respectively.

The median PNI value was found to be 42.2 (range: 14–66). Patients were divided into two groups based on their median PNI values as low (≤42.2) and high (>42.2) PNI groups. When PNI groups were compared, patients with low PNI values were seen to be older than the patients with high PNI values (p=0.005). No significant correlation was observed between PNI and smoking status, histopathology, comorbidity, tumor stage, performance status, and treatment modality. The comparisons of the clinicopathological features of the patients according to their PNI values are presented in Table 2.

The median OS of patients with low PNI and high PNI was 380.00 (95% CI: 347.00–412.96) days and 568.00 (95% CI: 515.52–620.48) days, respectively, and the difference was statistically significant (p=0.009). A low PNI was highly associated with a short survival time, and the mortality rate of the low PNI group was 1.5 times higher than that of the high PNI group (hazard ratio [HR]: 1.50; 95% CI: 1.08–2.08). However, no statistically significant difference was observed between PNI values in terms of PFS (p=0.328) [Figs 1, 2].

Univariate analysis and Cox regression model were applied to better define risk factors associated with OS. Smoking (p=0.006), histopathology (p=0.036), treatment modality (p=0.001), Eastern cooperative oncology group performence status (ECOG PS) (p=0.001), TNM stage (p=0.001), and PNI (p=0.009) were found as poor prognostic factors. Multivariate analysis showed that nonsurgical systemic treatments, advanced tumor stage, and low PNI (≤42.2, p=0.016) were significant independent predictors of OS (Table 3).

We performed a univariate analysis to identify the risk factors linked to PFS, and smoking (p=0.001), treatment modality (p=0.001), ECOG PS (p=0.001), and TNM stage (p=0.001) were found to be significant prognostic factors. After multivariate analysis, advanced stage, nonsurgical treatments, and presence of bone metastases (p=0.001) were determined as independent risk factors for PFS. However, PNI had no influence on PFS (p=0.328) [Fig. 2] (Table 4).

Table 1: Clinical characteristics of the study population

	Mean±SD	n	%
Age, year	59.9±9.4		
BMI, kg/m²	24.6±4.1		
Gender			
Male		205	88.7
Female		26	11.3
Smoking			
Nonsmoker		19	8.2
Active smoker		91	39.4
Former smoker		121	52.4
Histopathology			
Adenocarcinoma		107	46.3
Squamous cell carcinoma		88	38.1
Others*		36	15.6
ECOG PS			
0		103	44.6
1		95	41.1
2		28	12.1
3		5	2.2
TNM stage			
1B+2A+2B		32	13.9
3A		69	29.9
3B		24	10.4
4		106	45.9
Treatment			
No treatment		3	1.3
Chemotherapy		109	47.2
Chemotherapy and radiotherapy		50	21.6
Others**		69	29.9

*: Large cell carcinoma or NSCLC not otherwise specified (NOS). **: Neoadjuvant chemotherapy+surgery, surgery+adjuvant chemotherapy, or surgery+adjuvant chemoradiotherapy. BMI: Body mass index, ECOG PS: Eastern cooperative oncology group performence status, TNM: Tumour stage

Discussion

Our study demonstrated that a low PNI was an independent poor prognostic factor, and a low PNI was associated with a 1.5-fold reduction in survival. The systemic inflammatory response has an important role in cancer development. Indices containing various inflammatory parameters are used for the prognosis of patients with cancer. Lung cancer is one of the most fatal cancer types, with a 5-year survival rate of 25%. Therefore, high-risk patients must be identified using prognostic parameters. PNI is calculated based on the

Table 2: Association between PNI and clinicopathological features

Parameters	PNI				
	≤42.2		>42.2		p
	n	%	n	%	
	118	51.1	113	51.9	
Age					
<60	48	40.7	67	59.3	**0.005**
≥60	70	59.3	46	40.7	
Gender					
Male	111	94.1	94	83.2	**0.009**
Female	7	5.9	19	16.8	
Smoking					
Nonsmoker	7	5.9	12	10.6	0.259
Active smoker	44	37.3	47	41.6	
Former smoker	67	56.8	54	47.8	
Histopathology					
Adenocarcinoma	50	42.4	57	50.4	0.141
Squamous cell carcinoma	52	44.1	36	31.9	
Others*	16	13.5	20	17.7	
Comorbidity					
None	67	56.8	56	49.6	0.520
Single	28	23.7	33	29.2	
Multiple	23	19.5	24	21.2	
ECOG PS					
0	45	38.1	58	51.3	0.089
1	52	44.1	43	38.1	
2+3	21	17.8	12	10.6	
TNM stage					
1B+2A+2B	15	12.7	17	15.0	0.121
3A	28	23.7	41	36.3	
3B	15	12.7	9	8.0	
4	60	50.8	46	40.7	
Treatment					
Chemotherapy	62	52.5	47	42.7	0.287
Chemotherapy and radiotherapy	25	21.2	25	22.7	
Others**	31	26.3	38	34.5	

*: Large-cell carcinoma or NSCLC not otherwise specified (NOS). **: Neoadjuvant chemotherapy+surgery, surgery+adjuvant chemotherapy, or surgery+adjuvant chemoradiotherapy. PNI: Prognostic nutritional index, ECOG PS: Eastern cooperative oncology group performence status, TNM: Tumour stage, NSCLC: Non-small cell lung cancer

serum albumin concentration and lymphocyte count in the peripheral blood, and it is used to determine the nutritional and immunological status of patients with gastrointestinal cancer.[4,6,9]

In 2011, Proctor et al.[10] reported that PNI is a prognostic factor for all cancers independent of the tumor site. Additionally, Yao et al.[11] showed that PNI is a useful indicator in the prognosis of patients with malignant pleural mesothelioma.

In addition to neutrophils, T and B lymphocytes play crucial roles in tumor inflammation and immunology. According to preclinical studies, neutrophils stimulated by the tumor growth factor-mediated signaling pathway may promote tumor growth. The predictive role of neutrophil or lymphocyte counts in inflammation or immune tumor progression may be limited, and they are not associated with survival prognosis, but together they have a strong predictive role in survival.[12]

A close relationship exists between albumin and lymphocyte levels and the presence of an inflammatory response in patients with cancer. Hypoalbuminemia is generally seen in patients with advanced cancer and is usually accepted as an indicator of malnutrition and cachexia. Proinflammatory mediators, such as interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha secreted from the tumor, downregulate albumin synthesis. Furthermore, these cytokines play a role in malignant transformation, neoangiogenesis, and cancer progression.[13,14] Therefore, hypoalbuminemia suggests a poor prognosis in patients with cancer.

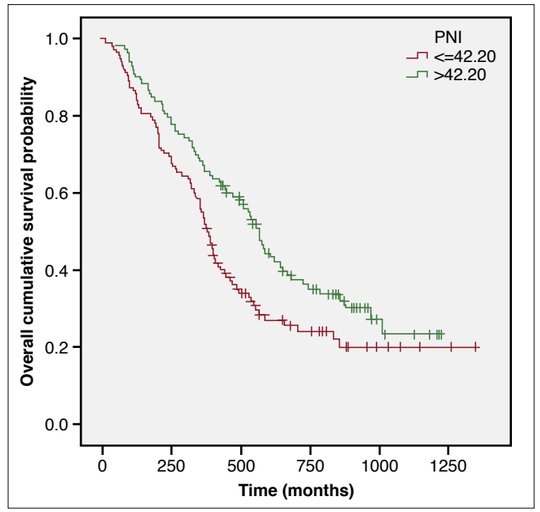

Figure 1: Kaplan–Meier survival curve for overall survival of the two PNI groups (p=0.009)
PNI: Prognostic nutritional index

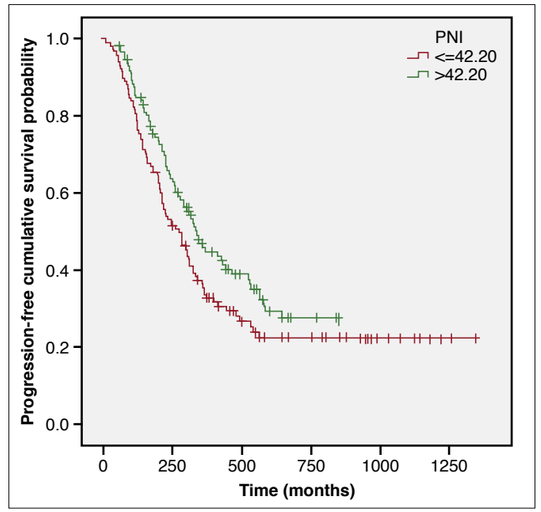

Figure 2: Kaplan–Meier survival curve for progression-free survival of the two PNI groups (p=0.328)

The relationship between the lymphocyte count with the immune system and cancer has been investigated, and malnutrition severity has been found to increase with a decrease in lymphocyte count.[15–17] Lymphocytes inhibit proliferation, invasion, and migration of cancer cells through T cell-mediated immune response.[18]

CD4+ Th cells can increase the effect of CD8+ cytotoxic T lymphocytes and induce the antitumor inflammation response through IL-2 release. Chronic inflammatory reactions contribute to tumor growth and invasion. Lymphocytopenia induced by systemic inflammatory reactions shows that cellular immunity is impaired, and it provides information regarding the severity and prognosis of the disease.[19]

Therefore, although PNI was initially considered an indicator of the nutritional status of a patient, it is likely an indicator of systemic inflammation. Furthermore, the presence of inflammatory response has been suggested to be associated with increased mortality and malnutrition, resulting in poor performance status in patients with cancer.[20–25]

The systemic inflammatory response is manifested through increased basal metabolism, loss of nonadipose tissue, and decreased performance and life expectancy in patients with lung cancer.[26–30] Scott et al.[31] showed that systemic inflammatory response is associated with an increase in weight loss, a decrease in performance status, an increase in fatigue, and a shortened life expectancy.

Few studies have investigated whether PNI is a prognostic factor for OS in patients with NSCLC. Although different PNI values are used in current studies, median values are generally accepted as threshold values. In these studies, the relationship between low PNI and poor prognosis has been found to be statistically significant.[11,19,32,33] Wang et al.[34] found that PNI had an independent effect on survival in patients with NSCLC treated with platinum-based chemotherapy.

In our study, we used the median PNI value of 42.2. Nonsurgical systemic treatment, advanced disease, and low PNI were evaluated as independent poor prognostic factors for OS. Mortality risk was seen to increase 1.5-fold in patients with low PNI values compared to the patients with high PNI values. In a meta-analysis by Hu et al.[35]

Table 3: Univariate and multivariate analyses of clinicopathological parameters for the prediction of OS in patients with NSCLC

Variable	Univariate					Multivariate			
	n	KM ST	95% CI		p	HR	95% CI		p
			L.B.	U.B.			L.B.	U.B.	
Age, years									
<60	115	470.00	353.99	586.01	0.073				
≥60	116	390.00	284.06	495.94					
Gender									
Male	205	439.00	357.39	520.61	0.746	**2.21**	1.07	4.57	**0.032**
Female	26	470.00	220.87	719.13		–	–	–	–
Smoking									
Nonsmoker	19	322.00	101.29	542.71	**0.006**	1.64	1.17	2.31	**0.004**
Active smoker	91	388.00	342.68	433.32		2.20	0.99	4.93	0.054
Former smoker	121	533.00	444.51	621.49		–	–	–	**0.007**
Histopathology									
Adenocarcinoma	107	555.40	38.94	479.08	**0.036**				
Squamous cell	88	690.10	56.52	579.31					
Large cell carcinoma	4	611.25	189.82	239.20					
NOS	32	403.11	57.34	290.71					
Comorbidity									
None	123	439.00	322.90	555.10	0.835				
Single	61	508.00	316.87	699.13					
Multiple	47	445.00	320.29	569.71					
Treatment									
Chemotherapy	109	322.00	241.11	402.89	**<0.001**	–	–	–	**0.015**
Chemoradiation	50	494.00	393.07	594.93		**1.89**	1.07	3.33	**0.028**
Others*	69	969.00	758.26	1179.74		1.04	0.57	1.90	0.901
ECOG PS									
0	103	64.05	435.46	686.54	**<0.001**				
1	95	53.44	382.27	591.73					
2–3	33	56.85	127.58	350.42					
TNM stage*									
1B+2A+2B	32	996.65	870.90	1122.39	**<0.001**	–	–	–	<0.001
3A	69	678.59	581.70	775.48		2.73	1.26	5.93	**0.011**
3B	24	589.52	380.25	798.78		4.56	1.74	11.96	**0.002**
4	106	372.31	312.57	432.06		5.28	2.23	12.53	**<0.001**
Bone metastasis									
Present	55	262.00	197.64	326.36	**<0.001**				
Absent	176	543.00	472.56	613.44					
PNI									
≤42.20	118	380.00	347.04	412.96	**0.009**	**1.50**	1.08	2.08	**0.016**
>42.20	113	568.00	515.52	620.48		–	–	–	–

*: Neoadjuvant chemotherapy and surgery, surgery and adjuvant chemotherapy, or surgery and chemoradiation. OS: Overall survial, NSCLC: Non-small cell lung cancer, KM: Kaplan–Meier, ST: Survival table, CI: Confidence interval, L.B.: Lower bound, U.B.: Upper bound, HR: Hazard ratio, NOS: NSCLC not otherwise specified, ECOG PS: Eastern cooperative oncology group performence status, TNM: Tumour stage, PNI: Prognostic nutritional index.

that involved patients with NSCLC, low PNI was associated with advanced TNM stage and tumor progression; thus, low PNI indicated a shortened life span of patients.

Current studies have not investigated the relationship between PFS and PNI. In our study, although the relationship between PNI and PFS was not significant, disease recurrence was earlier in patients with a low PNI value.

This study has several limitations. This was a retrospective, single-center study with a relatively small sample size and had a few female participants.

Conclusion

In conclusion, PNI (≤ 42.2) at diagnosis is an independent biomarker of poor outcome in patients with NSCLC. As a

Table 4: Univariate and multivariate analyses of clinicopathological parameters for the prediction of PFS in patients with NSCLC

Variable	Univariate					Multivariate			
	n	KM ST	95% CI		p	HR	95% CI		p
			L.B.	U.B.			L.B.	U.B.	
Age, years									
<60	115	294.00	233.37	354.63	0.307				
≥60	116	280.00	233.38	326.62					
Sex									
Male	205	289.00	252.40	325.60	0.072				
Female	26	220.00	110.07	329.94					
Smoking									
Nonsmoker	19	185.00	160.83	209.17	**<0.001**	1.38	0.99	1.89	0.051
Active smoker	91	247.00	190.13	303.87		1.91	1.11	3.28	**0.019**
Former smoker	121	320.00	265.27	374.73		–	–	–	**0.033**
Histopathology									
Adeno	107	262.00	194.75	329.25	0.099				
Squamous	88	314.00	268.05	359.95					
Large cell carcinoma	4	359.00	*	*					
NOS	32	229.00	155.55	302.45					
Comorbidity									
None	123	312.00	251.45	372.55	0.349				
Single	61	276.00	195.10	356.90					
Multiple	47	259.00	178.40	339.60					
Treatment									
Chemotherapy	109	208.00	174.53	241.47	**<0.001**	1.35	0.81	2.25	0.253
Chemoradiation	50	312.00	266.99	357.01		**1.92**	1.15	3.20	**0.012**
Others*	69	569.00	423.01	714.99		–	–	–	**0.034**
ECOG PS									
0	103	314.00	285.07	342.93	**<0.001**				
1	95	288.00	241.04	334.96					
2–3	33	149.00	79.22	218.78					
TNM stage									
1B+2A+2B	32	883.51	731.47	1035.56	**<0.001**	–	–	–	**0.001**
3A	69	458.68	375.31	542.06		**2.99**	1.53	5.85	**0.001**
3B	24	452.62	267.86	637.37		**3.20**	1.37	7.49	**0.007**
4	106	232.79	195.89	269.70		**4.20**	1.93	9.14	**<0.001**
Bone metastasis									
Present	55	160.00	123.67	196.33	**<0.001**	1.40	0.96	2.05	0.080
Absent	176	320.00	290.58	349.42		–	–	–	–
PNI									
≤42.20	118	254.00	195.45	312.55	0.328				
>42.20	113	311.00	258.91	363.09					

*: Neoadjuvant chemotherapy and surgery, surgery and adjuvant chemotherapy, or surgery and chemoradiation. PFS: Progression-free survival, NSCLC: Non-small cell lung cancer, KM: Kaplan-Meier, ST: Survival table, CI: Confidence interval, HR: Hazard ratio, L.B.: Lower bound, U.B.: Upper bound, NOS: NSCLC not otherwise specified, ECOG PS: Eastern cooperative oncology group performence status, TNM: Tumour stage, PNI: Prognostic nutritional index.

biomarker of systemic inflammatory response in NSCLC, PNI can be a useful tool to predict the prognosis because it is simple, easily available, and inexpensive. Furthermore, we suggest that intensive supportive care may be required to improve prognosis in those with low PNI values.

Conflicts of interest

There are no conflicts of interest.

Ethics Committee Approval

The study was approved by the Süreyyapaşa Chest Diseases and Chest Surgery Training and Research Hospital Scientific Ethics Committee (No: 235-2021, Date: 22/11/2021).

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Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept – D.E., M.Ö.A., F.K.; Design – D.E., M.Ö.A., Ü.A.A.; Supervision – F.K., D.E., M.Ö.A., Ü.A.A.; Funding – D.E., M.Ö.A., F.K.; Data collection &/or processing – F.K., M.Ö.A.; Analysis and/or interpretation – F.K., Ü.A.A., D.E.; Literature search – F.K., M.Ö.A.; Writing – F.K., M.Ö.A., D.E.; Critical review – D.E., M.Ö.A.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN Estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209–49. [CrossRef]
2. Kara F, Keskinkılıç B. Türkiye Kanser İstatistikleri 2017. TC Halk Sağlığı GM 2021;22–52. Available at: https://hsgm.saglik.gov.tr/depo/birimler/kanser-db/istatistik/Turkiye_Kanser_Istatistikleri_2017.pdf Accessed Jan 20, 2023.
3. Woodard GA, Jones KD, Jablons DM. Lung Cancer Staging and Prognosis. Cancer Treat Res 2016;170:47–75. [CrossRef]
4. Balkwill F, Mantovani A. Inflammation and cancer: Back to Virchow? Lancet 2001;357:539–45. [CrossRef]
5. Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Nihon Geka Gakkai Zasshi 1984;85:1001–5. Japanese.
6. Tomita M, Shimizu T, Ayabe T, Yonei A, Onitsuka T. Preoperative neutrophil to lymphocyte ratio as a prognostic predictor after curative resection for non-small cell lung cancer. Anticancer Res 2011;31:2995–8.
7. Qiu C, Qu X, Shen H, Zheng C, Zhu L, Meng L, et al. Evaluation of prognostic nutritional index in patients undergoing radical surgery with nonsmall cell lung cancer. Nutr Cancer 2015;67:741–7. [CrossRef]
8. Goldstraw P, Crowley J, Chansky K, Giroux DJ, International Association for the Study of Lung Cancer International Staging Committee; Participating Institutions, et al. The IASLC Lung Cancer Staging Project: Proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM Classification of malignant tumours. J Thorac Oncol 2007;2:706–14. Erratum in: J Thorac Oncol 2007;2:985. [CrossRef]
9. Nozoe T, Kimura Y, Ishida M, Saeki H, Korenaga D, Sugimachi K. Correlation of pre-operative nutritional condition with post-operative complications in surgical treatment for oesophageal carcinoma. Eur J Surg Oncol 2002;28:396–400. [CrossRef]
10. Proctor MJ, Morrison DS, Talwar D, Balmer SM, Fletcher CD, O'Reilly DS, et al. A comparison of inflammation-based prognostic scores in patients with cancer. A glasgow inflammation outcome study. Eur J Cancer 2011;47:2633–41. [CrossRef]
11. Yao ZH, Tian GY, Wan YY, Kang YM, Guo HS, Liu QH, et al. Prognostic nutritional index predicts outcomes of malignant pleural mesothelioma. J Cancer Res Clin Oncol 2013;139:2117–23. [CrossRef]
12. Yao Y, Yuan D, Liu H, Gu X, Song Y. Pretreatment neutrophil to lymphocyte ratio is associated with response to therapy and prognosis of advanced non-small cell lung cancer patients treated with first-line platinum-based chemotherapy. Cancer Immunol Immunother 2013;62:471–9. [CrossRef]
13. Rothschild MA, Oratz M, Schreiber SS. Serum albumin. Hepatology 1988;8:385–401. [CrossRef]
14. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature 2008;454:436–44. [CrossRef]
15. Dunn GP, Bruce AT, Ikeda H, Old LJ, Schreiber RD. Cancer immunoediting: from immunosurveillance to tumor escape. Nat Immunol 2002;3:991–8. [CrossRef]
16. Smyth MJ, Hayakawa Y, Takeda K, Yagita H. New aspects of natural-killer-cell surveillance and therapy of cancer. Nat Rev Cancer 2002;2:850–61. [CrossRef]
17. Seiler WO. Clinical pictures of malnutrition in ill elderly subjects. Nutrition 2001;17:496–8. [CrossRef]
18. Chen DS, Mellman I. Oncology meets immunology: the cancer-immunity cycle. Immunity 2013;39:1–10. [CrossRef]
19. Li XL, Yao ZH, Wan YY, Mou XY, Ni YH, Sun EL, et al. Prognostic impact of prognostic nutritional index in advanced (stage IIIB/IV) non-small cell lung cancer patients. Neoplasma 2019;66:971–77. [CrossRef]
20. Kinoshita A, Onoda H, Imai N, Iwaku A, Oishi M, Fushiya N, et al. Comparison of the prognostic value of inflammation-based prognostic scores in patients with hepatocellular carcinoma. Br J Cancer 2012;107:988–93. [CrossRef]
21. Li QQ, Lu ZH, Yang L, Lu M, Zhang XT, Li Jet al. Neutrophil count and the inflammation-based glasgow prognostic score predict survival in patients with advanced gastric cancer receiving first-line chemotherapy. Asian Pac J Cancer Prev 2014;15:945–50. [CrossRef]
22. O'Callaghan DS, O'Donnell D, O'Connell F, O'Byrne KJ. The role of inflammation in the pathogenesis of non-small cell lung cancer. J Thorac Oncol 2010;5:2024–36. [CrossRef]
23. Feng JF, Chen QX. Significance of the prognostic nutritional index in patients with esophageal squamous cell carcinoma. Ther Clin Risk Manag 2014;10:1–7. [CrossRef]
24. Pinato DJ, Shiner RJ, Seckl MJ, Stebbing J, Sharma R, Mauri FA. Prognostic performance of inflammation-based prognostic indices in primary operable non-small cell lung cancer. Br J Cancer 2014;110:1930–5.
25. Mohri Y, Inoue Y, Tanaka K, Hiro J, Uchida K, Kusunoki M. Prognostic nutritional index predicts postoperative outcome in colorectal cancer. World J Surg 2013;37:2688–92. [CrossRef]
26. Staal-van den Brekel AJ, Dentener MA, Schols AM, Buurman WA, Wouters EF. Increased resting energy expenditure and weight loss are related to a systemic inflammatory response in lung cancer patients. J Clin Oncol 1995;13:2600–5.
27. Scott HR, McMillan DC, Watson WS, Milroy R, McArdle CS. Longitudinal study of resting energy expenditure, body cell mass and the inflammatory response in male patients with non-small cell lung cancer. Lung Cancer 2001;32:307–12.
28. McMillan DC, Scott HR, Watson WS, Preston T, Milroy R, McArdle CS. Longitudinal study of body cell mass depletion and the inflammatory response in cancer patients. Nutr Cancer 1998;31:101–5.
29. Simons JP, Schols AM, Buurman WA, Wouters EF. Weight loss and low body cell mass in males with lung cancer: relationship with systemic inflammation, acute-phase response, resting energy expenditure, and catabolic and anabolic hormones. Clin Sci (Lond) 1999;97:215–23.
30. Martín F, Santolaria F, Batista N, Milena A, González-Reimers E, Brito MJ, et al. Cytokine levels (IL-6 and IFN-gamma), acute phase response and nutritional status as prognostic factors in lung cancer. Cytokine 1999;11:80–6. [CrossRef]
31. Scott HR, McMillan DC, Forrest LM, Brown DJ, McArdle CS, Milroy R. The systemic inflammatory response, weight loss, performance status and survival in patients with inoperable non-small cell lung cancer. Br J Cancer 2002;87:264–7. [CrossRef]
32. Kos FT, Hocazade C, Kos M, Uncu D, Karakas E, Dogan M, et al. Assessment of prognostic value of "neutrophil to lymphocyte ratio" and "prognostic nutritional index" as a sytemic inflammatory marker in non-small cell lung cancer. Asian Pac J Cancer Prev 2015;16:3997–4002. [CrossRef]
33. Shimizu K, Okita R, Saisho S, Maeda A, Nojima Y, Nakata M. Preoperative neutrophil/lymphocyte ratio and prognostic nutritional index predict survival in patients with non-small cell lung cancer. World J Surg Oncol 2015;13:291. [CrossRef]
34. Wang J, Liu Y, Mi X, Shao M, Liu L. The prognostic value of prognostic nutritional index (PNI) and neutrophil to lymphocyte ratio (NLR) for advanced non-small cell lung cancer treated with platinum-based chemotherapeutics. Ann Palliat Med 2020;9:967–78. [CrossRef]
35. Hu Y, Shen J, Liu R, Feng Z, Zhang C, Ling L, et al. Prognostic value of pretreatment prognostic nutritional index in non-small cell lung cancer: A systematic review and meta-analysis. Int J Biol Markers 2018;33:372–8. [CrossRef]

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